

# Human Papillomavirus Infection, Awareness, and Vaccine Acceptability and Uptake among Gay, Bisexual, and Other Men who have Sex with Men in Aotearoa, New Zealand

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## Abstract

### Background

Gay, bisexual and other men who have sex with men (GBM) experience significant health inequity resulting from anal HPV-related disease. In 2017, all males under the age of 27 became eligible for funded HPV vaccination in Aotearoa New Zealand (NZ), potentially addressing this inequity over time. Monitoring and evaluating the impact of communicable disease interventions are essential public health functions, but GBM are a minority population that have no sampling frame and are not identifiable within administrative health datasets. Therefore, alternative methods for collecting HPV-related health data are needed to inform evidence-based public health programmes for this population. To date, no HPV-related data in NZ are published for GBM beyond anogenital wart prevalence and international data are limited, with no countries providing surveillance data on HPV vaccination coverage or impact disaggregated by sexual orientation. The WHO and UNAIDS second-generation surveillance (SGS) for HIV offers a model for focussed data collection among GBM. These data can be used to inform public health decision making and programmes that address health inequities experienced by GBM.

### Aim

This thesis seeks to improve understanding of HPV among GBM in NZ to inform public health interventions and identify areas for future research.

### Approach

The data from three cross-sectional convenience studies, conducted between 2014 and 2018, are analysed and presented. Prior to the change in public funding for HPV vaccination, the Gay Auckland Periodic Sex Survey (GAPSS) and the Gay Online Sex Survey (GOSS) HIV behavioural surveillance programme opportunistically included HPV-related questions to establish baseline data for GBM on HPV-related knowledge and HPV vaccine acceptability and uptake in 2014. In 2015, the HPV infection in males study (HIMS), a feasibility study, collected oral and anal specimens from three populations of males attending clinical settings to test for HR-HPV infection, alongside a survey that repeated the HPV-related questions from GAPSS and GOSS. After the change in public funding for HPV vaccination, the 2018 round of the Ending HIV (EHIV) Survey, an online behavioural survey targeted to GBM, repeated the HPV-related knowledge and HPV vaccine acceptability and uptake measures from GAPSS and GOSS to monitor progress.

## Findings

The results of the HIMS feasibility study found a high burden of anal high-risk HPV (HR-HPV) infection among GBM participants attending clinical settings, while finding no anal HR-HPV infections among heterosexual male participants. Two out of every five ( $n=21/51$ , 41%) GBM participants tested positive for anal HPV-16 or HPV-18 infection, the most oncogenic but vaccine-preventable HR-HPV types. Conversely, oral HR-HPV prevalence was low, with only two out of 71 (3%) GBM participants testing positive for oral HR-HPV infection. HPV infection prevalence data was paired with behavioural survey data in this study, demonstrating the feasibility of conducting bio-behavioural surveillance across the clinical settings included in the study.

The majority ( $n=1615/3135$ , 52%) of GBM participants of the 2014 GAPSS and GOSS surveys were unaware of the range of HPV-related diseases that affected males. Self-reported knowledge was associated with higher education level, disclosure of sexual orientation to healthcare providers, and living with HIV. Knowledge of the HPV vaccine and its effectiveness for males was reported by 17% ( $n=531/3113$ ) of GBM in 2014, lower than knowledge of the HPV-related diseases that affect males.

In 2014, less than 3% of all GBM participants ( $n=92/3107$ ) of the GAPSS and GOSS surveys reported receiving any dose of the HPV vaccine. Associations were found with sociodemographic and behavioural variables, but analyses were limited by the low number of participants reporting vaccination. Close to four out of every five ( $n=2433/3115$ , 78%) participants reported willingness to receive the HPV vaccine if provided at no cost. Being recruited online and reporting knowledge of any HPV-related disease or the HPV vaccine, were independently associated increased willingness to receive the vaccine for free. In contrast, less than one in eight ( $n=388/3107$ , 13%) would be willing to receive the HPV vaccine if required to pay.

Almost two thirds ( $n=2002/3173$ , 63%) of GBM in NZ would be comfortable having their sexual orientation recorded confidentially on administrative health datasets. In 2014, GBM participants of GAPSS and GOSS were asked to rate their comfort with having their sexual orientation recorded on these databases. Reporting a bisexual or “other” sexual identity, holding a tertiary qualification, and not believing their healthcare provider to be aware of their sexual orientation were independently associated with reporting non-comfort. The inclusion of sexual orientation measures in administrative health databases in NZ would facilitate clinical surveillance of HPV-related disease, treatment, and vaccine uptake among GBM.

In 2018, among the younger GBM now eligible for funded HPV vaccination, uptake had significantly increased from 2% in 2014 to 31%. Compared to 2014, among those GBM aged

between 16 and 26 years, significant increases were also found in HPV-related disease knowledge, HPV vaccine awareness and vaccine uptake. These increases remained significant after controlling for sociodemographic and behavioural variables. In contrast, no changes were identified for HPV vaccine acceptability under either cost condition. These findings indicate that progress on improving these HPV-related outcomes among GBM is being made. However, additional programmes to further improve HPV vaccine uptake among eligible GBM are needed to reach the herd immunity threshold.

## Conclusion

To our knowledge, these data present the first baseline and follow-up data on HPV-related variables among GBM pre- and post-funding of HPV vaccination for males. Differences in HPV-related variables were identified by sociodemographic and behavioural variables that can be utilised to inform public health programming and delivery to address the HPV-related health inequities experienced by GBM in NZ.

This thesis demonstrates the feasibility of using existing SGS programmes for HIV to inform public health and research related to the control and prevention of HPV among GBM. However, to fully realise SGS for HPV among the GBM population, the inclusion of sexual orientation measures in administrative health datasets must also be investigated to enable HPV-related clinical surveillance of this population.

**To my parents, Henry (1957–2020) and Dawn Ludlam.**

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Ehara taku toa i te toa takitahi, engari kē he toa takitini

*My success is not mine alone, but that of my community*

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**It is thanks to the public health and community advocates mentioned above that future generations of men growing up in Aotearoa New Zealand are protected from HPV-related disease.**

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## List of Abbreviations

|             |  |
|-------------|--|
| Ab          | Antibody   |
| ACCESS      | Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Blood-borne Viruses |
| ADHB        | Auckland district health board   |
| AGW         | Anogenital warts   |
| AIN         | Anal intraepithelial lesion  |
| AOR         | Adjusted odds ratio  |
| ASHS        | Auckland sexual health service   |
| ATP         | According to protocol  |
| BGO         | Big Gay Out  |
| CDC         | Centres for disease control and prevention   |
| DARE        | Digital anal-rectal examination  |
| DHB         | District Health Board  |
| DNA         | Deoxyribonucleic acid  |
| EPHF        | Essential public health function   |
| EHIV Survey | Ending HIV survey  |
| ESR         | Institute of Environmental Science and Research  |
| FBMC        | Freemans Bay medical centre  |
| FDA         | US food and drug administration  |
| GAPSS       | Gay Auckland periodic sex survey   |
| GBM         | Gay, bisexual and other men who have sex with men  |
| GOSS        | Gay online sex survey  |
| GP          | General practice/general practitioner  |
| HAART       | Highly active antiretroviral therapy   |
| HDEC        | Health and disability ethics committee   |
| HIMS        | HPV in males study   |
| HIV         | Human immunodeficiency virus   |
| HPV         | Human papillomavirus   |
| HR-HPV      | High-risk HPV  |
| HSIL        | High-grade squamous intraepithelial lesion   |
| IARC        | International Agency for Research on Cancer  |
| ITT         | Intent to treat  |
| LGBTIQ+     | Lesbian, gay, bisexual, transgender, intersex, questioning/queer, and wider “rainbow” community                                      |
| LR-HPV      | Low risk HPV   |
| LSIL        | Low-grade squamous intraepithelial lesion  |
| MoH         | Ministry of Health New Zealand   |
| MSM         | Men who have sex with men  |
| MSW         | Men who have sex with women  |
| NATSAL      | National survey of sexual attitudes and lifestyles   |
| NGO         | Non-government organisation  |

|           |  |
|-----------|--|
| NHBS      | National HIV behavioural surveillance                |
| NHI       | National health index                                |
| NIR       | National immunisation registry                       |
| NZ        | Aotearoa, New Zealand                                |
| NZAF      | New Zealand AIDS Foundation                          |
| NZHS      | New Zealand health survey                            |
| OR        | Odds ratio   |
| PCR       | Polymerase chain reaction                            |
| PHE       | Public health England                                |
| PIS       | Participant information sheet                        |
| PLHIV     | People living with HIV                               |
| SCC       | Squamous cell carcinoma                              |
| SGS       | Second generation surveillance                       |
| SHC       | Sexual health clinic                                 |
| SIL       | Squamous intraepithelial lesion                      |
| SOGI      | Sexual orientation and gender identity               |
| SOS venue | Sex-on-site venue                                    |
| SPANC     | Study of prevention of anal cancer                   |
| STI       | Sexually transmitted infection                       |
| UAIC      | Unprotected anal intercourse with a “casual” partner |
| UNAIDS    | The Joint United Nations Programme on HIV/AIDS       |
| VLP       | Virus-like particle                                  |
| WHO       | World Health Organization                            |

# Chapter 1: Introduction and scope of the thesis

## Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) globally and estimated to be the second most costly STI, making up 45% of all STI-related medical costs among American youth in 2000 (1). Over 120 different HPV types are identified that infect humans, most of which cause benign asymptomatic infections. However, there are two groups of HPVs that cause disease; those that are classified as “low-risk” (LR) including those that cause warts, and those that are classified as “high-risk” (HR) and are oncogenic.

HPV is a necessary causal pathogen for anogenital warts (AGWs), and the majority of squamous cell carcinomas (SCC) of the cervix, vagina, vulva, oropharynx, penis, and anus. Incidence of HPV-related oropharyngeal and anal cancers have been increasing among males over time. Gay, bisexual, and other men who have sex with men (GBM) are particularly susceptible to anal HR-HPV infection. The incidence of anal cancer among this population is equivalent to that of cervical cancer among women before introducing cervical screening programmes (2).

In 2007, Australia was the first country to introduce the HPV vaccine to school-age females and has documented dramatic declines in the incidence of AGWs and cervical pre-cancerous lesions among vaccinated cohorts (3). These declines in AGWs have also been seen among heterosexual males through the effect of herd immunity, but no decline was observed among GBM over the same period (4). In 2013 and 2017 respectively, both Australia and Aotearoa New Zealand (NZ) extended the female-only school-based vaccination programmes to include males, with NZ also offering a “catch-up” vaccination programme for those up to the age of 26 years. These gender-neutral vaccination programmes have the potential to virtually eliminate HPV-related disease over time in countries that offer them. Other more economically developed countries are now considering how best to address the growing HPV-related health inequity experienced by males and GBM.

Determining the success and impact of these vaccination programmes on the health inequity experienced by GBM will require monitoring and surveillance among this population. However, information that identifies sexual orientation is not included in administrative clinical datasets used for clinical surveillance, effectively rendering GBM invisible in administrative public health data systems. Therefore, additional forms of surveillance are required.



## Studies included in the thesis

This thesis is presented as a series of observational epidemiological studies themed around measuring and monitoring the prevalence of HPV infection, HPV-related knowledge, and HPV vaccine awareness, acceptability, and uptake among GBM in NZ. The thesis draws upon data collected by three studies.

**HPV Infection among Males Study (HIMS):** Conducted in 2015, HIMS is a novel anonymous cross-sectional clinic-based feasibility study aiming to measure the prevalence of oral and anal HPV infection among males attending three health care settings in the inner Auckland area: a sexual health clinic (SHC), a general practitioner (GP) clinic, and a hospital-based outpatient clinic for people living with HIV (PLHIV). The study sought to recruit equal numbers of three distinct populations of males: GBM living with HIV, GBM who are HIV-negative/unknown, and heterosexual males who are HIV-negative/unknown. The candidate led this study.

**Gay Auckland Period Sex Survey (GAPSS) and Gay Online Sex Survey (GOSS):** These are two anonymous repeat cross-sectional community and internet-based surveys that recruit a large and diverse sample of GBM residing in NZ. The GAPSS survey recruits GBM in Auckland through community-based sampling at NZ's largest Pride fair day, GBM-orientated bars, and GBM-specific sex-on-site venues. The GOSS survey recruits GBM online through GBM-specific dating websites and mobile dating apps. In February 2014, questions were included to measure HPV-related disease knowledge and HPV vaccine awareness, acceptability, and uptake. The candidate was a co-investigator in this study.

**Ending HIV Survey (EHIV Survey):** Conducted by the New Zealand AIDS Foundation (NZAF), the EHIV Surveys are repeat anonymous cross-sectional online surveys of GBM recruited through social media, mobile dating apps, and GBM-specific websites. The surveys aim to capture large and diverse samples of GBM residing in NZ. The HPV-related questions included in the 2014 round of GAPSS and GOSS were repeated in the November 2018 round of the EHIV Survey, providing an updated measure of HPV-related disease knowledge and HPV vaccine awareness, and acceptability and uptake. The candidate designed and led this study.

## Thesis aims

The thesis aims to collate evidence and further understanding of HPV among GBM in NZ to inform public health interventions and future research. The overarching aim will be approached through addressing each of the following specific aims:

1. Assess oral and anal HPV infection prevalence among GBM attending outpatient and primary healthcare clinics (Chapter 4).
2. Explore awareness of HPV-related disease that can affect males among a community and online sample of GBM (Chapter 5: Section 2).
3. Explore HPV vaccine awareness and acceptability under different price scenarios among a community and online sample of GBM (Chapter 5: Section 3).
4. Describe HPV vaccine uptake among a community and online sample of GBM, prior to the extension of public funding of HPV vaccination for males in NZ (Chapter 5: Section 4).
5. Compare HPV vaccine uptake among an online sample of GBM pre- and post-extension of public funding of HPV vaccination for males in NZ (Chapter 6).
6. Describe the willingness to have sexual orientation recorded on administrative databases among a community and online sample of GBM (Chapter 7).

## Thesis structure

The thesis is organised to answer the overall thesis aim. Each research aim is addressed by chapters describing and analysing the results of the three studies used in the thesis:

**Chapter two** explores the literature surrounding HPV relevant to this thesis, dividing it into five sections: the biology of HPV, sampling of HPV and GBM, the epidemiology of HPV infection and related disease among GBM, HPV prevention and treatment, and HPV in the NZ context.

**Chapter three** presents a systematic literature review of HPV vaccine uptake among GBM.

**Chapter four** presents the HIMS feasibility study methods followed by the results, covering the sociodemographic characteristics and oral and anal HR-HPV infection prevalence for the three population groups and the three study settings.

**Chapter five** describes the GAPSS and GOSS surveys methods, followed by three analyses using the combined GAPSS and GOSS 2014 samples. These explore awareness of HPV-related disease and HPV vaccine acceptability, awareness, and uptake.

**Chapter six** outlines the methods of the EHIV Survey, then used the cross-sectional samples of GBM collected through GOSS 2014 and EHIV Survey 2018 to compare measures of HPV-related disease knowledge and HPV vaccine awareness, acceptability, and uptake. This offers baseline and follow-up data before and after the 2017 extension of public funding for HPV vaccination to include males in NZ.

**Chapter seven** examines the acceptability of having sexual orientation recorded on administrative databases among the cross-sectional community and online sample of GBM recruited in the 2014 round of GAPSS and GOSS.

**Chapter eight** synthesises and grounds the main findings from the thesis into the broader field of study and offers considerations for public health approaches and avenues for future research, followed by concluding remarks.

## Taking a public health approach to HPV among GBM

This thesis seeks to take a public health approach to addressing HPV-related health inequities among GBM. And yet, as a discipline, public health has struggled to create a shared framework for the operationalisation of public health at national and international levels, against which public health activities can be evaluated. Here, a way forward is suggested.

In 1998, the World Health Organization (WHO), developed a list of essential public health functions (EPHFs) through the International Delphi Study (see *Table 1*) (5). In response to rapidly changing health and social environments, the EPHFs sought to provide clarity and international consensus on centralising, operationalising, and evaluating public health activities.

Table 1: Essential Public Health Functions identified by the World Health Organization international Delphi study, 1998 (5)

| # | Function   |
|---|--|
| 1 | Prevention, surveillance, and control of communicable and noncommunicable diseases |
| 2 | Monitoring of health situation   |
| 3 | Health promotion   |
| 4 | Occupational health  |
| 5 | Protecting the environment   |
| 6 | Public health legislation and regulations  |
| 7 | Public health management   |
| 8 | Specific public health services  |
| 9 | Personal health care for vulnerable and high-risk populations                      |

In 2018, the WHO revisited the EPHF framework and its operationalisation at a regional level, identifying only two out of the six WHO regions having direct examples of integrating EPHFs into their regional frameworks (6).

While NZ is a member of the United Nations and therefore the World Health Organization (WHO), the operationalisation of EPHFs has not been directly translated nor explicitly referenced in government bodies tasked with providing public health activities (7). Instead,

NZ government has taken a universal but decentralised approach, with public health functions, services, and programmes being provided through contracting of district health boards (DHBs), non-government organisations (NGO), academic institutions, and private providers (8). Within this model, the Public Health Clinical Network outlined five core public health functions in 2015 to provide leadership for public health units across the 12 DHBs and strengthen the performance of contracts they hold with the Ministry of Health's Director of Public Health (see Table 2) (9).

Table 2: The core functions, descriptions and actions of the Public Health Clinical Network, NZ.

| Core function                         | Description   | Actions  |
|---------------------------------------|---|--|
| 1. Health assessment and surveillance | Understanding health status, health determinants, and disease distribution. | <ul style="list-style-type: none"> <li>Monitoring, analysing, and reporting on population health.</li> <li>Detecting and investigating disease clusters and outbreaks (both communicable and non-communicable).</li> </ul>   |
| 2. Public health capacity development | Enhancing our system's capacity to improve population health.               | <ul style="list-style-type: none"> <li>Developing and maintaining public health information systems.</li> <li>Developing partnerships with Māori and Pacific communities.</li> <li>Developing human resources</li> <li>Conducting research, evaluation, and economic analysis.</li> <li>Planning, managing, and providing expert advice on public health programmes.</li> <li>Quality management for public health.</li> </ul> |
| 3. Health promotion                   | Enabling people to increase control over and improve their health.          | <ul style="list-style-type: none"> <li>Developing public and private sector policies.</li> <li>Creating physical, social, and cultural environments supportive of health.</li> <li>Strengthening communities' capacities to address health issues.</li> <li>Supporting people to develop skills.</li> <li>Working in partnership with other parts of the health sector.</li> </ul>   |
| 4. Health protection                  | Protecting communities against public health hazards.                       | <ul style="list-style-type: none"> <li>Developing and reviewing public health laws and regulations.</li> <li>Supporting, monitoring and enforcing compliance with legislation.</li> <li>Identifying, assessing, and reducing communicable disease risks.</li> <li>Identifying, assessing and reducing environmental health risks.</li> <li>Preparing for and responding to public health emergencies.</li> </ul>               |
| 5. Preventive interventions           | Populations programmes delivered to individuals.                            | <ul style="list-style-type: none"> <li>Developing, implementing and managing primary prevention programmes.</li> <li>Developing, implementing and managing secondary prevention programmes.</li> </ul>   |

Adapted from Williams et al. 2015 (9)

Using the framework created by the Public Health Clinical Network, Figure 1 presents the chapters within the thesis and their alignment with the core public health function approach. Monitoring and surveillance of communicable disease are core functions cited by both the WHO and Williams et al., this facilitates identifying health inequities and assessing their

extent. Health promotion also features in both frameworks, this seeks to raise awareness of both the disease and the interventions or treatments among the populations of interest. Williams et al. then differ from the WHO framework and present the categories of Public Health Capacity and Preventive Interventions.

In this thesis, preventive interventions speak to the provision of HPV vaccination programmes, while development of capacity is framed as developing and maintaining information systems through the expansion of data collected (sexual orientation) and its use for programme monitoring and evaluation (changes over time).

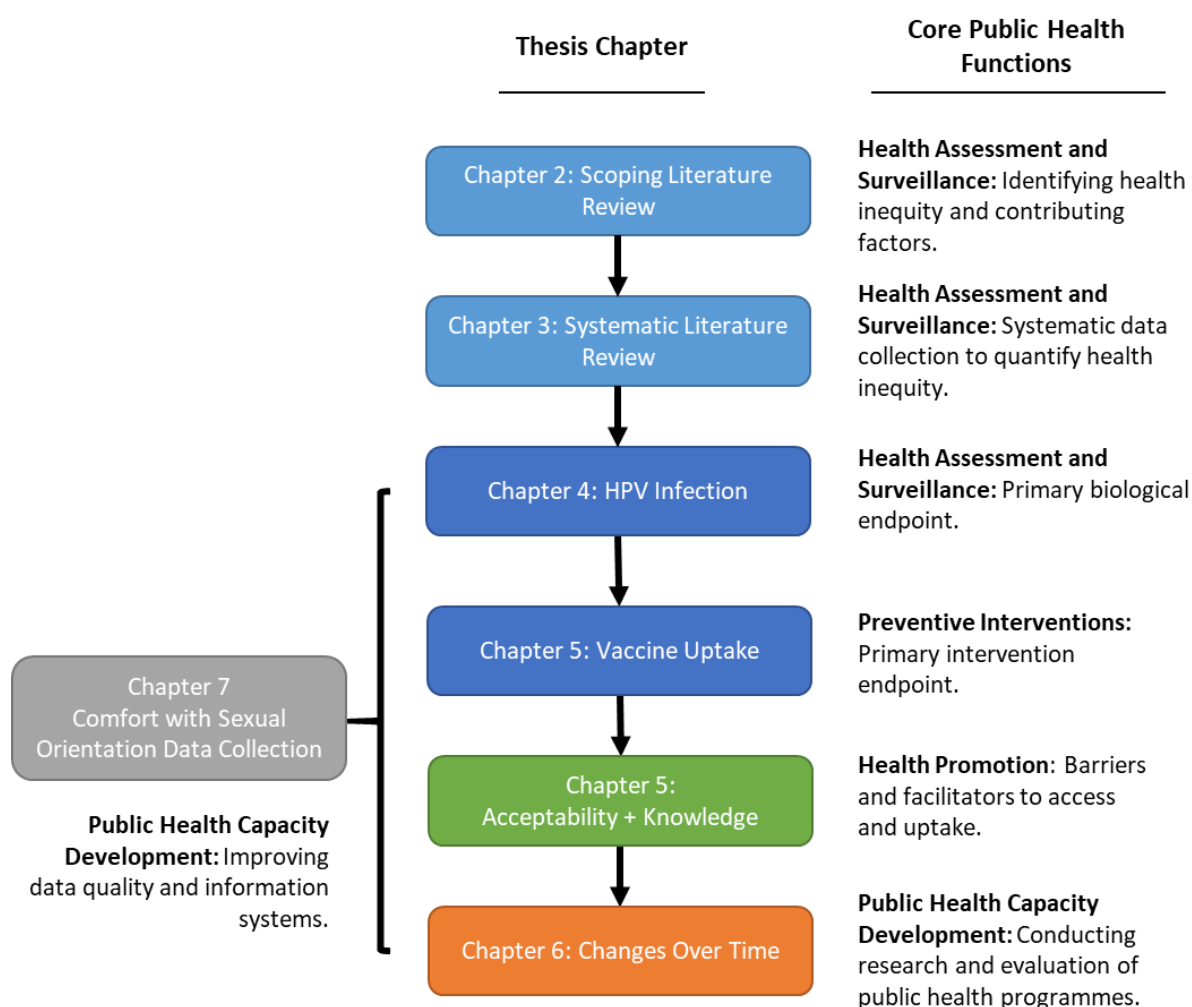


Figure 1: Diagrammatic representation of the thesis approach and its relation to core public health functions to inform programming, interventions, and policy for the control of HPV infection and related disease among GBM in NZ.

# Chapter 2: Review of the literature

## Introduction

The background literature review provides the foundation of the thesis. The review aims to present the evidence available for GBM and the HPV-related diseases that affect them, providing a rationale for the approach taken for measuring HPV-related variables necessary to inform effective public health programmes that control or eliminate HPV-related disease among GBM.

Five topic areas were identified that provided the framework for the research question (see *Figure 2*). Each topic area relates to a section of the literature review and a more comprehensive explanation for each is provided in the next section.

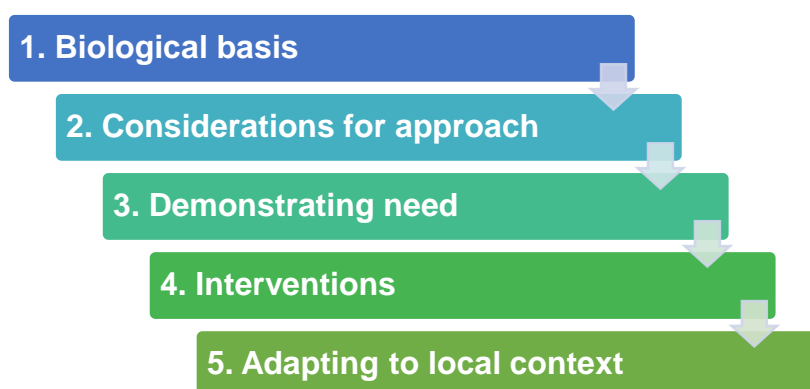


Figure 2: Diagrammatic representation of the themes for the literature review

## Structure of the literature review

Using the framework above, the literature review is split into five sections, each covering a topic area necessary for informing a public health approach to the control and potential elimination of HPV-related disease among GBM. Each section is closed with a synopsis of the main points. These are carried forward into the approach taken in the thesis.

The exploration of HPV virology, infection and disease at each anatomical site, and clinical diagnosis and treatment are not intended to be exhaustive but are provided to add context to the complexity in which the research question is set.

**Section 1 Biology:** The biological vulnerability of anatomical sites to HPV infection provides insights and explanations as to why GBM experience a greater burden of HPV-related disease (**biological basis**). Understanding how HPV is transmitted, how it replicates, and why some infections result in disease is essential to identifying when and where in the HPV lifecycle we might intervene to prevent its transmission and development of disease.

**Section 2 Sampling:** Exploring the techniques and limitations to how HPV infection and HPV-related diseases are detected provides an understanding for the rationale and design of studies aiming to measure prevalence and incidence. The section also covers defining and recruiting of GBM and explores the strengths and limitations of these approaches (**considerations for approach**).

**Section 3 Epidemiology:** The epidemiology of HPV infection and related disease among GBM quantifies the burden of disease experienced by GBM (**demonstrating need**). Quantification of other factors critical to the success of HPV control programmes, such as awareness of HPV-related disease and vaccination among GBM are explored in this section.

**Section 4 Treatment and Prevention:** Investigating the options available for the treatment and prevention of HPV infection and related disease is key to understanding why vaccination is the best option for controlling HPV-related disease among GBM (**interventions**).

**Section 5 Aotearoa NZ Context:** Geographic and cultural differences can influence the transmission and prevention of disease (**adapting to the local context**). Exploring what is already known about HPV and GBM in NZ can inform the approach taken by this thesis.

**Section 6 Synthesis of Background:** Synthesising these insights from the other sections provides the foundational knowledge built upon throughout this thesis.

## A narrative review approach

A narrative approach to the literature review, adapted from Demiriz et al. and represented below in Figure 3, was used to gather the published literature on epidemiological topics in Section Three and Section Four of this chapter (10). The approach provides confidence that, while imperfect, a large cross-section of the literature has been searched and reviewed to meet the section's purpose, aims and objectives. Key limitations of this approach include:

- only one literature database was used for these searches. Grey-literature reports may contain additional results not found in these reviews,
- additional screening of the references of included papers was limited and not widely incorporated into the approach taken,
- paper authors were not contacted for information where results specifically for GBM had been collected but not presented.

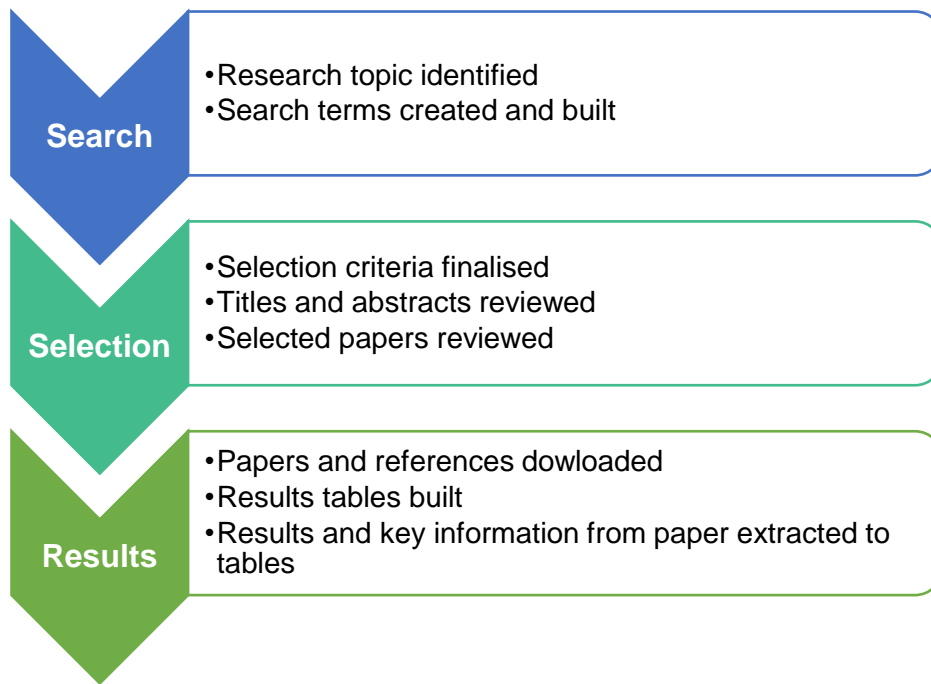


Figure 3: Diagrammatic representation of the narrative literature review approach taken in Chapter Two, Section Three and Section Four.



## Section One: The biology of human papillomavirus

### Purpose

To understand the biology of HPV, its transmission and lifecycle, and identify the targets that can be utilised for prevention, screening and treatment programmes to control and potentially eliminate HPV-related disease. Exploring the HPV lifecycle also explains why some populations, such as GBM, experience a greater burden of HPV-related disease compared to others.

### Aims

- a. Describe the discovery of HPV and oncogenic potential.
- b. Explore HPV transmission at different male anatomical sites.
- c. Describe the HPV lifecycle and mechanisms for oncogenesis.

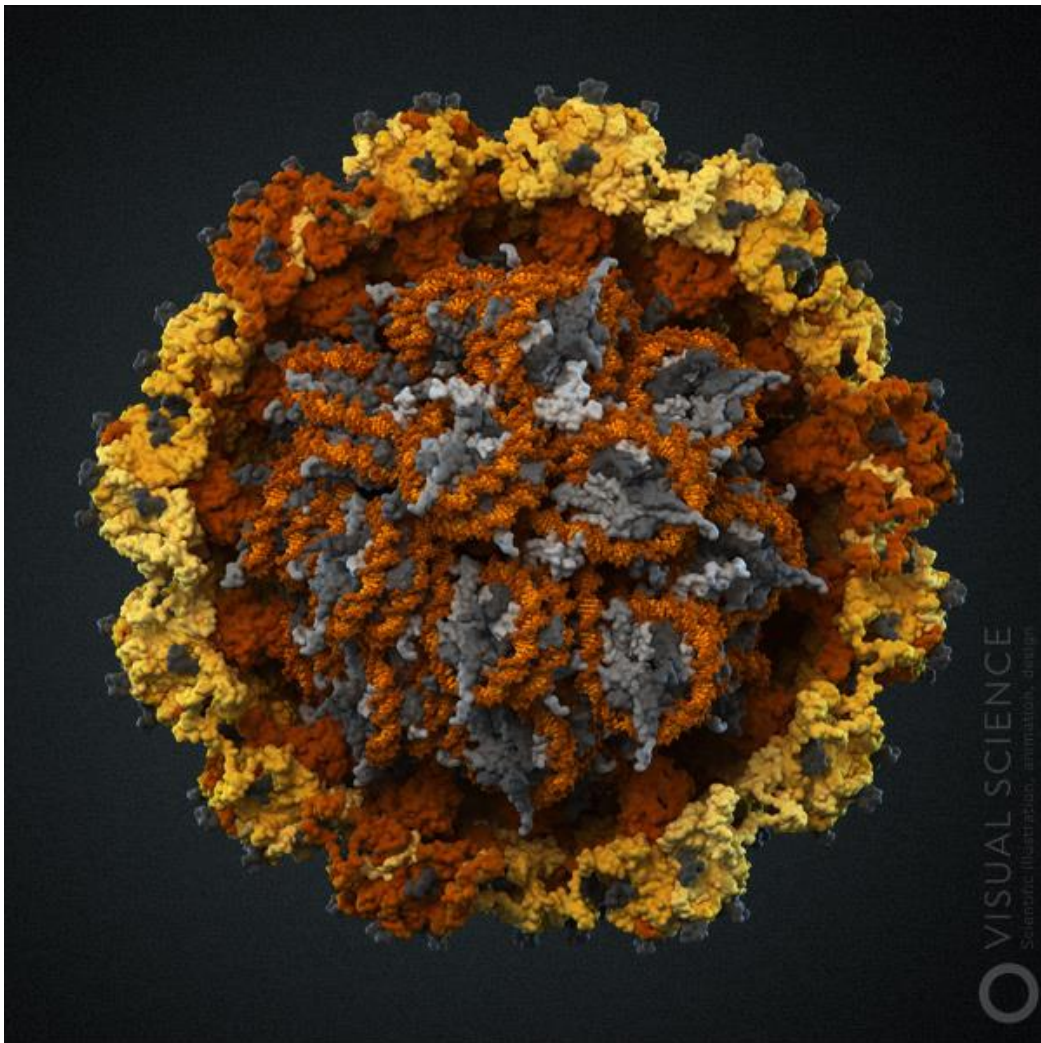


Figure 4: Computer generated cut-through visualisation of human papillomavirus type 16, based on protein and molecular structures. Taken from Visual Science (11)

## Taxonomy of papillomaviruses and human papillomaviruses

Agents that have evolved with their host over long expanses of time typically cause chronic infections that have little or no clinical symptoms (12). It has been proposed that papillomaviruses emerged over 350 million years ago and can now be found in a wide range of animal hosts from birds and reptiles to mammals (13, 14).

Papillomaviruses are non-enveloped viruses that have an icosahedral structured capsid containing their genetic material, double-stranded DNA (see Figure 4). The capsid is made up of two types of structural viral proteins: the major capsid protein L1, and the minor capsid protein L2. Expression of L1 protein alone is both necessary and sufficient for the formation of virus-like particles, which are used in current HPV vaccines (15).

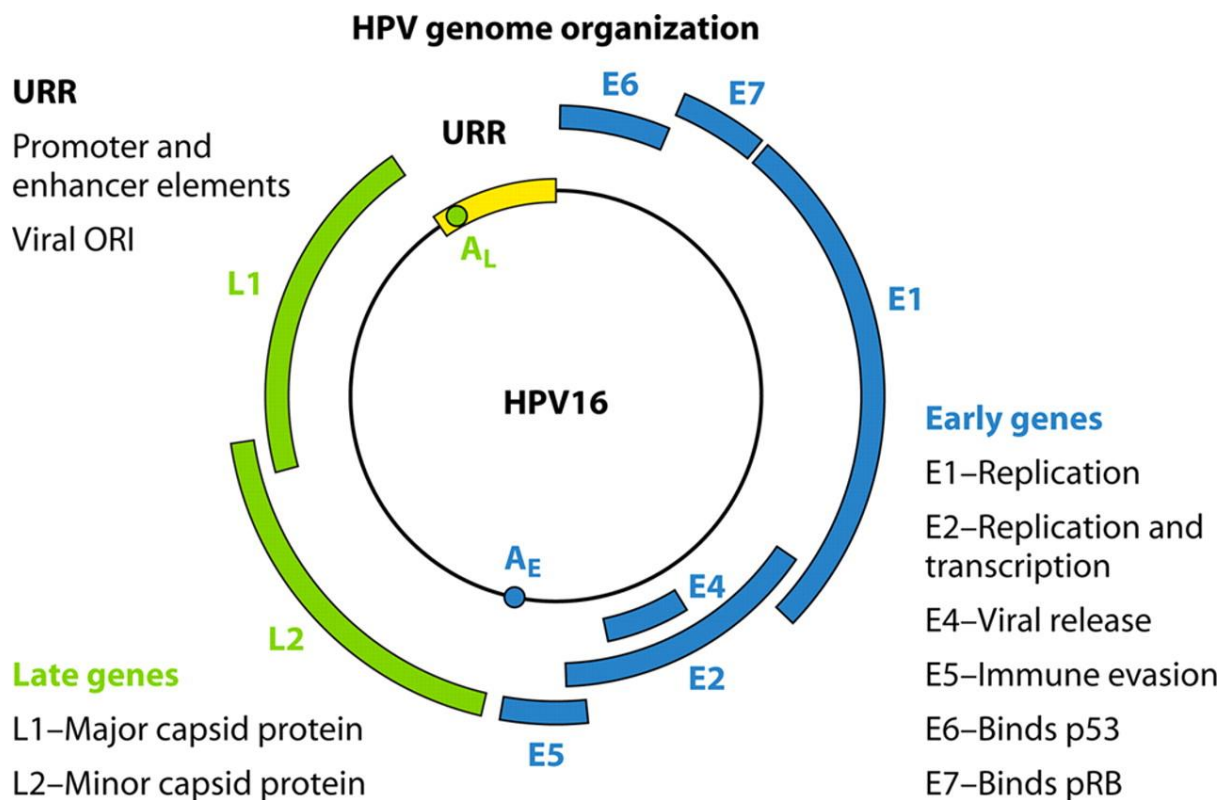


Figure 5: Diagrammatic representation of the organisation of an HR-HPV genome and encoded viral proteins. The genome is organised based on the position and timing and expression of the coded proteins (early vs late) (16).

Classic taxonomic terms for viruses such as “strain” and “serotype” used by the International Committee on Taxonomy of Viruses are not applicable to papillomaviruses (17). Standard culturing techniques are not able to produce papillomaviruses, therefore “strains” cannot be identified, and as most infections with papillomaviruses do not generate a robust immune response, the term “serotype” is also difficult to apply (15). Because of these limitations,



## History of human papillomaviruses and their link to cancer

A possible link between sexual activity and cervical cancer was first proposed as far back as 1842, when Domenico Rigoni-Stern of Verona noted that the cancer occurred more frequently among married women and widows than among nuns who had taken a vow of abstinence (22). It was not until the 1970s that an infectious agent was considered the cause, and at this time, the prime suspect was herpesvirus (23). Around the same time, Harald zur Hausen used DNA hybridisation to identify HPV strains in plantar and flat warts (HPV-14) (23).

The first HPV type was isolated from a form of cancer in 1978. The work was done by Stefania Jablonska and Gerard Orth, who used zur Hausen's methods to isolate HPV-5 from a form of skin cancer involving epidermodysplasia verruciformis (24). At the same time, zur Hausen and colleagues Herbert Pfister, Lutz Gissman and Matthias Durst continued to isolate new HPV strains, including HPV-6 from genital warts and HPV-8, another HPV type causing epidermodysplasia verruciformis (25, 26). zur Hausen and colleagues then used HPV-6 to create a DNA probe and identified HPV-11 in genital warts, laryngeal tumours and some cervical cancer specimens (27). Using HPV-11 as a probe, Durst et al. identified HPV-16 among 11 out of 18 cervical cancer specimens they tested (28). Syrjanen et al. suggested in their 1983 observations that HPV may play a role in oral squamous cell cancers, and in 1984, Borshart et al. from zur Hausen's group identified HPV-18 in several cervical cancer specimens, further increasing the association between HPV and cervical cancer (29, 30).

The discovery of these novel viruses outlined above shows that progress has been based on utilising existing genetic code to hybridise and isolate novel types. This has potentially limited the field of discovery, as novel HPV types will only be found that are closely related to those already identified.

## Classification of HPV based on oncogenic potential

It was not until 2007 that the International Agency for Research on Cancer (IARC) released a statement concluding that there was "sufficient" evidence to confirm the role of HPV in cancers of the penis, anus, oral cavity, oropharynx and tonsils, in addition to cervical cancers and other cancers of the vagina (31).

Table 3 summarises the IARC Working Group's conclusions in relation to HPV types, with Group 1 being evaluated as having sufficient evidence and Group 2 (A and B) having limited evidence for carcinogenicity (31). The HPV types covered in Groups 1 and 2 are classified as high-risk (HR) HPV types.

Table 3: Human papillomavirus types assessed by IARC Monograph Working Group, adapted from Bouvard et al. 2009 (31)

| Group           | HPV Types                                  | Evidence for carcinogenicity  |
|-----------------|--|---|
| Alpha HPV Types |  |   |
| 1               | 16   | Most potent HPV type, known to cause cancer at several sites  |
| 1               | 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 | Sufficient evidence for carcinogenicity   |
| 2A              | 68   | Limited evidence for carcinogenicity  |
| 2B              | 26, 53, 66, 67, 70, 73, 82                 | Limited evidence for carcinogenicity  |
| 2B              | 30, 34, 69, 85, 97                         | Classified by phylogenetic analogy to HPV types with sufficient or limited evidence for carcinogenicity |
| 3               | 6, 11                                      | -   |
| Beta HPV Types  |  |   |
| 2B              | 5, 8                                       | Limited evidence for carcinogenicity  |
| 3               | Other beta and gamma types                 |   |

Of all the HPV types identified to date, HPV-16 has been classified as the most oncogenic (31). The 2007 IARC Monograph Working Group collated and evaluated the evidence relating to the causal associations between the various HPV types and cancers found at different anatomical sites (21). The working group identifies a causal link with oncogenic potential based on the following criteria: a strong statistical association (relative risk), replication across multiple separate studies, quality of studies, risk increases with exposure, the specificity of an association, and randomised control trials (where available). The following categories are used to classify the evidence relevant to carcinogenicity in humans:

*Sufficient evidence for carcinogenicity:* the group considers that there is a causal relationship between exposure to the agent and human cancer. Chance, bias and confounding in studies has been ruled out with reasonable confidence.

*Limited evidence for carcinogenicity:* a positive association has been observed between exposure and disease, but chance, bias and confounding could not be reasonably ruled out.

*Inadequate evidence for carcinogenicity:* studies examined are lacking in quality, consistency and statistical power to allow a conclusion to be made or no data on cancer in humans are available.

*Evidence suggesting lack of carcinogenicity:* several studies of adequate quality show there is no positive association between exposure and any studied cancer.

## Human papillomavirus transmission

Human papillomaviruses exclusively infect the basal cells of the stratified epithelium tissue (cutaneous and mucosal). Therefore, HPV is primarily transmitted via direct skin-to-skin contact. However, this contact can be considered both casual, as is the case for the majority of HPV types that infect the cutaneous epithelium, and sexual being the primary route of transmission for HPV types that infect the mucosal epithelium.

For infection to occur and establish, it is generally thought that a micro-abrasion or tear in the epithelial layers that make up the skin must be present as this allows the HPV virion access to the basement membrane and the basal epithelial layer (see *Figure 7*) (32, 33).

### ***Sexual transmission of human papillomavirus and GBM***

An agent is considered a sexually transmitted infection (STI) if the primary mode of transmission is through sexual contact. The majority of HPV types that belong to the alpha-papillomavirus genus are tropic to the mucosal epithelium and are primarily transmitted to these sites through sexual contact.

By definition, GBM are males that have sexual contact with males, this means that the routes of sexual transmission for HPV are different to those between opposite sex sexual partners. The sexual activities engaged in by GBM are important for understanding the potential routes of HPV transmission among this population and identify possible prevention interventions. Sexual practices between males can include, but is not limited to, mutual masturbation, genital-to-genital contact, genital-to-oral sex (receptive and insertive), anal-to-oral sex (receptive or insertive), and anal sex (receptive and insertive). Each of these sexual practices can be engaged in by opposite sex sexual partners, but the practice of anal sex is more frequent among GBM compared to heterosexuals. In the 2014 round of the NZ GAPSS and GOSS surveys, 82.6% of GBM who reported a casual male sex partner also reported engaging in anal sex with this casual male sex partner in the previous six months (34). By comparison, in the 2012 round of the UK Natsal survey, 13.8% of males reported any anal sex with a female sex partner in the previous 12 months, but reported 62.9% vaginal sex in the previous four weeks (35).

The cervix and anus are particularly vulnerable to HPV infection during sexual contact. It is at these sites that HPV has direct access to the “transformation zone” or the squamocolumnar junction during penetrative sexual activity (36, 37). At this site, a process of metaplasia occurs whereby columnar epithelial cells are constantly being replaced by squamous epithelial cells, allowing HPV direct access to susceptible epithelium cells without the need for a micro-abrasion or tear (see *Figure 7*) (32, 33).

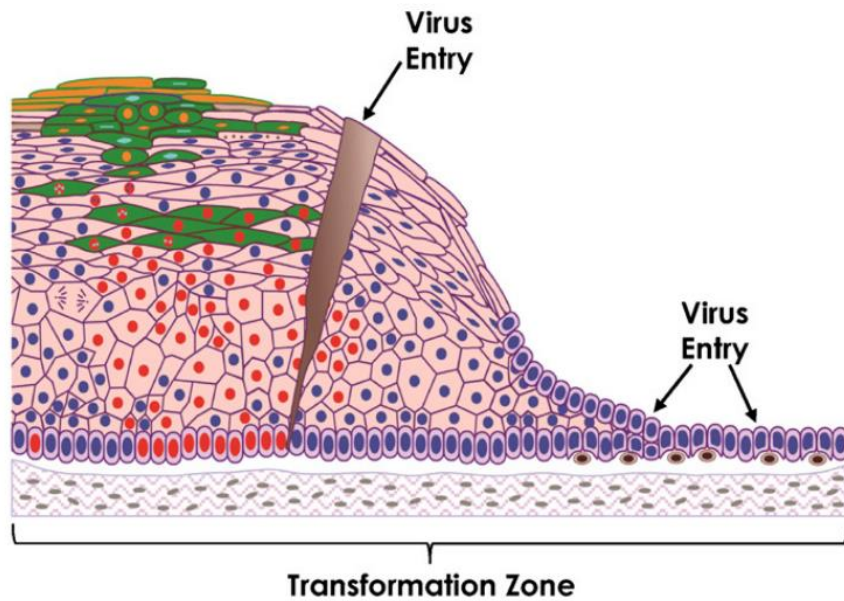


Figure 7: Diagrammatic representation of the process of HPV entry at the endocervix. Firstly, through the stratified epithelium via a microwound, and secondly, at the transformation zone via direct infection of basal epithelial cells. Taken from Doorbar et al. (38)

Within the oral cavity, the tonsils and the base of the tongue are susceptible to HPV infection due to the presence of reticulated epithelium found at the base of crypts within the stratified squamous epithelium, providing similar direct access to susceptible cells without the need for a micro-abrasion (39).

The penis is less vulnerable to mucosal HPV infection as compared to the other sites mentioned above. The penis is an external sexual organ and the larger area of keratinised epithelium found here may reduce the susceptibility to infection with HR-HPV types that infect mucosal sites. However, squamous epithelial cells under the foreskin are susceptible to infection with HR-HPV types, with circumcision showing some protective effect (40).

***Other potential routes of human papillomavirus transmission***

Consistent condom use has shown some protective effect against HPV infections but is not fully protective (41-43). Therefore, other transmission routes are needed to explain HPV transmission beyond penetrative sexual activity. Cutaneous HPV types such as HPV-1 and HPV-2 have been demonstrated to be transmitted by fomites, as viral shedding from the dry epidermis is common (44). However, it is unclear whether mucosal HR-HPV types can be transmitted via fomites, particularly surfaces that may be contaminated with genital secretions, mucus, saliva or other fluids containing shed virus from these mucosal sites.

For healthcare providers, the potential for non-sexual transmission of HR-HPV types through contact with skin and bodily fluids during clinical inspections and surgeries are of particular concern. Meyers et al. exposed HPV-16 to 11 common clinical disinfectants and then

measured the infectivity of the exposed viruses (45). They found that these disinfectants had no effect on HPV-16 infectivity, further adding to the biological potential for the fomite transmission of HPV.

As described earlier, there is no culturing technique to produce large titres of HPV for experimental purposes, meaning experiments rely on detecting HPV DNA or using virus-like proteins (VLPs) consisting of only the viral capsid proteins to demonstrate the presence of HPV. The benefit of VLPs is that they can still model the infection pathway prior to viral replication, making them more suitable for demonstrating HPV transmission potential.

The importance of differentiating between detecting HPV DNA and demonstrating transmission potential is apparent in two studies. Anderson et al. were able to detect HPV DNA on swabs taken from a sex toy 24 hours after having cleaned a toy that had been inserted into the vagina (46). However, experiments by Ding et al. using HPV-16 pseudoviruses (VLPs) showed that while there were high levels of survivability (detection) in the environment, up to several days, those pseudoviruses exposed to cervicovaginal secretions and those exposed to desiccation exhibited lower levels of infectivity (44).

Malagon et al. report that HPV transmission is unlikely to occur through hand-to-genital contact (adjusted hazard ratio: 0.5 [95% CI: 0.1–1.8] for concordance of HPV infection on female genitals and male hand) compared to genital-to-genital contact (adjusted hazard ratio: 19.3 [95% CI: 11.8–31.8] female and male HPV genital infection concordance) between heterosexual couples (47). Further research is needed to determine if other routes of infection are present for HR-HPVs and used to inform behavioural change and harm-minimisations interventions.

### ***High-risk human papillomavirus and oncogenesis***

From initial infection to the shedding of virus, the lifecycle of HPV takes between six to twelve weeks (48). While there is heterogeneity between HPVs, such as between those that cause AGWs and those that cause cancers, there are similarities in their lifecycles. Viral replication relies on the epithelial cell differentiation process, with infection commencing at the basal cell layer (early infection) and infectious HPV virions being formed and shed in the upper layers of the epithelial strata (late infection) (49, 50).

There appear to be two factors that make HR-HPV types oncogenic compared to other HPV types:

1. The E6 and E7 proteins of HR-HPV types bind to target host cell proteins with greater affinity than other HPV types, driving continuous cell division and replication.



2. HR-HPV types are more likely to produce a persistent infection and are less likely to clear compared to other HPV types. A persistent infection provides greater opportunity for disruption of viral genes and their integration into the host genome.

### ***Viral clearance and persistence and oncogenesis***

An estimated 90% of incident HR-HPV infections become undetectable through current testing techniques within two years (51, 52). Clearance of HPV infection is generally defined as two (or greater) consecutive negative test results in a given period following an initial positive result (53). Clearance of HPV infection is independent of seroconversion to HPV (54). HR-HPV infections at non-cervical sites are estimated to clear faster than in the cervix (55).

Viral persistence appears to be a significant factor in the development of HSIL, with HR-HPV types being more likely to establish a persistent infection compared to LR-HPV types (38). In 2018, Jin et al. report on the incidence of HSIL among GBM participants in the Study of the Prevention of Anal Cancer (SPANC) cohort, with an incidence of 10.3 per 100 person-years (95%CI: 8.1-13.2) (56). They report HSIL incidence was lowest among participants who consistently tested negative to HR-HPV at baseline and 12-month visits (3.2 per 100 person-years) as compared to those with persistent HPV-16 infection (33.6 per 100 person-years, hazard ratio:10.10, 95% CI: 4.21-24.3) and persistent infection of other HR-HPV types (21.4 per 100 person-years, hazard ratio: 6.60, 95%CI: 2.92-15.0).

### ***Viral genome disruption and incorporation and oncogenesis***

Viral genetic disruption and incorporation during cell division have a greater chance of occurring with a longer duration of infection. As mentioned above, HR-HPV types are more likely to result in persistent infection and have a greater probability of genetic disruption and incorporation.

During the early experiments conducted by Borshart et al., they discovered that, among the tumours tested, HPV-18 frequently becomes integrated into the host's DNA (29). An essential feature of this integration is that the genes coding for the HPV proteins E6 and E7 remain intact and continues to be expressed, while the E2 gene is disrupted (57).

In infections that do not result in oncogenesis, as the E6 and E7 proteins drive cell and viral replication, the viral E2 protein will be produced in quantities large enough to downregulate their production, and the cell will return to its normal differentiation process. With the loss of the E2 gene, the protein can no longer be expressed, and the feedback loop for the cell cycle becomes deregulated and immortalised, resulting in oncogenesis (13).

## Latency and reactivation of HPV infections

Differentiating between incident and latent infections has implications for the control and prevention of HPV-related disease. If the majority of HPV infections detected are reactivation of latent infections, it emphasises the importance of early vaccination against HPV, before acquiring initial infection. Similarly, a screening programme will not capture latent HPV infections through current testing techniques as the infection is not active and producing (shedding) virus.

The biological basis and theory for HPV latency has been well established (58-60). However, limited data exist in human studies. The consensus has been that most HPV infections are incident infections, and a subset of active infections result from reactivation of latent HPV, which are triggered among immunocompromised individuals, such as PLHIV and transplant recipients (61-63).

A longitudinal cohort study by Twisk et al. provides evidence that estimates of reactivation of latent HPV infection may be more common than previously considered (64). The authors identified “incident” anal HPV infections among GBM who had previously tested negative for HPV infection on at least two prior bi-annual follow-up appointments and reported no sexual exposure. This conservative measure included no report of insertive or receptive anal intercourse, no oral-anal contact, and no fisting for six months prior to follow-up appointment (n=157/714). It is worth noting that this definition does not exclude those who may have experienced anal-digital stimulation and used or shared sex toys. Among sexually non-exposed GBM, the incident rate for HPV-16 was 5.7/100 PY (95% CI: 2.4—13.6) with no significant difference observed between these men and those defined as highly sexually exposed (>2 anal sex partners and reporting fisting or rimming), with an incidence rate ratio of 1.8 (95% CI: 0.6—4.5, p-value: 0.24).

## Progression of HPV-related cancers

High-risk HPV types infect mucosal sites, characterised by squamous epithelial cells. Once the life cycle of these cells is disrupted, and continuous cell replication and division occurs, lesions begin to develop (13). Since the time of writing, the understanding of the natural history of HPV from infection to invasive SCC has shifted from a linear progression through the stages of pre-cancer to invasive cancers, to a more nuanced one that may be related not only to the infecting HPV type but also the cell type that is being infected.

Findings of studies on the cervical transformation zone have suggested that, dependent on the epithelial cell type infected, cervical HSIL are not always preceded by LSIL (65). Not all infections are confined to the ectocervix and transformation zone, and it has been demonstrated that HR- HPV types can infect the columnar cells in the endocervix, which do

not support the development of LSIL (66). However, the anal and cervical transformation zones differ, and further studies are needed to determine if the infection and development pathways also differ between these sites (67).

Fang et al. argue that the current evidence is inconclusive to support either of the proposed pathways and further research is needed for anal SCC (68). They propose that it may be the case that both pathways are viable for the development of anal HSIL and SCC.

What is clear, however, is that development of anal HSIL is associated with HR-HPV infection. Lui et al. described that among patients with anal LSIL (N=168, 87% PLHIV, 92% GBM) attending a New York hospital, those infected with HR-HPV types HPV-16/-18 at baseline visit were more likely to present with HSIL at follow-up compared to those infected with non-HPV-16/-18 types or were HPV-negative (presenting with HSIL: 67%, 25%, and 7% respectively; p-value:<0.001) (69).

### ***Spontaneous regression of HPV-related lesions***

The natural history of HPV-related cancer development at non-cervical sites is emerging compared to what is known for cervical cancers. Spontaneous regression is an important parameter as it influences the effectiveness of screening programmes and the potential harm caused by early clinical intervention of identified cases.

Poynten et al. describe the rates of progression and spontaneous regression of AIN among a community cohort of GBM recruited into the Study of the Prevention of Anal Cancer (SPANAC) study, almost all of whom were GBM (>95%) (70). They found evidence of “composite” HSIL (cHSIL) (positive cytological or histological HSIL) clearance rate of 22.0 per 100 PY (95% CI 18.8–25.8) across the study period (70). Higher clearance rates were associated with younger age, an AIN2 diagnosis rather than AIN3, smaller lesion size, and not having a persistent HR-HPV infection. Clearance was also higher for incident cHSIL diagnosed during the study period at 44.5 per 100 PY (95% CI 33.1-60.1), comparable to the CIN2/3 regression estimates of 33–40% among HIV-uninfected women (71).

## Synthesis of main findings on the biology of HPV

- Papillomaviruses are only detectable using DNA-based testing technologies such as PCR and hybrid-capture.
- Mucosal tropic HPVs are transmitted by direct skin-to-skin contact and therefore primarily during penetrative sexual intercourse.
- HR-HPVs infect the basal epithelial layer of stratified epithelium, which is exposed through micro-abrasions that occur during sexual activity.
- Direct access through “transformation zones” found at the cervical and anal canal increase susceptibility to HPV infection at these sites.
- The HPV vaccine utilises the HPV L1 proteins to form VLPs and illicit immune memory in the host, creating Abs against the highly conserved L1 protein. This blocks viral entry to host cells, explaining the high efficacy and sterilising immunity seen for the HPV vaccine.
- Incorporation of HR-HPV genes and disruption of the viral and host genome is a causal mechanism for oncogenesis. Persistent infections, reinfection and reactivation of HR-HPV infections provide the opportunity for viral gene integration to occur.

## Section Two: Sampling of HPV infection and HPV-related disease among GBM

### Purpose

This section is broken into two parts. Part one seeks to explore the current sampling methods and detecting HPV infection and related disease among males. Part two defines GBM and explores methods for recruiting GBM into studies. Understanding the rationale, the strengths, and the limitations in sampling methods for both HPV and GBM will aid in critically interpreting the epidemiological estimates for the burden of HPV among this population in Section Three.

### Aims

- a. Describe the methods of sampling HPV infection and related disease at various anatomical sites in males.
- b. Explore the methodology for defining and recruiting GBM into public health research.

## Section Two – Part 1: Measuring HPV infection and related disease among GBM

### ***Purpose***

The range of HPV-related disease among males and the range of anatomical sites affected adds to the complexity of monitoring the burden of these viruses and the impact of health interventions to address them. This section seeks to identify the

### ***Aims***

- a. Explore sampling for the detection of HPV at male anatomical sites susceptible to HPV infection.
- b. Describe the methods for the detection of HPV-related disease that affects males.

### ***Biological sampling and detection of HPV infection among GBM***

Infection with HPV is necessary, though not sufficient, for the development of HPV-related disease. Therefore, determining the prevalence and incidence of HPV infection is essential to understanding the force of infection, the rate at which susceptible individuals experience infection. A greater prevalence of infection drives a greater incidence of infection within sexually connected communities. Finding these measures and identifying the groups within the population that are most affected, facilitates the development and targeting of research and public health programmes.

The focus of this thesis is on HPV among GBM; therefore, the exploration of sampling in this section is related to the detection of HPV infection for this purpose rather than for clinical diagnostic purposes. The clinical relevance of HPV infection detected at any point in time for HPV-related non-cervical disease is unclear, though there is consensus that for most HPV-related cancers, repeat and persistent HR-HPV infection is associated with the progression of disease (69).

### ***Detection of HPV***

Two methods have been widely used for the detection of HPV infection, the first being polymerase chain reaction (PCR) and the second being hybrid capture 2 (72). PCR is the more sensitive of the two assays, but it also detects HPV infections that may not be clinically relevant (73).

As with most studies that seek to compare prevalence estimates obtained through biological sampling, some variation in the results between studies can be explained by sampling techniques, sample handling and storage, and the specificity and sensitivity of detection methods used. This is particularly relevant for HPV prevalence studies as there has been no “gold standard” in the sampling or detection methods for the different male anatomical sites

that HPV infects, nor the range of diseases HPV causes at these sites. For example, studies published before the 2012 meta-analysis on anal HPV infection and related anal cancers by Machalek et al. had used “in house” assays to detect HPV in their samples (73).

Since this time, PCR-based assays have been widely agreed to be the detection method of choice, with some countries now moving to use PCR detection as a component of their cervical cancer screening programmes in place of solely cytological techniques, including NZ (74, 75). However, questions remain about the best sampling and detection methods for HPV-infection and screening at other anatomical sites.

Dunne et al. conducted a systematic review of the literature in 2006 on the prevalence of HPV infection among males (43). They identified that samples collected for studying HPV infection are generally collected via the rubbing or rotation of a swab brush to capture cellular material and reported that seven of the 40 studies included used beta-globulin levels to assess whether there was sufficient cellular material in the sample to conduct PCR analysis.

#### *Sampling of the anal canal for HPV infection*

There appears to be a consensus across studies that biological samples from the anal compartment are best collected using a swab. Sampling of the anal compartment for HPV infection is the same as that for the collection of anal samples for chlamydia or gonorrhoea testing. However, there is variation in the type of swab used, the sample collection method using the swab, the storage of the sample, and the methods of DNA extraction from the sample for PCR analysis.

High-resolution anoscopy has been used in some studies for sample collection as this allows the clinician to visualise the anal environment and more thoroughly sample the area. However, this is a highly invasive method for the patient, is expensive, complicated and time consuming compared to other techniques, requires specific training to use on the part of the clinician and also has the potential to cause harm to the patient if not used correctly.

Self-collected or patient-collected sampling has proved to be a successful and acceptable method for STI screening, and more recently, has been proposed for cervical screening programmes. Tamalet et al. found self-collected anal samples to be an acceptable and accurate method to measure HPV infection prevalence among PLHIV patients in France (N=116, 84% male, 60% GBM), with 91% of patients agreeing to participate in the study and 91% (n=94/106) of the self-collected swabs containing sufficient material for testing (76).

Yared et al. compared agreement between self-collected and clinician-collected anal swab samples for the detection of anal HPV infection among HIV-negative GBM recruited through sexual health services in the USA (N=90), finding a moderate interrater agreement for all HPV types tested between pairs ( $\kappa = 0.51-0.63$ ) (77). Overall, among clinician collected and

self-collected samples, a similar number did not contain adequate cellular material for analysis (n=5 vs. n=6, respectively). However, clinician-collected samples showed a greater detection of any HR-HPV types than self-collected samples (55.1% vs 42.3%, p-value=0.021).

#### *Sampling of the penis for HPV infection*

The penis is an external sexual organ compared to the anus, cervix or the oral cavity; therefore, the sampling techniques used are varied and depend on the area of the penile region being studied.

The use of urine samples has also been investigated to detect urethral HPV infection, as urine samples are already commonly collected to detect chlamydia and gonorrhoeal infections. Aung et al. explored urine positivity for HR-HPV types and LR-HPV types 6 and 11 among heterosexual men under the age of 25 years attending a SHC who had tested positive for chlamydia. They demonstrated that the odds of detecting HPV6/11 were significantly greater in those cases with AGWs closer to the urethra (OR:40.20, 95% CI: 19.78—81.70) compared to those who presented with no AGWs, and HR-HPV types detection was lower among circumcised men compared to uncircumcised men (OR 0.31; 95% CI: 0.14 to 0.65) (78). The authors conclude that the passing of urine over areas affected by AGWs or over the foreskin likely contributed to the findings, limiting the application of urine testing for detecting HPV infection.

In their 2006 systematic review, Dunne et al. report that sampling the glans, corona, prepuce, and shaft of the penis yield the most consistent and adequate samples for the detection of HPV infection, while sampling of urine, semen, scrotum and the urethra yielded more varied and inadequate samples (43). Additionally, in the HIM Study, Giuliano et al. used three separate swabs to sample different sections of the penile area (coronal sulcus and glans, shaft of the penis, and finally the scrotum), which were then combined for analysis (79) .

#### *Sampling of the oropharynx and oral cavity for HPV infection*

Sampling of the oral cavity is potentially more problematic than other anatomical sites. The surface area to be sampled is large and there are multiple structures within this environment. Furthermore, the cells that are susceptible to HPV infection are within pits and therefore may not be readily accessible using a swab method as can be used for anal and penile sampling. However, both swabbing and oral rinsing methods have been used to collect samples for HPV detection.

In 2001, Garcia-Closas et al. directly compared the oral rinse and swabbing methods for sampling human genomic DNA and determined that while both were adequate to detect the presence of human DNA using PCR, the oral rinse provided a greater amount (80). This is



important for studies that are looking to sample oral HPV, as it demonstrates that oral rinses collect a greater number of human cells compared to swabbing and are more likely to contain the host cells for HPV. The yield of potential host cells is also crucial because inadequate sample purification due to PCR inhibition has been shown to underestimate the prevalence of oral HPV infection (81). Furthermore, oral rinsing is easier to conduct than oral swabbing and may be more acceptable to study participants as they can do the procedure themselves.

#### *Sampling the blood for antibodies against HPV*

Testing for antibodies against HPV can provide an estimate of cumulative or lifetime exposure to HPV rather than point- or age-specific infection prevalence. Measuring the seroprevalence of anti-HPV antibodies (Ab) also removes the need to sample HPV infection prevalence at each anatomical site. Drawing blood from patients allows for the testing of circulating Ab against HPV types. Testing uses VLPs of the HPV type being tested and Abs will bind to these if present in the sample.

The clinical and epidemiological relevance of HPV seroprevalence is not clear. It appears that only a minority of HPV infections result in seroconversion and that this is dependent on the anatomical site of infection. There appears to be a greater level of seroconversion among cervical and anal HPV infection compared to those of the oropharynx and penis (82, 83). Furthermore, the duration and concentration of antibodies raised to infection is unclear but is lower than that induced by vaccination with HPV VLPs (72). This raises whether seroconversion is protective against future infection or facilitates the clearance of infection, though it has been demonstrated that seroconversion is not necessary for clearance (84).

In a nationally representative sample of men in the USA collected between 2003 and 2004, the seroprevalence against HPV types 6, 11, 16 and 18 ranged between 2% to 6% and was considerably lower compared to women in the same sample (85). Seroprevalence was significantly associated with age, with males aged 50-59 years having a 14-fold greater risk of seropositivity compared to males aged 14-19 years in the sample (85).

Among studies that have looked at GBM, the seroprevalence is much greater. In a USA study based in a Seattle clinic that recruited GBM between 1989 and 1995, the overall seroprevalence among HIV-positive and HIV-negative GBM for HPV types 6 and 16 ranged between 32% and 48%, respectively (86). Seroprevalence was also associated with age in this study, particularly those aged over 35 years.

A study of seroconversion after incident HPV infection at different anatomical sites among GBM aged 16-20 years by Zou et al. supports the finding that seroconversion is more likely to occur during anal HPV infection, with seroconversion following incident anal infection with LR-HPV types 6/11 significantly greater than after incident penile infections with the same

types (OR 6, 95% CI: 2-21) (87). However, at baseline, seroprevalence for LR-HPV types 6/11 (16.5%) was significantly greater than that for HR-HPV types 16/18 (5.5%), in contrast to the studies above where HR-HPV seroprevalence is greater. In the study, seroconversion (seroincidence) rates were significantly higher following incident anal infections with LR-HPV types 6/11 compared to HR-HPV types 16/18 (OR 15, 95% CI: 2-118).

### ***Detection of anogenital warts***

The majority of AGWs are painless and may go unnoticed by the patient, particularly if they are present at internal anatomical sites. Clinical diagnosis of AGWs is made through visual inspection of the anogenital region (88). AGWs can be present in the anogenital tract (urethra, anal canal). HPV types 6 and 11 have also been associated with conjunctival, nasal, oral, and laryngeal papillomas outside of the anogenital region (89).

### ***Detection of HPV-related lesions: cytology, histology and biopsy***

The methods for detecting cancers and pre-cancerous lesions caused by HR-HPV infection are similar to those of non-HPV-related cancers. Cytological and histological techniques are used to detect, characterise and grade lesions caused by HPV infection at the various anatomical sites.

Collection of cellular material is important for cytological analyses. The Bethesda classification system is used to categorise cytological samples collected from the anal canal (see Table 4) (90). In a single visit randomised control trial, Wiley et al. compared nylon-flocked swabs to Dracon swabs for the specificity and sensitivity of collecting anal cellular material for cytological testing and prediction of HSIL among GBM (91). They found comparable sensitivity (48% vs. 47%, respectively) but greater specificity for nylon-flocked swabs (76% vs. 69%). In contrast to the collection of samples for HPV infection prevalence, direct comparisons of self-collected and clinician-collected specimens for AIN cytology screening were not comparable, with clinician collected samples providing greater specificity in two USA based studies (92).

For histology, as with cervical screening for HPV-related lesions, diluted acetic acid can be applied within the anal canal to aid in visualising SILs and is most often utilised during anoscopy to visualise, take biopsies or remove HSIL or anal carcinomas. This technique has also shown value in detecting oral lesions but limited benefit when used for penile lesions due to these being present in keratinised cells (93, 94). Acetic acid causes coagulation of nuclear proteins and cytokeratins that cause the colouration of the tissue. Therefore, squamous cell tissue will appear unaffected as the acid will not penetrate beyond the top layer of keratinised cells, which have few nuclear proteins, while lesions will appear white as these cells have more nuclear proteins due to the continued cellular proliferation.

For anal histology, the Lower Anogenital Squamous Terminology (LAST) system is used to grade anal squamous lesions (95). Table 4 summarises the terminology and equivalent stages of dysplasia (abnormal cell growth/development) prior to the development of squamous cell carcinoma (SCC).

Table 4: Terminology for grading anal dysplasia for cytology and histology (96)

|                         | <b>Bethesda, Used for Cytology</b> | <b>LAST, Used for Histology</b> |
|-------------------------|------------------------------------|---------------------------------|
| No dysplasia            | No dysplasia                       | No dysplasia                    |
| Atypia                  | ASC-US                             |                                 |
|                         | ASC-H                              |                                 |
| Mild dysplasia          | LSIL                               | AIN1                            |
| Severe dysplasia        | HSIL                               | AIN2                            |
|                         |                                    | AIN3                            |
| Squamous cell carcinoma | SCC                                | SCC                             |

Abbreviations: AIN, anal intraepithelial neoplasia; ASC-H, atypical cells cannot exclude HSIL; ASC-US, atypical cells of unknown significance; HGAIN, high-grade anal intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion; LAST, Lower Anogenital Squamous Terminology; LGAIN, low-grade anal intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial lesion; SCC, squamous cell carcinoma.

Emerging data suggest cytology and anoscopy with histological findings have only modest agreement for the detection of AIN, potentially reducing their effectiveness for screening programmes. Four studies performing both cytology and anoscopy with biopsy report 12% to 25% of subjects with no cell lesions or malignancies detected in cytological examination have HSIL detected during anoscopy (97-100). Conversely, three of these four studies also report an average of 13% of patients with abnormal cytology results also receive histological results reporting no abnormalities or not receiving a biopsy during anoscopy for further analysis, indicating that HSIL were missed (97-100). Another limitation for the potential of cytological screening for anal HPV-related disease is that abnormal anal cytology is not associated with anal condyloma (AGWs) nor LSIL (98, 101).

Despite the limitations of cytological screening for AIN, Lima et al. make the recommendation in their systematic literature review and meta-analysis that anal swab-based cytology be considered as a potential triaging method for PLHIV patients, a population at greater risk of developing HPV-related anal cancers (96). Table 5 provides a summary of the meta-analysis findings for the sensitivity and specificity for each testing method. However, in the 2016 study by Jin et al., they identified that the low specificity for anal cytological abnormality cut-off would result in unmanageable referral rate (66.2%) among community recruited GBM PLHIV for anoscopy (100).

Table 5: Meta-analysis results for the sensitivity and specificity of anal swab-based test to detect high-grade AIN, comparison of cytology, histology and PCR (96)

| <b>Test and detection threshold</b> | <b>Sensitivity summary estimate</b> | <b>Specificity summary estimate</b> |
|-------------------------------------|-------------------------------------|-------------------------------------|
| HGAIN with any SIL as the cut-off   | 82%                                 | 45%                                 |
| HGAIN with any HSIL as the cut-off  | 44%                                 | 79%                                 |
| HR-HPV DNA detection                | 91%                                 | 27%                                 |

HGAIN = high-grade anal intraepithelial neoplasia

SIL = squamous intraepithelial lesion

HSIL = high-grade squamous intraepithelial lesion

HR-HPV = high-risk human papillomavirus

## Synthesis of Part One: Measuring HPV infection and related disease in males

- There is a diversity in the anatomical sites of males infected by HPV, but sampling methods remain similar across them.
- The collection of cellular material for identifying HPV DNA through PCR testing is used to detect both HPV infection and presence in HPV-related lesions and cancers.
- The use of hybrid capture assays to detect HPV infection is not as sensitive as PCR-based testing but may have greater specificity.
- The techniques or tools used to obtain the greatest yield of cellular material for testing of HPV infection at the various anatomical sites are as follows:
  - Swabbing to sample the anal canal.
  - Mouthwash to sample the oral compartment.
  - Swabbing to sample the penile surface.
- Seropositivity studies are useful in determining probable lifetime or cumulative exposure to HPV among the population, though are limited by the possibility of low seroconversion following HPV infections, which also seems to vary by anatomical site of infection.
- For HPV-related diseases, clinical diagnoses are made using validated techniques and methods:
  - Visual inspection is used for detection of AGWs, with additional biopsy and PCR testing if required.
  - Visualisation with acetic acid and collection of cellular material through biopsy for HPV-related lesions at all anatomical sites.
  - Cytology and histology for identifying and grading abnormal lesions
- To detect AIN among GBM, HR-HPV DNA testing has a high sensitivity, but low specificity compared to cytological and histological detection.
- In patient versus clinician collected samples, clinician-collected samples were found to have greater detection of HR-HPV anal infection and greater specificity for AIN cytology.

## Section Two – Part Two: Sampling GBM

### **Purpose**

Gay, bisexual and other men who have sex with men (GBM) have been identified as a population that is vulnerable to anal HPV infection and related disease. Defining this population is necessary to recruit study samples to measure aspects of their health status, identify health inequities compared to other groups, and monitor progress in addressing these inequities over time.

### **Aims**

- a. Explore the dimensions of sexual orientation used to define GBM.
- b. Explore methods used to recruit GBM for public health research.

### Defining GBM for public health research and surveillance

In the previous section, HPV and the diseases that it causes among males were identified and defined. In public health research, it is necessary to define the population of focus to develop a sampling frame with which to recruit a study sample. Here the purpose is to define GBM, the population focussed upon in this thesis.

### **Dimensions of sexual orientation**

Sexual orientation is comprised of three interrelated dimensions, attraction, behaviour and identity (see Figure 8).

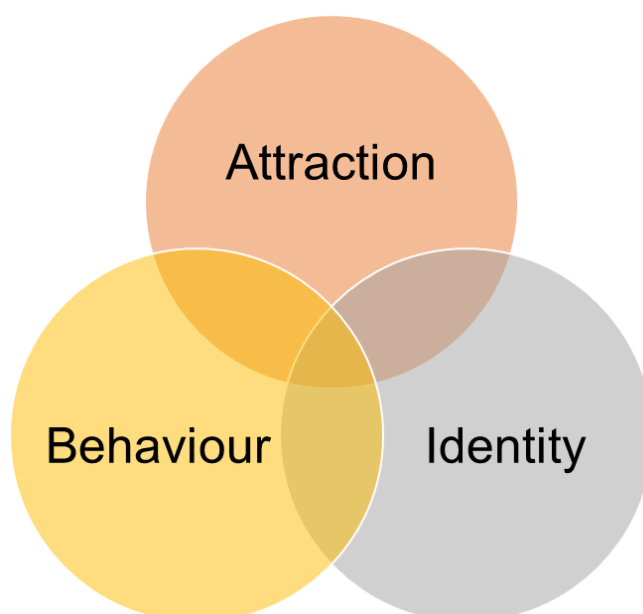


Figure 8: Visual representation of sexual orientation and the relationship between each of the three aspects of sexual orientation: attraction, identity and behaviour.

In brief, sexual behaviour refers to the sex and gender of sexual partners that sexual activity is engaged with. Attraction is the strength and direction of sexual attraction to sex and gender. Sexual identity are the words and descriptions used by individuals to describe themselves, publicly or privately (102).

Sexual identity is tied to social contexts such as language and cultural norms (103). The sexual identities of gay, bisexual, homosexual, and queer are specific to a Western and colonial cultures and may not exist in other cultures and contexts.

Specific to te ao Māori (*Māori world view*), the sexual identity *takatāpui* is derived from a description of “an intimate partner of the same sex” but has been reclaimed to be more inclusive of broader LGBTIQ+ identities (104). Te Tiriti o Waitangi is the founding document of Aotearoa New Zealand and, at a high level, the document seeks equity for Māori in all activities in NZ that affect Māori, which includes research and public health programming (105). Therefore, throughout this thesis, ethnicity has been included in analyses to reflect the experience of Māori, and *takatāpui* has been included as a sexual identity. An important aspect of the thesis is the aim to identify between group differences in HPV-related outcomes within the GBM population, of which ethnicity is one. Where differences are found, these can be used to inform the development of public health programmes that are responsive and appropriate to these intersections.

Measuring different dimensions of sexual orientation results different samples (*see Table 6*). Therefore, it is necessary to determine which aspect(s) of sexual orientation is most relevant to the research question. For the scope of this thesis, sexual behaviour is an epidemiologically important factor as HPV is sexually transmitted and males have not previously been eligible to receive funded HPV vaccination in NZ. Sexual identity is also an important factor to consider, as those who self-identify with a particular sexual identity are more likely to engage with related sexual behaviours and reflecting these identities in public health information and interventions can enable them to be targeted to those most at risk.

Table 6: Proportion reporting non-exclusive same-sex sexual attraction, sexual behaviour, and non-heterosexual identity by gender among nationally representative survey samples

| Author                    | Year      | Country   | Attraction |        | Behaviour |        | Identity |        |
|---------------------------|-----------|-----------|------------|--------|-----------|--------|----------|--------|
|                           |           |           | Male       | Female | Male      | Female | Male     | Female |
| Smith (106)&              | 2003      | Australia | 7.0        | 13.4   | 6.0       | 8.5    | 2.6      | 2.3    |
| Copen (107)*              | 2011-2013 | USA       | 8.0        | 18.9   | 6.2       | 17.4   | 3.9      | 6.8    |
| Ministry of Health (108)# | 2014-2015 | NZ        | 5.5        | 16.1   | 4.2       | 6.5    | 2.3      | 3.7    |
| Geary (109)+              | 2010-2012 | UK        | 6.5        | 11.5   | 5.5       | 6.1    | 2.8      | 2.7    |

& Sample 16-59 years, lifetime sexual attraction, lifetime sexual experience "contact you felt was sexual", identity current.

\* Sample age 18-44 years, "current" sexual attraction, sexual behaviour refers to specific acts dependent on gender, and females were also asked if they had "ever experienced any sexual experience of any kind with another female", identity current.

# Sample 16-74 years, attraction in the last 12 months, lifetime sexual experience "contact you felt was sexual", identity current.

+ Sample aged 16-74 years, lifetime sexual attraction, lifetime sexual experience involving genital contact, identity current.

### **Time**

Time is an important factor to consider in communicable disease research. In relation to sexual orientation, prevalence of these dimensions varies by age and lifetime vs current experience (110, 111). This can introduce measurement error if the correct timeframe for these measures is not considered or specified. Described in Chapter Two: Section One, repeat and persistent infection with HR-HPV types are associated with development of HPV-related cancers, and therefore both lifetime and current sexual behaviour are likely to be indicators of risk (70).

### **Defining GBM**

By definition, the term GBM encompasses two dimensions of sexual orientation, identity (gay and bisexual) and behaviour (men who have sex with men), It also encompasses gender identity (identifying as male). This population definition of GBM encompasses those at risk from the sexual transmission of HPV through male-to-male sexual contact, those at risk of developing HPV-related disease that affects males, and a self-identifying population within NZ that can be targeted with public health messages and interventions that are culturally specific.

### **Sample size**

Sample size is considered in relation to statistical power to detect differences in variables within the sample.



Table 6 shows that GBM are defined by low prevalence indicators (dimensions of sexuality) within national probability samples, resulting in a reduced number of GBM recruited within the overall sample. Therefore, to detect between group differences within a GBM sample, such as differences by ethnicity, other methods are required that recruit larger samples of GBM.

### ***Sampling frame***

Data in relation to the dimensions of sexual orientation are not captured within administrative health datasets in NZ, nor are they fully captured through Census (with the exception of cohabiting same-sex couples) (112, 113). The development of a sampling frame requires an accurate denominator of the sample population, and this does not exist for GBM in NZ. Estimates for the prevalence of the different dimensions of sexual orientation are provided through the 2014 NZ Health Survey, Sexual and Reproductive Health Module (see *Table 6*). However, factors such as geographic macro and micro-clustering of GBM to urban centres in NZ, may mean that sampling frames for the general population are not applicable to GBM and result in an underestimation of prevalence (113).

### ***Error and bias***

There are two types of error, systematic and random (114). Random error is due to chance and can be controlled through statistical methods. Systematic errors are the result of bias introduced into research through methods employed and can be difficult to control for as they are largely unknown. There are two key sources of systematic error in survey methodologies, sample biases and measurement biases.

Sample biases result in sample recruited not being representative of the population it seeks to study. When sampling GBM, participation bias and non-response bias should be considered. Same-sex sexual behaviour and identity are stigmatised and therefore participants may not wish to participate in a study targeted to GBM or respond to questions that require disclosure of sexual orientation.

Measurement biases result in data not accurately reflecting the factors they seek to measure. When measuring dimensions of sexual orientation, social desirability bias and recall bias are particularly important. Participants may not wish to disclose sensitive and stigmatised sexual behaviours, such as receptive anal intercourse, and therefore may report that they have not engaged in these behaviours. Some questions may ask participants to accurately recall lifetime prevalence of a behaviour or the number of sexual partners over a time period, these may be difficult to recall accurately, particularly if the event occurred many years ago or they are asked to accurately recall a large number of sexual partners over an extended time period.

## ***Sampling methods used in public health research and GBM***

Outside of experimental research on the efficacy of treatments and interventions, public health research and surveillance seeks to use observational research to provide an accurate and robust picture of disease and risk factors among the population. There are a number of methodologies employed to provide this, but not all are appropriate or ethical for capturing the experience of GBM. Acquiring a large and diverse sample of GBM requires compromise between external and internal validity.

### *Census*

Sexual orientation measures are not captured through census data in NZ, with the exception of extrapolating same-sex cohabiting couples (113). Inclusion of sexual orientation measures would allow for the development of an accurate sampling frame for GBM as it would provide a denominator for the GBM population in NZ. However, social desirability and response biases could result in an underestimate, particularly in households where disclosure of sexual orientation may not be safe for the individual.

### *Administrative health databases*

To date, sexual orientation measures are not captured in administrative health datasets in NZ, which include medical records and laboratory data (112). Inclusion of sexual orientation measures would allow GBM to be identified through clinical surveillance, enabling clinical data to be disaggregated for this population and health inequities to be identified and tracked over time. However, these require GBM to disclose sexual orientation measures when accessing healthcare and over 50% of GBM in NZ do not believe their GP is aware of their sexual orientation (115). Furthermore, there has been opposition from clinical organisations within NZ to the collection of sexual orientation in these datasets (112). Additionally, differences in healthcare literacy, access to healthcare and navigating the healthcare system have been described in the literature for different populations in NZ, despite the provision of a public healthcare system (8). Therefore, estimates provided through health databases are likely to be an underestimate of true prevalence.

### *Enhanced and sentinel surveillance*

Enhanced surveillance in NZ relies on “going back” to clinicians after a notification for additional information, rather than extracting the data directly from health records (116, 117). This can result in missing or minimal additional information being reported. For example, in 2017, HIV, syphilis and gonorrhoea became notifiable diseases, legally requiring clinicians to complete enhanced surveillance upon diagnosis of these disease, primarily for contact tracing requirements (118). However, the fields that are legally required to be completed do not include sexual orientation data (117).

The Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Blood-borne Viruses (ACCESS) utilises partnerships with multiple clinical sentinel surveillance networks to track changes in testing and diagnoses of these diseases among key populations, including GBM. The project combines sentinel and enhanced surveillance through collaboration with these sentinel settings to extract de-identified data that includes sexual orientation measures from clinical records. However, these measures are not standardised across all settings and still rely on patient disclosure of sexual orientation to healthcare providers (119).

#### *National probability samples*

Few countries have regularly included sexual orientation variables in research conducted using national probability samples. Of those that have, a range of different questions have been used that have measured different aspects of sexual orientation, reducing comparability (see *Table 6*) (109). In the USA, sexual orientation questions have been included across national surveillance surveys with the aim to quantify and reduce health disparities based on sexual orientation (120). However, there is no accurate population denominator for GBM in NZ, and as such, a sampling frame for this population cannot be created from which to draw a probability sample. National probability samples that have included measures of sexual orientation have resulted in under three percent of males identifying as GBM (see *Table 6*) (121). This results in a small sub-sample GBM population that does not have the statistical power to detect between group differences (such as by age or ethnicity) (122).

#### *Clinical and healthcare samples*

Clinical and healthcare settings provide an obvious recruitment setting for health-based research. In these settings, patients are often actively seeking care related to health issues relevant to the research in question. For research seeking to recruit GBM, disclosure of sexual identity or behaviours routinely occurs in these settings, particularly in relation to sexual health. These settings also provide an opportunity to acquire biological specimens ethically and accurately, such as swabs to test for HPV infection.

Recruiting GBM PLHIV from clinical and healthcare settings has been a common way to reach this population since the beginning of the AIDS pandemic in 1982, with many creating cohorts from the enrolled patients at various specialist clinics (123, 124). HIV-negative GBM have been recruited through specialist sexual health clinics where disclosure of sexual behaviours is part of routine practice. However, this results in a bias the sample compared to the general population of GBM by selecting those who may have engaged in sexual behaviours that place them at greater risk of acquiring STIs, have greater access to healthcare, have greater health literacy, and who are more comfortable disclosing their sexual identity and behaviours (125).

### *Respondent-driven sampling*

Respondent-driven sampling (RDS) combines chain-referral sampling with weighted measures based on respondent network size to approximate probability data (126). Researchers have used this method for HIV-related behavioural surveillance of GBM in several European countries to provide more robust estimates among this key affected population (124). Similar to clinical recruitment, collection of biological samples is facilitated through this method, as respondents can be asked to come to a physical location where study procedures can be carried out. A feasibility study using this method did not prove successful in Auckland, NZ (127). Low recruitment was the main limiting factor, with half of the initial “seed” participants not resulting in second wave recruitment. However, two cases of chlamydia were detected within the sample, indicating that the initial recruitment was targeted to sexually active GBM at risk of STIs and HIV, and therefore also likely to be at risk for HPV infection.

### *Convenience samples*

Cross-sectional convenience and opportunistic sampling methods are routinely used in HIV behavioural surveillance for GBM as they provide large and diverse samples of GBM, facilitating statistical power to detect between group differences (124). Cohort studies are also routinely used to explore longitudinal changes in factors of interest over time among GBM, such as engagement with risk and protective behaviours and use of preventative tools.

There are inherent biases in convenience samples, particularly in relation to recruitment. Sampling biases, such as selection bias and non-response bias, are difficult to control for through statistical methods once introduced (121). For example, the setting of recruitment is important to consider as it has been demonstrated to result in populations of GBM with different sociodemographic and behavioural characteristics (128).

Nevertheless, researchers have developed these methods to overcome the inherent issues with recruiting GBM through the methods described above. Repeatable sampling of GBM populations using these methods, with attempts made to control for sampling and response biases, have resulted in reliable and robust data on which public health decisions for these populations are based (129).

### ***Second generation surveillance***

Surveillance using infection and disease case notification is an essential public health function, but measures of sexual orientation are not captured in administrative health datasets in NZ, which includes laboratory diagnoses. As described in detail above, GBM and other sexual orientation minorities are invisible within these datasets. Therefore, researchers

and public health decision makers cannot monitor the burden of HPV infection and related disease among GBM using these datasets.

In response to the HIV pandemic, the WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS), released guidelines for second generation surveillance in 2000 (130). Second generation surveillance aims to ensure surveillance be scalable, responsive, and appropriate to the local epidemic through the following principles:

1. Concentrating strategic information resources to reduce the spread of infection and providing care for those infected.
2. Concentrate data collection in key populations at greater risk of exposure.
3. Compare information on prevalence and risk behaviours to build an informative picture of changes in the epidemic over time.
4. Make use of other sources of information, such as disease surveillance and health surveys, to increase understanding of the epidemic and risk behaviours.

Though recruiting GBM through repeat cross-sectional convenience sampling to monitor changes in HIV-risk behaviours over time were not novel, the UNAIDS and WHO guidelines provided legitimacy to the research and described the added explanatory power that behavioural surveillance contributed to clinical surveillance.

To build a comprehensive picture of the HPV epidemic among GBM, additional and specific data sources are required. The principles and components of HIV second generation surveillance can be applied to HPV-related disease in NZ, under which GBM would be considered a key risk population for anal HPV-related disease (see *Figure 9*).



Figure 9: Components of second generational surveillance, adapted for HPV (130).

## Synthesis of Part Two: Sampling of GBM

- Measuring dimensions of sexual orientation yield different populations and should be based on the research question being explored.
  - For this thesis, the interest is an STI. Therefore, sexual behaviour and sexual identity are dimensions of interest to identify a discreet population for the targeting of surveillance and public health programmes.
- With no population denominator for GBM, a sampling frame cannot be created for this population. Probability and random samples drawn from the total population do not recruit a sample of GBM with statistical power to detect between group differences, e.g., by ethnicity.
- Government-collected administrative databases provide clinical surveillance data, and the inclusion of sexual orientation measures within these tools should be prioritised (122).
- Cross-sectional convenience samples present a focussed, statistically powered method of collecting a diverse sample of GBM. While subject to sampling biases, they recruit large and diverse samples of GBM with sufficient statistical power to detect between group differences.
- Second generation surveillance, which utilises both clinical and behavioural surveillance methods, concentrates epidemic-specific information to increase explanatory power for evidence-based public health decision making on disease control and prevention. These principles can be applied to anal HPV-related disease among GBM.

## Synthesis of Section Two: Sampling of HPV infection and HPV-related disease among GBM

### Sampling HPV

- Detection of HPV relies on DNA-based testing at any anatomical site or type of HPV-related disease. Collection of cellular material from the affected anatomical site is necessary for testing, providing commonality despite the range of affected anatomical sites, HPV types and forms of HPV-related diseases.
  - Swabs are used at the penile and anal sites.
  - A rinse is used for sampling of the oropharyngeal site.
  - Swabs and biopsies can be taken from lesions and neoplasia to determine the presence of HPV.
- HPV testing is not currently clinically indicated for the diagnosis or screening of HPV-related disease in males. Therefore, research to determine HPV infection prevalence must occur independently of routine healthcare.
- Quantifying HPV-related disease relies on presentation, testing, clinical diagnosis and recording in administrative databases and clinical records. Access, quality, and healthcare availability are inequitable across a range of measures, including sexual orientation.

### Sampling GBM:

- Sexual orientation has various dimensions, including attraction, behaviour, and identity. Determining the dimension measured in research is driven by the study question and scope as this also determines the population.
- In NZ, sexual orientation measures are not included in administrative health databases that record HPV-related disease diagnoses and outcomes.
- Recruiting a sample of GBM that is adequately powered to answer the research aims will determine the most appropriate and feasible method to use.
  - In lieu of collecting sexual orientation measures in administrative healthcare databases in NZ, cross-sectional studies are often the most appropriate studies to undertake sexual health research as they recruit large and diverse samples of GBM.
  - Clinical settings provide access to GBM utilising with healthcare, enabling both collection of specimens and the delivery of clinical interventions such as vaccination.

## Section Three: Prevalence of HPV infection and related disease among GBM

### Purpose

This section aims to describe the existing literature reporting the prevalence of HPV infection and related disease among GBM. Presented in two parts, the first covers HPV infection at the various anatomical sites that are susceptible to HPV infection among males – penile, anal and oral. The second part explores the prevalence of the HPV-related diseases at these anatomical sites that result from HPV infection among GBM.

### Aims

1. Explore the existing published literature examining HPV infection among GBM.
2. Explore the existing published literature relating to HPV-related disease among GBM.



## Section Three: Part One – Epidemiology of HPV infection among GBM

### **Purpose**

Sexual practices among GBM differ to those of men who have sex with women (MSW), meaning the routes of sexual transmission between GBM will be different to that between MSW and women and impacting the rates of HPV infection, site of infection and development of HPV-related disease. Part one seeks to explore the prevalence of HPV infection among GBM at each anatomical site to determine if all sites are impacted equally or if particular sites are most affected. The relevant anatomical sites are the anal compartment, the oral cavity, and the penile area.

### **Aims**

- a. Explore the prevalence of HPV infection among GBM at the different male anatomical sites affected by HPV-related disease.

### **Anal HPV infection among GBM**

Machalek et al. conducted a systematic literature review and meta-analysis in 2012 on the prevalence of anal HPV infection among GBM, with the meta-analysis focussing on the prevalence of AIN among GBM (73).

A total of 31 studies were included in the meta-analysis for the prevalence of anal HPV infection among GBM, most of which were conducted in North America. The authors include a total of 4868 samples (29 studies) from GBM PLHIV and 4487 samples (18 studies) HIV-negative GBM. Of these samples, 86% and 64% were from studies recruiting in North America for PLHIV and HIV-negative GBM, respectively.

The authors report that they found no association between the recruitment setting and the reporting of any HPV type or HR-HPV types alone. This is despite the majority of studies recruiting GBM PLHIV from clinical settings (68% of the GBM PLHIV samples), while HIV-negative GBM were mostly recruited from community settings (68% of the HIV-negative GBM samples).

The overall prevalence of any anal HPV infection was greatest among GBM PLHIV (92.6%) compared to HIV-negative GBM (63.9%), and this finding held when limiting to HR-HPV anal infections (73.5% vs. 37.2%, respectively) (see *Figure 10*) (73). GBM PLHIV were also found to have the greater prevalence of both HPV-16 (35.4%) and HPV-18 (18.6%) anal infection compared to HIV-negative GBM (12.5% and 4.9%, respectively) (see *Figure 10*) (73).

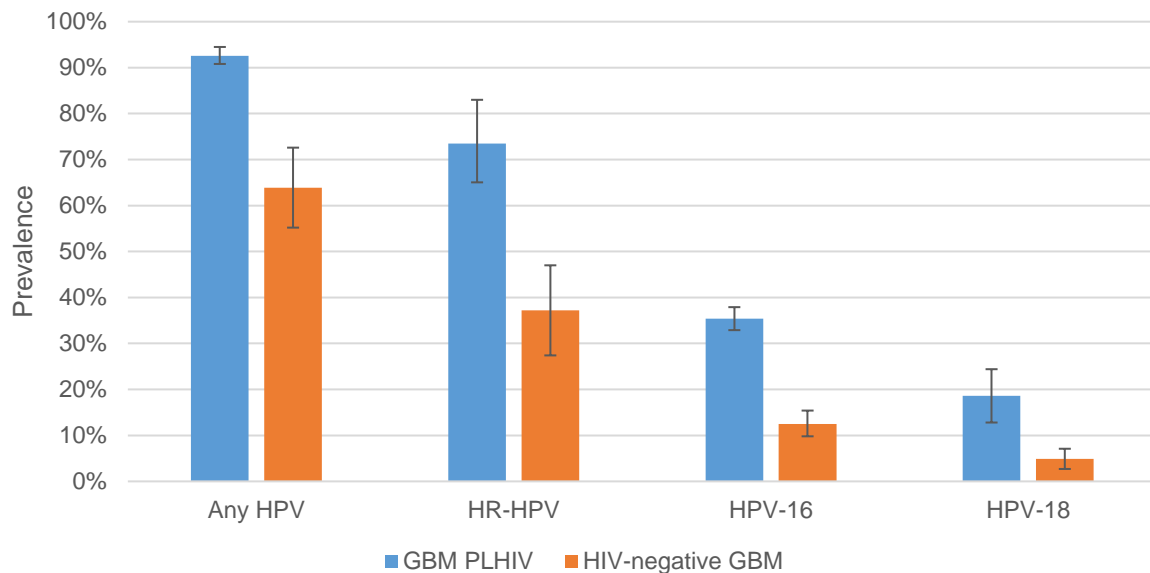


Figure 10: Combined prevalence of anal HPV infection among GBM by HIV status and HPV type, results from the meta-analysis by Machalek et al. 2012 (73).

Repeating the search terms used in the 2012 systematic literature review by Machalek et al. in the PubMed database: (((men who have sex with men)[Title/Abstract] OR MSM)[Title/Abstract] OR homosexual men[Title/Abstract])) AND ((human papillomavirus)[Title/Abstract] OR HPV[Title/Abstract])

A total of 19 papers had been published since 2012. Of these papers, one by Pontyten et al. contained data on HPV anal infection prevalence among GBM. However, this paper used secondary prevalence data collected by Chin-Hong et al. that had been included in the 2012 systematic literature review and meta-analysis by Machalek et al. (131, 132). The study by Pontyten et al. notes that the prevalence of anal HPV infection from Chin-Hong et al.'s study does not appear to decline with age among GBM (see *Figure 11*) (131). This suggesting that this may be due to the continued acquisition from new sexual partners throughout life by GBM compared to women, as indicated from behavioural surveillance data among these two populations (132). Age-specific anal HPV infection data among GBM collected by Vajdic et al. in 2009 support these findings (133).

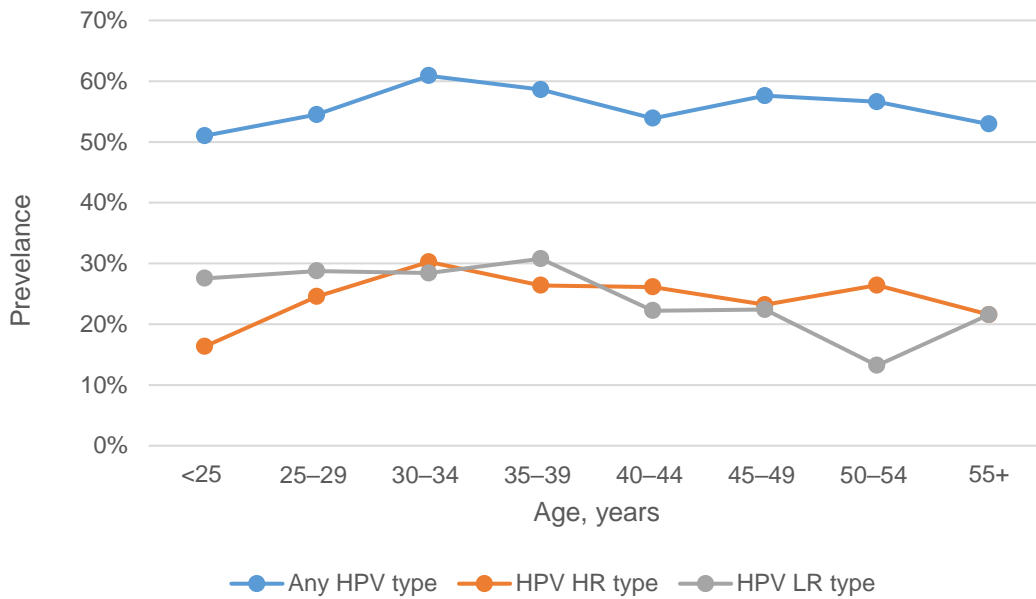


Figure 11: Prevalence of anal HPV infection among HIV-negative GBM, by age group and HPV risk-type. High-risk (HR) types include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 73; low-risk (LR) types include 6, 11, 53–55, 66, Pap 155, and Pap 291. Taken from Chin-Hong et al. 2004 (131)

Additional criteria were added to the search terms to include:

- Specifying anal infection prevalence.
- Including the terms “gay” and “bisexual”.

((((((((male[Title/Abstract]) OR men[Title/Abstract]))) AND (((gay[Title/Abstract]) OR bisexual[Title/Abstract]) OR MSM[Title/Abstract]))) AND ((HPV[Title/Abstract]) OR human papillomavirus[Title/Abstract]))) AND ((anal[Title/Abstract]) OR rectal[Title/Abstract])) AND ((infection[Title/Abstract]) OR prevalence[Title/Abstract])

With the addition of these search terms, a total of 217 papers published since 2012 were returned. Included among these papers was a 2018 systematic review of the literature by Marra et al. that explored anal HPV infection among males by sexual behaviour and HIV status (134). Inclusion criteria for this review were:

1. Time published: 1986 up to June 2018
2. using (PCR)-based assays to detect anal HPV DNA in men,
3. reporting of type-specific anal HPV prevalence in men by HIV status and sexual orientation

Marra et al. used the search terms (((“papillomaviridae” OR “papillomavirus”) or “HPV”) AND (“anal canal” OR “anus” OR “anal”)), to return a total of 4435 papers, of which 79 were included in the analysis. Among the combined sample (N=23700), n=1805 were HIV-negative MSW, n=924 were MSW living with HIV, n=8213 were HIV-negative GBM, and

n=12758 were GBM living with HIV. The majority of participants were recruited in Europe (36%) or North America (34%).

The findings of this review support those found by Machalek et al. that report GBM living with HIV have a near-ubiquitous prevalence of anal HPV infection with any HPV-type but also greater infection prevalence with HR-HPV types including HPV-16, which is the causal pathogen for the majority of anal cancers (see Table 7). The prevalence and anal infection with any HPV type and both HR-HPV types 16 and 18 among HIV-negative GBM were lower than that among GBM living with HIV but greater than that found among both HIV-negative MSW and MSW living with HIV.

Table 7: Estimates of anal HPV infection prevalence among males by HPV-type detected, HIV-status and sexual orientation from the meta-analysis by Marra et al. (134)

| HPV type | Population group |           |                  |           |
|----------|------------------|-----------|------------------|-----------|
|          | HIV-negative GBM | GBM PLHIV | HIV-negative MSW | MSW PLHIV |
| Any HPV  | 47%              | 81%       | 12%              | 44%       |
| HPV-16   | 14%              | 30%       | 3%               | 11%       |
| HPV-18   | 6%               | 16%       | 0.4%             | 4%        |

GBM = gay, bisexual and other men who have sex with men  
MSW = men who have sex with women

### ***Penile HPV infection among GBM***

There have been few extensive studies examining the prevalence of penile HPV infection among GBM. Much of the existing literature explores the prevalence of penile HPV infection among MSW and the relation with cervical HPV prevalence and risk of cervical cancer (135, 136).

Modifying the search terms used previously to identify studies of anal HPV infection prevalence and altering to specify penile HPV infection, the following search terms were run in PubMed:

(((((HPV[Title/Abstract]) OR human papillomavirus[Title/Abstract])) AND ((infection[Title/Abstract]) OR prevalence[Title/Abstract])) AND (((penis[Title/Abstract]) OR penile[Title/Abstract]) OR genital[Title/Abstract])) AND ((((((gay[Title/Abstract]) OR bisexual[Title/Abstract]) OR MSM[Title/Abstract]) OR GBM[Title/Abstract]) OR homosexual[Title/Abstract])) AND ((men[Title/Abstract]) OR male[Title/Abstract]))

The search returned 111 papers, of which 20 reported HPV infection prevalence at penile sites by sexual orientation, four of these repeated findings previously reported in earlier publications of the same cohort and were not included in the table. Except one, all studies utilised a cross-sectional study design to determine the prevalence of penile HPV infection among their samples. Differences were present in the sampling and recruitment methods,

the population targeted for recruitment, study recruitment site, penile areas sampled, and tests used to detect HPV in samples collected. A limitation of the literature review search criteria used is that it excluded studies that recruited and identified GBM in their samples but did not describe this in their title or abstracts.

Overall, the prevalence of penile infection with any HPV type (at any penile site and among all populations studied) ranged from 9.5%—69.2% (see *Table 8*). Studies that investigated and reported the quadrivalent HPV vaccine strains separately (n=11) found prevalence of infection among GBM with HPV-16 (range: 0.0%—11.9%) was greater than that of HPV-18 (range:0.0%—5.7%) and HPV-6 (range:1.5%—10.2%) greater than HPV-11 (range:0.0%—17.1%).

Table 8: Prevalence of penile HPV infection among GBM

| Author           | Year of Publication | Country       | Sample size             | Population   | Study design   | Any HPV prevalence                | HR-HPV prevalence   | LR-HPV prevalence   |
|------------------|---------------------|---------------|-------------------------|--|--|-----------------------------------|---|---|
| Van Bilsen (137) | 2019                | Netherlands   | N=116                   | 2015-2016<br>MSM were recruited based on HIV and penile HPV status in a previous cohort recruited through sexual health clinic, Amsterdam.<br>MSM PLHIV=51%<br>HPV vaccinated=2% | Clinical cohort.<br>Penile samples for HPV testing were physician-obtained from two anatomical sites: shaft and external foreskin tissue; glans, coronal sulcus and inner blade of the foreskin. | Total =57%                        | Any HR-HPV<br>Shaft=24%<br>Glans=9%<br><br>HPV-16:<br>Shaft=5%<br>Glans=2%<br><br>HPV-18:<br>Shaft=3%<br>Glans=2% | Any LR-HPV<br>Shaft=38%<br>Glans=32%<br><br>HPV-6:<br>Shaft=8%<br>Glans=2%<br><br>HPV-11:<br>Shaft=2%<br>Glans=0% |
| Strong (138)     | 2019                | China, Taiwan | N=171 at 6mth follow-up | 2015-2016.<br>Sexually experienced MSM, 20 years of age and older. Recruitment through LGBTQ community health centres.   | Clinical cohort study. Three-year baseline to follow-up.<br>Anal and penile samples taken at baseline, 6mth, 12mth, 24mth, 36mth.  | At 6mth follow-up:<br>Total=16.5% | At 6mth follow-up:<br>Any HR-HPV=10.4%  | At 6mth follow-up:<br>Any LR-HPV type=7.7%  |
| Kahn (139)       | 2019                | USA           | N=145                   | 2012 to 2015 among MSM PLHIV aged 18-26 years  | Phase II vaccine trial. Cohort.<br>Penile/scrotal, perianal, anal, and oral samples were tested for 61 HPV types.  | Total=40%                         | Any HR-HPV=8%<br><br>HPV-16=2%<br>HPV-18=0%   | Any LR-HPV=NR<br><br>HPV-6=6%<br>HPV-11=5%  |

| Author          | Year of Publication | Country | Sample size | Population  | Study design  | Any HPV prevalence                                       | HR-HPV prevalence   | LR-HPV prevalence   |
|-----------------|---------------------|---------|-------------|---|---|--|---|---|
| Ucciferri (140) | 2018                | Italy   | N=90        | Attendees of Infectious Diseases Clinics in Central, Italy.<br>n=45 GBM PLHIV   | Clinical cross-sectional study.<br>Inclusion criteria were: self-reported sexual intercourse with a man; no HPV vaccination; absence of ongoing HPV infection clinical signs.<br><br>Swabs from urethral mucosa, and coronal sulcus | Total=27.8%<br>HIV-negative GBM=28.9%<br>GBM PLHIV=28.9% | NR  | NR  |
| Qian (141)      | 2017                | China   | N=465       | Self-reporting anal sex with men in the past three months, age ≥18 years, living in Beijing City at the time of the survey.<br>n= 459 HIV-negative GBM<br>n=212 GBM PLHIV | Cross-sectional community venue, snowballing and online recruitment in Beijing.<br><br>Genital swab from the coronal sulcus of the glans penis using a saline moistened swab.   | HIV-negative GBM=36.7%<br>GBM PLHIV=39.8%                | HPV-16<br>HIV-negative GBM=4.5%<br>GBM PLHIV=4.6<br><br>HPV-18<br>HIV-negative GBM=4.2%<br>GBM PLHIV=5.1% | HPV-6<br>HIV-negative GBM=6.6%<br>GBM PLHIV=10.2<br><br>HPV-11<br>HIV-negative GBM=3.1<br>GBM PLHIV=3.4 |
| Xin (142)       | 2017                | China   | N=198       | July 2015 and October 2016. Men attending an STD clinic in Beijing Ditan Hospital.<br>n=88 GBM, of which n=72 (82%) GBM PLHIV   | Cross-sectional clinical study.<br>Genital sample by rotating saline water moistened nylon flocked swab around the penile shaft, glans, coronal sulcus and scrotum for about 2 minutes.   | MSW=50.9%<br>GBM=36.4%                                   | HPV-16<br>MSW=5.5%<br>GBM=3.4%<br><br>HPV-18<br>MSW=3.6%<br>GBM=5.7%                                      | HPV-6<br>MSW=19.1%<br>GBM=6.8%<br><br>HPV-11<br>MSW=20.0%<br>GBM=17.1%                                  |

| Author             | Year of Publication | Country | Sample size | Population   | Study design  | Any HPV prevalence        | HR-HPV prevalence   | LR-HPV prevalence   |
|--------------------|---------------------|---------|-------------|--|---|---------------------------|---|---|
| Tsikas (143)       | 2018                | Greece  | N=294       | 2015 in Athens, Greece. Recruitment from hospital outpatient STI and HIV clinics. Males, 18-55 years. n=89 (30%) GBM | Clinical single-centre cross-sectional study. Samples rubbing a saline-wetted swab over the entire surface of the penis starting with the shaft of the penis and then the glans of the penis/coronal sulcus | GBM=14.6%<br>MSW=26.3%    | NR  | NR  |
| Raghavendran (144) | 2017                | India   | N=274       | GBM PLHIV. Recruited through clinical services and NGO outreach recruitment in two cities in India.                  | Cross-sectional study. Two centres: clinical and NGO. Emery paper was gently rubbed across the penile skin and scrotal area followed by swabbing with a moist swab.   | Penile=55%<br>Scrotal=54% | Any HR HPV<br>Penile=15%<br>Scrotal=13%<br><br>HPV-16<br>Penile=4%<br>Scrotal=2.3%<br><br>HPV-18<br>Penile=2.2%<br>Scrotal=2.7% | Any LR-HPV<br>Penile=15%<br>Scrotal=13%<br><br>HPV-6/-11<br>Penile=3.3%<br>Scrotal=4.6% |



| Author     | Year of Publication | Country   | Sample size | Population   | Study design  | Any HPV prevalence                                    | HR-HPV prevalence  | LR-HPV prevalence  |
|------------|---------------------|-----------|-------------|--|---|---|--|--|
| Blas (145) | 2015                | Peru      | N=200       | March and September 2011.<br>GBM. Being a male 18 years of age or older, self-reported anal sex with another man within 12 months prior to enrollment, live in Lima, Peru.<br>n=101 HIV-negative GBM<br>n=99 GBM PLHIV | Cross-sectional study among MSM in Lima, Peru. Participants were recruited through respondent-driven sampling (RDS) starting from Clinica Cayetano Heredia.<br>External genital lesion inspection and swab collection of lesions, collection of swab specimens separately from the glans, coronal sulcus, penis shaft and scrotum.  | Any HPV:<br>HIV-negative GBM=22.4%<br>GBM PLHIV=44.3% | Any HR-HPV<br>HIV-negative GBM=27.9%<br>GBM PLHIV=38.5%<br><br>HPV-16<br>HIV-negative GBM=6.5%<br>GBM PLHIV=11.9%<br><br>HPV-18<br>HIV-negative GBM=1.9%<br>GBM PLHIV=3.7% | HPV-6<br>HIV-negative GBM=9.9%<br>GBM PLHIV=14.5%<br><br>HPV-11<br>HIV-negative GBM=1.8%<br>GBM PLHIV=7.3% |
| Zou (87)   | 2014                | Australia | N=200       | October 2010 and September 2012.<br>GBM aged 16-20 years.  | Cohort study, one-year follow-up.<br>Recruitment through online platforms, community venues and SHS clinics in Melbourne.<br>Self-collected penile swab. A paper emery board to gently exfoliate the entire penile shaft and glans penis and uncircumcised, the inner and outer aspects of the foreskin if uncircumcised. Then rolled a saline-moistened swab firmly over these areas | At baseline:<br><br>Any HPV=9.5%                      | At baseline:<br><br>Any HR-HPV=7.5%<br><br>HPV-16=1.5%<br><br>HPV-18=1.0%  | At baseline:<br><br>Any LR-HPV=6.5%<br><br>HPV-6=1.5%<br><br>HPV-11=2.0%                                   |

| Author        | Year of Publication | Country     | Sample size | Population   | Study design   | Any HPV prevalence   | HR-HPV prevalence  | LR-HPV prevalence   |
|---------------|---------------------|-------------|-------------|--|--|--|--|---|
| Van Aar (146) | 2013                | Netherlands | N=778       | July 2010 and July 2011.<br>HIV-negative GBM (n=461) and GBM living with HIV (n=317).<br>GBM recruited from 3 populations at two sites in Amsterdam. | Prospective cohort study.<br>HIV-negative participants primarily recruited at the Amsterdam Cohort Study.<br>PLHIV were recruited from 2 clinics: the city sexually transmitted infection clinic and an HIV outpatient clinic<br><br>Self-collected penile swab. Participants were asked to rub the swab firmly over the skin of the penile shaft, including the outside of the foreskin, if present, for 20 seconds | At baseline:<br><br>Any HPV:<br>HIV-negative GBM=29.6%<br>GBM PLHIV=49.5 | At baseline:<br><br>Any HR-HPV:<br>HIV-negative GBM=16.3%<br>GBM PLHIV=32.2%<br><br>HPV-16:<br>HIV-negative GBM=4.1%<br>GBM PLHIV=7.9%<br><br>HPV-18:<br>HIV-negative GBM=1.7%<br>GBM PLHIV=4.7% | At baseline:<br><br>Any LR-HPV:<br>HIV-negative GBM=19.6%<br>GBM PLHIV=36.6%<br><br>HPV-6:<br>HIV-negative GBM=3.9%<br>GBM PLHIV=9.1%<br><br>HPV-11:<br>HIV-negative GBM=3.0%<br>GBM PLHIV=7.3% |

| Author        | Year of Publication | Country | Sample size | Population   | Study design  | Any HPV prevalence    | HR-HPV prevalence   | LR-HPV prevalence  |
|---------------|---------------------|---------|-------------|--|---|-----------------------|---|--|
| Darwich (147) | 2013                | Spain   | N=733       | PLHIV attending outpatient clinic.<br>n=538 GBM PLHIV<br>n=195 MSW PLHIV   | Single-center, prospective cohort attending the Outpatient-HIV-Clinic of Hospital Germans Trias i Pujol (Badalona, Spain).<br><br>Clinician collected urethral and penile swabs:<br>first 2 cm of the urethral epithelium, a saline prewetted swab was used to obtain cells from the four quadrants of the penile shaft, glans (rubbed with emery paper), and coronal sulcus. | NR                    | At baseline:<br><br>Any HR-HPV:<br>NR<br><br>HPV-16:<br>GBM<br>PLHIV=4.8%<br>MSW<br>PLHIV=6.8%<br><br>HPV-18:<br>GBM<br>PLHIV=0.9%<br>MSW<br>PLHIV=1.6% | At baseline:<br><br>Any LR-HPV:<br>NR<br><br>HPV-6:<br>GBM<br>PLHIV=8.1%<br>MSW<br>PLHIV=8.9%<br><br>HPV-11:<br>GBM<br>PLHIV=2.4%<br>MSW<br>PLHIV=1.6% |
| Ghosh (148)   | 2012                | India   | N=129       | Patients attending clinics of National AIDS Prevention and Control Organization.<br>n=26 GBM<br>n=45 female commercial sex workers<br>n=58 people who inject drugs | Cross-sectional clinical study of patients attending the STI or de-addiction clinics. In West Bengal.<br><br>Genital scrape samples collected from glans penis and coronal sulcus in males and cervical squamocolumnar junction in females  | Any HPV:<br>GBM=69.2% | Any HR-HPV:<br>NR<br><br>HPV-16:<br>GBM=0%<br><br>HPV-18:<br>GBM=0%   | NR   |

| Author              | Year of Publication | Country  | Sample size | Population  | Study design  | Any HPV prevalence   | HR-HPV prevalence  | LR-HPV prevalence   |
|---------------------|---------------------|--|-------------|---|---|--|--|---|
| Nyitray (149)       | 2011                | Mexico, Brazil and USA   | N=4074      | <p>June 2005 to December 2009.</p> <p>Males from São Paulo, Cuernavaca, and Tampa.</p> <p>Eligibility criteria included aged 18–70 years, no history of anal cancer or genital warts, and no current STI symptoms or diagnosis including self-reported HIV.</p> <p>n=170 MSM,<br/>n=214 MSWM<br/>n=3326 MSW</p> | <p>Cross-sectional study of a prospective cohort.</p> <p>Recruited through community and venue-based sampling as well as clinical and military samples.</p> <p>A clinician used a saline-wetted swab to sweep 360° around the coronal sulcus and glans penis, and if present, a retracted prepuce. A second swab was used to sample the entire surface of the penile shaft while a third was used to sample the scrotum</p> | <p>Any HPV:<br/>MSM=50.1%<br/>MSWM=60.3%<br/>MSW=53.1%</p>         | <p>Any HR-HPV:<br/>MSM=29.7%<br/>MSWM=39.6%<br/>MSW=30.0%</p> <p>HPV-16:<br/>MSM=8.5%<br/>MSWM=10.6%<br/>MSW=7.7%</p> <p>HPV-18:<br/>MSM=3.7%<br/>MSWM=3.0%<br/>MSW=2.2%</p> | <p>Any LR-HPV:<br/>MSM=36.0%<br/>MSWM=50.8%<br/>MSW=42.1%</p> <p>HPV-6:<br/>MSM=9.1%<br/>MSWM=11.8%<br/>MSW=6.0%</p> <p>HPV-11:<br/>MSM=4.4%<br/>MSWM=3.3%<br/>MSW=1.2%</p> |
| Goldstone (150)     | 2011                | Multinational study: enrolled from 17 sites in Australia, Brazil, Canada, Croatia, Germany, Mexico, Spain, and the United States | N=602       | <p>November 2004 to May 2007.</p> <p>HIV-negative GBM.</p> <p>Aged 16–27 years with five or less lifetime male or female sexual partners.</p> <p>No concurrent STI nor living with HIV.</p>   | <p>Randomised control trial vaccine efficacy trial.</p> <p>Baseline swab specimens were collected separately from the penile and scrotal areas. A metal nail file was used to rub the penile skin gently and swabbed to collect material.</p>   | Any HPV=NR   | <p>Any HR-HPV=NR</p> <p>HPV-16:<br/>Penile=3.5%<br/>Scrotal=3.1%</p> <p>HPV-18:<br/>Penile=3.1%<br/>Scrotal=2.1%</p>   | <p>Any LR-HPV=NR</p> <p>HPV-6:<br/>Penile=4.4%<br/>Scrotal=3.8%</p> <p>HPV-11:<br/>Penile=2.0%<br/>Scrotal=1.5%</p>   |
| Van der Snoek (151) | 2003                | Netherlands  | N=258       | <p>February 1999 to February 2000.</p> <p>n=241 HIV-negative GBM<br/>n=17 GBM PLHIV</p>   | <p>A cross-sectional clinic-based sample of men attending the sexual health clinic of the Erasmus MC, Rotterdam.</p> <p>Samples were collected using a dry swab sampling the coronal sulcus only.</p>   | <p>Any HPV:<br/>HIV-negative GBM=15.8%<br/>GBM<br/>PLHIV=23.5%</p> | NR   | NR  |

Studies that separated populations based on HIV status (n=6) found GBM PLHIV had a greater prevalence of penile infection with any HPV type (range: 23.5%—49.5%) as compared to HIV-negative GBM (range: 15.8%—36.7%), similar to estimates in those studies found for anal HPV infection prevalence. Exploration of penile HPV infection prevalence by other sociodemographic variables such as by age and ethnicity within published studies was limited.

Authors describe their study population characteristics but are often limited by sample size to detect differences between sub-groups within the study population. For example, Nyitray et al. published their findings from the HPV in Men (HIM) study, a large multi-national cohort examining HPV prevalence among men (149). The study did not specifically target GBM for recruitment, but classified men based on lifetime and recent sexual behaviours, providing a direct comparison of penile HPV infection prevalence between different sexual orientation populations. A total of 170 gay and 214 bisexual men were recruited in the study, compared to 3326 MSW. The overall prevalence of any HPV type was 50%, 60% and 53% among gay males, bisexual males, and MSW respectively. For HR-HPV types, the prevalence was 30%, 40% and 30% among gay, bisexual, and MSW, respectively. Of those HPV types responsible for the greatest disease burden (HPV-6,-11,-16,-18) the prevalence was 23%, 26% and 16% among gay males, bisexual males, and MSW, respectively. For HPV-16, that associated with greatest oncogenic potential, the prevalence found were 8.5%, 10.6%, and 7.7% among gay, bisexual and MSW respectively.

The studies identified in this review have recruited GBM who are potentially more sexually active, and therefore at greater risk of acquiring HPV. This could result in an over-estimation of penile HPV infection prevalence compared to the wider population of GBM. As covered in Chapter Two, Section Two: Part Two, the studies targeted recruitment at sites where sexual identity and behaviours are routinely disclosed (healthcare) or settings where GBM gather to find sexual partners (bars, venues, and online spaces). These settings allow a large and diverse convenience sample of GBM to be recruited but may not be generalisable to the wider GBM population.

Among a nationally representative sample of N=1868 men, who took part in the US National Health and Nutrition Examination Survey between 2013 and 2014 in the United States, the overall prevalence of genital HPV infection (with any HPV type) was 45.2% among men aged 18 to 59 years, 25% of men were infected with any HR-HPV type, and 4.3% with HPV-16 (152). The survey did not differentiate men based on sexual behaviours or sexual identity, but it is likely that due to the recruitment method employed, greater than 95% of the sample are MSW.

Findings from the US National Health and Nutrition Examination Survey and the Niytray et al. study support those found in the search specific to GBM. Similar to HPV infection prevalence at the anal site, there appears to be a high prevalence of infection with any HPV type at the penile site but infection with the HPV-16, the HR-HPV type that causes the majority of HPV-related cancers among males, is less prevalent.

### ***Oropharyngeal HPV infection among GBM***

The oropharyngeal region is susceptible to HPV infection due to the presence of reticulated epithelial cells within crypts. However, as previously explored in Chapter 2, Section One: The biology of human papillomavirus, the oral transmission routes of HPV are not well understood but likely result from direct epithelial contact of oral and genital sites and shedding of virus from these sites through oral sexual activity.

The following search terms were used in PubMed to identify papers that explored oropharyngeal HPV infection among GBM:

```
(((((((((human papillomavirus[Title/Abstract]) OR HPV[Title/Abstract]) OR papillomavirus[Title/Abstract]))) AND ((infection[Title/Abstract]) OR prevalence[Title/Abstract]))) AND (((oral[Title/Abstract]) OR oropharyngeal[Title/Abstract]) OR throat[Title/Abstract])) AND (((gay[Title/Abstract]) OR bisexual[Title/Abstract]) OR homosexual[Title/Abstract])) AND ((male[Title/Abstract]) OR men[Title/Abstract]))
```

The search returned 23 results, of which four studies specified they recruited GBM and measured oral HPV infection in their titles or abstracts. One study was excluded as it did not report the HPV infection prevalence among GBM participants in the study (153). Of the three remaining studies, two recruited GBM through sexual health clinic settings and two recruited young GBM (those within the age range eligible for HPV-vaccination in the USA, 26 years and under) (*see Table 9*).

Published estimates of oral HPV infection prevalence among GBM are considerably lower than that of anogenital infection. The prevalence of oral infection with any HPV type ranged from 8.4%—24.2% and with any HR-HPV type from 4.7%—6.0%. Infection prevalence with HPV types covered by the quadrivalent vaccine was lower still, with HR-HPV types 16 and 18 ranging from 0.5%—1.1% and LR-HPV types 6 and 11 ranging from 0.0%—2.0%.

Oral HPV infection prevalence was greater among PLHIV compared to HIV-negative GBM (154). However, these data come from one study among those identified in the review by Halkitis et al., in which they separated the GBM study population based on HIV-status, reporting the prevalence of oral HPV infection with any HPV, HR-HPV and LR-HPV to be greater among those living with HIV compared to those who were HIV-negative.

Compared to the general population, oral HPV infection with any HPV type is greater among GBM in the studies found in this search. In 2010, Kreimer et al. published a meta-analysis of pooled oral HPV infection prevalence among 4581 “healthy individuals”, which they defined as individuals without cancer, pre-cancers or immune suppression (155). Oral infection prevalence of any HPV type was estimated at 4.5%, any HR-HPV types were 3.5%, and men (n=1017) and women (n=3690) had similar prevalence of any oral HPV detected (4.6% vs. 4.4%, respectively). However, a greater infection prevalence with HPV-16 (1.3%) was found by Kreimer et al. compared to that among the GBM from the studies identified in this review (range: 0.7%—1.1%).

Table 9: Prevalence of oropharyngeal HPV infection among GBM

| Author         | Year of Publication | Country | Sample size | Population  | Study design  | Any HPV prevalence  | HR-HPV prevalence  | LR-HPV prevalence   |
|----------------|---------------------|---------|-------------|---|---|---|--|---|
| Halkitis (154) | 2019                | USA     | N=486       | 2015<br>GBM aged 22-25 years.<br>Both HIV-negative GBM (n=453) and GBM PLHIV (n=33)   | Computer-assisted cross-sectional survey as part of a prospective cohort study via venue and internet-based sampling strategies.<br>Self-collected oral mouthwash samples and anal swabs.   | Any HPV type = 8.8%<br><br>HIV-negative GBM= 7.7%<br>GBM PLHIV= 24.2% | Any HR-HPV type = 4.7%<br><br>HIV-negative GBM= 4.2%<br>GBM PLHIV= 12.1% | Any LR-HPV type= 3.1<br><br>HIV-negative GBM= 2.6%<br>GBM PLHIV= 9.1% |
| Meites (156)   | 2016                | USA     | N=922       | July 2012–August 2014<br>Age 18–26 years, assigned male sex at birth; and eligible for the HPV vaccine, based on sexual behaviour.            | GBM attending three sexual health clinics in two US cities.<br>Three types of biological specimens: anal swab, oral rinse, and blood. Self-collected anal and oral specimens.<br>Venepuncture by clinical staff.<br>Oral specimen by oral rinse and gargle.   | Any HPV type = 8.4%   | Any HR-HPV type = 4.9%<br><br>HPV-16= 1.1%<br>HPV-18=0.5%                | Any LR-HPV type= NR<br><br>HPV-6= 0.8%<br>HPV-11= 0.0%                |
| King (157)     | 2015                | UK      | N=151       | October 2010 to July 2012<br>Men aged 16–40 years, who reported anal or oral sex with another man in the last five years,<br>HIV-negative GBM | Cross-sectional study of GBM attending a sexual health clinic in London, UK.<br>Computer-assisted self-interview questionnaire and anogenital specimens (first-void urine, intra-anal swab and external genital swab (glans penis/coronal sulcus/penile shaft/scrotum/perianal area)), collected by a study nurse.<br>Oral specimen collected by oral rinse and gargle. | Any HPV type = 13.9%  | Any HR-HPV type = 6.0%<br><br>HPV-16= 0.7%<br>HPV-18=0.7%                | Any LR-HPV type= NR<br><br>HPV-6= 2.0%<br>HPV-11= 0.0%                |



## Synthesis of Part One: Prevalence of HPV infection among GBM

- A limited number of studies have been published specifically describing HPV infection prevalence among GBM.
  - The greatest number of published studies explore anal HPV infection among GBM, with two systematic literature reviews and meta-analyses published on this topic.
  - Fewer studies were identified that describe penile HPV infection prevalence among GBM, and fewer still on oral HPV infection prevalence.
- Due to GBM representing a small proportion within the total population, few studies are powered to explore differences of infection prevalence of subgroups within GBM samples, for example, by age or ethnicity.
  - While some studies limited their population to younger GBM, specifically those aged 26 years and younger, the majority had not explored variation in HPV infection prevalence by age among GBM.
  - Where reported, greater prevalence of HPV infection at any anatomical site was found among GBM PLHIV.
- With the limitations in mind, some patterns emerge from the published data.
  - Of the different HPV types:
    - infection with any HPV type is common,
    - infection with any HR-HPV type is less prevalent,
    - infection with HPV-16, the most oncogenic type, is most prevalent among HR-HPV infections.
    - infection with HPV-18 is less prevalent than HPV-16.
  - Of the different anatomical sites among GBM:
    - anal HPV infection is most prevalent,
    - penile infection is more prevalent than oral infection,
    - oral is least prevalent.

## Section Three: Part Two – Prevalence of HPV-related disease among GBM

### ***Purpose***

Diagnosis and notification of disease cases is the primary form of clinical surveillance. As previously covered in Chapter Two, Section Two: Part Two, measures of sexual orientation are not routinely captured during case notification in administrative health datasets. Measuring the impact of HPV vaccination among GBM requires monitoring case notifications among this population over time. Therefore, additional surveillance and prevalence studies are required to estimate the burden of HPV-related disease among GBM.

### ***Aims***

- a. Explore the published literature relating to the prevalence of HPV-related diseases that affect GBM: anogenital warts and HPV-related cancers at the anal, penile, and oropharyngeal sites.

### ***Anogenital warts among GBM***

Anogenital warts are considered a common STI and present as single or multiple papules on the perineum, perianal area, penis, anus, scrotum, and urethra. It is estimated that over 90% of AGWs are caused by HPV 6 and HPV 11 (158).

In a 2013 systematic review by Patel et al., they report that the median annual incidence of new AGW cases among males was 137 per 100,000 and was 120.5 per 100,000 among females (159). They also reported the prevalence of AGWs to range between 0.06% and 5.1% among males, while among women, this ranged between 0.13% and 4.0% (159). The authors note that there was a greater incidence and prevalence of AGW among those patients who underwent a genital examination compared to those studies that reviewed clinical databases or records alone, indicating a pool of undiagnosed AGWs in the general population (159). The authors also noted the majority of studies that recruited representative population samples were from more economically developed western countries (USA, Canada, Northern Europe, and Australia), limiting the generalisability of these estimates to less economically developed countries.

The incidence of AGWs appears to peak soon after sexual debut among the general population of men and women and declines with age (160). Though this trend is similar for GBM, the decline is not as marked with age and potentially demonstrates ongoing new sexual partner exchange/acquisition throughout life, placing GBM at greater risk of repeated HPV infection and related disease (161).

Search terms:

(((((prevalence[Title/Abstract]) OR incidence[Title/Abstract])) AND  
(((((((genital[Title/Abstract]) OR anogenital[Title/Abstract]) OR penile[Title/Abstract]) OR  
anal[Title/Abstract]) OR oral[Title/Abstract]) OR oropharyngeal[Title/Abstract])) AND  
((wart[Title/Abstract]) OR condylomata[Title/Abstract])) AND ((((((gay) OR bisexual) OR  
homosexual)) AND ((male) OR men))) OR (((men who have sex with men) OR MSM) OR  
GBM))

The search was limited to publications that mentioned any of the search terms in their title or abstract between January 2001 and January 2020. The search returned 19 articles, of which five reported data on the prevalence or incidence of anogenital warts among GBM (see *Table 10*). Eleven studies did not contain data on the incidence or prevalence of AGWs, and three studies did not stratify the prevalence or incidence of AGWs among GBM in their sample.

Prevalence of AGWs among GBM ranges considerably across the studies from 2.3%—39.9%. The prevalence of anal warts (range: 4.0%—28%) is greater than that of warts in the penile area (range: 1.6%—10.6%). Of those studies that reported AGW prevalence and HIV status, there was little difference in the prevalence of anal warts (HIV-negative: 24.9%, PLHIV: 27.9%), with no studies identified that reported AGWs of the penile area separately based on HIV-status.

Two studies were identified that reported AGW diagnoses among first-time attendees to sexual health clinics, one in the USA and one from Australia, that enable comparison between GBM to MSW populations. The study by Llata et al. found no difference in AGW prevalence between GBM (7.5%) and MSW (7.5%) populations (162). By comparison, Chow et al. reported a greater prevalence of AGWs among MSW patients (13.7%) compared to GBM patients (5.6%). Reported penile wart prevalence is considerably higher among MSW (13.7%) compared to that among GBM (1.6%). The difference in AGW prevalence by anatomical area could indicate that though there might be no overall difference in AGW prevalence between GBM and MSW, such as found by Llata et al., there could be in site affected as found by Chow et al. However, the two prevalence estimates in the study by Chow et al. come from two different time periods (MSW prior to 2002—2008 and GBM 2008—2013). Anal wart prevalence was not reported for MSW.

Table 10: Prevalence and incidence of anogenital warts among GBM

| Author      | Year of Publication | Country | Sample size | Population  | Study design   | Prevalence of anogenital warts (any location) | Penile or testicular                             | Anal or peri-anal               |
|-------------|---------------------|---------|-------------|---|--|---|--|---------------------------------|
| Galea (163) | 2017                | Peru    | N=341       | <p>Inclusion criteria of:</p> <ul style="list-style-type: none"> <li>• born anatomically male;</li> <li>• age ≥18 years;</li> <li>• had any anal intercourse with a man during the previous 12 months;</li> <li>• residing in metropolitan Lima;</li> <li>• HIV-negative;</li> <li>• willing to commit to twice-yearly clinic visits for 24 months;</li> <li>• had not participated in an HIV or HPV vaccine study</li> </ul> | <p>Cross-sectional analysis of baseline data collected as part of a prospective cohort.</p> <p>Recruited between February 2012 and February 2013.</p> <p>Mixture of sampling methods used include venue-based sampling; online through social media; and by snowball sampling.</p> | HIV-negative GBM: 39.9%                       | HIV-negative GBM:<br>Penile=10.6%<br>Testes=1.5% | HIV-negative GBM:<br>Anal=24.9% |

| Author     | Year of Publication | Country | Sample size                           | Population  | Study design  | Prevalence of anogenital warts (any location)   | Penile or testicular | Anal or peri-anal |
|------------|---------------------|---------|---------------------------------------|---|---|---|----------------------|-------------------|
| Neme (164) | 2015                | Kenya   | N=1137<br><br>n=852<br>GBM<br>(74.9%) | <p>HIV-negative men reporting high-risk sexual behaviour, defined as:</p> <ul style="list-style-type: none"> <li>• having sex with men,</li> <li>• sex in exchange for money,</li> <li>• recent sexually transmitted infections,</li> <li>• serodiscordant sex partners,</li> <li>• or multiple sex partners.</li> </ul> <p>Classification based on reported gender of sexual partners in the previous three months.</p> <ul style="list-style-type: none"> <li>• Both men and women</li> <li>• Men only</li> <li>• Women only</li> </ul> | <p>Baseline data from a prospective observational study of populations at "high-risk" of HIV acquisition. Invited to attend the SHC and participate in the study.</p> <p>Participants were recruited through community outreach, local voluntary counselling and testing sites, and links with local LGBTIQ+ groups.</p> <p>Visual inspection of the external genitalia and the perianal area if the participant reported receptive anal sex or anorectal symptoms.</p> | <p><u>Prevalence:</u><br/>HIV-negative MSM:<br/>n=4/176 (2.3%)<br/>HIV-negative MSW:<br/>n=6/285 (2.1%)<br/>HIV-negative MSMW<br/>n=23/676 (3.4%)</p> <p><u>Incidence:</u><br/>MSM: 8.2/100 PY<br/>MSW: 2.5/100 PY<br/>MSMW: 5.8/100 PY</p> | NR                   | NR                |

| Author        | Year of Publication | Country   | Sample size   | Population  | Study design  | Prevalence of anogenital warts (any location)                   | Penile or testicular  | Anal or peri-anal   |
|---------------|---------------------|-----------|---|---|---|---|---|---|
| Chow (165)    | 2015                | Australia | N=32,256<br><br>N=8978 (27.8%)<br>GBM                               | All new patients attending the Melbourne SHC for the first time were included in the study.<br><br>Men reporting any sexual contact with another man in the past 12 months or the 12 months before any previous visit to MSHC were defined as GBM | Retrospective cohort analysis investigating all new patients attending the SHC between February 2002 and December 2013.<br><br>GBM attending the SHC prior to 2008 were excluded in this analysis.<br><br>MSW patients attending the SHC after 1 January 2008 were excluded from the analysis due to herd immunity effects of the female HPV vaccination programme. | GBM:<br>N=503/8978 (5.6%)<br><br>MSW: NR                        | GBM:<br>N=141/8978 (1.6%)<br><br>MSW:<br>N=1656/12112 (13.7%) | GBM:<br>N=362/8978 (4.0%)<br><br>MSW: NR                              |
| Llata (162)   | 2014                | USA       | N=241630<br><br>GBM:<br>n=29534 (12.2%)<br>MSW:<br>n=113206 (46.9%) | All patients attending STD clinics in the STD Surveillance Network. January 2010 to December 2011.<br><br>Men who reported sex with a man ever or who self-identified as gay, homosexual, or bisexual were defined as GBM.                        | Cross-sectional analysis of patients attending clinics that are part of the STD Surveillance Network, comprising 12 collaborating state and local health departments that implement similar protocols for collecting and analysing enhanced surveillance data.  | GBM:<br>N=2215/29534 (7.5%)<br><br>MSW:<br>N=8451/113206 (7.5%) | NR  | NR  |
| Darwich (166) | 2012                | Spain     | N=640<br><br>GBM:<br>n=473<br>MSW:<br>n=167                         | Inclusion criteria: <ul style="list-style-type: none"> <li>• Living with HIV</li> <li>• Male</li> <li>• &gt;18 years old,</li> <li>• No history of (or current) anal cancer.</li> </ul>   | Cross-sectional study based on the baseline visits of male PLHIV patients enrolled in a clinical cohort.<br><br>A clinical visual inspection and a digital rectal examination were performed at the baseline visit of patients.   | NR  | NR  | GBM PLHIV:<br>N=132/473 (27.9%)<br><br>MSW PLHIV:<br>N=25/167 (15.0%) |

The search criteria specified, and the reviewing process of articles, may result in the exclusion of publications that report the prevalence or incidence of AGWs among GBM as a sub-population or in the exclusion of studies where multiple STIs were reported.

Daugherty et al. described AGW prevalence among male participants of the 2013-2014 survey round of the US National Health and Nutrition Examination Survey (N=1757), a nationally representative survey, of which questions relating to same-sex sexual behaviour and self-reported history of AGW diagnosis were included (167). A total of 1681 men answered both questions, of which 5.7% (n=96) reported ever having a same-sex sexual partner. Among these men, 3.1% (n=3) reported a history of AGWs providing a weighted prevalence of 2.5%. This estimate is lower than the 7.5% prevalence estimate provided by Llata et al. from sentinel surveillance SHC network in the USA, reinforcing that recruitment from SHCs results in a biased sample of participants at greater risk of STI acquisition (162).

A limitation of the study by Daugherty et al. is that AGWs, particularly those of the anal and perianal region may go unnoticed by GBM. However, in the HIM study published by Nyitray et al., AGWs were diagnosed by study clinicians in 6.3% of MSW (n=82/1305) and 4.0% of GBM (n=7/176) (168). Of these, perianal warts and warts at the anal verge were diagnosed in <1% of both MSW and GBM. These findings may contradict the assumption that a large proportion of AGWs in the anal region go unnoticed among GBM and MSW.

#### *AGWs and HPV vaccine impact*

Surveillance of AGW diagnoses has been used to estimate the impact of HPV vaccination where vaccines that cover the LR-HPV types 6 and 11 have been utilised in vaccination programmes. This is because development of HPV-related cancers does not occur until later in life and therefore the benefits of HPV vaccination (given in early adolescence) will not be seen for many decades. Conversely, the HPV vaccine prevents AGWs, which can develop quickly after infection. As a result, the benefits of vaccination will be seen quickly after sexual debut.

Estimating standardised rates of AGWs among populations is another method that allows comparison between sub-groups, but many countries lack an accurate denominator for their GBM population and therefore cannot calculate rates for this group. Canvin et al. estimate the impact of the female-only HPV vaccination programme on young persons (<24yrs) attending SHC in England between 2009—2014 (169). They present age-standardised rates for AGWs among MSW using census data and for GBM (men who report GBM identity or behaviour at clinic visit) using estimates of sexual identity from NATSAL-3 (2.9% of the male population). They report that the incidence of genital warts diagnoses increased between 2009 and 2014 among GBM aged 15–19 years combined (439.4—458.2 per 100 000) and a

larger increase among GBM aged 20–24 years (1410.0—1894.4 per 100 000). By comparison, a decrease was observed in MSW aged 15–19 years between 2009 and 2014 (269.0—200.6 per 100 000) and among MSW aged 20–24 years (832.8—731.6 per 100 000). These data suggest that the female-only HPV vaccine programme provided herd immunity level effects for MSW but not for GBM. Rates of AGWs among GBM in this study are not only increasing but are double that of their MSW peers. The findings contrast to those studies identified above, in which prevalence estimates are lower or similar among GBM compared to MSW.

Australia was the first country to implement HPV vaccination among females in 2007 and then extend to include males in 2013. Before the extension of the vaccine to males, two studies were published that explored trends in AGW diagnoses among Australian SHC attendees that also identified GBM in the study populations.

In 2013, Ali et al. reported a decrease in AGW diagnoses among Australian born patients under the age of 30yrs who attended any of the eight SHCs in the surveillance network for the first time between January 2004 and December 2011 (4). In this study, the GBM population were not stratified by age, but the proportion diagnosed with AGW declined by 24.7% between 2007 and 2011 (8.5%—6.4%,  $p=0.04$ ). This was in contrast to the 30.5% ( $p=0.03$ ) increase in Chlamydia diagnoses among this group over the same period. The authors hypothesise that the reason for the finding was that more asymptomatic GBM were triaged into the SHCs during the study period, resulting in the relative proportion of GBM attendees increasing substantially during that time.

In 2014, Chow et al. published a retrospective analysis of prevalence estimates of AGWs among Australian-born new attendees of the Melbourne SHC in Australia between 1 July 2004 to 30 June 2014, to explore the impact of the female-only vaccination programme on AGW diagnoses among vaccine eligible and ineligible populations (170). They also reported an overall decline in genital warts among GBM, from 7.8% in 2004 to 5.2% in 2014 ( $p$ -value:  $<0.001$ ), which remained after separating GBM by age. The authors note that among their GBM patients, the decline was not seen in anal wart diagnoses ( $p$ -trend=0.24) but only in penile wart diagnoses ( $p$ -trend=0.04) between 2007—2014. They hypothesise that the anal epithelium may be more susceptible to AGW infection or development than the penile epithelium.

Both Ali et al. and Chow et al. describe an overall increase in the number of GBM attending SHCs in Australia between 2007 to 2014 as an explanation for the decline of AGWs seen among GBM in their samples, with greater asymptomatic screening occurring and resulting in a lower positivity rate for STIs that are symptomatic, such as AGWs. This hypothesis is



supported by the significant increase in Chlamydia diagnoses among GBM reported by Ali et al. over the same period ( $p$ -trend=0.03), being an asymptomatic STI in the majority of cases.

### ***HPV-related cancers among GBM***

Globally, the most common HPV-related cancer is cervical cancer, with 100% of cervical cancers believed to be attributable to HPV infection. Cervical cancer is the second most common cancer among women in less economically developed countries and the seventh most common among more economically developed countries (171). Women are also affected by HPV-related cancers of the vulva, vagina, oropharynx and anus.

Among countries that have successfully implemented cervical screening programmes, cervical cancer rates have declined over time, yet remain greater than other HPV-related cancers (172). In contrast, data from cancer registries in the USA, UK, Australia, and Europe indicate that rates of oral and anal HPV-related cancers have been rising steadily over time, particularly among males (39, 171, 173-177). It has been hypothesised that the reason for this increase is a change in sexual behaviour, with greater practice of oral and anal sex in these countries over time. Oropharyngeal cancers caused by HPV are more difficult to define from clinical records due to tobacco and alcohol use also being causal factors. This is similar to penile cancers, with an estimated 50% being caused by factors other than HPV infection (178).

Among all HPV-related cancers diagnosed in 2005 in Australia, roughly a third were among males, with the majority of these being oral cancers (171). However, Grulich et al. also noted that it was the rates of HPV-related anal cancers among males in Australia that have seen the largest positive average annual percentage change (2.58% per year) between 1982 and 2005 compared to other HPV-related cancers among both men and women, which also increased but at a lower rate (171). In general, few countries collect sexual behavioural data that can be linked to cancer diagnoses. However, higher rates of HPV-related anal cancers have been observed among GBM PLHIV cohorts compared to rates seen in the general male population (179). Rates of HPV-related anal cancers among this group are estimated to be similar to those among women prior to the introduction of cervical screening programmes and continue to increase (2).

### ***HPV-related anal lesions and cancer among GBM***

Much of the data on the rates of anal cancer and precancerous anal lesions among GBM has been collated and reviewed in the 2012 systematic literature review and meta-analysis by Machalek et al. However, additional studies since this publication have been sought and included where more recent data has been published with methods considered of quality similar to those included in the review article.

### *Anal cytological abnormalities among GBM*

The 2012 meta-analysis by Machalek et al. included 19 studies that reported the prevalence of anal cytological abnormalities among GBM (73). Of these 19 studies, 17 included data on GBM PLHIV and six on HIV-negative GBM. Among the GBM PLHIV included in the analysis, 84% were recruited through clinical settings, while among the HIV-negative GBM, 87% were recruited through community settings. Of the total HIV-negative GBM sample, 70% were from a single community-based North American study (73).

The prevalence of anal LSIL was significantly greater ( $p=0.010$ ) among GBM PLHIV (27.5%) compared to HIV-negative GBM (6.6%) (see *Table 11*). The prevalence of HSIL was also greater among GBM PLHIV (6.7%) compared to HIV-negative GBM (2.7%) all though this difference was not significantly different ( $p=0.11$ ).

### *Anal histological abnormalities among GBM*

High-resolution anoscopy was used to histologically identify anal abnormalities in eight studies included in the 2012 meta-analysis by Machalek et al. Similar to other analyses in this paper, the majority of GBM PLHIV were recruited through clinical settings (88%), and the majority of HIV-negative GBM were recruited through community-based settings (94%).

Among GBM PLHIV, the prevalence of low-grade squamous intraepithelial lesion (LSIL) (AIN1, AIN2) was 28.6%, and the prevalence of high-grade squamous intraepithelial lesion (HSIL) (AIN3) was 23.9% (see *Table 11*) (73). For HIV-negative GBM in the analysis, the prevalence of low-grade AIN was 8.4%, and high-grade AIN was 15.2%. The meta-analysis found significant differences between HIV-positive and HIV-negative GBM in the prevalence of either low-grade AIN ( $p=0.029$ ) or high-grade AIN ( $p=0.48$ ).

Table 11: Pooled prevalence of cytological and histological anal canal abnormalities among GBM, by HIV status

| Type of anal canal abnormality           | Pooled Prevalence (% [95% CI]) |                  |
|--|--------------------------------|------------------|
|  | HIV-negative GBM               | GBM PLHIV        |
| <b><i>Cytological abnormalities</i></b>  |                                |                  |
| ASIL                                     | 18.5 (8.0–28.9)                | 57.2 (51.2–63.2) |
| LSIL                                     | 6.6 (1.1–12.1)                 | 27.5 (21.9–33.2) |
| HSIL                                     | 2.7 (0.0–5.1)                  | 6.7 (4.4–9.0)    |
| <b><i>Histological abnormalities</i></b> |                                |                  |
| ASIL                                     | 29.2 (12.3–46.2)               | 55.1 (39.7–70.5) |
| LSIL                                     | 8.4 (5.8–11.0)                 | 28.6 (18.4–38.8) |
| HSIL                                     | 15.2 (0.0–30.9)                | 23.9 (12.8–35.0) |

ASIL = any squamous intraepithelial lesions.

LSIL = low-grade squamous intraepithelial lesions.

HSIL = high-grade squamous intraepithelial lesions.

Adapted from the systematic literature review and meta-analysis by Machalek et al. (73): Only pooled prevalence estimates have been presented.

#### *Anal cancer among GBM*

Of the nine studies included in the meta-analysis by Machalek et al., six collected data from either HIV/AIDS or cancer registries and three were observational cohort studies (73). Only two of these studies reported data on HIV-negative GBM but all nine reported data for GBM PLHIV.

Figure 12 presents the pooled incidence estimates from the meta-analysis. For HIV-negative GBM, the incidence of anal cancer was 5.1 per 100 000 person-years. The overall incidence of anal cancer for GBM PLHIV is 45.9 per 100 000 person-years. The estimate for GBM PLHIV is further broken down into pre- and post-highly active antiretroviral therapy (HAART) era estimates due to the increase in life expectancy gained through the provision of HAART post-1996. The pre-HAART estimate of anal cancer incidence for GBM PLHIV is reported as 21.8 per 100 000 person-years, while post-HAART the estimate is 77.8 per 100 000 person-years. This indicates that while the provision of HAART has dramatically increased the life expectancy of those who acquire HIV, it has not reduced the development of anal cancer among this population compared to HIV-negative GBM.

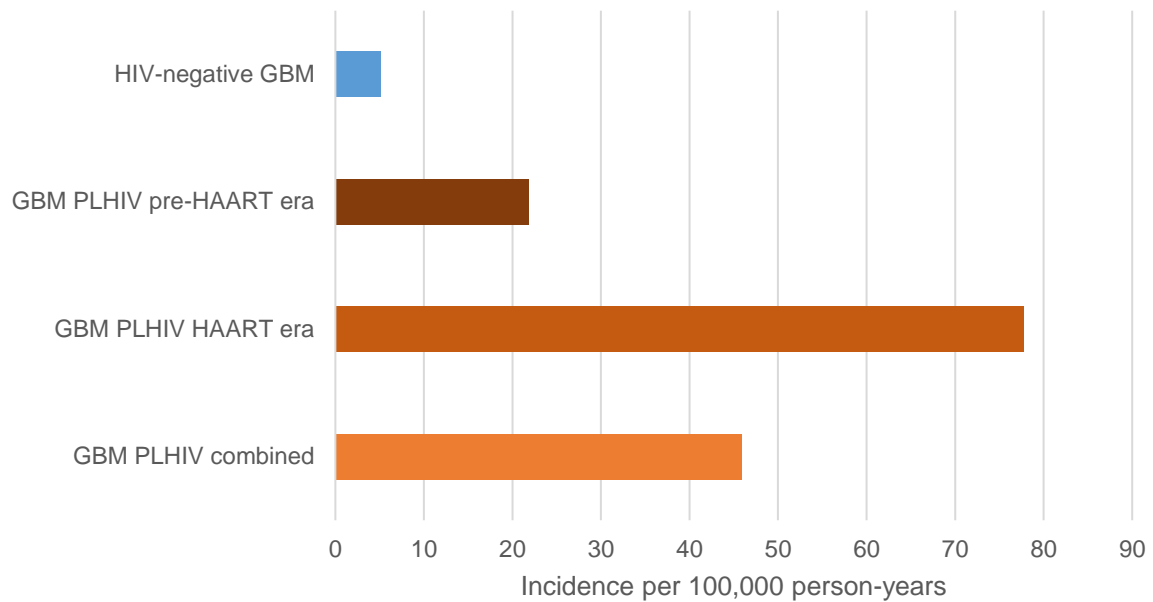


Figure 12: Pooled incidence of anal cancer among GBM, by HIV status. HAART = highly active antiretroviral therapy. HAART era is considered 1996 and onwards. Adapted from Machalek et al. 2012 (73)

#### *HPV-related penile cancer among GBM*

Systematic reviews by Backes et al. and Miralles-Guri et al. estimate an overall HPV prevalence of 50% among all penile cancer cases examined (178, 180). The complex anatomy of the penis and the range of cancers that are present creates uncertainty surrounding the staging of cancers that affect this area, making classification tools such as the Bethesda system difficult to apply (181). Histologically, HPV is most commonly found in keratinising and basaloid squamous cell carcinomas of the penis (182).

The incidence of penile cancer is greater in less economically developed countries, with estimates exceeding 4 per 100,000 person-years, less common in more economically developed countries ranging from 0.1 to 1.5 per 100,000 person-years, and extremely rare in countries where infant circumcision is common practice (178, 183). In Australia, the incidence of penile cancer remained steady between 1985 and 2005, with the incidence in 2005 reported as 0.7 per 100,000 person-years (171).

Pubmed search terms:

((((prevalence) OR incidence)) AND ((((((penile) OR penis)) AND (((cancer) OR carcinoma) OR lesion) OR neoplasia))) OR PIN)) AND (((((men who have sex with men) OR MSM) OR GBM)) OR (((gay) OR bisexual) OR homosexual)) AND ((men) OR male)))

Limiting the search terms to only the title and abstract returned zero results. The search was repeated to expand the search to cover all search fields. A total of 97 items were returned

from the expanded search, of which one study reported data specifically on HPV-related penile cancer prevalence among GBM (see *Table 12*).

Table 12: Prevalence and incidence of HPV-related penile lesions and cancers among GBM

| Author   | Year of Publication | Country | Sample size   | Population   | Study design  | Any penile lesions     | PIN  | Penile Cancer                              |
|--|---------------------|---------|---|--|---|------------------------|--|--|
| Kreuter (184)  | 2008                | Germany | GBM PLHIV N=263   | October 2003 and December 2006.<br><br>White, GBM PLHIV were screened every six months for HPV-related diseases in the context of a sub-study of the German "Kompetenz-Netzwerk HIV/AIDS". | Standardized HPV-screening program at the Department of Dermatology of the Ruhr University Bochum.<br><br>Penile lesions were categorised as follows: condylomata acuminata; lesions suspicious of PIN; subclinical lesions; and unspecific lesions.  | GBM PLHIV N=10 (3.8%)  | GBM PLHIV N=10 (3.8%)                          | GBM PLHIV N=0                              |
| <b>The following studies do not present results specifically for GBM participants, but can provide indicative data</b> |                     |         |   |  |   |                        |  |  |
| Fuchs (185)  | 2016                | Germany | N=400 PLHIV<br><br>N=392 GBM PLHIV<br>N=8 non-GBM PLHIV | PLHIV attending the outpatient clinic at Bochum Hospital, Germany.   | Prospective observational study. Participants followed up every 3-12mths depending on test results.<br><br>For detection of penile HPV-related disease: the glans, penis, foreskin, corona, sulcus, frenulum, scrotum, inguinal and perianal skin were inspected, and penile swabs collected. Cytology used the Bethesda classification system. | PLHIV (all) =14 (3.5%) | PLHIV (all) PIN 1=6 (1.5%)<br>PIN 2/3=7 (1.8%) | PLHIV (all)=1 (0.3%)                       |
| Saunders (186)   | 2017                | UK      | N=249010<br><br>Males n=117937<br><br>GBM n=1279 (1.1%) | Cancer survivors who received treatment for cancer.<br><br>Data analysed from 2010—2014.   | Hospital-based Cancer Patient Experience Survey (CPES) sent annually to all patients aged 16+ years who were treated for cancer in an NHS hospital during a three-month period.   | NR                     | NR   | All men N=331 (0.3%)<br><br>GBM N=8 (0.6%) |

The 2008 study by Kreuter et al. reports on the prevalence of penile cancer among a German patient cohort of GBM PLHIV (184). PIN was detected in 11/263 (4.2%) patients, though there were no cases of penile cancer. Compared to the estimates provided through the global estimates on rates and prevalence of penile cancers, the GBM PLHIV in this study experienced considerably greater incidence of PIN. This aligns with the greater incidence and prevalence of other HPV-related cancers among this population.

Two studies were excluded but may provide data to further understand the prevalence of HPV-related penile cancers among males (see *Table 12*). The first, by Fuchs et al., did not separately report HPV-related penile cancer prevalence among their GBM participants (185). The second, by Saunders et al., did not report cancer prevalence that included those patients who had died over the study period nor did they identify HPV-related penile cancers separately to other forms of penile cancers (186).

Few data have been published on rates of penile cancers among GBM due to several reasons explored in Chapter Two, Section Two: Part Two. One of the biggest obstacles remains that few cancer registries or clinical administrative databases record patients' sexual identity or behaviour, making linkage of cases to these variables impossible. Another consideration is that the incidence of penile cancer peaks at the age of 70yrs and homosexual behaviour would have been illegal for most of these men's lives, making them less likely to disclose their sexual behaviour (183). This also has implications for recruiting older GBM in these settings, through which GBM are routinely sampled, as they are likely to be under-represented in these clinical GBM samples if they are less likely to disclose their sexual identity or same-sex sexual behaviours.

#### *HPV-related oropharyngeal cancer among GBM*

Oral cancers are the fifth most common cancer reported in European countries and include squamous cell cancers of the oral cavity, the oropharynx, hypopharynx, larynx, sinonasal tract and the nasopharynx (187). Prevalence of these cancers is greater among males compared to females, though rates among both these populations are increasing while the prevalence of non-tobacco non-alcohol-related cancers is decreasing over time (171). Greater prevalence of oral cancers have been reported among PLHIV (the majority of whom are GBM) compared to those found among the HIV-negative and wider population (188).

Search terms PubMed:

(((((prevalence) OR incidence)) AND (((((head) AND neck)) OR (((oral) OR throat) OR pharyngeal) OR oropharyngeal))) AND (((cancer) OR carcinoma) OR lesion) OR neoplasia))) AND (((((cancer) OR carcinoma) OR lesion) OR neoplasia)) AND (((oral) OR throat) OR pharyngeal) OR oropharyngeal))) AND (((((men) OR male)) AND ((gay) OR

homosexual) OR bisexual))) OR (((men who have sex with men) OR MSM) OR GBM))) AND (((HPV) OR human papillomavirus) OR papillomavirus)

The search returned 102 results; 86 reported only on oral HPV infection, did not report prevalence or incidence of oropharyngeal cancers, did not report on GBM, were clinical case studies or were laboratory methodological papers. Fifteen articles were selected that contained a relevant title for reviewing the abstract, of which none reported HPV-related oropharyngeal cancers by sexual orientation measures. Of the 15 papers for which the abstract was reviewed:

- two were excluded as they did not separately report the prevalence of HPV-related oropharyngeal cancers,
- seven were excluded as they did not identify GBM within their studies,
- two were excluded as they were methodological papers that did not report results,
- one identified GBM within their sample but did not report the prevalence separately for this population,
- one was excluded as it was a systematic literature review with a focus was on risk factors for the development of oral lesions and cancers and did not report prevalence from the studies (these studies did not identify GBM in their samples),
- one was an editorial article and included references to other studies, though these did not report HPV-related oral cancer prevalence or incidence among GBM,
- one was excluded as it did not report the results for oral cancer separately.

Key themes emerged from the papers identified above that provide insights into the difficulties with identifying published material on this subject and have been identified throughout this chapter, reinforcing the topics explored in sampling GBM in Chapter Two, Section Two: Part Two. Saunders et al., Heck et al., and Frisch et al. utilise cancer registry data or an equivalent administrative medical database in their papers to provide a prevalence estimate of oral cancers utilising ICD coding (189). However, this coding does not identify the causal root of the cancer, rather ICD coding classifies malignant neoplasms based on tumour site. In addition to HPV-related oral cancers not being readily being identifiable from administrative datasets, measures of sexual orientation that could be utilised to identify GBM are also not included as has been identified as a barrier to providing accurate measures of GBM health throughout this chapter.



## Synthesis of Part Two: Prevalence of HPV-related disease among GBM

- HPV infection is common among GBM, but the development of invasive HPV-related cancers at these sites are comparatively rare. Therefore, HR-HPV infection is necessary but not sufficient for the development of invasive cancer, with most infections clearing or being suppressed by the immune system.
- The majority of studies published burden of HPV-related disease among GBM have estimated the prevalence of anal HPV-related lesions and cancers, including two systematic literature reviews and meta-analyses.
- Comparatively fewer studies were identified that reported on the prevalence or incidence of other HPV-related diseases that affect males:
  - Six studies were identified that explored AGW prevalence among GBM
  - One study was identified that specifically reported HPV-related penile cancer prevalence among GBM.
  - No studies were identified that specifically reported HPV-related oral cancers among GBM.
- The prevalence of AGWs is the most commonly reported HPV-related disease that affects GBM.
- Compared to MSW or the general population of males:
  - GBM experience a similar prevalence of penile warts.
    - Greater prevalence of anal warts.
  - GBM experience a greater prevalence of anal cancers and lesions.
  - No data were found allowing comparison of prevalence of incidence for penile cancers.
- GBM PLHIV experience a greater prevalence of HPV-related disease compared to HIV-negative GBM.

## Synthesis of main findings in Section 3: Prevalence of HPV infection and related disease among GBM

- Quantifying HPV-related disease among GBM is necessary to demonstrate both the need and subsequent impact of HPV vaccination and prevention efforts among this population.
- Accurately quantifying the burden of disease among GBM is problematic due to the lack of sexual orientation data recorded in administrative health databases globally.
- Identifying HPV-related cancers from cancer registry or other forms of administrative health databases is limited by the use of ICD coding that identifies the site and form of cancer but can lack data on the causal agent or mechanism of oncogenesis if not used in diagnosis.
- Studies employing convenience and cross-sectional designs are appropriate for the research question and provide estimates among sexually active GBM who are at risk of acquiring HPV infection and developing disease.
- The factors outlined above and earlier in Chapter Two, Section Two: Part Two published data are limited for HPV infection and related disease among GBM, particularly for oral and penile sites.
- Despite these limitations, themes emerge from the literature.

### **HPV infection:**

- Anal HPV infection is prevalent among GBM and almost ubiquitous among GBM PLHIV.
- Oral and penile HPV infection are rare compared to anal infection, though penile infection is more common than oral infection among GBM.

### **HPV-related disease:**

- AGWs are common among GBM affecting both penile and anal sites.
- Of the HPV-related cancers that affect GBM, anal cancers and lesions are the most commonly reported.
- GBM PLHIV experience a greater prevalence of both HPV infection and related disease. This is of particular concern as GBM are over-represented among HIV diagnoses both in NZ and globally.

## Section Four: Treatment and prevention of HPV-related disease

### Purpose

Screening and treatment of pre-cancerous lesions and vaccination have been successfully utilised to control and prevent HPV-related cancers among women. Each of these is potentially relevant for GBM. However, HPV screening and vaccination programmes will need to be designed and adapted to be appropriate and effective for GBM and the HPV-related cancers that affect this population.

However, the design and creation of effective interventions will have little impact if the target population do not perceive the disease to affect them, are not aware of the interventions and programmes, or are not willing to use them. Awareness of HPV-related diseases, awareness of HPV vaccination, and acceptability of receiving the HPV vaccine are measures that might predict prevention uptake. Measuring the prevalence of these factors can aid in the design and targeting of health promotion messages and evaluate their impact if measured over time.

This section explores the literature in relation to these topics and informs the direction of this thesis.

### Aims

1. Explore treatment and prevention tools available for HPV-related diseases affecting GBM
2. Explore awareness among GBM of the HPV-related diseases that affect GBM, the HPV vaccine, and willingness to receive the HPV vaccine.

## Part One: Screening, treatment, and prevention interventions against HPV-related disease among GBM

### **Purpose**

The benefits and harms of any public health intervention – whether prevention, screening or treatment – must be understood before a recommendation can be made. Here, existing interventions and their efficacy and appropriateness for GBM in relation to HPV-related disease are explored with the aim to identify those that would be best to prioritise for this population.

### **Aims**

- a. Explore the literature relating to screening for HPV-related cancers among GBM.
- b. Explore the literature relating to the treatment of HPV-related disease among GBM.
- c. Describe the efficacy of HPV vaccination among GBM for the prevention of HPV infection and HPV-related disease.
- d. Describe the efficacy of condoms for the prevention of HPV infection and HPV-related disease among GBM.

### **Screening for HPV-related cancers in GBM**

The natural history and progression of HR-HPV infection and subsequent development of HPV-related cancers at the various anatomical sites have been covered earlier in this thesis (see *Chapter 2: Section One*).

Screening has a dual purpose, firstly identifying malignant cancers that require immediate clinical intervention, and secondly, precancerous lesions that can be either managed through follow-up testing where they either regress or progress and require intervention. The success of cervical cancer screening programmes comes from treating high-grade precancerous lesions to prevent invasive cancers.

The rates of anal SCCs among GBM are estimated to be similar or greater than cervical cancer rates prior to the introduction of cervical screening. This prioritises the development of screening programmes for this form of cancer to mimic the success of cervical screening programmes (2). Two forms of screening for anal cancers and pre-cancers have been proposed: the use of high-resolution anoscopy and digital anal rectal examination (190). High-resolution anoscopy uses colposcope to magnify and examine the perianal and intra-anal epithelium, through which a trained healthcare provider can examine and take biopsies of any suspicious lesions by applying acetic acid (5%) and Lugol iodine where required (191). With digital anal rectal examination, the healthcare provider examines the anal passage with a finger and is able to palpate any lesions they detect. These can then be referred on for further examination with an anoscope if thought necessary.

Additional research is focussed on identifying biomarkers with greater sensitivity and specificity in identifying patients experiencing HPV-related HGAIN or malignant neoplasia. Jin et al. reported that compared to anal cytology, HR-HPV viral load testing and detection of E6/E7 mRNA had similar sensitivity (78.4 and 75.4 respectively vs. 83.2%) and greater specificity (68.0 and 69.4 respectively vs. 52.4%) (192).

The natural history of oropharyngeal and penile pre-cancer progression is not as well understood, and therefore the benefits of screening and treatment are also uncertain. To date, the proportion of cancers affecting these sites that are caused by HPV-infection are lower compared to the cervical and anal sites. However, screening for HPV infection and of HR-HPV infection persistence, in particular, has been utilised as a risk measure alongside PAP-smears in cervical cancer screening programmes (193). This form of screening and monitoring of persistent HR-HPV infections could also apply to the other anatomical sites affected by HPV as persistent infection with HR-HPV types appears to be the biological basis for the development of the majority of HPV-related cancers.

### ***Treatment of HPV-related diseases in GBM***

There is a range of treatments available for the variety of HPV-related disease affecting GBM. Though HPV can infect various anatomical sites, there are essentially three forms of HPV-related disease: condyloma (warts) and neoplasia and invasive cancer. In this section we will explore the treatments available for these forms of HPV-related disease.

#### *Treatment of HPV-related condyloma*

The most commonly used therapies to treat condyloma are ablation with cautery or laser, topical medications, and cryotherapy. The treatment process can be time-consuming, particularly if the patient has a number of condylomata, and involves discomfort for the patient. As condyloma are relatively benign, and up to 30% of cases will spontaneously clear within six months, the clinical benefit and cost of treating condyloma has been questioned (194). This is further called into question considering that treating the condyloma does not treat the underlying viral infection and subsequently recurrence rates of condyloma are significant, laying between 25-40% within 12 months (195). However, most patients will wish to receive treatment due to the physical appearance and stigmatising nature of warts.

A systematic review of the published randomised control trials by Lacey et al. in 2013 as part of the guidelines on the management of AGWs produced for European Branch of the International Union against Sexually Transmitted Infections, noted the recurrence rates for each form of therapeutic intervention, ranging from 6%—26% for imiquimod cream to 13%—100% for podophyllotoxin solution (see *Table 13*) (196).

Table 13: Summary of the results of randomized controlled trials of therapies for anogenital warts among HIV negative patients: modified from Lacey et al. (196)

| Treatment                     | Range of clearance rates based on an intention to treat analysis | Range of clearance rates based on a per protocol analysis ( <i>determined at time in weeks; range</i> ) | Range of recurrence rates ( <i>determined at time in weeks; range</i> ) |
|-------------------------------|--|---|---|
| Podophyllotoxin solution 0.5% | 45-83%   | 55-83% (3-6)  | 13-100% (8-21)  |
| Podophyllotoxin cream 0.15%   | 43-70%   | 43-70% (4)  | 6-55% (8-12)  |
| Imiquimod cream 5%            | 35-68%   | 55-81% (16)   | 6-26% (10-24)   |
| Cryotherapy                   | 44-75%   | 67-92% (6-10)   | 21-42% (4-12)   |
| TCA                           | 56-81%   | 81-84% (8-10)   | 36% (8)   |
| Electrosurgery                | 94-100%  | 94-100% (1-6)   | 22% (12)  |
| Scissors excision             | 89-100%  | 89-100% (6)   | 19-29% (40-48)  |

TCA = Trichloroacetic acid

Note: Clearance rates and recurrence rates are not directly comparable as clearance was measured at different times from the start of treatment and high loss to follow up was often experienced in the trials.

#### *Treatment of HPV-related neoplasia and invasive cancers*

From controversial studies on cervical cancer progression rates, it was demonstrated that there was a significant benefit to clinical intervention due to high progression rates in CIN2/3 to invasive cancer (197). However, among male patients attending an anal cancer screening clinic between 2004-2011, Tong et al. recorded higher rates of spontaneous regression for HGAIN (23.5/100PY, 95% CI 15.73–35.02) compared to rates of progression (7.4/100PY, 95%CI: 4.73–11.63) (198). This makes the benefit of clinical intervention for anal pre-cancers unclear, though there may be benefit for GBM PLHIV who experience the highest rates of HPV-related cancers.

Chemoradiotherapy has been established as the standard of care used to treat HPV-related neoplasia and invasive cancers (199). Though concurrent chemotherapy and chemoradiation are less invasive than surgery, they can cause collateral damage to the surrounding healthy tissues. Furthermore, the anatomical sites among men affected by HPV-related cancers are structurally complex and the interventions used to treat them can significantly disrupt these tissues. In an effort to better document and standardise late effects of anal SCC and post-chemotherapy treatment outcomes, Core outcomes for clinical trials of CRT for anal cancer (CORMAC) have been defined (200). These include toxicity (anal incontinence, faecal urgency, pelvic fistula, stoma, skin loss) and impact on life (physical function, sexual function, health-related quality of life). Therefore, prevention through vaccination is better than cure as current treatment can effect men's ability to engage in anal sexual intercourse, an important and normative sexual behaviour among GBM.

A Cochrane review conducted by Macaya et al. in 2012 found a lack of suitable evidence to guide the clinical management and treatment of AIN (201). The literature search conducted for this review, and the subsequent evaluation of the findings of this search, produced only one randomised control trial that had a limited number of participants and found no significant difference between the placebo and treatment arms of the trial. The authors recommended that more randomised control trials are needed to be conducted to guide clinical intervention and guidelines in this area.

For anal cancer, similar to condyloma, the relapse rates for anal cancers and neoplasia post-intervention are high, particularly among GBM PLHIV with rates up to 80% within two years after surgery (194). Anal stenosis post-surgery is also a frequent occurrence. Nigro et al. demonstrated the efficacy of combined chemotherapy and chemoradiation for treating anal cancers in the 1980s, and this has become recommended practice, though surgical intervention may still be indicated (202, 203). Novel technology to deliver much more focussed radiation to minimise collateral tissue damage have also been developed, and HPV-related cancers appear to be particularly susceptible to forms of radiotherapy (204).

### ***HPV vaccination and efficacy among males***

Vaccines for HPV were developed as a response to the global burden of cervical cancers, of which 100% are thought to be caused by HR-HPV types. However, with the rising rates of HPV-related cancers among males, the poor uptake of HPV vaccination among females in some countries, and the lack of cross-protection to GBM provided by a female-only vaccination programme, HPV vaccination is increasingly being considered for males.

#### *Development of HPV vaccines*

In 1991, Frazer and Zhou had successfully developed a technique to produce HPV capsid proteins that in turn, self-assembled into VLPs (205). The technique was further developed and refined by the pharmaceutical company Merck, conducting six clinical trials between 1997 and 2004 to show the efficacy of the first HPV vaccine Gardasil, a quadrivalent vaccine against HPV types 6, 11, 16, and 18 (206). At a similar time, between 1999 and 2003, the company GlaxoSmithKline was developing a similar vaccine called Cervarix, which is a bivalent vaccine against HPV types 16 and 18. Both the Gardasil and Cervarix vaccines were first approved for use by the USA Food and Drug Administration (FDA) in 2006 and 2009, respectively (207, 208).

#### *HPV vaccines available*

Two vaccines were developed and brought to market between 2007 and 2013; Cervarix produced by GlaxoSmithKline and Gardasil produced by Merc. Both vaccines utilise the VLP technology to create pseudoviruses using the major capsid proteins specific to the HPV

types that cause the burden of HPV-related clinical disease (see Table 14). Between 2007 and 2013, the Broad-Spectrum HPV Vaccine Study determined the efficacy of inclusion of additional HPV types into the formulation of Gardasil to create Gardasil9, a nonavalent vaccine against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 (209). The Gardasil9 vaccine was first approved for use by the USA FDA in 2014 and is the vaccine scheduled for use in NZ.

Table 14: Vaccine composition of a 0.5ml dose of HPV vaccine.

|   | <b>Gardasil</b> | <b>Gardasil9</b> | <b>Cervarix</b> |
|---|-----------------|------------------|-----------------|
| Oncogenic protein subunit component L1 VLP, µg    |                 |                  |                 |
| HPV-16  | 40              | 60               | 20              |
| HPV-18  | 20              | 40               | 20              |
| HPV-31  |                 | 20               |                 |
| HPV-33  |                 | 20               |                 |
| HPV-45  |                 | 20               |                 |
| HPV-52  |                 | 20               |                 |
| HPV-58  |                 | 20               |                 |
| Verrucous protein subunit component L1 VLP, µg    |                 |                  |                 |
| HPV-6   |                 | 30               |                 |
| HPV-11  |                 | 20               |                 |
| Adjuvant  |                 |                  |                 |
| Amorphous aluminium hydroxyphosphate sulphate, µg | 225             | 500              |                 |
| 3-O-Desacyl-4'-monophosphoryl lipid (MPL) A, µg   |                 |                  | 50              |
| Aluminium hydroxide salt, µg                      |                 |                  | 500             |

VLP = viral-like protein

Taken from Harper et al. 2017 (210)

### *HPV vaccine efficacy among males*

The efficacy of quadrivalent Gardasil was examined in 4065 HIV-negative males aged 16 to 26 years old recruited from 18 countries into a randomised, double-blind, placebo-controlled trial between 2004 and 2008 (211). The trial sought to examine the effectiveness of the quadrivalent vaccine in preventing extragenital lesions, which were defined as anogenital warts, penile, perineal or perianal intraepithelial neoplasia (of any grade), or cancers at these sites. Among the according to protocol (ATP) group, the efficacy against all clinical endpoints was 90.4% and 65.8% among the intention to treat (ITT) group (see Table 15) (211, 212).



Table 15: Efficacy of Gardasil in males for the prevention of HPV-related clinical endpoints among ATP and ITT populations of GBM

|  | ATP % Efficacy (95% CI) | ITT % Efficacy (95% CI) |
|--|-------------------------|-------------------------|
| <b>External genital lesions</b>                    |                         |                         |
| HPV-6, -11, -16, -18                               | 79.0 (-87.9 to 99.6)    | 70.2 (23.0 to 90.2)     |
| <b>Persistent anogenital infection<sup>β</sup></b> |                         |                         |
| HPV-6, -11, -16, -18                               | 48.8 (11.6, 71.2)       | 43.6 (19.5 to 60.8)     |
| <b>AIN-any grade</b>                               |                         |                         |
| Any type <sup>α</sup>                              | 54.9 (8.4–79.1)         | 25.7 (-1.1–45.6)        |
| HPV-6, -11, -16, -18                               | 77.5 (39.6–93.3)        | 50.3 (25.7–67.2)        |
| AIN 2/3  | 74.9 (8.8–95.4)         | 54.2 (18.0–75.3)        |
| <b>Persistent anal infection<sup>β</sup></b>       |                         |                         |
| HPV-6, -11, -16, -18                               | 94.9 (80.4–99.4)        | 59.4 (43.0–71.4)        |

<sup>α</sup> Seronegative to HPV6, 11, 16, 18 and DNA negative to 6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 56, 58, and 59 at enrolment.

<sup>β</sup> Persistence is defined as detecting the same HPV type (6, 11, 16, or 18) in an anogenital swab or biopsy specimen on consecutive visits at least 6 (+/-1) months apart.

AIN: Anal intraepithelial neoplasia; AIN 2/3: Anal intraepithelial neoplasia grade 2 or 3; ATP: According to Protocol; CI: Confidence interval; HPV: Human papillomavirus; ITT: Intention-to-treat.

Table adapted from Schiller et al. 2012 (212)

Data from Giuliano et al. 2011 (211) and Palefsky et al 2011 (213)

### *HPV vaccine efficacy among GBM*

Of the males recruited into the trial, 602 reported same-sex sexual behaviour and were enrolled in a concurrent study assessing the effectiveness of quadrivalent Gardasil to prevent HPV infection and AIN (213). Among the ATP group, vaccine efficacy of 77.5% was recorded after three years follow-up in preventing AIN of any grade caused by the HPV types included in the vaccine. The vaccine also demonstrated an efficacy of 94.9% among the ATP group and 59.4% among the ITT group in preventing persistent anal infection with the HPV types included in the vaccine. Though the differences between the ATP and the ITT groups are considerable, it is important to note that the ITT group will include males who received only one dose of vaccine and also included those who were Ab seropositive or DNA positive for HPV infection upon enrolment (211, 213).

Immunobridging studies have been conducted in males for the nonvalent Gardasil. These have provided evidence that the immune response elicited by the vaccine was similar to that among women, which was sufficient to prevent genital warts and CIN of any grade with high efficacy (214). Immunobridging studies have also been conducted among HIV-positive males aged 22 to 61 years and showed that greater than 95% of these participants seroconverted

after vaccination but that the antibody titres produced in response to vaccination were half that seen among HIV-negative participants of a similar age (215).

#### *Herd immunity threshold for HPV vaccination*

A meta-analysis of HPV modelling studies reported that population-level impacts of HPV vaccination are seen with as little as 20% coverage among females but suggest that herd immunity and potential elimination of the HPV types included in the vaccine would not be realised until coverage is 80% among both women and men (216). HPV vaccination coverage among vaccine eligible populations in NZ (64%) remains lower than the 80% herd immunity target set by MoH in 2015 (217, 218). The HPV vaccine, in its various forms, is proving to be incredibly effective for the prevention of HPV infection and related diseases by providing sterilising immunity among women (219, 220). Evidence is emerging that as little as one dose may be as effective in preventing cervical cancer as the previously recommended three doses of the quadrivalent vaccine (221). However, data on the effectiveness of single dose and long-term efficacy for males and GBM remains uncertain.

#### ***Effectiveness of condoms for the prevention of HPV infection and related disease among GBM***

Limited published articles were identified that provided evidence relating to the effectiveness of condom use in preventing HPV acquisition specifically among GBM. Consistent and correct condom use during penetrative sexual behaviours is most likely to prevent anal and oral HPV infection and development of disease due to the requirement for penetrative sexual activity to reach susceptible anatomical sites and the demonstrated impermeable material of condoms to viral particles (222). However, in a longitudinal study of GBM attending an SHC, Donà et al. found no association with reported consistent condom use and incident anal HPV infection or clearance among men in their study after controlling for sociodemographic and behavioural variables but found an association with tertiary education and reporting receptive anal sex (223).

Two studies were found that demonstrated lower prevalence of AGWs among men who report consistent condom use, though these studies did not identify GBM in their samples (224). This is despite the theory that condoms provide limited protection against LR-HPV types that cause AGWs as these viruses can infect areas not covered by the male condom, such as the testes and larger pubic and perianal areas.

The problematic nature of accurately measuring condom use and the associated biases have been well described in the literature (225, 226), as has measuring wider sexual behavioural and participation in studies relating to sexual behaviour (227). These factors combined with the methodological issues with recruiting GBM and accurately measuring HPV infection and related diseases among this population, described in Chapter Two, Section Two: Part Two,

illustrate the complexities of providing definitive high-quality evidence on this research area specifically for GBM.

*Evidence from the wider literature on the effectiveness of condoms for the prevention of HPV infection and related disease*

Two systematic literature reviews were identified that explored condom use in relation to preventing HPV infection and cervical neoplasia (228, 229). The earlier review by Manhart et al. published in 2002 identified 20 studies that provided inconsistent evidence of the effectiveness of condoms in preventing cervical HPV infection, with odds ratios ranging from 0.2 (95% CI: 0.1—0.6) to 1.6 (95% CI: 0.8—3.3), of which five of the six studies included in the review were cross-sectional studies (229). Lam et al. published their literature review in 2014, the review similarly focused on women but only included longitudinal studies and excluded populations that were primarily PLHIV. Lam et al. concluded that consistent condom use was protective against both cervical HPV infection and aided the regression of cervical neoplasia (228). However, only four out of the eight studies provided evidence of significance, with those showing non-significance having larger populations and adjusting for other factors such as the number of recent sexual partners, which demonstrated greater significance.

Some of the highest quality evidence of the potential effectiveness of condoms preventing HPV infection and disease comes from a 2003 randomised control trial conducted by Hogewoning et al. that demonstrated a significant association between condom use compared to non-use on the regression of cervical intraepithelial neoplasia (p-value=0.03) and clearance of HPV infection (p-value=0.02) (230). Such effects have not been demonstrated among GBM for either anal or oral HPV-related neoplasia but could be a direction for future study.

## Synthesis of Part One: Screening, treatment and prevention interventions against HPV-related disease among GBM

- Few data specifically identify GBM in studies of HPV-related disease treatment, screening and prevention interventions.
- Complexities with accuracy identifying HPV-related cancers and pre-cancers from administrative health datasets further compound the of research in this area.
- High regression rates have been recorded for AGWs, indicating that prevention is more effective than currently available treatments.
- The Australian SPANC study has demonstrated that HR-HPV types 16 and 18 are correlated to anal HSIL development and lower spontaneous regression rates.
- Screening for early detection and monitoring for HR-HPV infections and lesions could be a suitable intervention for populations most at risk of developing HPV-related cancers. One such population that has been identified is GBM PLHIV.
- Detection of HSIL at the various anatomical sites is invasive and the benefits of detecting and treating HSIL beyond cervical HSIL has not been definitively demonstrated to outweigh the harms of intervention.
- HPV vaccination offers the most effective (and most ethical) intervention to prevent HPV-related disease and associated morbidity and mortality among GBM.
- Condoms are a widely available and acceptable prevention tool, and there is strong evidence that consistent and correct use promotes cervical HPV infection clearance and lesion regression among women. However, no studies were identified that demonstrated condoms prevented anal HPV infection among GBM.

## Section Four: Part Two – Awareness of HPV-related disease and vaccine acceptability among GBM

### ***Purpose***

Awareness of a disease, the interventions to prevent or treat it, and the acceptability of these interventions are important components of the health belief model and health literacy and promotion. Exploring HPV-related awareness and vaccine acceptability among GBM can provide insights into the upstream determinants of HPV vaccine uptake among this population.

### ***Aims***

- a. Explore the literature relating to knowledge and awareness of HPV-related disease and HPV vaccination among GBM.
- b. Explore the literature relating to HPV vaccine acceptability among GBM.

### ***Health belief model and HPV vaccination***

Knowledge of HPV and acceptability of the HPV vaccine have been demonstrated to be associated with HPV vaccination uptake (231, 232). Limited examples in literature are available that explore these factors among GBM. However, internationally, awareness of HPV related disease and HPV vaccination is lower among males compared to females (233).

Knowledge and awareness are associated but may not predict vaccine uptake alone. Walling et al. conducted a systematic review of studies that evaluated the impact of different interventions on HPV vaccine uptake, which included studies providing behavioural interventions that sought to increase knowledge and vaccine acceptability among different populations, ranging from school children to commercial sex workers (234). Their findings indicate that behavioural interventions alone demonstrated increases in knowledge but had limited effects on HPV vaccination uptake. The authors recognise the complexity in delivering programmes seeking to increase HPV vaccination, including the socio-political environment, targeting either the individual, their parent(s), caregiver(s), or healthcare provider, and the availability and ability to access healthcare and HPV vaccination.

The Health Belief Model is one theoretic framework that seeks to explain the predictors of health interventions (235, 236). Each of the potential barriers or facilitators identified by Walling et al. can be situated within the health belief model with the recognition that each facilitator is necessary but is not sufficient on its own to translate to HPV vaccination uptake, rather public health programmes must target multiple facilitators to achieve greater uptake.

### ***Knowledge and awareness of HPV among GBM***

Knowledge and awareness of HPV infection and related disease have been measured in different ways throughout the literature. Participants have been asked questions (open or prompted) or have been provided with statements and asked to identify if they are true or false. Some studies have presented the prevalence of knowledge or awareness, while others have created a knowledge score and examined factors associated with greater scores. This section will explore the prevalence of knowledge of HPV and related disease and awareness of HPV vaccination.

#### *Knowledge of HPV and related disease*

In general, the majority of GBM participants in the selected studies report having “heard of HPV”, ranging from 45% of GBM in the 2007 study by Pitts et al., to 93% of GBM in the 2011 study by Wheldon et al. (see *Table 16*). Self-reported knowledge appears higher among women and GBM, but will be affected by age of participants, the year the study was conducted, and the site from which participants were sampled. For example, Pitts et al. sampled GBM attending a community event in Australia in 2005, which was before the start of the female-only school-based vaccination programme in this country in 2007 (237).

Knowledge that HPV causes genital warts appears greater than knowledge of the causal relationship between HPV and various cancers, the prevalence of this knowledge being greater among GBM and women as compared to heterosexual men. From the selected studies focussed on GBM, a greater proportion of participants report knowing that HPV causes anal cancer compared to knowing that it causes oral and penile cancers. However, among GBM, the overall prevalence of HPV-related cancer knowledge is lower than 50%.

#### *Awareness of HPV vaccine*

The prevalence of awareness of HPV vaccine was generally greater than knowledge of HPV-related disease among those included in the studies (see *Table 16*). A greater proportion of women report awareness compared to males, both GBM and heterosexual, though this is unsurprising given the majority of these studies among women took place after the introduction of female-only vaccination programmes. Among males, awareness of the HPV vaccine appears to be greater among heterosexual males compared to GBM, which could be explained by heterosexual men being exposed to the HPV vaccine promotion and uptake through their female partners.

Wheldon et al. asked their young GBM participants two questions: (1) if they were aware that “*there is a vaccine for girls and women that prevents certain types of HPV*” to which 75% reported they were; and (2) if they were aware that “*there is a vaccine for boys and men that prevents certain types of HPV*” to which 25% reported they were (238). Therefore, these

young GBM may be exposed to the HPV vaccine through females of a similar age while not being aware of the benefits to males. This may also be the case for heterosexual males who report a higher prevalence of HPV vaccine awareness compared to GBM.

Table 16: Studies reporting HPV and HPV-related disease knowledge and HPV vaccine awareness prevalence by gender and sexual orientation

| Author                   | Year | N    | Heard of HPV | HPV causes:   |             |             |               | There is an HPV vaccine |
|--------------------------|------|------|--------------|---------------|-------------|-------------|---------------|-------------------------|
|                          |      |      |              | Genital warts | Anal cancer | Oral cancer | Penile cancer |                         |
| <b>GBM</b>               |      |      |              |               |             |             |               |                         |
| Pitts (237)              | 2007 | 384  | 45%          | -             | -           | -           | -             | -                       |
| Brewer (239)             | 2010 | 312  | 79%          | 46%           | 32%         | 25%         | -             | -                       |
| Gilbert (240)            | 2011 | 312  | -            | -             | -           | -           | -             | 76%                     |
| Wheldon (238)            | 2011 | 179  | 93%          | 57%           | 43%         | 39%         | 31%           | 25%*                    |
| Pelullo (207)            | 2012 | 566  | 55%          | -             | 53%         | 45%         | -             | 41%                     |
| Fenkl (241)              | 2015 | 163  | -            | 69%           | 56%         |             |               |                         |
| Bjekic (242)             | 2016 | 270  | 65%          | -             | 29%         | 17%         | 14%           | 13%                     |
| Feeney (243)             | 2019 | 1660 | -            | -             | -           | -           | -             | 32%                     |
| <b>Heterosexual Men†</b> |      |      |              |               |             |             |               |                         |
| Brewer (239)             | 2010 | 296  | 62%          | 34%           | 15%         | 21%         | -             | -                       |
| Pitts (244)              | 2010 | 2556 | 38%          | 42%           | -           | -           | -             | -                       |
| Reiter (245)             | 2010 | 297  | 61%          | 34%           | 14%         | 21%         | 17%           | 63%                     |
| Marlow (233)             | 2012 | 1189 | 48%          | 51%           | -           | -           | -             | 69%                     |
| Little (246)             | 2015 | 175  | 80%          | 57%           | 29%         | 33%         | -             | -                       |
| <b>Women</b>             |      |      |              |               |             |             |               |                         |
| Dursun (247)             | 2009 | 1427 | 45%          | -             | -           | -           | -             | -                       |
| Pitts (244)              | 2010 | 2634 | 63%          | 46%           | -           | -           | -             | -                       |
| Marlow (233)             | 2012 | 1220 | 74%          | 50%           | -           | -           | -             | 85%                     |
| Tung (248)               | 2016 | 417  | -            | 68%           | -           | -           | -             | -                       |

‡ Asked only of those who had heard of HPV.

\* Asked if participants knew about the vaccine prevented HPV-related disease in boys and men.

† Includes studies in which sexual orientation data was not collected – a general sample of men.

- not reported

### **HPV vaccine acceptability among GBM**

There is heterogeneity in the methods used to measure HPV vaccine acceptability among the literature, with studies reporting acceptability, willingness and intention to be vaccinated among their participants. Studies have also examined vaccine acceptability under different conditions, such as vaccine efficacy and cost. This section will explore the prevalence of theoretical acceptability and willingness of GBM to be vaccinated against HPV, as the

intention to receive the HPV vaccine may be more influenced by local availability and healthcare provision.

Nadarzynski et al. published a systematic review of the literature in 2014 on the prevalence and factors related to HPV vaccine acceptability among GBM (249). This review notes a combined acceptability prevalence of 56% among the pooled population of GBM (see *Table 17*). The majority of studies in this review recruited a cross-sectional and venue-based sample of GBM, of which the majority were males who were white European, educated and aged between 16-70 years. Despite no geographic restrictions placed on study inclusion criteria, the half of the 16 studies were conducted in the USA, and only two studies being identified that took place outside of Western countries.

Since the review by Nadarzynski et al., several studies have been published that also report vaccine acceptability among GBM populations. The GBM in these samples report a higher prevalence of HPV vaccine acceptability as compared to the pooled prevalence by Nadarzynski et al. with a range of 72-88% (see *Table 17*). Similar to the 2014 review, these studies are cross-sectional, and the majority of participants were white European.

Few studies reported acceptability under different cost scenarios, but among those that did, there was a noticeable decline in the number of GBM who would be willing to be vaccinated if they were required to pay for it.

### ***Uptake of HPV vaccination among GBM***

Few data were found for HPV vaccine uptake among GBM in the literature. Additional data may be published in grey literature or government websites. In Chapter 3, the candidate conducts a systematic literature review to further explore HPV vaccination uptake among GBM.



Table 17: Studies reporting HPV vaccine acceptability or willingness among GBM participants, whether fully funded or required the participant to pay

| Author  | Year        | Country     | N           | HPV Vaccine Acceptability/Willingness |                  |
|---|-------------|-------------|-------------|---------------------------------------|------------------|
|   |             |             |             | Free                                  | Paid             |
| <i>Studies included in 2014 Nadarzynski systematic review</i> |             |             |             |                                       |                  |
| Simatherai (250)  | 2009        | Australia   | 200         | NR                                    | 47%              |
| Reiter (251)  | 2009        | USA         | 312         | 74%                                   | NR               |
| Sundstrom (252)   | 2010        | Sweden      | 75          | 79%                                   | 7%               |
| Hernandez   | 2010        | USA         | 88          | 75%                                   | NR               |
| Wheldon (238)   | 2011        | USA         | 179         | 36%                                   | NR               |
| Colon-Lopez (253)   | 2012        | Puerto Rico | 58          | 21%                                   | NR               |
| Al-Naggar   | 2012        | Malaysia    | 46          | 0%                                    | NR               |
| Rank (254)  | 2012        | Canada      | 1169        | 67%                                   | NR               |
| Sanchez (255)   | 2012        | USA         | 116         | 86%                                   | NR               |
| Lau (256)   | 2013        | Hong Kong   | 542         | 79%                                   | 29%              |
| <b>Nadarzynski (249)</b>                                      | <b>2014</b> | -           | <b>5185</b> | <b>56%</b>                            |                  |
| <i>Additional studies published since 2014</i>                |             |             |             |                                       |                  |
| Cummings (257)  | 2015        | USA         | 1457        | 88%                                   | NR               |
| Giuliani (258)  | 2015        | Italy       | 296         | 72%                                   | 73% <sup>†</sup> |
| Marra (259)   | 2016        | Netherlands | 1053        | 85%                                   | NR               |
| Sadlier (260)   | 2016        | Ireland     | 302         | 78%                                   | 51%              |
| Bjekic (242)  | 2016        | Serbia      | 270         | 46.3%                                 | NR               |

† Of those that would be willing to receive the HPV vaccine  
NR – not reported

## Synthesis of Part Two: Awareness of HPV-related disease and vaccine acceptability among GBM

- In the collected studies, the majority of GBM were aware of HPV, but fewer were aware of the various HPV-related diseases that affect males, with awareness of HPV being a causal agent of oral and penile cancers being lower than AGWs and anal cancer.
- HPV vaccine awareness varied across the studies identified though this may be due to the year and populations in which the studies recruited their participants.
- The HPV vaccine appears highly acceptable to GBM, with the majority willing to receive the vaccine if provided through a funded programme, particularly in more recently published studies.
- Despite high acceptability, vaccine uptake prevalence was less than 20% in the two studies that reported uptake among GBM. However, these studies were conducted in the USA, where the provision of vaccination is through healthcare providers and largely dependent on health insurance coverage. In wider studies, school-based and publicly funded programmes resulted in greater coverage.

## Synthesis of Section Four: Treatment and prevention of HPV-related disease

### **Treatment and prevention:**

- The HPV vaccine has a demonstrated efficacy among GBM in preventing persistent anal HPV infection with HPV-16 and -18 and for the prevention of HPV-related AIN.
- Considerable difference in efficacy was observed between ATP and ITT populations, underpinning the recommendation of three doses, particularly for those older individuals accessing vaccination through catch-up programmes in NZ.
- The GBM in the vaccination studies were aged 16—26 years and were sexually active, reinforcing the importance of early vaccination.
- Implementation of vaccination programmes to prevent HPV-related disease is preferable to screening and treatment for several reasons.
  - It is more ethical to prevent HPV-related disease than to screen and treat. This is particularly true if prevention interventions can be targeted to those at greatest risk, such as among GBM where rates of anal HPV-related cancers are estimated to be greater or equivalent to rates of cervical cancers among women.
  - There is no evidence that treatment for HSIL is effective in prevention of anal cancer, although a randomised study of HSIL treatment versus observation is currently in progress (261).
  - Treatments for anal HPV-related cancers (and AGWs) are less effective than those for cervical cancer, making a screening and treatment programme unlikely to be effective.
  - High coverage of HPV vaccination could result in the elimination of HPV-related disease through community immunity effects.

### **Awareness and acceptability:**

- Awareness of HPV-related disease that affects males is less than 50% among GBM.
- Awareness of the HPV vaccine was comparable to awareness of HPV-related disease among GBM.
- Despite low awareness, HPV vaccine acceptability was high if provided at no-cost. However, this fell when there was a requirement to pay.
- Few studies were identified that reported on HPV vaccination uptake among GBM. This will be explored in a systematic literature review in Chapter Three.

## Section Five: HPV-related data among GBM in Aotearoa, New Zealand

### Purpose

This section explores the published literature relating to HPV and GBM in Aotearoa New Zealand, examining the areas previously explored: infection and disease prevalence, knowledge, vaccine awareness and acceptability, and vaccine uptake.

### HPV infection prevalence among GBM in Aotearoa, New Zealand

No published data were identified on the prevalence of HPV infection or Ab seropositivity among GBM in Aotearoa, New Zealand. Data related to HPV infection among the wider population of males is limited. The Dunedin Multidisciplinary Health and Development Study examined HPV Ab seropositivity among their cohort of male participants at the age of 32 years (N=450) to HPV types 6, 11, 16 and 18 (262). Dickson et al. reported that overall Ab seropositivity to HR HPV-16/-18 was 21%, for LR HPV-6/-11 was 5%, and 25% for any of the four HPV types tested. The study does collect data on sexual identity and behaviours, but the results were not disaggregated for GBM.

### HPV-related disease prevalence among GBM in Aotearoa, New Zealand

#### ***Anogenital warts***

Sexual orientation data are not routinely collected in national surveillance data related to STI diagnoses, meaning that diagnoses of AGWs cannot be disaggregated for GBM. National surveillance data collected in 2015 by the Institute of Environmental Science and Research (ESR) from diagnostic laboratories and sexual healthcare providers reported N=881 primary diagnoses of AGW among males in Aotearoa, New Zealand, compared to N=584 cases among females (263). An overall decline in the primary diagnosis of AGW was reported between 2012 and 2016, among both males and females (*see Figure 13*), which may in part be due to the implementation of the HPV vaccination programme (160).

(a) Sexual Health Clinics



(b) Family Planning Clinics

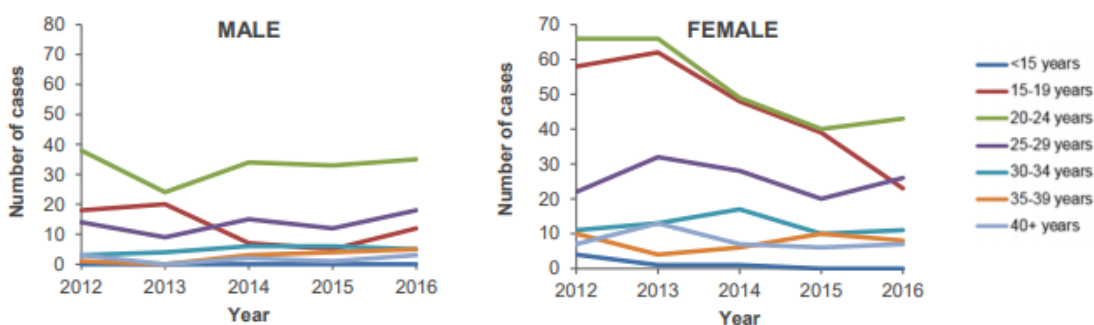


Figure 13: Number of genital wart cases (first presentation) recorded in (a) sexual health clinics and (b) family planning clinics, by sex and age group, 2012—2016 (160).

Oliphant et al. noted a decrease in AGW diagnoses among male and female first-time attendees under the age of 20 years to Auckland Sexual Health Services (ASHS) between 2007 and 2010 (264). Among first-time male attendees under the age of 20 years, this decrease was from 11.5% in 2007 to 6.9% in 2010. The decrease among females of the same age was greater (13.7% vs. 5.1%). The decline in males may reflect the herd immunity effect of vaccinating the sexual partners of heterosexual males compared to the greater impact of direct vaccination among females.

Data on self-reported AGW diagnosis is available from the Gay Auckland Period Sex Survey (GAPSS) and the Gay Online Sex Survey (GOSS), the HIV behavioural surveillance programme for GBM in NZ. Among the combined sample of GBM participants (N=3138) from the 2011 GAPSS and GOSS surveys, 1.9% self-reported an AGW diagnosis in the previous 12 months (265). The lower prevalence among this sample compared to the Oliphant et al. findings is likely reflective of the difference in sampling methods for these studies.

**HPV-related cancers**

Bruni et al. from the Institut Català d'Oncologia, Information Centre on HPV and Cancer provide crude HPV-related cancer incidence rates among New Zealand men and women based on published data (266).

Table 18 provides the crude and age-standardised incidence rates for each HPV-related cancer based on data accessed in 2018, looking at the period between 2008—2012.

Table 18: Burden of HPV-related cancers in NZ, 2008—2012, by sex (266)

| Anatomical site of Cancer | Incidence rate per 100,000/year |         |
|---------------------------|---------------------------------|---------|
|                           | Males                           | Females |
| Cervical                  | -                               | 7.9     |
| Anal                      | 0.6—1.0                         | 0.7—1.7 |
| Vulval                    | -                               | 1.0—2.4 |
| Vaginal                   | -                               | 0.7—1.0 |
| Penile                    | 0.1—0.6                         | -       |
| Oropharyngeal             | 3.3                             | 0.7     |

Elwood et al. published a comparison of oropharyngeal and oral cavity cancer trends between New Zealand and Queensland, Australia that reported the 2010 age-standardised incidence rate of oropharyngeal cancers among males in NZ to be 4.1 per 100,000 persons/year (267). They also report a doubling in oropharyngeal cancer incidence among males in NZ between in the past decade, with an estimated annual percentage change in the incidence of 11.9%, with this increase in incidence not found among females. However, the data were not disaggregated by sexual orientation and could not identify HPV-related oropharyngeal cancers separately due to utilisation of administrative medical databases and the limitations of ICD codes.

The increase in HPV-related oropharyngeal cancers in NZ was supported by a more recent study by Lucas-Roxburgh et al. (268) They retrospectively examined the HPV positivity of 267 stored oropharyngeal biopsies recorded on the NZ Cancer Registry between 1996 and 2012 and reported that the proportion found to be HPV-positive had increased over this time (AOR: 5.65, 95% CI: 2.60—12.30, p-value=<0.01). Of the included biopsies, 78.3% were from males, but no significant difference was found in the proportion that were HPV-positive between males and females (AOR: 1.36, 95% CI:0.68—2.66, p-value=0.38). The data collected in the Cancer Registry does not include sexual orientation, and therefore the results could not be disaggregated for GBM.

### HPV-related knowledge and HPV vaccine awareness and acceptability among GBM in Aotearoa New Zealand

There are no New Zealand data published on GBM knowledge of the HPV virus or related disease, nor are there data on GBM awareness or acceptability of the HPV vaccine. However, Chelimo et al. investigated these topics among a cross-sectional survey of undergraduate students undertaking tertiary healthcare education, of which 19% (n=38)

identified as male (269). Among these males, 66% reported having heard of HPV, 42% had heard of the HPV vaccine, and 66% would be willing to accept the vaccine for free. These findings were generally lower than the findings for females in the same study (n=159), of whom 65% reported having heard of HPV, 57% reported having heard of the HPV vaccine, and 90% would be willing to receive the vaccine for free.

### HPV vaccination coverage among GBM in Aotearoa New Zealand

The New Zealand National Immunisation Register (NIR) was created to record vaccine coverage, timeliness of scheduled dosage and was primarily focussed on childhood vaccinations. From 2013, some adult vaccines (Influenza, MMR and Tdap) delivered through primary care started to be recorded on the NIR, which also includes HPV vaccines given as part of the catch-up programmes for non-school aged females (270). The NIR collects data on gender, but it does not record sexual orientation. Therefore, data is available on vaccine coverage for males, but cannot be disaggregated for GBM.

As of December 2017, the MoH data on final dose coverage of the HPV vaccine among the female 2003 birth cohort was 67% (271). Males became eligible for vaccination in July 2017, but the data has not been reported at the time of writing, though estimates place the male vaccination coverage as equivalent to the female (217).

## Synthesis of Section 5: HPV in the Aotearoa New Zealand context

- Data are available for males in NZ covering a range of HPV-related data none are disaggregated by sexual orientation.
- Data available for GBM are limited to self-reported AGW diagnoses.
- Data collected through administrative clinical datasets are not disaggregated by sexual orientation, and as a result, HPV vaccination coverage and diagnosed HPV-related disease cannot be presented for GBM in NZ.
- There are no published data on the knowledge of HPV-related diseases affecting males among GBM in NZ.
- Until 2017, the HPV vaccine has been promoted as a “cervical cancer vaccine” as only females have been eligible for funded vaccination, reflected in the lower acceptability reported by Chelimo et al. among males in their study (272).
- As of July 2017, males up to the age of 26 years are eligible for funded Gardasil9 vaccination in NZ (273). However, data on sexual orientation are not collected in the National Immunisation Register (NIR) dataset.



## Summary of Chapter Two: Review of the Literature

### **Biological basis of HPV risk among GBM:**

- Transmission of HPV is through direct skin-to-skin contact.
- The anal transformation zone increases GBM vulnerability to anal HPV infection during anal intercourse.
- Repeat and persistent infection with HR-HPV types increase risk of developing HPV-related cancers.

### **Considerations for thesis approach:**

- Detection of HPV infection requires collection of cellular samples for PCR analysis from site of infection: swabs for penile and anal, and rinse for oral.
- Quantifying HPV-related disease burden relies on presentation, testing, diagnosis and recording in administrative health databases.
- Sexual orientation has various dimension that can be measured. Decisions on which measure to use must be driven by the research question.
- Cross-sectional convenience samples, routinely used in behavioral surveillance, recruit large and diverse samples of GBM with statistical power to detect between group differences.

### **Demonstrating need among GBM:**

- Few published studies describe HPV infection among GBM. Of those that do, studies describing anal HPV infection prevalence are the most extensively published compared to oral and penile infection.
- Among GBM, HPV infection is common, particularly at the anal site and among GBM PLHIV. However, infection with HR-HPV type 16 is comparatively rare.
- AGWs is the most commonly reported HPV-related disease among GBM.
- Anal HPV-related cancers are the most commonly reported HPV-related cancer among GBM, compared to HPV-related cancers at the oral and penile sites.

### **Interventions to prevent HPV infection, development of disease, and treat HPV-related disease:**

- Few studies in the published literature explore treatment for HPV-related disease among GBM.
- Barrier prevention methods such as condoms are not fully effective.
- Regression of AGWs and anal HSIL HPV-related anal cancers is common.
- HPV vaccination offers the most effective intervention for the prevention of HPV-related disease among GBM.
- Knowledge of HPV-related disease and HPV vaccination are low among GBM in the published studies.
- The HPV vaccine is highly acceptable to GBM.
- The prevalence of HPV vaccination uptake remains low among GBM in the limited number of studies that have described this.

### **Adapting findings to the local context:**

- Data relating to HPV infection, related disease and vaccination are scarce in NZ.
- No published data were found relating to HPV-related knowledge, HPV vaccination awareness or acceptability, and HPV vaccination uptake among GBM in NZ.
- As of January 2017, all individuals aged 26 years and under are eligible for publicly funded HPV vaccination in NZ.

# Chapter 3: Human Papillomavirus Vaccine Uptake among Gay, Bisexual and Other Men Who Have Sex with Men: A Systematic Review of the Literature

## Background

Gay, bisexual and other men who have sex with men (GBM) are a population that is particularly susceptible to HPV-related disease, anogenital warts and anal cancers (4, 274, 275).

Data on the true burden of disease experienced by this population are limited as sexual orientation, behaviours and identity are stigmatised and difficult to capture in a meaningful and representative way. Consequently, they are often not reported in national-level statistics such as hospitalisation data (276).

Globally, HPV vaccination programmes have traditionally been targeted as female-only, and much of the conversation around HPV-related disease focused on cervical cancer prevention, a significant and preventable source of morbidity and mortality for women.

In terms of public health, these programmes also had a secondary benefit of protecting the sexual partners of vaccinated women, and at a population level once a community-immunity threshold of women have been vaccinated. These programmes were also seen to be cost saving, protecting the population while only vaccinating half (277, 278). However, GBM gain little to no benefit from a female-only vaccination programme as their sexual partners are primarily or include males (4).

A number of countries have extended funded HPV vaccination to include all males due to increasing evidence surrounding the health inequity experienced by GBM with a female-only vaccination programme, the burden of HPV-related disease, and HPV vaccine efficacy among GBM and heterosexual males (213), and sub-optimal vaccine uptake among women (279). In the USA, HPV vaccination has been recommended for all males up to the age of 26 years to prevent anogenital warts since 2009, and among GBM up to the age of 26 years for the prevention of anal cancer precursors since December 2011 (280).

A vaccine that has been promoted as a female-only and “cervical cancer vaccine” may not be perceived as relevant to GBM. The concern is that among males eligible for HPV vaccine funding, but who are not captured through school-based vaccination programmes or are captured opportunistically through healthcare attendance, uptake could be lower among GBM. Studies have shown that while the HPV vaccine has high acceptability among GBM (281), there are relatively low levels of HPV-related disease knowledge or vaccine awareness among this population (237-239, 255, 282, 283).

Seven years after the recommendation for HPV vaccination to be provided to GBM up to the age of 26 years of age to prevent anogenital warts and HPV-related anal pre-cancers, this systematic literature review seeks to gather evidence of uptake among this population.

## Methods

### Research Question

What is the prevalence of HPV vaccination uptake among GBM?

### Aim

This systematic literature review seeks to collate and summarise existing evidence on the prevalence of HPV vaccination uptake among GBM.

### Registration of review

This review was registered at Prospero ID number: CRD42018107405

### Inclusion criteria

Items were included in the review if they:

- were written in English,
- presented data on HPV vaccination prevalence disaggregated by sexual orientation or sexual behaviour among males,
- were cross-sectional in design,
- were in the format of peer-reviewed articles, conference abstracts or posters, theses, and government or NGO reports.

### Exclusion criteria

Items were excluded from the review if they:

- were in a language other than English,
- did not present data on HPV vaccination uptake disaggregated by sexual identity or sexual behaviour among males,
- were randomised control trials, intervention studies, cohort studies, or computer modelling,
- were news stories, websites, blogs.

### Databases and grey literature

Due to the scope of the research question, data relevant to this review could be found from a range of sources that include both peer-reviewed publications and conference abstracts, as well as grey literature such as government and organisational reports.

### ***Databases searched***

- Medline (Ovid)
- Embase
- Cochrane Library
- Web of Science
- Scopus

### ***Grey literature databases searched***

- nzresearch.org.nz
- Australian Medical Index
- OpenGrey (Europe)
- New Zealand Ministry of Health
- World Health Organization
- Centers for Disease Control and Prevention
- Public Health England & Wales

### Development of search strategy

A set of key papers were collected that met the inclusion criteria described above. These were identified through online searches and identification within the references of these papers.

From these papers, a set of keywords and Medical Subject Heading (MeSH) terms were identified relevant to the research question. These were then used to develop search strategies for the various databases included in this review.

A three-stage search strategy was developed. Firstly, a combination of keywords and MeSH terms were used to search Medline and Embase, while key words linked with Boolean operators were used to search Web of Science, Cochrane and Scopus databases.

For government, organisational, and other grey literature databases, systematic or advanced search terms are not available. Most often these utilise word-matching algorithms, meaning that all words included in a string are searched for individually and results applied – this can lead to an overwhelming number of results for long strings, most of which are irrelevant to the search topic. In these cases, the search was limited to a few key terms:

- HPV/"human papillomavirus" (if quotations allowed)
- Vaccine/vaccination
- Gay/Homosexual/Men/MSM (depending on the website)

- e.g., NZ MoH had few “men”-related pages, while PHE had thousands, but PHE used the term “MSM” allowing the focus to be narrowed

Lastly, abstracts from recent key conferences that could include HPV-related research were searched. These included: International Papilloma Virus Conference (2017 and 2018) and the 2017 Australasian Combined HIV/AIDS and STI Conference.

A restriction to only items published in the English language was placed on the search strategies where possible.

### ***Search strategy***

Below is the keyword search strategy used for Medline broken down into the PICO categories:

#### *Population*

- ((gay OR bisexual OR homosexual OR queer) AND (men OR male OR males)) OR
- (MSM OR “men who have sex with men” OR “sexual orientation”)

#### *Intervention*

- (HPV OR “human papillomavirus” OR papillomavirus OR “human papilloma virus”) AND
- (vaccine OR vaccination)

#### *Comparison*

- Not applicable

#### *Outcome:*

- (uptake OR coverage OR prevalence)

Table 19 shows the full search strategy used for Medline, including keywords, MeSH terms and the results returned for each search line.

Table 19: Search strategy for Medline including keywords and MeSH terms

| Search # | Search Statement  | Result items |
|----------|---|--------------|
| 1        | gay.mp.   | 9567         |
| 2        | bisexual.mp.  | 7281         |
| 3        | homosexual.mp.  | 9128         |
| 4        | queer.mp.   | 912          |
| 5        | 1 or 2 or 3 or 4  | 19987        |
| 6        | men.mp. or MEN/   | 462583       |
| 7        | Male/   | 7903444      |
| 8        | 6 or 7  | 7976183      |
| 9        | 5 and 8   | 16527        |
| 10       | "Sexual and Gender Minorities"/   | 1206         |
| 11       | "men who have sex with men".mp.   | 9261         |
| 12       | 9 or 10 or 11   | 24270        |
| 13       | Papillomaviridae/ or "human papillomavirus".mp.   | 41447        |
| 14       | Vaccination/ or Vaccines/ or vaccin*.mp.  | 343040       |
| 15       | uptake.mp.  | 349339       |
| 16       | coverage.mp.  | 110362       |
| 17       | PREVALENCE/ or prevalence.mp.   | 618400       |
| 18       | 15 or 16 or 17  | 1065398      |
| 19       | 14 and 18   | 30067        |
| 20       | VACCINATION COVERAGE/   | 246          |
| 21       | PAPILLOMAVIRUS VACCINES/ or HUMAN PAPILLOMAVIRUS RECOMBINANT VACCINE QUADRIVALENT, TYPES 6, 11, 16, 18/ | 6527         |
| 22       | 19 or 20 or 21  | 34818        |
| 23       | 12 and 13 and 22  | 166          |
| 24       | limit 23 to English language  | 160          |

## Item selection

Search results were exported to EndNote(X8) and the duplicates removed within and between databases. Grey literature search results were copied and pasted to Excel, with separate sheets for each database. The full text was then retrieved for the included studies.

## Data extraction and quality assessment

Items were critically appraised using the STROBE checklist for cross-sectional studies and, for each study, the "Quality Assessment Tool for Quantitative Studies" form produced by the Effective Public Health Practice Project was completed (284). Using this tool, the studies

were assessed for their quality of evidence (potential for bias and confounding, and external validity), though this was limited by the scope of the review being cross-sectional data.

Subsequently, the following data were extracted: year of publication, year of recruitment, country of study, population recruited, age range, sexual orientation/proportion identifying as GBM, sample size, vaccination uptake among GBM, study design, and quality of evidence (strong, moderate, weak).

Where multiple studies were published using the same study population sample, the study containing the total study population and data relevant to the research question was included. For periodic surveys, such as the NHBS Survey, each item was included where they sampled at different time points.

The measurement of vaccination prevalence was considered to be the proportion of those in the sample who reported receiving at least one dose of the HPV vaccine rather than completion of the vaccination schedule. The distinction between receiving one dose and completing the schedule is not made in some studies, meaning that vaccination prevalence is likely an overestimate of the vaccination completion rate.

Six studies provide stratification of the sample based on sexual orientation with the majority of these men identifying as gay/homosexual. Classification of GBM was self-reported in the majority of studies either as sexual identity or having engaged in sex with another man. For seven studies, this was part of the eligibility criteria for participants. For the study by Moores et al., it was assumed that all males attending the sexual health clinic specifically for GBM were indeed GBM, and this was not a sociodemographic variable that was reported in the study (285).

# Results

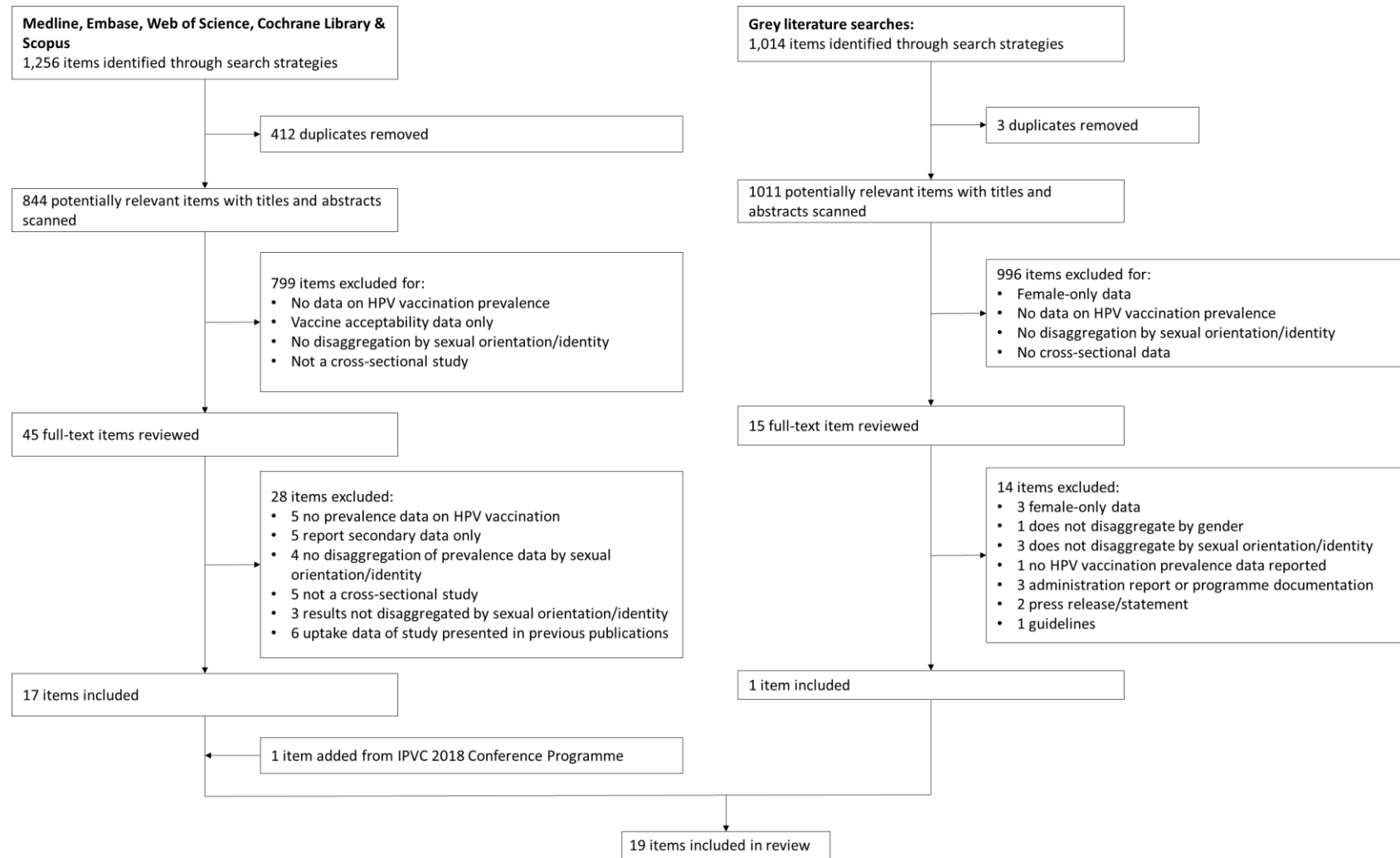


Figure 14: Flow diagram of literature screening and selection process



## Study selection

Figure 15 shows that a total of 2,270 items were returned through the various searching strategies, with 60 full-text items reviewed, resulting in 18 items being included in the review. Additionally, through the searching of relevant conference programmes, a single item was identified for inclusion, leading to 19 records meeting the inclusion criteria.

## Study characteristics

The studies were conducted in four high-income countries (14 USA, 2 UK, 2 Canada, 1 Hong Kong/PR China) and specifically sought to recruit GBM or disaggregated the sample by sexual behaviour or identity (*see Table 20*).

Each study employs a cross-sectional approach. However, the recruitment methods, site of recruitment, year of recruitment, and data collection methods vary across the 19 studies. The pilot study by Iyenger et al. was included in the review as it took a cross-sectional approach to the monitoring of HPV vaccination uptake among GBM while simultaneously assessing the feasibility of offering HPV vaccination through sexual health clinic settings in the UK, which has since been implemented.

Three of the 19 studies (16%) recruit males over the age of 26 years and do not provide an estimate of HPV vaccination prevalence among those aged 18-26 years for whom the vaccine is recommended, one of which is the UK pilot study using the UK eligibility criteria for funded HPV vaccination of GBM up to the age of 45 years. The remaining studies recruit GBM up to the age of 26 years or separately report HPV vaccination prevalence for this age range.

Year of recruitment is of particular importance in the context of understanding vaccination prevalence among USA GBM, with HPV vaccination being recommended for all males up to the age of 26 years as of 2009 and specifically for GBM at the end of 2011. The 14 studies from the USA included in this review recruited GBM across the period of 2011-2017. In Canada, Hong Kong and the UK, HPV vaccination had not been implemented when the studies included in this review were conducted.

The measurement of vaccination prevalence varies across the studies, with the majority reporting those who had received “any dose”, had “initiated” or had “ever received” HPV vaccination. Eight studies do not make a distinction between HPV vaccination schedule initiation and completion.

Table 20: Characteristics of the studies and study populations describing the prevalence of HPV vaccination uptake among GBM

| Author             | Year published | Year of recruitment | Country             | Population  | Age range (mean)              | Sexual orientation/identity/behaviour (% GBM)                            | Sample size   | Vaccination uptake GBM (%)                             | Study design   | Quality of evidence |
|--------------------|----------------|---------------------|---------------------|---|-------------------------------|--|---|--|--|---------------------|
| Choi (286)         | 2018           | 2014—2015           | Hong Kong, PR China | Students from 4 Hong Kong universities  | Males, under the age of 22yrs | Self-report<br>Bisexual or homosexual: 4.5% (13%)                        | N=888<br>All male: 306<br>GBM: 40   | Yes: 1/36 (2.6%)<br><br>Unsure: 3/39 (7.7%)            | Cross-sectional  | Weak                |
| Cummings (257)     | 2015           | 2011                | USA                 | Online survey, MSM dating website   | 18-26yrs (22.5)               | Self-report<br>100%<br>Hetero=0.4%<br>Homo/gay=78%<br>Bi=19%<br>Other=3% | N=1457  | Any does: 98/1457 (6.7%)                               | Cross-sectional  | Moderate-weak       |
| Daniel-Ulloa (287) | 2016           | 2013                | USA                 | National Health Interview Survey  | 18-30yrs                      | Self-report<br>1.5% (3.4%)   | N=6444<br>Male: 3003<br>GBM: 101  | Initiated: 8/101 (7.9%)<br><br>Completed: 3/101 (3.0%) | Cross-sectional  | Moderate            |
| Fisher (288)       | 2016           | 2013                | USA                 | New Orleans residents completing National HIV Behavioral Surveillance (NHBS) Survey | 18-26yrs                      | Self-report<br>GBM: 217<br>Bisexual: 170<br>Gay: 3<br>Mi:39              | N=358<br><br>Eligible for HPV=217<br><br>Answered identity and vaccination =208 | Ever received HPV vaccination: 31/208 (14.9%)          | Cross-sectional, venue-based                               | Moderate-weak       |
| Fontenot (289)     | 2016           | 2014-2015           | USA                 | Focus groups, Boston health centre LGBTQ youth-group/space                          | 18-26yrs (20.8)               | Only YMSM eligible for study=100%  | N=34  | Vaccine initiated 20/34 (58.8%)                        | Cross-sectional survey, focus-group, community recruitment | Weak                |

| Author        | Year published | Year of recruitment  | Country | Population  | Age range (mean) | Sexual orientation/identity/behaviour (% GBM)  | Sample size | Vaccination uptake GBM (%)   | Study design  | Quality of evidence |
|---------------|----------------|----------------------|---------|---|------------------|--|-------------|--|---|---------------------|
| Gerend (290)  | 2016           | 2014-2015            | USA     | Geospatial smartphone dating app for MSM                      | 18-26yrs         | Eligible if identify as gay/bi or ever had sex anal with man = 100%<br><br>Gay=254 (75.6%)<br><br>Bi=37 (11.0%)<br><br>Other=14 (4.2%)<br><br>Missing= 31 (9.2%) | N=336       | Any dose: 70/336 (20.8%)   | Cross-sectional, online survey  | Moderate-weak       |
| Gorbach (291) | 2017           | 2012-2014            | USA     | YM-HPV Study, 3 STD clinics LA and Chicago                    | 18-26yrs         | Eligible if assigned male at birth and identify as GBM or engaged in oral/anal sex with a man= 100%  | N=1033      | Any dose: 111/1033 (10.7%)<br><br>Complete: 37/1033 (3.6%)<br><br>Unsure: 225/1033 (21.8%) | Cross-sectional, clinic-based, confidential computer-assisted interview     | Moderate-weak       |
| Iyanger (292) | 2017           | June 2016-March 2017 | UK      | GBM attending 42 sexual health and HIV clinics across England | 16-45yrs         | Self-reported = 100%   | N=18,875    | Any dose: 8580/18875 (45.5%)   | Pilot study, cross-sectional, opportunistic recruitment of clinic attenders | Moderate            |

| Author       | Year published | Year of recruitment | Country | Population   | Age range (mean) | Sexual orientation/identity/behaviour (% GBM)   | Sample size                 | Vaccination uptake GBM (%)                                  | Study design  | Quality of evidence |
|--------------|----------------|---------------------|---------|--|------------------|---|-----------------------------|---|---|---------------------|
| Jones (293)  | 2016           | 2012–2013           | USA     | Kentucky. A convenience sample survey of local LGBT. Online survey distributed through LGBT social media, posters, and LGBT print media. | 18-64yrs         | GBM: 136<br><br>Sexual partners of men:<br>All men: 93 (68%)<br>Mostly men 29 (21%)<br>Both men & women 11 (8%)<br>Mostly women 3 (2%)<br>All women 0 | N=218<br>GBM: 136 (62%)     | Among males in sample 19-26yrs: 78 (10.3%)                  | Cross-sectional, survey completed online or paper-based | Moderate-weak       |
| Kahle (294)  | 2017           | 2012                | USA     | Online survey using banner ads, social media, and peer referral. Sexually active.  | 18yrs+           | Eligible if male and ever had oral/anal sex with man = 100%   | N=2794                      | Total sample: 205/2794 (7%)<br><br>18-26yrs: 154/1098 (14%) | Cross-sectional, online convenience sample              | Moderate-weak       |
| Little (246) | 2015           |                     | Canada  | Survey at student health clinics at two Greater Vancouver universities and two colleges. Targeting males                                 | 19-26yrs         | Self-reported<br>Homosexual or gay: 12 (6.9%)<br><br>Bisexual: 9 (5.1%)<br><br>Other: 3 (1.7%)  | N=175<br>GBM: 24 (13.7%)    | GBM vaccinated: 4/24 (16.7%)                                | Cross-sectional, convenience sample, clinic-based       | Weak                |
| Mansh (295)  | 2016           | 2013-2014           | USA     | National Health Interview Surveys  | 18-26yrs         | Self-identified.<br>Not given   | N=4119<br>GBM: not provided | Hetero: 8.3%<br>GBM: 12.7%                                  | Cross-sectional,  | Moderate            |

| Author       | Year published | Year of recruitment | Country | Population   | Age range (mean) | Sexual orientation/identity/behaviour (% GBM)                     | Sample size              | Vaccination uptake GBM (%)   | Study design  | Quality of evidence |
|--------------|----------------|---------------------|---------|--|------------------|---|--------------------------|--|---|---------------------|
| Meites (296) | 2014           | 2011                | USA     | National HIV Behavioral Surveillance System.<br>Trained interviewers used handheld computers to administer, in English or Spanish, a standardized, anonymous questionnaire | 18+yrs           | Eligible if male and ever report having a male sex partner = 100% | N=9819<br>18-26:<br>3221 | Total:<br>262/9819<br>(2.7%)<br>18-26:<br>157/3221<br>(4.9%)   | Cross-sectional, venue-based, time-space sampling at locations where MSM congregate, such as bars, clubs, and social organizations. | Moderate            |
| Meites (297) | 2018           | 2017                | USA     | Vaccine Impact in Men (VIM) study enrolled MSM and transgender women in Seattle, Chicago, and Los Angeles.   | 18–26 years      | Eligible if MSM or transwoman 100%                                | N=693                    | Any dose:<br>276/693<br>(39.8%)<br><br>All three doses:<br>140 (20%),<br><br>Unvaccinated:<br>274 (39.5%)<br><br>Unsure:143<br>(20.6%) | Cross-sectional, clinic-based   | Moderate-weak       |

| Author            | Year published | Year of recruitment | Country | Population  | Age range (mean) | Sexual orientation/identity/behaviour (% GBM)                | Sample size                                   | Vaccination uptake GBM (%)   | Study design  | Quality of evidence |
|-------------------|----------------|---------------------|---------|---|------------------|--|---|--|---|---------------------|
| Moore (285)       | 2015           | 2013-2014           | Canada  | Survey administered to men registering for STI testing services at a clinic specifically for MSM, Ottawa, Ontario | 18-69yrs (37)    | Recruited men attending MSM sexual health clinic = 100%      | N=280<br>n=272 completed vaccination question | 44/272 (16.2%)   | Cross-sectional, clinic-based, convenience sample   | Weak                |
| Nadarzynski (298) | 2018           | 2015                | UK      | Adverts on Facebook to MSM 16-26yrs. Participants encouraged to invite MSM peers.                                 | 14-63yrs (22)    | Self-reported (100%)<br>Gay= 93%<br>Bisexual= 5%             | N=1508<br>n=1420 answered vaccination         | Any dose: 43/1420 (3.0%)<br>Completed: 6/1420 (0.4%)<br>Unsure: 377/1420 (26.5%) | Cross-sectional, online convenience sample, snowball recruitment  | Moderate-weak       |
| Oliver (299)      | 2017           | 2014                | USA     | National HIV Behavioral Surveillance (NHBS) Survey.   | 18yrs+           | Eligible if male and report ever having sex with a man= 100% | N=10161<br>18-26yrs: n=2892                   | Any dose:<br><br>All GBM: 860/10161 (8.5%)<br><br>18-26yrs: 497/2892 (17.2%)     | Cross-sectional, venue-based, time-space sampling at locations where MSM congregate, such as bars, clubs, parks and social organisations. | Moderate            |

| Author         | Year published | Year of recruitment | Country | Population  | Age range (mean) | Sexual orientation/identity/behaviour (% GBM)             | Sample size   | Vaccination uptake GBM (%)  | Study design                         | Quality of evidence |
|----------------|----------------|---------------------|---------|---|------------------|---|---|---|--------------------------------------|---------------------|
| Reiter (300)   | 2015           | 2013                | USA     | Harris Interactive LGBT Panel, a subset of the Harris Poll Online Panel, a voluntary research panel constructed using online and offline recruitment strategies.    | 18-26yrs         | Self-identify (100%)<br>Gay=309 (72.2%)<br>Bi=119 (27.8%) | N=428   | Any dose:<br>56/428 (13%)   | Cross-sectional, online survey       | Moderate-weak       |
| Thompson (301) | 2016           | 2009-2013           | USA     | The National College Health Assessment (NCHA) II. A national survey that collects data at universities regarding health status, health behaviours, and perceptions. | 18-26yrs         | Self-reported<br>2013:<br>GBM=668/6244<br>(10.7%)         | N=107,716<br>2013:<br>n=6244<br><br>Male:<br>n=6244<br><br>Removed if reported "unsure" if received HPV vaccine | 2013<br>All males:<br>2677/6244<br>(42.9%)<br><br>Gay: 145/352<br>(41.2%)<br><br>Bisexual:<br>74/168<br>(44.1%)<br><br>Other: 59/148<br>(39.6%) | Cross-sectional, randomised sampling | Moderate            |

## Results of studies

Vaccination prevalence varied considerably across the studies, ranging from 2.6% to 58.8% (see *Table 20*). Of the studies included in the review, five studies were determined to provide “moderate” quality evidence, all of which were from repeat periodic surveys in the USA. Two present data from the National Health Interview Surveys (NHIS) (296, 302), two from the National HIV Behavioral Surveillance (NHBS) (287, 295), and one from National College Health Assessment (NCHA) (301). The NHBS surveys specifically recruit GBM, while both the NHIS and the NCHA seek to collect a representative sample of the study population, with GBM making up a proportion.

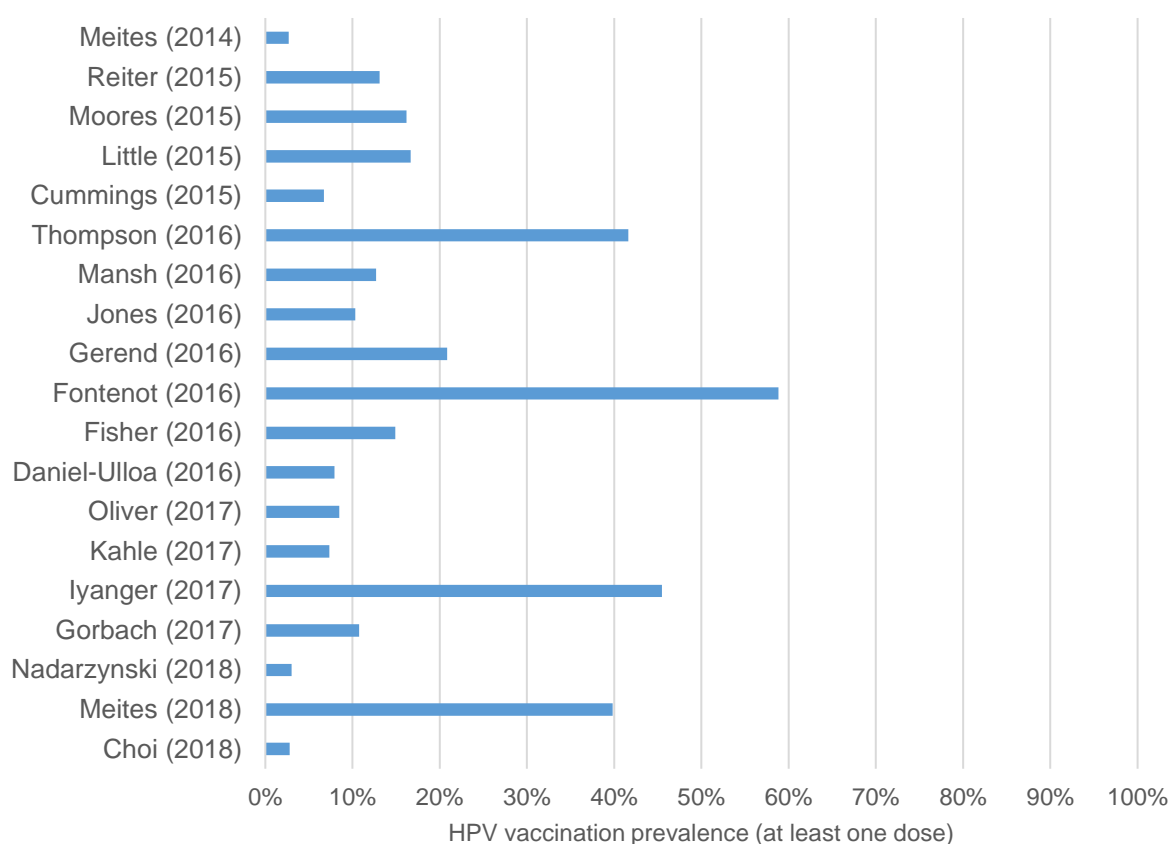


Figure 15: Prevalence of HPV vaccination uptake, any dose (%), among GBM, all ages, by year.

Overall, there does not appear to be a clear correlation between vaccination prevalence and the year in which the study took place (see *Figure 15*). However, the five studies identified above provide evidence of increasing vaccination prevalence among GBM over time in the USA. Daniel-Ulloa et al. and Mansh et al. utilise the NHIS in 2013 and 2014, respectively, though it is unclear from the abstract by Mansh et al. the difference between the population identified by Daniel-Ulloa et al. (287, 295). Daniel-Ulloa et al. found an HPV vaccination prevalence of 7.9% among the GBM in their 2013 sample, while Mansh et al. present a prevalence of 12.7% from their 2013-2014 sample. Meites et al. and Oliver et al. present



data collected through the NBHS surveys conducted in 2011 and 2013, respectively (296, 302). The prevalence of vaccination among GBM aged 18-26 years in the 2011 sample was 4.9% and 17.2% in 2013 sample. Additionally, Thompson et al. report data on HPV vaccination prevalence among GBM students attending tertiary institutions in the USA who took part in the NCHA surveys between 2009 and 2013, showing a statistically significant increase in HPV vaccination uptake among male students identifying as gay, bisexual or unsure over this period (301).

Three studies sampled GBM university/college students, each in a different country (USA, Canada and HK/China), and using a different sampling method. GBM students from the USA 2013 sample had greater vaccine uptake prevalence (41.6%) (301) compared to those in Canada and HK/China (16.7% and 2.6%, respectively) (246, 286).

Four studies recruited GBM through online social media or dating apps (298, 303-305). The earliest of these recruited GBM aged 18-26 years in 2011, reporting a vaccination prevalence of 6.7% (303). Of the three conducted in the USA, Gerend et al. report the greatest vaccination prevalence of 20.8% among their 2014-2015 sample of GBM aged 18-26 years (304).

Four studies recruited GBM through clinic-based services, two from the USA and one from Canada and the UK (285, 292, 297, 306). Iyenger et al. report the greatest prevalence of HPV vaccination uptake (45.5%) among GBM aged 16-45 years attending sexual health clinics in the UK. The men in this sample were receiving the vaccine at enrolment, compared to GBM in the other three studies who were asked to recall if they had received the HPV vaccine, demonstrated by the findings from Meites et al. with 20.6% of the men in their sample reporting being unsure if they had been vaccinated against HPV (297).

Thirteen studies were identified that reported findings for GBM aged 26 years and younger, for whom the vaccine is recommended. Of those studies, 11 were undertaken in the USA, and vaccination prevalence ranged between 2.8%—58.8% (see *Figure 16*).

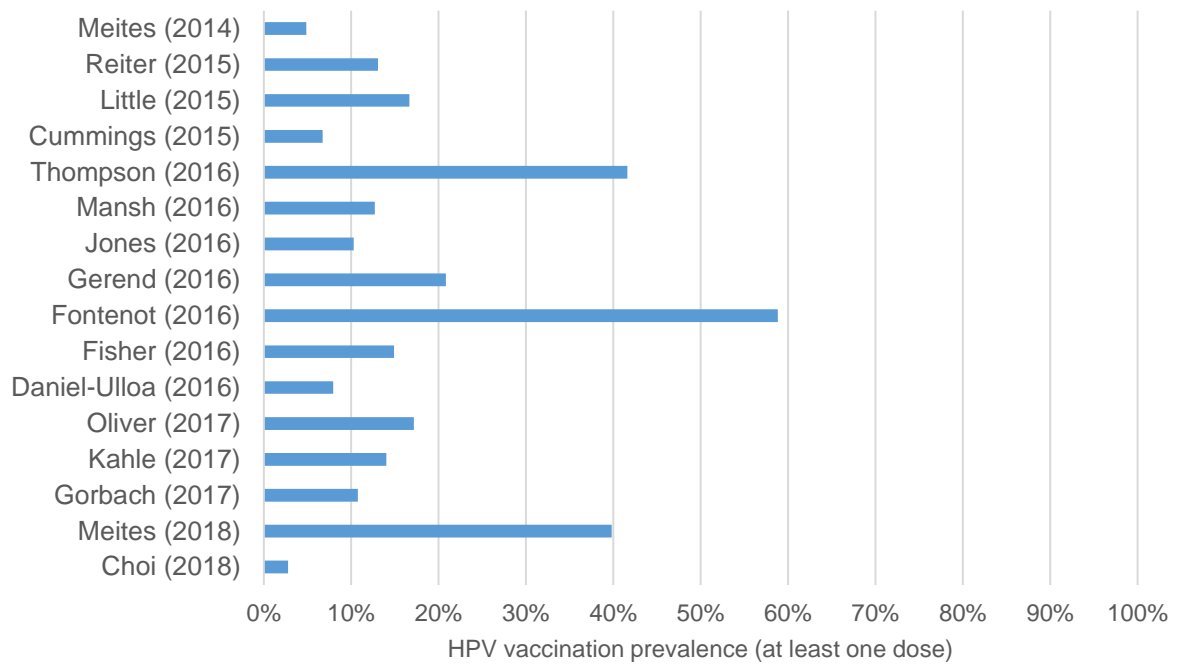


Figure 16: Prevalence of HPV vaccination uptake, any dose (%), among GBM aged under 26 years, by year.

### Risk of bias across studies

The studies included in this review are all cross-sectional, and therefore subject to the inherent bias associated with this study design. Using the “Quality Assessment Tool for Quantitative Studies”, cross-sectional studies could not attain a quality rating greater than “Moderate” across the sections applicable to cross-sectional studies (selection bias, study design, confounders, and data collection methods).

Due to the nature of the research question, which sought to identify the prevalence of HPV vaccination among GBM, the study design most suited to capture these data is cross-sectional. While appropriate, this study design is at greater risk of bias depending on the methodology used. These studies are subject to recruitment and selection bias as participants are not randomised once enrolled, meaning the representativeness of the sample relies on the recruitment method and controlling of confounders in analyses. Of the studies included in this review, eight demonstrated methodology that sought to reduce recruitment and selection bias through some form of randomisation to select participants, standardised and repeatable recruitment methods, seeking to recruit a large and diverse sample of the population being studied, and capturing data to control for known confounders in the analyses.

The measure of HPV vaccination prevalence included those who reported receiving any dose of the vaccination schedule, meaning that vaccination prevalence estimates within

these studies are likely an over-estimate of true HPV-vaccination completion, and therefore protection among GBM populations included in the review.

However, this may be offset by the majority of studies asking GBM to self-report HPV vaccination status, which is subject to recall bias. This is demonstrated in the study by Meites et al., where 20.6% of their sample report being unsure if they have received the HPV vaccine (297). This could lead to underestimating HPV vaccination prevalence among these samples, particularly when males receive the HPV vaccine earlier in childhood through school-based vaccination programmes that can often include vaccinations against other diseases.

The majority of studies limit the population to those aged 18-26 years, those eligible to participate in studies without parental consent and the upper age limit for HPV vaccination recommendation in the USA, either during study recruitment or in analyses. This will likely underestimate the true prevalence of HPV vaccination uptake among vaccine eligible GBM, particularly in countries that focus on school-based vaccination programmes, such as Canada, New Zealand and Australia. Conversely, these studies do not sample GBM outside the vaccine eligible age cohorts, resulting in an overestimation of HPV vaccination prevalence among the GBM population, as a whole.

The sample of GBM in the studies by Choi et al., Fontenot et al., and Little et al. are considerably smaller than other samples of GBM within the review, limiting the external validity and statistical power to show differences among those who have or have not received the vaccine.

Almost all studies in this review rely on self-reported identification as GBM or engaging in same-sex sexual behaviour. Homosexual identity and same-sex sexual behaviour remain stigmatised even among countries with legal protections for these populations, meaning that these studies will be subject to participation and reporting bias based on social desirability to not identify as GBM. Men who do not identify as GBM may be more marginalised and less likely to engage with healthcare services and therefore be less likely to seek, be offered or accept HPV vaccination, potentially resulting in an overestimation of vaccination uptake prevalence in these studies due to these men not being included in the denominator.

As identified in Chapter Two, Section Two: Part Two, without the standardised collection of sexual orientation data in census or nationally representative datasets, it is difficult to ascertain the denominator against which a sampling frame for GBM can be created to recruit a sample of GBM large enough determine statistically significant differences between groups (e.g. by ethnic group).

## Discussion

### Overview

To the candidate's knowledge, this is the first study to systematically review HPV vaccination prevalence among GBM.

While the optimal level vaccination coverage among this population required to provide a community-immunity effect is uncertain, findings from this review indicate that vaccination uptake is considerably lower than those reported among female peers in the countries from which studies in this review have been conducted (279).

This is of particular concern for the USA where HPV vaccination has been recommended and available for all males up to the age of 26 years since 2009. Other countries included in this review had not provided the HPV vaccine to males or GBM at the time these studies were conducted, providing a partial explanation for the low vaccination prevalence seen.

### Strengths

Few limitations were placed on the search strategies with the exception of English language, decreasing the potential for relevant items being excluded from search results. Given the research question's scope, a further restriction could be to limit the inclusion of items published post-2009 as this is the year that HPV vaccination was first approved for males. However, no items included in the review were published before 2009, indicating that this approval partly drove research on HPV vaccine uptake among GBM.

The review searched a diverse range of online databases, covering peer-reviewed journals, conference abstracts and grey literature. The inclusion criteria reflected the research question's scope, seeking data from community, national, and global levels.

Search terms were inclusive and returned a large selection of material against which robust selection criteria were applied to identify relevant items. Inclusion of terms such as "sexual orientation" led to capturing items with data on GBM where they were not the primary study population.

The wider public health organisations included in the secondary search strategy capture data and monitor vaccine uptake globally, which would enable the review to include items based on these data or have been translated into English. However, the search returned few items that met the inclusion criteria for this review, which is likely a reflection of the limitations discussed below.

## Limitations

At the time of writing, few countries have implemented HPV vaccination for males or specifically for GBM, limiting the amount of research on this subject and data collected by government or non-government organisations. Grey literature and public health organisation databases were included in the search strategy for this review, but few countries can provide vaccination coverage or uptake data among males, and fewer still collect linked data that would allow disaggregation by sexual orientation.

Search terms differed between sites used in the secondary search strategy due to search functionality on the websites and databases searched. The inability to use the complete search strategy combining all the keywords and statements may mean that relevant items were missed across the various sites. Doing a single search for each term and combining the results could overcome this but would result in a large number of irrelevant items that would need to be reviewed.

A number of items returned from the secondary search strategy of organisational websites linked to other material or collections, and it was not immediately clear from scanning the abstract what these links contained. As these links contained secondary material, it was decided that they would be excluded early in the review process. However, there could be relevant material within these links for the review that might be included in a tertiary search process.

## Discussion of results

Results demonstrate that tracking changes in HPV vaccination uptake among GBM is problematic if done in an opportunistic and non-systematic approach. However, the strongest data come from repeat studies conducted in the USA designed to monitor HIV-related behavioural change over time among GBM. Though these data have their limitations and findings cannot be generalised to the wider GBM population of the USA, by keeping biases consistent in each round, they can provide a robust estimate and demonstrate significant changes in prevalence over time.

Additionally, for the USA, these data are limited as they do not provide the statistical power required to identify differences by sociodemographics within states, which could then inform targeted public health action to address inequities.

The delivery of the vaccination and those eligibility criteria for vaccination can vary by country or state, such as private insurance and healthcare providers in the USA, and through publicly funded school-based vaccination programmes in Australia. The results from the USA must be considered in the context of the health system in place in this country. Access to health insurance, and therefore healthcare, is likely to be a major determinant of HPV vaccination.

This is illustrated when comparing the findings of Oliver et al. from the 2014 NHBS survey and those of Thompson et al. from the 2013 NCHA survey (301, 302). The NHBS surveys recruit a diverse range of GBM from across the USA through GBM-associated venues, and the NCHA surveys use a random sampling method to recruit among those attending tertiary education. Among GBM of the same age group (18-26 years), a vaccine prevalence of 17.2% and 41.6% was recorded by Oliver et al. and Thompson et al., respectively. Despite differences in recruitment methodology, these findings point to the difficulties in achieving equitable vaccination coverage when provided through non-publicly funded healthcare and a non-school-based vaccination programme.

The USA (2009) and Australia (2013) made HPV vaccination available for males earlier than other countries. In Australia, vaccination is fully-funded by the federal government and provided through schools or primary care at no additional cost to the individual up to the age of 19 years, but while the vaccine is recommended for all GBM with no age restrictions, it is not publicly-funded for those over the age of 19 years (307). Compared to the USA, where vaccination is recommended for males up to the age of 26 years, but eligibility for vaccination provision may vary by individual insurance providers and programmes. This may partially explain Australia's lack of published data despite being an early implementer of male HPV vaccination. Those males aged 19 years in 2013 will have reached the age of 24 years in 2018 (the time this review was conducted), limiting the number of GBM able to participate. Those vaccinated through school-based programmes in 2013 will have reached the age of 18 in 2018. Therefore, it will be some years before the population-level impacts of a gender-neutral vaccination programme is seen among GBM.

It is recommended that HPV vaccination be provided at an early age to be most effective and ideally before sexual debut, further limiting the number of countries that could estimate HPV vaccination uptake among GBM. For those countries that have implemented or recommended HPV vaccination for males, the time since HPV vaccination programme implementation will limit the age of vaccinated cohorts eligible to participate in research studies and outwardly identify as GBM or have engaged in same-sex sexual behaviour.

While HPV vaccination is recommended for all males for the prevention of anogenital warts, it is specifically recommended for the prevention of anal HSIL and anal cancer among GBM. The recommendation for the prevention of more serious disease among GBM may motivate healthcare providers to be more proactive in recommending or encouraging vaccination of patients they know to be GBM. However, disclosure of sexual orientation to healthcare providers is complex and not all GBM will feel safe or comfortable to do so, which could mitigate the overall effect (115). However, the study by Thompson et al. included in this review indicated no difference in HPV-vaccination uptake among all males in their 2013

sample of college attendees and those identifying as non-heterosexual (301). Conversely, Agenor et al. report that GBM are more likely than heterosexual males to report HPV vaccination in the 2013-2014 rounds of the National Health Interview Surveys (308).

## Conclusions

Overall, vaccination uptake among eligible GBM in the studies included in this review is sub-optimal to convey possible herd immunity effects for HPV-related disease within these populations (216). The majority of GBM in these samples were unvaccinated, despite being eligible for the HPV vaccine, and therefore at risk of acquiring and developing HPV-related disease.

While country-level reporting of HPV vaccination prevalence is disaggregated by gender, it is not available by sexual orientation. It is unlikely that a true prevalence of HPV vaccination uptake among GBM can be ascertained through the current methodology and routine data collection, as illustrated by the heterogeneity of estimates across years presented in this review. Therefore, research that uses a systematic and repeated sampling of GBM populations can and should be used to provide evidence of changes and trends over time to inform public health action.

# Chapter 4: HPV infection prevalence among males in Aotearoa, New Zealand

## Section One: Methods: Feasibility Study of HPV Infection Prevalence among Males

### Introduction

The HPV Infection among Males Study (HIMS) is a cross-sectional feasibility study. The study measures oral and anal HPV infection, HPV-related knowledge, and HPV vaccine acceptability and uptake among males aged 16-49 years recruited through non-random purposive sampling with quotas at outpatient and primary healthcare clinical settings in Auckland, NZ.

The study was conducted at the Department of Social and Community Health and the Department of General Practice and Primary Health Care, both within the Faculty of Medical and Health Science at the University of Auckland. Funding for the study was provided through the Feasibility Research Grant from the Health Research Council of New Zealand (grant number: #14/572) (309).

### Candidate's involvement

The candidate was involved in the study conception, development, design, protocol development, application to funding bodies, and initial application for ethical approval. The majority of this foundational work occurred prior to the candidate's official enrolment into the PhD programme. Regulatory body approval, study consultation, subsequent changes to study procedures and protocol, additional ethical approval, study fieldwork, data cleaning and analyses, and report production were conducted principally by the candidate within the PhD enrolment period (*see Co-authorship Form*).

The candidate was supported in the study conception, ethics and funding applications, study material and protocol development, data analyses, and report production by Dr Peter Saxton, Dr Helen Petousis-Harris, Dr Mark Thomas, Dr Nikki Turner, and Prof Bruce Arroll. Dr Helen Petousis-Harris was the Principle Investigator for this feasibility study.

### ***Study settings and laboratory involvement***

At Auckland District Health Board (ADHB) Adult Infectious Disease Outpatient Clinic at Auckland City Hospital, Dr Rupert Handy and Dr Steve Richie acted as advisors in the development of study protocols at this setting and ensured quality control throughout the study recruitment period.



At Auckland Sexual Health Services (ASHS), also part of ADHB, Dr Murray Reid and Nurse Practitioner Suzanne Werder acted as site leads and ensured quality control for the HIMS study protocols. Clinical Directors Dr Nicky Perkins and Dr Sunita Azariah acted as advisors in the development of study protocols for the ASHS site.

At Freemans Bay Medical Centre (FBMC) general practice, Dr Alison Copland was responsible for study enrolment, quality control for study protocols and advised on study protocol development for the general practice setting. Practice manager Rebecca MacCormick ensured quality control and delivery of participants' biological samples to LabPlus for processing and analysis.

At LabPlus diagnostic laboratory at Auckland City Hospital, Dr Fahimeh Rahnema and Dr Kitty Croxson were responsible for laboratory protocols, conducting and the quality assurance of the HPV PCR testing. Dorothy Schumack, Ross Hewett and Daniel Wong acted as advisors in setting up the laboratory protocols and supplies, and also ensured that participants' biological samples delivered from ADHB settings, and externally from FBMC, were processed correctly.

### Feasibility study design and rationale

Studies examining HPV infection prevalence among GBM and other males, explored in Chapter Two: Section Three: Prevalence of HPV infection and related disease among GBM, utilise sexual health and other clinical settings that facilitate the collection of biological samples. Other established study methods for recruiting GBM include sampling from community settings frequented by GBM and online opportunistic sampling, as seen in studies examining HPV-related knowledge among GBM (*see Chapter Two, Section Two: Part Two*). However, collection of biological specimens through community and online settings is difficult and untested for the study of HPV infection prevalence.

A feasibility study design was utilised for HIMS for the following reasons:

- Uncertainty and limited local evidence of recruiting males, particularly GBM, for HPV infection prevalence studies:
  - Difficulties in collecting biological samples in GBM community settings, such as gay bars and fair days, particularly for anal sampling.
  - Difficulties with recruiting heterosexual males as a comparison group for biological sampling, with concerns around the acceptability of anal sampling among this population.
  - Limited evidence of comparability of effectiveness in self-collected versus clinician-collected samples for anal sampling at the time of study conception.
  - HPV seroprevalence studies underestimate HPV infection point prevalence.

- No clinical guidelines or routine testing for the diagnosis of HPV infection at the time of the study.
  - No laboratory offering testing for the detection of HPV infection in NZ.
  - Feasibility of setting up laboratory procedures and processes for the study of HPV infection.
  - No guidelines for collection or storage of oral and anal samples for detection of HPV infection.
  - Limited data for laboratory testing of oral and anal HPV infection.
  - The expected prevalence of HPV infection at different anatomical sites for GBM could not be provided for power calculations.
- Limited local study data relating to the recruitment of GBM participants through outpatient and primary care settings.
  - The expected recruitment rate could not be provided for power calculations.

In critically reflecting on the potential uncertainties within the study methods, a feasibility study was envisioned to provide evidence to inform gaps in the methods for a larger study.

#### Feasibility study aims:

1. Provide power calculation estimates for a larger study:
  - a. Provide estimates for anatomical site-specific HPV infection prevalence among males attending study settings.
  - b. Provide recruitment rate estimates for males in outpatient and primary healthcare clinical settings.
2. Provide study process and protocol experience and feedback at various study settings:
  - a. Feasibility of laboratory testing for HPV infection, including sample delivery, processing and provision of results.
  - b. Feasibility of recruiting GBM through outpatient and primary healthcare settings.
  - c. Feasibility of conducting additional biological and questionnaire data collection through clinical services.

#### Setting

The setting for this project was three healthcare recruitment sites in the Auckland region: the Infectious Diseases outpatient clinic at Auckland City Hospital, the Sexual Health Clinic at Greenlane Clinical Centre, and the Freemans Bay Medical Centre (FBMC), an inner-city general practice. These sites were chosen on the basis of:

- 1) The Auckland region has been shown to have a higher population of GBM than other regions (113).
- 2) Clinical settings are also settings through which the HPV vaccine is delivered, specifically for catch-up vaccination programmes in NZ.
- 3) The Infectious Disease clinicians at Auckland City Hospital have a high caseload of GBM PLHIV.
- 4) The Sexual Health Clinic at Greenlane Clinical Centre has a high caseload of GBM, in addition to heterosexual males.
- 5) FBMC has a high caseload of GBM patients.
- 6) The investigating research group has a working relationship with the relevant clinical teams at Auckland City Hospital and the Greenlane Clinical Centre.

### ***General practitioner setting***

Formative research identified three general practices in central Auckland that historically have a high GBM caseload: CityMed, FBMC and Cairnhill Health Centre. Subsequently, ethics approval was gained, and an approach made to FBMC that was accepted. The acceptance was by a single general practitioner at the practice, Dr Alison Copland, with the support of Mrs Rebecca MacCormick, Practice Manager.

### **HIMS Consultation and ethics**

Consultation on this project was undertaken with Mr Maihi Makiha, the Community Engagement Officer Māori at the New Zealand AIDS Foundation (NZAF) representing both tangata whenua (*indigenous person with tribal ties to the local area*) and takātapui populations. Consultation was undertaken with Mr Bruce Kilminster, CEO of Body Positive, a non-government organisation (NGO) supporting PLHIV. Further consultation was undertaken with Dr Nicky Perkins and Dr Sunita Azariah, the Clinical Directors of the Auckland Sexual Health Services (ASHS), Greenlane Clinical Centre; and with Dr Rupert Handy, Clinical Director of the Infectious Disease Department at Auckland City Hospital. Each provided a letter of support for the ethics application process.

Ethics approval was gained through University of Auckland Human Participant Ethics Committee (Ref: 012721) on 1<sup>st</sup> October 2014. Further ethics approval was sought and gained through the Health and Disabilities Ethics Committee (HDEC) (Ref: 15/NTB/5) on the 12 March 2015 to meet the requirements of the ADHB Research Office. Approval for the study to be conducted in ADHB settings (Auckland City Hospital and Greenlane Clinical Centre) was gained through the ADHB Research Office on 17 March 2015.

Stakeholder meetings were undertaken with both staff of the relevant departments at Auckland City Hospital and Greenlane Clinical Centre in December 2014 to address potential

issues surrounding recruitment and the impact on the normal consultation process at these settings. Once she had accepted the invitation to participate in the study, a meeting was also undertaken with Dr Copland at FBMC in April 2015. Valuable feedback from stakeholders was received due to these consultation processes, and subsequent changes to the recruitment protocol were made. Changes to the procedure included: provision of shared Recruitment Sheets at ASHS, making study approach at the end of the consultation, provision of recruitment documents and signage to display in waiting rooms, and completion of the survey by the participant in the waiting room post-consultation to reduce the impact on consultation times.

### ***Recruiter training session***

Before study commencement, the candidate conducted a training session at each of the settings where recruitment for the study would be occurring. This was delivered by the candidate and covered all aspects of the study process: participant approach, information sheets, recording response rate, sample collection and delivery, questionnaire, and koha. Recruiting clinicians were provided with further opportunity to ask questions and provide feedback.

### **Study populations**

The study design was a cross-sectional feasibility study, recruiting specific populations through purposive sampling and quotas at the hospital and primary care settings. An overview of the study populations and quotas allocated to each study setting is shown in Figure 17.

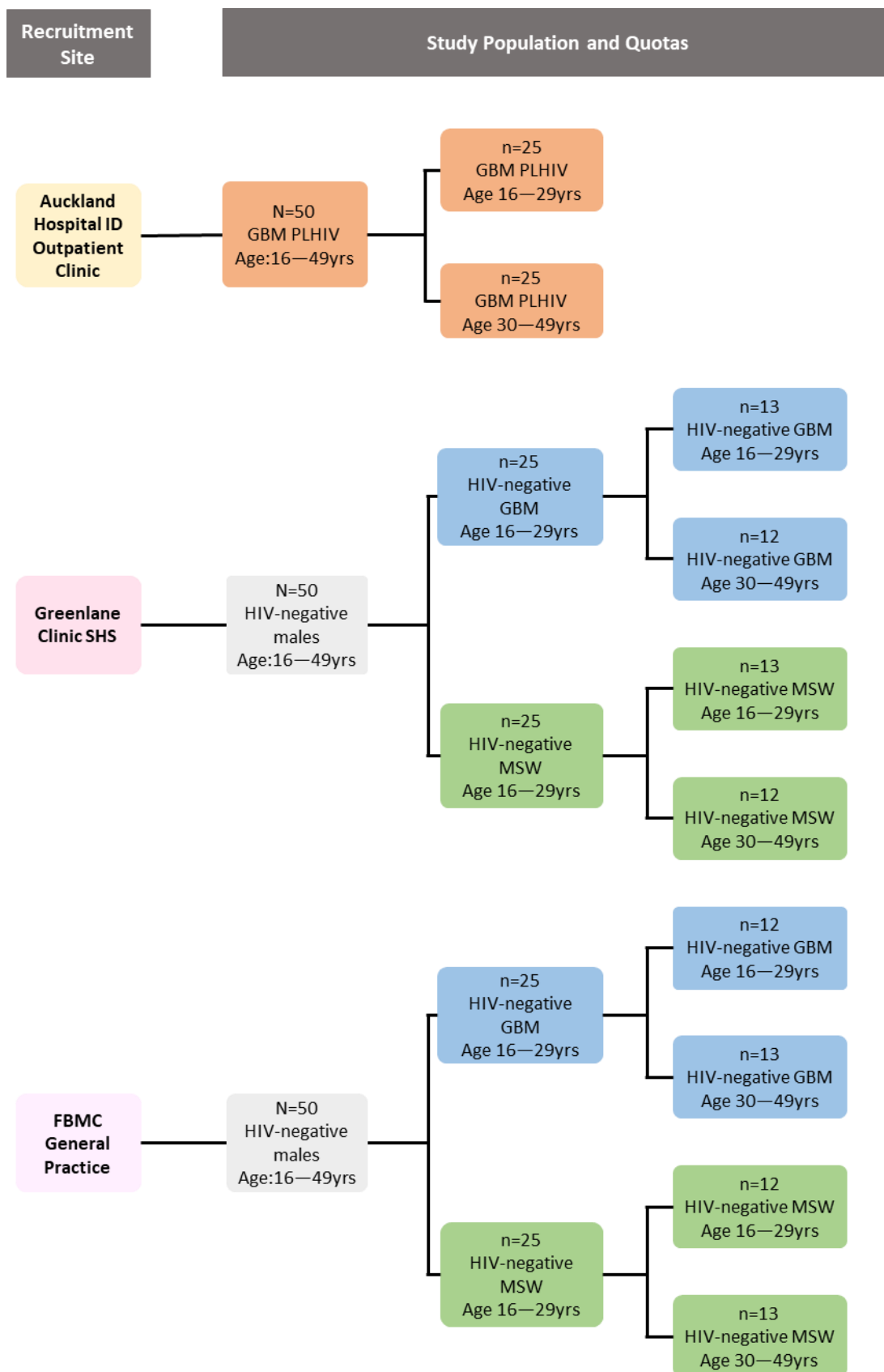


Figure 17: Flow diagram of HIMS feasibility recruitment populations and quotas by recruitment site.

### ***GBM PLHIV***

Clinicians at this setting were asked to recruit a sample of 50 GBM PLHIV participants, of whom 25 were to be 16-29 years of age and 25 were to be 30-49 years of age. It was known that all patients recruited at this setting were living with HIV, and clinicians did not ask this during eligibility screening. Participants at this setting were eligible if they were: born biologically and identified as male, identified as homosexual/gay/bisexual, between 16-49 years of age and resident in the Auckland region.

It was possible for GBM living with HIV to be recruited from the two other study sites. Therefore, HIV status was sought through the questionnaire to include in the data analysis. If a GBM participant recruited at these two other sites indicated that they were living with HIV, they were then included in the GBM PLHIV population during analysis, regardless of the site of recruitment.

### ***HIV-negative GBM***

Clinicians at Greenlane Clinical Centre and FBMC were asked to recruit GBM participants as both these settings are known to have a high caseload of GBM patients. Clinicians at these settings were asked to recruit a total sample of 50 GBM participants, of whom 24 were to be 16-29 years of age (12 at each site) and 26 were to be 30-49 years of age (13 at each site). Participants at this setting were eligible if they were: born biologically and identified as male, identified as homosexual/gay/bisexual, between 16-49 years of age and resident in the Auckland region.

### ***HIV-negative heterosexual males***

Heterosexual male patients are seen at both Greenlane Clinical Centre and FBMC. Clinicians at these settings were asked to recruit a total sample of 50 heterosexual participants, of whom 24 were to be 16-29 years of age (12 at each site) and 26 were to be 30-49 years of age (13 at each site). Participants at this setting were eligible if they were: born biologically and identified as male, identified as heterosexual/straight, aged between 16-49 years of age and resident in the Auckland region.

Of note, Auckland Sexual Health Services underwent a review midway through 2015. As of July 2015, all patients were triaged prior to booking to identify priority groups. Male priority groups include GBM, Māori, Pacific, unemployed or on a social benefit, under 25 years of age, and by GP referral. This may have resulted in fewer heterosexual males, particularly older men, accessing the service and therefore affected recruitment for this study.

## Study procedures

An overview of the study processes and procedures used in both ADHB settings can be viewed in Figure 18. Initially, it was envisioned that a practice nurse complete study the procedures at the FBMC GP setting but this was not feasible at this setting. Therefore, study procedures were similar across all settings.

In brief, the following procedures are followed at the ADHB settings:

1. The clinician approaches their client at the end of their regular consultation to gauge interest in participation.
2. If they are interested, the study procedures are explained and the Participant Information Sheet (PIS) (*see Appendix B: HIMS Feasibility Study PIS*) and the PIS: Storage of Specimens for Future Research (FUR) (*see Appendix C: HIMS Feasibility Study FUR*).
3. If the patient consents to participate, they are screened for eligibility.
4. If eligible, the clinician uses a pre-packaged study kit and assigns a unique study ID provided in the kit.
5. Samples are taken by the clinician, the ID sticker attached to the samples and sent to the laboratory for testing through the normal process.
6. The ID sticker is attached to the questionnaire and provided to the participant to complete in the waiting room.
7. The completed questionnaire is returned to a secure drop box at the reception, and the participant is given the koha before leaving the clinic and study.

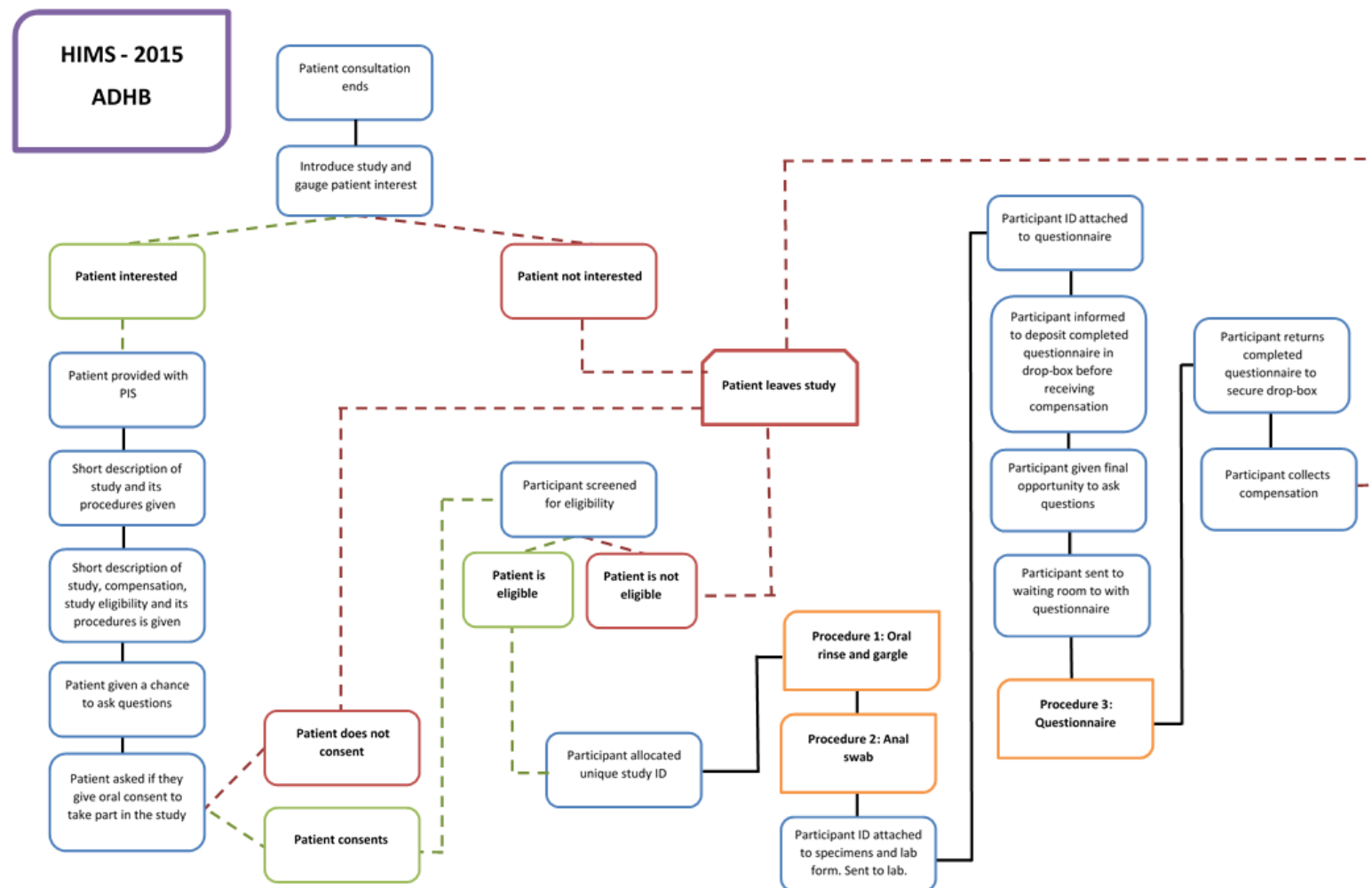


Figure 18: Stepwise diagrammatic representation of study processes at the ADHB setting.



### ***Participant approach and recruitment processes***

Recruitment took place between April and August 2015. In all settings, participants were approached by the clinician undertaking the patient consultation. Patients were approached and offered a PIS and a PIS-FUR if they were interested in participating in the study. The clinician provided the participant with the PIS and PIS-FUR and explained the study's main purpose, processes, and ethical concerns. The patient was then asked to provide verbal informed consent if they wished to participate or could decline.

If a participant agreed to take part in the study, they were then screened for eligibility and allocated into one of the study population groups as detailed below. General study eligibility criteria were as follows:

1. Born biologically and identify as male,
2. Are aged between 16-49 years of age,
3. Are resident in the Auckland region,
4. Can read and speak English,
  - That is, are able to understand the PIS and the study protocol so that they can provide 'Informed Consent'.
  - This will already have been established when Informed Consent was gained.

Each recruiting clinician maintained a record of all patients seen at each clinic and recorded whether these patients were potentially eligible for participation in the study, whether the patients consented to participate or declined participation. This record of recruitment rate was documented by each clinician on their Response Sheet after each patient was seen as: "Accept", "Decline" or "Not Eligible".

After a participant had completed all the study processes (screening, sample collection and questionnaire), they could collect their *koha* (compensation for participants experience and time). *Koha* was provided in the form of a NZ\$20.00 equivalent voucher for Westfield Shopping Centres. For each participant successfully recruited, the study site was provided with NZ\$20.00 to be deposited into a shared clinical fund upon study completion.

### ***Sample collection, storage and sample delivery processes***

There were no special requirements or refrigeration required for the storage of samples collected during this study. However, oral samples needed to be processed within 72 hours of collection. This meant that the candidate needed to work closely with the laboratory to ensure this could be done.

LabPLUS were employed to analyse all samples collected during this feasibility study. It was decided that LabPLUS would be the preferred laboratory as they receive and process samples directly from both Auckland City Hospital and Greenlane Clinical Centre. Therefore, the study could use existing delivery pathways, and clinicians would not need to treat or store the samples collected in this study differently compared to their usual processes.

At FBMC, however, there was no existing pathway for delivery to LabPLUS. In this situation, the candidate used the preferred courier service of LabPLUS so that charges could be made to this account and included in the final invoice. This required the receptionist at FBMC to call LabPLUS so that an online booking could be made. However, this proved a time-consuming process in a busy general practice, and they requested an alternative system be used. Therefore, the candidate collected and delivered samples from FBMC to LabPLUS when required.

Two samples were collected: an oral rinse and an anal swab. The oral rinse was collected by providing participants with a Falcon™ tube containing a premeasured 10ml of ethanol-containing mouthwash (Listerine® was used), which they were requested to hold within the mouth and rinse vigorously for 30 seconds then gargle for a further 5 seconds. This allowed for effective sampling of the oropharynx. The anal swab was obtained using a flocked swab inserted 3-5cm into the anal passage, after which it was slowly rotated as it was withdrawn for 10-15 seconds to sample the mucosal lining. The swab was then immersed in universal transport medium and vigorously swirled to release the captured cells.

After samples were processed and analysed, the remaining sample was put into frozen storage at LabPLUS. Upon study completion, the candidate collected these samples and placed in frozen storage at the University of Auckland as per the information provided in both the HDEC ethics application and the PIS-FUR.

## Study measurements

### ***Study recruitment rate***

At each site, clinicians recruiting for the study were provided with individual recruitment tracking sheets. They used this sheet to record each approach throughout the study and continued onto a new sheet if required.

Each approach could be classified as an “Accept”, a “Decline” or a “Not Eligible”. Those who did not fit the study eligibility criteria were classed as “Not Eligible”. If a recruitment quota had been filled at a site (e.g., all 30–49 year-old GBM), then a patient wishing to participate and fitted that quota would be marked as ineligible.

### ***HIV status measurements***

As previously mentioned, it was assumed that all participants recruited at Auckland City Hospital would be living with HIV. However, there was the possibility that males living with HIV could be recruited at other settings.

In the questionnaire, a question was included that asked for the participants' HIV status at their last HIV test. The question was posed as the statement "*About HIV testing:*", with possible responses: "*I've never had an HIV test/AIDS test*", "*My last HIV test was negative*", and "*I am HIV positive*". From this we could classify our participants into three groups: "Never tested/HIV status unknown", "HIV-negative" and "HIV positive".

### ***HPV infection measurements***

Samples collected in this study were tested for the presence of HPV DNA. We tested for any HR-HPV types and specifically for HPV-16 and HPV-18. As previously mentioned LabPLUS were employed to undertake this laboratory analysis for the project and reported the findings to the investigator team.

LabPlus utilised the Cobas® 4800 HPV test, which at the time of the study, was primarily intended for use on cervical specimens (310). Primers are used to target nucleotides in the L1 region of the HPV genome and polymerase chain reaction to amplify target DNA specific to 14 HR-HPV types in a single analysis. The test specifically identifies HPV-16 and HPV-18 while also detecting the remaining HR-HPV types (31, 33, 39, 45, 51, 56, 58, 66 and 68).

HPV prevalence is reported in the following ways:

- Positive for HPV-16
- Positive for HPV-18
- Positive for HR-HPV other than HPV-16/-18 (HPV-31, 33, 39, 45, 51, 56, 58, 66 and 68).
- Positive for any HR-HPV, including HPV-16/-18

### ***Specimen validity***

A quarter (n=22 or 25%) of specimens were collected from the anal compartment were not suitable for laboratory analysis. Specimens were considered unsuitable for analysis if the  $\beta$ -globin control was not also amplified during the PCR procedure, indicating either a lack of sufficient genetic material or the presence of PCR inhibitors in the sample. Faecal samples are known to contain PCR inhibitors and purification of the sample seeks to isolate the genetic material from these inhibitors prior to PCR (311).

Table 21 summarises the distribution of these invalid samples overall, then by recruitment site and study population group. Overall, there were no invalid oral specimens collected. The proportions of invalid anal samples were greatest among HIV-negative GBM and participants recruited from the GP site.

Table 21: Validity of HPV specimens: total by anatomical site

|                         | Oral  |     |         |   | Anal  |    |         |    |
|-------------------------|-------|-----|---------|---|-------|----|---------|----|
|                         | Valid |     | Invalid |   | Valid |    | Invalid |    |
|                         | n     | %   | n       | % | n     | %  | n       | %  |
| <b>Total</b>            |       |     |         |   |       |    |         |    |
| Valid                   | 89    | 100 | 0       | 0 | 67    | 75 | 22      | 25 |
| <b>Site</b>             |       |     |         |   |       |    |         |    |
| Hospital                | 38    | 100 | 0       | 0 | 29    | 76 | 9       | 23 |
| SHC                     | 37    | 100 | 0       | 0 | 31    | 84 | 6       | 16 |
| GP                      | 14    | 100 | 0       | 0 | 7     | 50 | 7       | 50 |
| <b>Population Group</b> |       |     |         |   |       |    |         |    |
| GBM PLHIV               | 46    | 100 | 0       | 0 | 35    | 76 | 11      | 24 |
| HIV – GBM               | 25    | 100 | 0       | 0 | 16    | 64 | 9       | 36 |
| HIV – Het               | 18    | 100 | 0       | 0 | 16    | 89 | 2       | 11 |

Among the study sites, the greatest number of invalid anal samples were collected at Auckland Hospital (n=9), but the greatest proportion was collected at the general practice setting (50%). When exploring the distribution of invalid anal samples, we see that it is 24% (n=11) among GBM PLHIV, 36% (n=9) among HIV-negative GBM, and 11% (n=2) among HIV-negative heterosexual men.

### ***HPV-related measurements***

Questions relating to knowledge of HPV-related diseases that affect males, HPV vaccine awareness, vaccine acceptability, and vaccine uptake were included in the questionnaire. The questions were taken directly from the 2014 GAPSS and GOSS surveys to provide direct comparability (see *Chapter Five: Section One*).

#### *HPV-related disease and vaccine knowledge*

Knowledge of HPV was assessed under three components. Firstly, knowledge of the HPV virus was assessed through the question “*Before today, were you aware of human papillomavirus, also called “HPV”?*” with responses including “Yes”, “No” and “Not sure” (question not included in GAPSS and GOSS surveys). Secondly, we questioned participants regarding their knowledge of the range of HPV-related diseases affecting males; these included: penile and anal warts, anal cancer, mouth and throat cancer and penile cancer.

Possible responses for each of the diseases were “*I knew that*”, “*I wasn’t sure*” and “*I didn’t know that*”. Finally, we asked participants if they were aware that there was a vaccine available to protect against these diseases “*Gardasil - the vaccine used to protect girls against cervical cancer - also protects men against other cancers and genital warts*” with responses including “*I knew that*”, “*I wasn’t sure*” and “*I didn’t know that*”.

#### *HPV-vaccine acceptability and uptake*

Acceptability of the HPV vaccine was investigated under two different pricing conditions. Before being asked about acceptability, participants were informed that the vaccine required three injections for best efficacy – “*The NEXT three questions are about the Gardasil vaccine that requires three injections to give the best protection against HPV*”. The first pricing condition was fully funded “*I would get vaccinated with Gardasil<sup>®</sup> if it was offered for free*” with options including “*Yes*”, “*No*” and “*Not sure*”. The second pricing condition related to the 2015 price for the full three doses “*I would get vaccinated with Gardasil<sup>®</sup> if it cost \$500*” with the possible responses being “*Yes*”, “*No*” and “*Not sure*”.

The value of NZ\$500.00 was indicated as, at the time of the study, the quadrivalent HPV vaccine (Gardasil<sup>®</sup>) was NZ\$167.00 per dose if purchased from a clinical provider, with a complete course requiring three doses. The total amount was rounded for ease of interpretation. The price provided to participants in the survey did not consider the vaccine administration fee and consultation fee required, as this varies considerably by the clinical centre and DHB. These fees could also be waived if accessed through SHS by GBM.

#### ***Participant sociodemographic data***

Data were collected on participants’ demographics and sexual behaviours after first reminding participants that this was an anonymous study “*The following questions will help us learn more about HPV in different groups of people. Remember, this is an anonymous survey, meaning no-one can link this information back to you*”.

Participants were asked about their age, ethnicity, sexual orientation, HIV status, and lifetime number of sexual partners. The phrasing and possible responses to these questions can be found in the questionnaire.

#### **Consent for storage of samples for future research**

Participants were asked when entering the study if they would be happy for their samples to be stored for future research and provided with information relating to this through the separate PIS-FUR. However, an option within the questionnaire was also included for participants to opt-out of storing their samples if, upon reflection, that they did not wish for

them to be stored. As the questionnaire contained the participant's unique study ID, this allowed the destruction of samples linked to these IDs.

## Data entry and processing

### ***Study recruitment response sheets***

At each site, clinical team members who were recruiting were supplied with a Response Sheet. Upon study completion, these sheets were collected to analyse the response rate. The candidate was unable to collect all Response Sheets from Greenlane Clinical Centre as it appeared that some sheets had been inadvertently removed from the consultation rooms (there was no patient identifying information on these forms).

For each setting, the total under each heading of "Accept", "Decline" and "Not Eligible" was calculated for each recruitment sheet and then expressed as a total for each setting in a Microsoft Excel spreadsheet.

### ***Laboratory report data***

LabPLUS supplied the research team with laboratory reports containing the results of the HPV testing throughout the study period. These reports contained the unique participant ID and the result for each sample (anal/oral), and information relating to the validity of the sample.

The data from these reports were entered into a Microsoft Excel spreadsheet by the candidate, creating a single entry for each unique participant ID that contained the results for both samples and sample validity. This was imported into STATA v.13 and saved as a STATA dataset.

### ***Participant questionnaires***

A Data Entry Assistant was hired to double enter the questionnaires completed by participants throughout the study. Microsoft Access 2013 was used to create two databases for each round of data entry and a form to facilitate the data entry process linked to each database. A coding form to convert the questionnaire responses to numerical categorical data was created and provided to streamline data entry and importation into STATA software for analysis. After data entry had been completed, the candidate compared the two databases to check for inconsistencies for each entry, of which there were none.

### ***Dataset merging***

Both the laboratory report dataset and the questionnaire dataset were merged in STATA v.13, using the unique study ID to create a single line entry for each participant that contained both the results of their HPV testing and their questionnaire data. The combined

dataset was used for all further analysis relating to the participants. Study recruitment data were not included in the dataset.

## Analysis

### ***Analysis of recruitment***

For each study recruitment setting, the total for each outcome of: “Accept”, “Decline” and “Not Eligible” were calculated and expressed as a percentage of the total number of approaches. Taking only the percentage of “Accept” gives us an impression of the recruitment rate per 100 approaches.

Additional analyses of recruitment rate by sociodemographic characteristics are not available as this would require participants to disclose additional information to the clinician and study forms, which may have been a reason for declining to participate.

### ***Analysis of HPV prevalence***

Data on HPV prevalence was captured to meet the requirements of the study aims for the following grouping of HR-HPV types:

- HPV-16
- HPV-18
- Hr-HPV other than HPV-16/-18
- Any Hr-HPV, including HPV-16/-18

The infection prevalence for each of the above categories is described for the total population. Cross-tabulation of HPV infection prevalence with participants’ socio-demographic variables, study site of recruitment, and sexual behaviour are then presented for each of the study populations (GBM PLHIV, HIV-negative GBM, and HIV-negative MSW).

### ***Analysis of HPV knowledge and vaccine acceptability***

Measures of HPV-related knowledge and HPV vaccine acceptability are reported firstly for the total population, then at the recruitment site level and finally for each population group in the study.

The analysis was conducted for three groupings:

1. HPV-related disease knowledge.
  - a. Awareness of HPV prior to the study.
  - b. HPV causes AGWs.
  - c. HPV causes some anal cancers.
  - d. HPV causes some oral cancers.
  - e. HPV causes some penile cancers.

2. HPV vaccine knowledge.
3. HPV vaccine acceptability.
  - a. If offered fully funded.
  - b. If had to pay NZ\$500.00

Cross-tabulation of HPV infection prevalence with participants' sociodemographic variables, study site of recruitment, and sexual behaviour are then presented for each of the study populations (GBM PLHIV, HIV-negative GBM, and HIV-negative MSW). All analyses were performed using STATA v.13 IC.



## Section Two: Results of the HIMS Feasibility Study

### Introduction

For the purposes of this thesis, the HIMS feasibility study provides the first estimates of oral and anal HPV infection prevalence among GBM and other males in NZ.

Internationally, the data provide the first estimates of combined oral and anal HPV infection prevalence among GBM. For future analyses, these data can be investigated by a range of variables collected during the study such as HPV-related knowledge, recent sexual behaviours, HIV and STI testing behaviours, and HPV vaccination status.

### Feasibility study aims

1. Estimate the recruitment rates for the individual study sites to inform the recruitment period required for a larger study.
2. Estimate the oral and anal HR-HPV infection prevalence by study population and study site to inform power calculations for a larger study.
3. Identify the barriers to recruitment and data quality that would impact the implementation of a larger study.

### Overview of HIMS feasibility study

The methods and background of the HIMS feasibility study are covered in detail in the previous section (*see Chapter 4: Section One*). In brief, the HPV in Males Study (HIMS) was a cross-sectional, observational feasibility study that recruited males between the ages of 16 and 49 years from three healthcare settings (a general practice, a sexual health clinic and an adult infectious disease outpatient clinic). Recruitment occurred sequentially between April and August 2016, with the aim of recruiting 150 participants split equally into quotas based on age, HIV status and sexual identity (*see Figure 17*).

### Recruitment results

To monitor changes in HPV infection over time, recruitment must be viable, sustainable and reproducible. An essential component of the HIMS feasibility study was collecting data on recruitment in each study setting.

#### **Confirmation of study sites**

Three study sites located within the Auckland City region confirmed their willingness to participate in the HIMS feasibility study:

1. Auckland City Hospital - Adult Infectious Diseases Outpatient Clinic
2. Greenlane Clinical Centre – Auckland Sexual Health Services (ASHS) Clinic

### 3. Freemans Bay Medical Centre (FBMC) – General Practice

#### ***Staff recruiters at study sites***

Due to the nature of the different settings, the number of staff able to act as recruiters for the study varied. At FBMC, only one general practitioner was acting as a recruiter for the study, while at Auckland City Hospital, there were seven staff recruiting for the study. Staff at ASHS shared recruitment sheets and consultation rooms over the study period, and as such, the exact number of staff acting as recruiters is uncertain. However, the staff members acting as study partners at this setting estimated that between 12-14 staff recruited participants into the study over the study period.

#### ***Hours of recruitment at study sites***

At each setting, the number of hours during which recruitment could occur was limited by factors such as opening hours, staff availability and public holidays.

Participants were recruited at Auckland City Hospital while attending the outpatient clinic between 9 am and 1 pm on Wednesday, and 1:30 pm and 2:30 pm on Thursday.

Greenlane Clinical Centre hours are Monday to Friday 8:00 am to 5:00 pm with a late evening opening on Tuesday (8:00 pm) and a half-day on Wednesday (12:00 pm). These hours did not alter after the service review that was undertaken during the study period.

Freemans Bay Medical Centre hours are Monday to Saturday, opening at 8 am and closing at 6 pm, except Wednesday (8 pm), Friday (5 pm) and Saturday (9 am - 12noon). The general practitioner recruiting for the study worked three days per week (Monday, Wednesday and Friday). However, due to the requirement that specimens be processed within 24 hours of collection, the general practitioner was asked not to recruit on a Friday as oral samples would not be processed until the following Monday at the laboratory.

#### ***Delays and changes in recruitment at study sites***

Throughout the study recruitment period, several delays in recruitment were experienced at some of the study sites. During the recruitment period, ASHS underwent a service review that resulted in all patient bookings being triaged by staff as of 1<sup>st</sup> July 2016 to identify priority groups. Heterosexual males were not identified as a priority group, which may have resulted in fewer heterosexual males accessing the Greenlane clinic and therefore reduced the number approached to participate in the study. However, GBM remained a priority group.

Over the course of the recruitment period, the single general practitioner was not available to recruit participants for a total of three weeks. There were no delays or changes reported at the Auckland City Hospital setting.

### **Acceptance rate**

The acceptance rate was calculated as the proportion of participants accepting an invitation into the study among all participants eligible to participate. The acceptance rate was unable to be calculated by the different study populations, as questions relating to sexual identity and HIV status were not asked until after a participant had accepted.

The overall acceptance rate across all settings and recruiters was 42%. The Auckland City Hospital site reported the greatest average rate at 67% (min. 57%, max. 100%), compared to 31% at FBMC and 27% (min. 9%, max. 42%) at ASHS Greenlane (see *Table 22*).

### **HIMS feasibility study recruitment rate**

The recruitment rate was calculated as the number of participants who accepted the invitation into the study as a proportion of all approaches, including those found to be ineligible for the study. It is expressed as a rate per 100 approaches (see *Table 22*).

The overall recruitment rate for the HIMS feasibility study was 17 per 100 approaches. Unlike the acceptance rate, the recruitment rate was greatest at the ASHS Greenlane Clinic at 22 per 100 approaches and lowest at FBMC at 13 per 100 approaches.

Table 22: Study response rates: total by setting

| Measure                              | Study Site        |                                   |                               |         |
|--------------------------------------|-------------------|-----------------------------------|-------------------------------|---------|
|                                      | Auckland Hospital | Sexual Health Clinic <sup>a</sup> | General Practice <sup>b</sup> | Overall |
| Number of recruiters                 | 7                 | 12-14                             | 1                             | 20-22   |
| <b>Recruitment period</b>            |                   |                                   |                               |         |
| Total days                           | 195               | 194                               | 194                           | -       |
| Total weeks                          | 28                | 28                                | 28                            | -       |
| <b>Accepts</b>                       |                   |                                   |                               |         |
| Min.                                 | 3                 | 4                                 | -                             | -       |
| Max.                                 | 8                 | 8                                 | -                             | -       |
| Mean                                 | 5.29              | 5.67                              | -                             | -       |
| Overall                              | 37                | 17                                | 14                            | 68      |
| <b>Declines</b>                      |                   |                                   |                               |         |
| Min.                                 | 0                 | 9                                 | -                             | -       |
| Max.                                 | 4                 | 26                                | -                             | -       |
| Mean                                 | 2.57              | 15.33                             | -                             | -       |
| Overall                              | 18                | 46                                | 31                            | 131     |
| <b>Ineligible</b>                    |                   |                                   |                               |         |
| Min.                                 | 10                | 0                                 | -                             | -       |
| Max.                                 | 37                | 13                                | -                             | -       |
| Mean                                 | 22.57             | 4.67                              | -                             | -       |
| Overall                              | 158               | 14                                | 67                            | 239     |
| <b>Acceptance rate <sup>c</sup></b>  |                   |                                   |                               |         |
| Min.                                 | 57.14             | 13.33                             | -                             | -       |
| Max.                                 | 100.00            | 42.11                             | -                             | -       |
| Mean                                 | 67.27             | 22.08                             | -                             | -       |
| Overall                              | 67.27             | 22.08                             | 31.11                         | 41.79   |
| <b>Recruitment rate <sup>d</sup></b> |                   |                                   |                               |         |
| Min.                                 | 12.20             | 9.30                              | -                             | -       |
| Max.                                 | 27.78             | 42.11                             | -                             | -       |
| Mean                                 | 17.37             | 22.08                             | -                             | -       |
| Overall                              | 17.37             | 22.08                             | 12.5                          | 17.32   |

a - Incomplete collection of response sheets at Greenlane Clinical Centre. Response sheets were shared among recruiters.

b - Only one general practitioner was recruiting at this site

c - Denominator excludes those not eligible to participate in the study

d - Denominator includes all approaches and is expressed as a rate per 100 approaches

## HIMS feasibility study sample

At the end of the recruitment period, a total of 91 participants were enrolled in the study. Of these, laboratory results and questionnaires were available for 89 participants.

The questionnaire was not available for one participant. This may result from the participant either not completing the questionnaire or not handing it into the dropbox before leaving the study site. However, during the procedures training day at the study settings, staff were advised to ask participants if they had completed and returned their questionnaires before providing the koha, which should have minimised the likelihood of this occurring. It is also possible that the participant did not pick up the koha before leaving the clinic. For one other participant, laboratory results were not received. The reason for this is unclear.

### ***HIMS sample characteristics***

The feasibility study recruited 89 individuals with linked specimens and questionnaires. A similar number were recruited from Auckland Hospital (n=38) and ADHB Sexual Health Service (n=37) with 14 recruited from general practice. Of the three target populations, 46 were GBM PLHIV, 25 were HIV-negative GBM, and 18 were HIV-negative heterosexual men.

Table 23 describes the sample characteristics. Most of the study participants were GBM (79.8%), half (51.7%) were living with HIV, and 10.1% had never tested for HIV. More were aged 30 and over (60.7%) than under 30 (39.3%), approximately 40% were non-NZ European, and the majority (64.0%) reported more than 20 lifetime sexual partners.

Table 23 also describes how participant characteristics varied by recruitment setting. Respondents recruited from Auckland City Hospital were all GBM PLHIV and were proportionately older, non-European, and reported more lifetime sexual partners. Respondents recruited from the SHS and GP were broadly similar to each other, although those from the SHS were proportionately younger and less likely to be living with HIV.

Comparisons of the three study target populations are provided in Table 23. Although most (n=38) GBM PLHIV were recruited at the Auckland City Hospital, four were recruited at the SHS and four at the GP. In general, the GBM PLHIV were older, more ethnically diverse and reported more lifetime sexual partners. Participants allocated to the HIV-negative GBM group and the HIV-negative heterosexual group after screening were similar to each other except for their sexual identity; notably, half of each group were aged under 30 years. A number of the assumed HIV-negative GBM and heterosexual men had never tested for HIV.

Table 23: Participant characteristics: total by study population

| Characteristic           | Study population    |      |                    |      |                                |      |                 |      |
|--------------------------|---------------------|------|--------------------|------|--------------------------------|------|-----------------|------|
|                          | GBM PLHIV<br>(N=46) |      | HIV- GBM<br>(N=25) |      | HIV-<br>Heterosexual<br>(N=18) |      | Total<br>(N=89) |      |
|                          | n                   | %    | n                  | %    | n                              | %    | n               | %    |
| <b>HIV test status</b>   |                     |      |                    |      |                                |      |                 |      |
| Positive                 | 46                  | 100  | 0                  | 0.0  | 0                              | 0.0  | 46              | 51.7 |
| Negative                 | 0                   | 0.0  | 23                 | 92.0 | 11                             | 61.1 | 34              | 38.2 |
| Untested                 | 0                   | 0.0  | 2                  | 8.0  | 7                              | 38.9 | 9               | 10.1 |
| <b>Setting</b>           |                     |      |                    |      |                                |      |                 |      |
| Hospital                 | 38                  | 82.6 | 0                  | 0.0  | 0                              | 0.0  | 38              | 42.7 |
| SHS                      | 4                   | 8.7  | 20                 | 80.0 | 13                             | 72.2 | 37              | 41.6 |
| GP                       | 4                   | 8.7  | 5                  | 20.0 | 5                              | 27.8 | 14              | 15.7 |
| <b>Age</b>               |                     |      |                    |      |                                |      |                 |      |
| 16-29                    | 13                  | 28.3 | 13                 | 52.0 | 9                              | 50.0 | 35              | 39.3 |
| 30-49                    | 33                  | 71.7 | 12                 | 48.0 | 9                              | 50.0 | 54              | 60.7 |
| <b>Identity</b>          |                     |      |                    |      |                                |      |                 |      |
| Heterosexual             | 0                   | 0.0  | 2                  | 8.0  | 15                             | 83.3 | 17              | 19.1 |
| Bisexual                 | 5                   | 10.9 | 3                  | 12.0 | 3                              | 16.7 | 11              | 12.4 |
| Gay                      | 41                  | 89.1 | 20                 | 80.0 | 0                              | 0.0  | 61              | 68.5 |
| <b>Ethnicity</b>         |                     |      |                    |      |                                |      |                 |      |
| NZ European              | 23                  | 50.0 | 16                 | 64.0 | 15                             | 83.3 | 54              | 60.7 |
| Māori                    | 5                   | 10.9 | 2                  | 8.0  | 1                              | 5.6  | 8               | 9.0  |
| Pacific                  | 2                   | 4.4  | 0                  | 0.0  | 1                              | 5.6  | 3               | 3.4  |
| Asian                    | 8                   | 17.4 | 5                  | 20.0 | 0                              | 0.0  | 13              | 14.6 |
| Other                    | 8                   | 17.4 | 2                  | 8.0  | 1                              | 5.6  | 11              | 12.4 |
| <b>Lifetime Partners</b> |                     |      |                    |      |                                |      |                 |      |
| None                     | 1                   | 2.2  | 0                  | 0.0  | 0                              | 0.0  | 1               | 1.1  |
| One                      | 1                   | 2.2  | 0                  | 0.0  | 1                              | 5.6  | 2               | 2.3  |
| 2-5                      | 1                   | 2.2  | 3                  | 12.0 | 2                              | 11.1 | 6               | 6.7  |
| 6-10                     | 3                   | 6.5  | 2                  | 8.0  | 2                              | 11.1 | 7               | 7.9  |
| 11-20                    | 6                   | 13.0 | 6                  | 24.0 | 4                              | 22.2 | 16              | 18.0 |
| 21+                      | 34                  | 73.9 | 14                 | 56.0 | 9                              | 50.0 | 57              | 64.0 |

Note: "Study population" is based on assessment and allocation at screening. Hospital = ADHB Auckland City Hospital Adult Infectious Disease Outpatient Clinic, SHS = ADHB Greenlane Sexual Health Service; GP = Freeman's Bay Medical Centre general practice; "GBM" = gay, bisexual and other men who have sex with men; "Identity" = self-reported sexual identity from the questionnaire. Ethnicity is based on self-report in the questionnaire and coded according to the StatsNZ prioritisation system.

## HPV infection prevalence

### ***Oral HPV prevalence***

Overall, two respondents (2.3%) tested positive for HPV-16 in the oropharyngeal compartment; both were GBM PLHIV recruited from Auckland Hospital. Five respondents (5.6%) tested positive for high-risk non-HPV-16/18 type(s) (see *Table 24*). No respondents tested positive for HPV-18 in the oral compartment.

### ***Anal HPV prevalence***

The prevalence of HPV in the anal compartment was substantially higher, although the estimate was affected by a number of invalid samples (see *Table 21*). Of the valid samples, the prevalence of HPV-16 was 26.1%, and the prevalence of HPV-18 was 15.9%, with 31.3% having evidence of HPV-16/18 infection. Over half (54.1%) had evidence of a high-risk non-HPV-16/18 type.

### ***HPV 16/18 prevalence at either oral or anal compartment***

The aggregated measure of HPV-16/18 at either compartment was the same as that for the anal compartment due to the low frequency of oral infection. Thus, 31.3% of all respondents had any HPV-16/18 detected at the oral or anal compartment.

### ***HPV prevalence by study population***

Both oral and anal HPV infection prevalence differed markedly by study population group (see *Table 24*).

For oral HPV infection, GBM PLHIV were the only cases (n=2) of HPV-16 (4.4%), and 6.5% of this group also had a high-risk non-HPV-16/18 type (see *Figure 19*). HIV-negative GBM had no detectable HPV 16, 18 or other high-risk types in the oral compartment. Heterosexual HIV-negative men had no cases of HPV-16/18 but had the highest prevalence of non-HPV-16/18 types (11.1%).

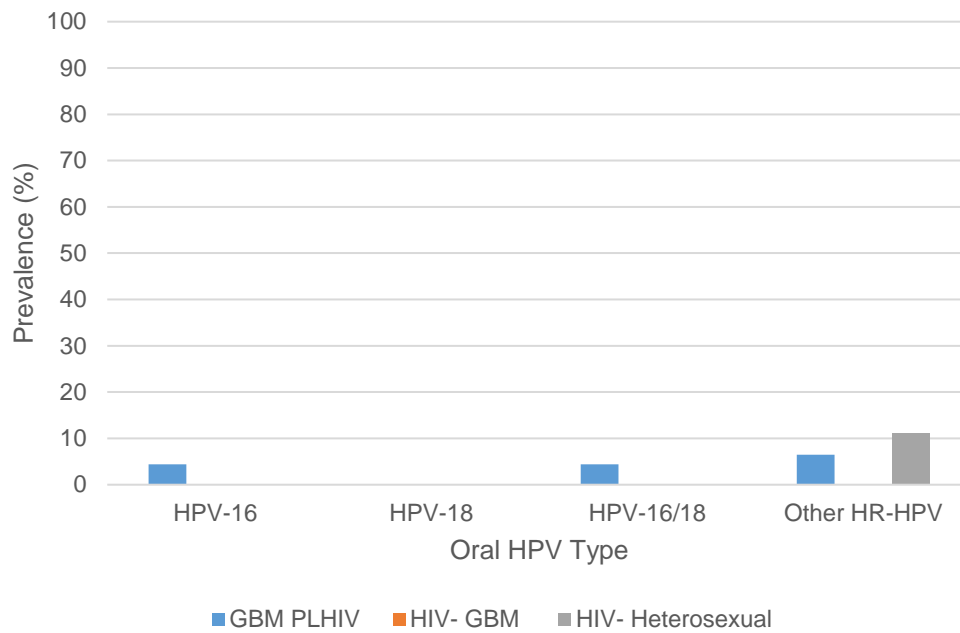


Figure 19: Prevalence of oral HPV infection by HPV type and study population.

For anal HPV infection, all cases were found in GBM with none identified in heterosexual males (see Figure 20). GBM PLHIV had the highest prevalence of infection for each type, being 46.0% for HPV-16, 25.0% for HPV-18, 54.3% for HPV-16/18, and 77.5% for high-risk non-HPV-16/18 types. In comparison, the prevalence of infection among HIV-negative GBM was 6.3% for HPV-16, 11.8% for HPV-18, 12.5% for HPV-16/18, and 50.0% for high-risk non-HPV-16/18 types.

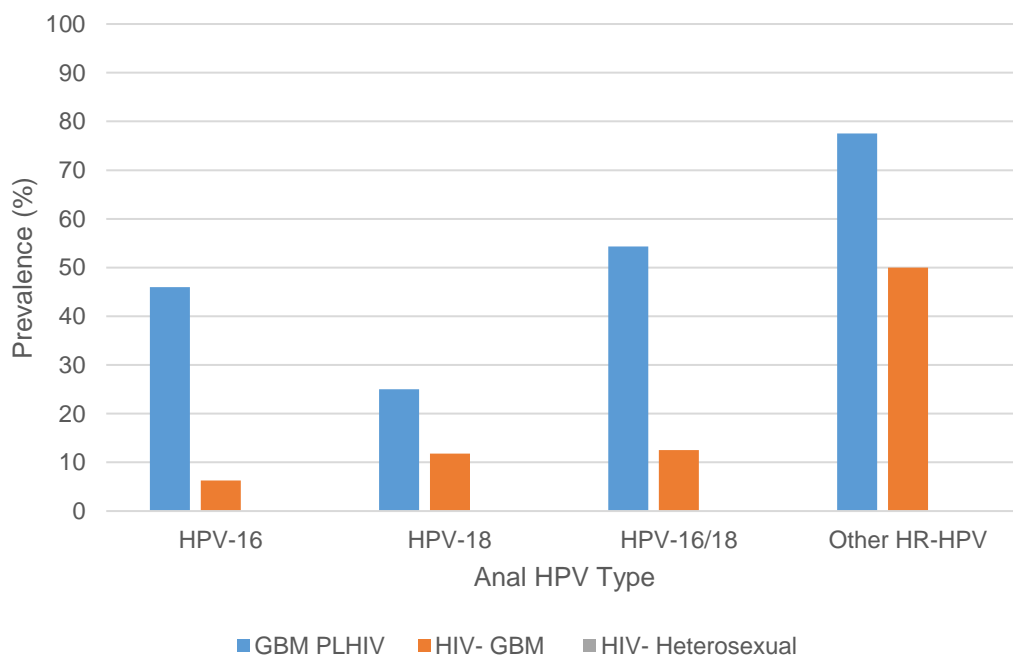


Figure 20: Prevalence of anal HPV infection by HPV type and study population.



### ***HPV prevalence by participant sociodemographic and behavioural characteristics***

Table 24 presents HPV prevalence by other participant characteristics, including age, sexual identity, ethnicity, and number of lifetime sexual partners. Older participants tended to have a higher proportion of anal HPV infection, whereas there was no clear association for oral HPV infection. Gay identified respondents tended to have a higher prevalence of anal HPV than bisexual identifying participants, who in turn had a higher prevalence of infection than respondents identifying as heterosexual; for oral HPV this appeared to be reversed. There was no clear association between ethnicity and oral HPV prevalence, but anal HPV-18 prevalence appeared to be higher among Māori participants and HPV-16 and HPV-18 anal prevalence appeared lower among Asian participants. HPV prevalence increased with greater numbers of lifetime sexual partners for both oral and anal HPV infection.

Table 24: HPV infection prevalence by anatomical site and participant characteristics among the total sample

| Characteristic           | Oral   |     |        |     |           |     |              |      | Anal   |      |        |      |           |      |              |      | Any Site HPV-16/18 |      |
|--------------------------|--------|-----|--------|-----|-----------|-----|--------------|------|--------|------|--------|------|-----------|------|--------------|------|--------------------|------|
|                          | HPV-16 |     | HPV-18 |     | HPV-16/18 |     | Other HR-HPV |      | HPV-16 |      | HPV-18 |      | HPV-16/18 |      | Other HR-HPV |      |                    |      |
|                          | N      | %   | N      | %   | N         | %   | N            | %    | N      | %    | N      | %    | N         | %    | N            | %    | N                  | %    |
| <b>Behaviour</b>         |        |     |        |     |           |     |              |      |        |      |        |      |           |      |              |      |                    |      |
| MSM                      | 71     | 2.8 | 71     | 0.0 | 71        | 2.8 | 71           | 4.3  | 53     | 34.0 | 53     | 20.8 | 51        | 41.2 | 58           | 69.0 | 51                 | 41.2 |
| Heterosexual             | 18     | 0.0 | 18     | 0.0 | 18        | 0.0 | 18           | 11.1 | 16     | 0.0  | 16     | 0.0  | 16        | 0.0  | 16           | 0.0  | 16                 | 0.0  |
| <b>Study pop</b>         |        |     |        |     |           |     |              |      |        |      |        |      |           |      |              |      |                    |      |
| GBM PLHIV                | 46     | 4.4 | 46     | 0.0 | 46        | 4.4 | 46           | 6.5  | 37     | 46.0 | 36     | 25.0 | 35        | 54.3 | 40           | 77.5 | 35                 | 54.3 |
| HIV- GBM                 | 25     | 0.0 | 25     | 0.0 | 25        | 0.0 | 25           | 0.0  | 16     | 6.3  | 17     | 11.8 | 16        | 12.5 | 18           | 50.0 | 16                 | 12.5 |
| HIV- Het                 | 18     | 0.0 | 18     | 0.0 | 18        | 0.0 | 18           | 11.1 | 16     | 0.0  | 18     | 0.0  | 16        | 0.0  | 18           | 0.0  | 16                 | 0.0  |
| <b>Setting</b>           |        |     |        |     |           |     |              |      |        |      |        |      |           |      |              |      |                    |      |
| Hospital                 | 38     | 5.3 | 38     | 0.0 | 38        | 5.3 | 38           | 7.9  | 31     | 41.9 | 30     | 23.3 | 29        | 48.3 | 34           | 73.5 | 29                 | 48.3 |
| SHC                      | 37     | 0.0 | 37     | 0.0 | 37        | 0.0 | 37           | 5.4  | 31     | 12.9 | 31     | 6.5  | 31        | 16.1 | 32           | 34.4 | 31                 | 16.1 |
| GP                       | 14     | 0.0 | 14     | 0.0 | 14        | 0.0 | 14           | 0.0  | 7      | 14.3 | 8      | 25.0 | 7         | 28.6 | 8            | 50.0 | 7                  | 28.6 |
| <b>Age</b>               |        |     |        |     |           |     |              |      |        |      |        |      |           |      |              |      |                    |      |
| 16-29                    | 35     | 2.9 | 35     | 0.0 | 35        | 2.9 | 35           | 0.0  | 29     | 17.3 | 28     | 14.3 | 28        | 21.4 | 29           | 51.7 | 28                 | 21.4 |
| 30-49                    | 54     | 1.9 | 54     | 0.0 | 54        | 1.9 | 54           | 9.3  | 40     | 32.5 | 41     | 17.1 | 39        | 38.5 | 45           | 55.6 | 39                 | 38.5 |
| <b>Identity</b>          |        |     |        |     |           |     |              |      |        |      |        |      |           |      |              |      |                    |      |
| Heterosexual             | 17     | 0.0 | 17     | 0.0 | 17        | 0.0 | 17           | 11.8 | 15     | 0.0  | 15     | 0.0  | 15        | 0.0  | 16           | 6.3  | 15                 | 0.0  |
| Bisexual                 | 11     | 9.1 | 11     | 0.0 | 11        | 9.1 | 11           | 0.0  | 9      | 22.2 | 9      | 11.1 | 9         | 33.3 | 9            | 44.4 | 9                  | 33.3 |
| Gay                      | 61     | 1.6 | 61     | 0.0 | 61        | 1.6 | 61           | 4.9  | 45     | 35.6 | 45     | 22.2 | 43        | 41.9 | 49           | 71.4 | 43                 | 41.9 |
| <b>Ethnicity</b>         |        |     |        |     |           |     |              |      |        |      |        |      |           |      |              |      |                    |      |
| NZ European              | 54     | 1.9 | 54     | 0.0 | 54        | 1.9 | 54           | 7.4  | 38     | 26.3 | 37     | 10.8 | 36        | 25.0 | 41           | 51.2 | 36                 | 25.0 |
| Maori                    | 8      | 0.0 | 8      | 0.0 | 8         | 0.0 | 8            | 12.5 | 6      | 16.7 | 7      | 57.1 | 6         | 50.0 | 7            | 57.1 | 6                  | 50.0 |
| Pacific                  | 3      | 0.0 | 3      | 0.0 | 3         | 0.0 | 3            | 0.0  | 3      | 33.3 | 3      | 0.0  | 3         | 33.3 | 3            | 33.3 | 3                  | 33.3 |
| Asian                    | 13     | 0.0 | 13     | 0.0 | 13        | 0.0 | 13           | 0.0  | 11     | 9.1  | 11     | 9.1  | 11        | 18.2 | 12           | 58.3 | 11                 | 18.2 |
| Other                    | 11     | 9.1 | 11     | 0.0 | 11        | 9.1 | 11           | 0.0  | 11     | 45.5 | 11     | 18.2 | 11        | 54.6 | 11           | 63.6 | 11                 | 54.6 |
| <b>Lifetime Partners</b> |        |     |        |     |           |     |              |      |        |      |        |      |           |      |              |      |                    |      |
| None                     | 1      | 0.0 | 1      | 0.0 | 1         | 0.0 | 1            | 100  | 1      | 100  | 1      | 100  | 1         | 100  | 1            | 100  | 1                  | 100  |
| One                      | 2      | 0.0 | 2      | 0.0 | 2         | 0.0 | 2            | 0.0  | 1      | 100  | 1      | 0.0  | 1         | 100  | 1            | 0.0  | 1                  | 100  |
| 2-5                      | 6      | 0.0 | 6      | 0.0 | 6         | 0.0 | 6            | 0.0  | 5      | 0.0  | 5      | 0.0  | 5         | 0.0  | 5            | 20.0 | 5                  | 0.0  |
| 6-10                     | 7      | 0.0 | 7      | 0.0 | 7         | 0.0 | 7            | 0.0  | 6      | 16.7 | 6      | 0.0  | 6         | 16.7 | 6            | 33.3 | 6                  | 16.7 |
| 11-20                    | 16     | 0.0 | 16     | 0.0 | 16        | 0.0 | 16           | 0.0  | 13     | 23.1 | 13     | 7.7  | 13        | 23.1 | 14           | 57.1 | 13                 | 23.1 |
| 21+                      | 57     | 3.5 | 57     | 0.0 | 57        | 3.5 | 57           | 7.0  | 43     | 27.9 | 43     | 20.9 | 41        | 36.6 | 47           | 59.6 | 41                 | 36.6 |

Note: "N" gives the denominator for that participant group with valid samples for each HPV test. Proportions are HPV prevalence in each participant group out of the valid samples.

"Study population" is based on assessment and allocation at screening. Hospital = ADHB Auckland City Hospital Adult Infectious Disease Outpatient Clinic, SHS = ADHB Greenlane Sexual Health Service; GP = Freeman's Bay Medical Centre general practice. "Behaviour" = assessment of sexual behaviour based on screening; "MSM" = men who have sex with men. "HIV-" = HIV-negative.

"Identity" = self-reported sexual identity from the questionnaire. Ethnicity is based on self-report in the questionnaire and coded according to the StatsNZ prioritisation system.

## HPV knowledge and awareness

Overall, two-thirds (65.2%) of participants had heard of HPV (see Table 25). Around half (48.9%) knew that HPV causes penile and anal warts. Few (34.5%) knew that HPV can cause anal cancer, and fewer still (24.1%) knew that HPV can cause mouth and throat cancer, or penile cancer (11.5%). Only a quarter (25.0%) knew that Gardasil can protect men and women against some cancers and warts.

Differences in HPV knowledge and awareness by study population is shown in Figure 21. GBM PLHIV and HIV-negative GBM were proportionately more likely to indicate awareness of HPV, that it is related to anal cancer, and that Gardasil can protect men and women.

Table 25: HPV-related disease knowledge and HPV vaccine awareness among total study sample

| Knowledge item   | Total (N=89) |      |
|--|--------------|------|
|  | n            | %    |
| <b>Before today, were you aware of human papillomavirus, also called “HPV”?</b>  |              |      |
| Yes  | 58           | 65.2 |
| Not sure   | 3            | 3.4  |
| No   | 28           | 31.5 |
| <b>“Human papillomavirus (HPV) is a virus that can cause...”</b>   |              |      |
| <b>Penile and anal warts</b>   |              |      |
| I knew that  | 43           | 48.9 |
| I wasn't sure  | 9            | 10.2 |
| I didn't know that   | 36           | 40.9 |
| <b>Anal cancer</b>   |              |      |
| I knew that  | 30           | 34.5 |
| I wasn't sure  | 11           | 12.6 |
| I didn't know that   | 46           | 25.9 |
| <b>Mouth and throat cancer</b>   |              |      |
| I knew that  | 21           | 24.1 |
| I wasn't sure  | 16           | 18.4 |
| I didn't know that   | 50           | 57.5 |
| <b>Penile cancer</b>   |              |      |
| I knew that  | 10           | 11.5 |
| I wasn't sure  | 23           | 26.4 |
| I didn't know that   | 54           | 62.1 |
| <b>“Gardasil – the vaccine used to protect girls against cervical cancer – also protects men against other cancers and genital warts.”</b> |              |      |
| I knew that  | 22           | 25.0 |
| I wasn't sure  | 12           | 13.6 |
| I didn't know that   | 54           | 61.4 |

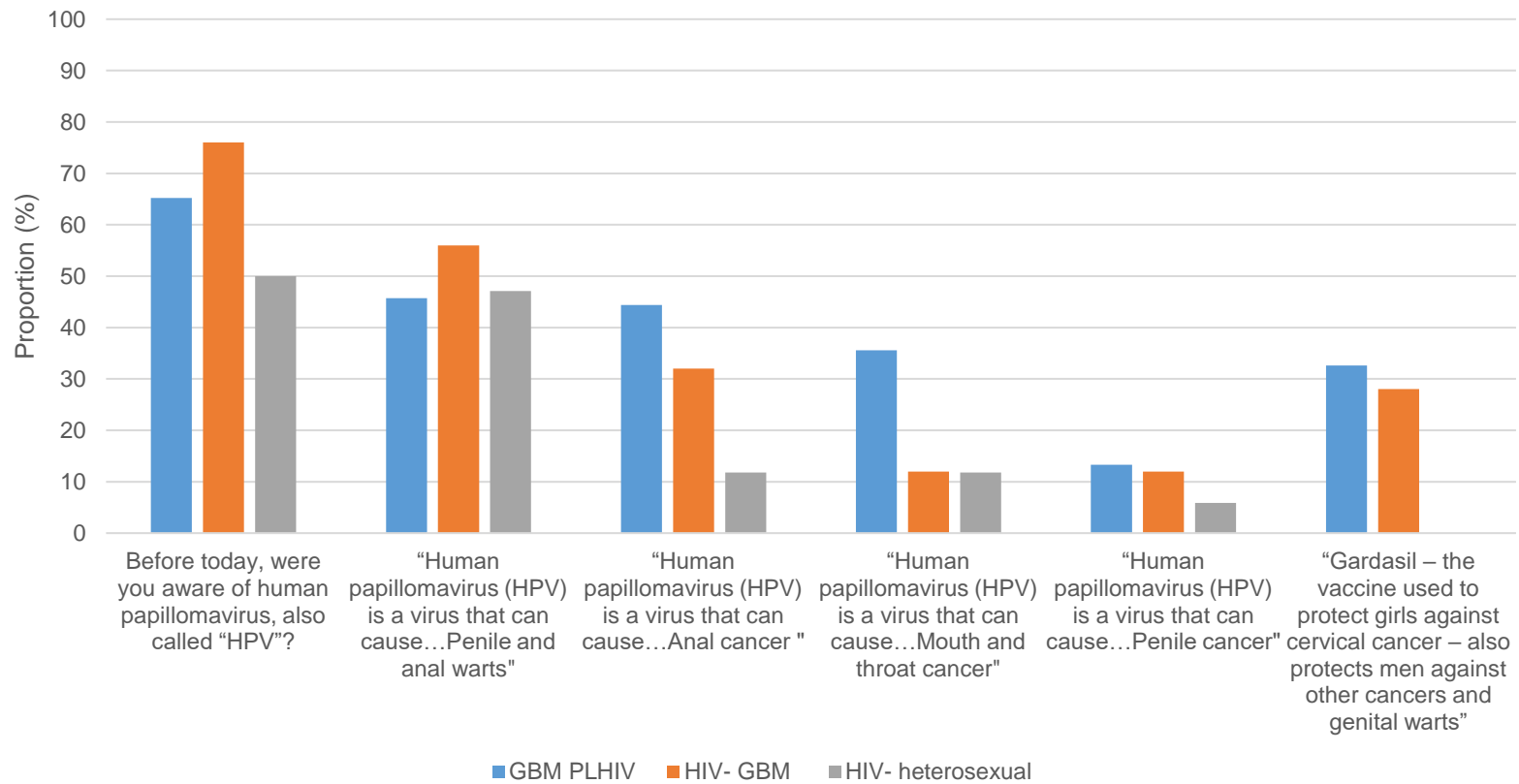


Figure 21: Proportion of respondents providing a positive response to HPV-related disease and HPV vaccine awareness questions, by study population

## HPV vaccine acceptability

The majority of participants (88.5%) indicated they would be prepared to be vaccinated with Gardasil if it were offered for free, with only 2.3% disagreeing (see Table 26). Support reduced to 13.6% if the full cost (\$500) had to be paid by respondents. A small proportion (6.8%) indicated that they had already received at least one dose of the vaccine.

Table 26: HPV vaccine acceptability and uptake among combined HIMS sample (N=89)

| Vaccine acceptability and uptake item                                     | GBM PLHIV<br>n=46<br>% | HIV- GBM<br>n=25<br>% | HIV- heterosexual<br>n=18<br>% |
|---|------------------------|-----------------------|--------------------------------|
| <b>“I would get vaccinated with Gardasil if it was offered for free.”</b> |                        |                       |                                |
| Yes   | 93.3                   | 92.0                  | 70.6                           |
| No  | 2.2                    | 4.0                   | 0.0                            |
| Don't know  | 4.4                    | 4.0                   | 29.4                           |
| <b>“I would get vaccinated with Gardasil if it cost \$500.00.”</b>        |                        |                       |                                |
| Yes   | 17.4                   | 12.0                  | 5.9                            |
| No  | 47.8                   | 36.0                  | 47.1                           |
| Don't know  | 34.8                   | 52.0                  | 47.1                           |
| <b>“I have already been vaccinated with Gardasil.”</b>                    |                        |                       |                                |
| Yes 1 shot  | 4.4                    | 4.0                   | 0.0                            |
| Yes 2 shots   | 2.2                    | 0.0                   | 0.0                            |
| Yes 3 shots   | 4.4                    | 0.0                   | 0.0                            |
| No  | 88.9                   | 96.0                  | 100.0                          |

Figure 22 shows differences in HPV vaccine acceptability and uptake by study population. Vaccine acceptability appeared to be higher among GBM PLHIV and HIV-negative GBM than among heterosexual males, and a higher proportion of GBM PLHIV stated that they had already received at least one dose of the vaccine (see Figure 22).

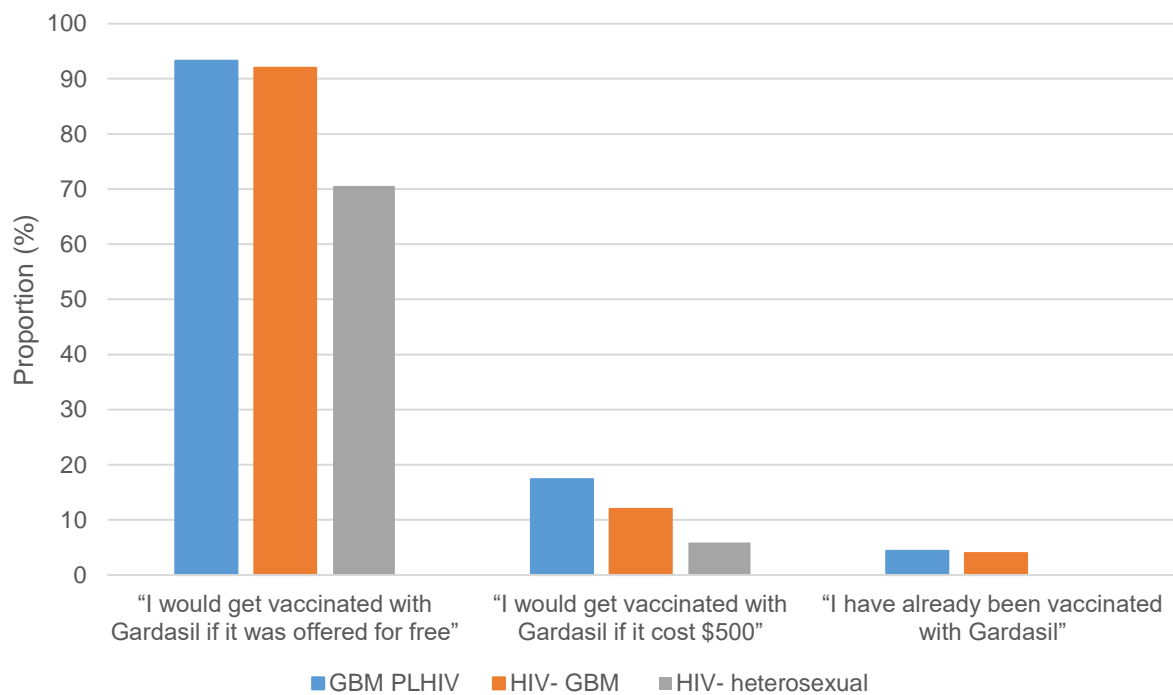


Figure 22: Proportion of study respondents providing a positive response to HPV vaccine acceptability and uptake variables by study population.

## Discussion

To the candidate's knowledge, this feasibility study presents the first data collected on anal HPV infection prevalence among males in NZ and the first among NZ GBM. It is also the first study to provide combined oral and anal HPV infection prevalence among males that can be linked to a range of sociodemographic, behavioural, and HPV-related knowledge and acceptability variables.

### **Strengths**

Recruitment from clinical settings enabled the linkage of biological data to sexual orientation and HPV-related data not routinely collected on administrative health records. These linked data can facilitate the identification of risk groups and targeting of public health interventions to groups within the wider GBM population based on sociodemographic or behavioural factors that would not be identified through clinical or behavioural research alone.

The recruitment of GBM through GP settings is not routinely used in GBM public health research. The use of a broader range of clinical settings resulted in different profiles of GBM than are recruited from one type of clinical setting alone.

The study was anonymous, and no results were returned to participants. This would have reduced participation bias for those more concerned about HPV and would have reduced social desirability bias in relation to responses to sexual behavioural questions within the self-administered survey.

A consistent recruitment approach was applied across the clinical settings. In absence of sampling frame for GBM in NZ, research that explores between group associations with HPV is reliant on opportunistic sampling methods that are repeatable and able to recruit large samples of GBM. The methods used in this feasibility study are scalable for a larger study that could recruit a large and diverse sample of GBM through clinical settings.

### ***Limitations***

The use of convenience sampling methods is widely accepted and use in GBM-related research, but the non-random sampling approach results in recruitment bias. Data cannot be generalised to wider GBM and heterosexual male population of NZ, and unmet recruitment quotas reduced power to detect differences. However, despite not being met, the purposive sampling and quotas in the study have been included to enable the statistical power to detect differences between groups of interest (age and HIV status).

Overall, a quarter of anal samples in study were invalid. A greater proportion of invalid samples were from HIV-negative GBM. If there were differences in HPV prevalence between valid and invalid samples, this could have affected the study findings. For the oral rinse, Listerine® was used and has been demonstrated to have antibacterial and antiviral properties that reduce the infectivity of the pathogen in the oral cavity (312, 313). While these properties may affect HPV and potentially disrupt the infectivity of the virus, it is unlikely to disrupt the viral DNA and therefore affect the results of this study.

HIV-status by self-report is subject to both reporting and social desirability biases. The anonymous, self-completed and voluntary nature of the study reduce the potential for this bias. In addition, some participants may be unaware that they are living with HIV (314). GBM are a population disproportionately affected by HIV, but GBM in this study who report being HIV-negative also report having tested for HIV at least once in their lifetime. However, whether this test was recent, and the sexual risk behaviours engaged in since this test were not asked as part of the questionnaire. A lower prevalence of HIV testing was reported among heterosexual males, but HIV prevalence among this population is comparatively low compared to GBM in NZ, despite SHS attendees being men who may have engaged in sexual behaviour that place them at risk of acquiring HIV infection (315).

GBM participants at both ASHS and FBMC were not excluded if they self-reported as living with HIV. This resulted in an over-sampling of GBM PLHIV despite quotas being in place for this population group and would overestimate the total HPV infection prevalence detect in the study population as a whole. This could be addressed through several approaches. Firstly, excluding participants at the analysis stage who report living with HIV from these recruitment sites. By monitoring the recruitment of GBM PLHIV at these sites during the recruitment period and updating quotas for HIV-negative GBM recruitment. Finally, by specifying the

living with HIV as an exclusion criterion at settings outside of the Auckland Hospital ID Outpatient Clinic. However, some participants may be uncomfortable or unwilling to disclose their HIV status to clinicians.

Knowledge and awareness questions were prompted rather than rely on recall and will have affected both recall and social desirability bias. Additionally, further HPV-related information was provided to participants prior to undertaking the survey through the Participant Information Sheet (PIS) (see *Appendix B: HIMS Feasibility Study PIS*) and the PIS: Storage of Specimens for Future Research (FUR) (see *Appendix C: HIMS Feasibility Study FUR*). However, the anonymous and self-completed nature of the survey and the neutral wording of the knowledge statements would reduce social desirability bias when selecting responses.

Factors such as smoking and other risk factors for oral HPV infection were not included in the questionnaire, and therefore, could not be adjusted for in the analyses. The feasibility study was not powered or designed to identify factors associated with HPV infection, rather this would be the purpose of the larger study. However, questions could have been piloted in the survey to assess the feasibility of obtaining responses to these questions in the various study settings.

### ***Recruitment***

Eighty-nine participants were recruited and provided complete data for over the seven-month study period. The overall recruitment rate of 17 per 100 approaches. When considering time periods, the weekly recruitment rate was close to one participant recruited per week of study (0.8/week), inclusive of all study settings.

Auckland hospital ID outpatient clinic has a largely older group, which may explain the large proportion of ineligible approaches recorded at this setting. In NZ, the majority of HIV diagnoses occur among GBM >30yrs (316). Patients living with HIV are seen every six months; therefore, most patients attending this clinic would likely have been seen at least once over the seven months of study recruitment.

At the Greenlane SHS clinic, ASHS underwent a major service review and restructure during the study period. This would have affected recruitment in terms of patient attendance to the clinic and additional demands on staff. As of July 2015, all patients were triaged and priority given to the following groups: GBM, of Māori or Pacific ethnicity, unemployed or receiving social support, under 25yrs of age, referred by a GP, experiencing symptoms, and contact of a recent diagnosis. In addition, the candidate was unable to retrieve all Response Sheets from this setting, affecting the calculation of recruitment rates for this site.

One GP agreed to participate in the study at Freemans Bay Medical Centre general practice. In primary healthcare, GP clinical time is under significant demand with appointments limited



to 10 minutes. Making study procedures streamline and be completed alongside a routine clinical visit required considerable consultation and adaptation. The GP recorded a greater proportion of declines and ineligible approaches compared to other study settings. The recruiting GP had three practice days per week and not all patients attending during the study period would have been of the target populations for the study (female or outside of the age range eligible for participation). During the study, the GP was also on annual leave for a three-week period, which would have affected recruitment numbers.

Despite these variations and limitations in recruitment, the overall study population was diverse in terms of age, ethnicity and sexual identity, reflecting both the study quotas and the Auckland region's diverse population.

Recruitment outside of the central Auckland district may have increased the diversity seen within the study population. Recruitment from ASHS and GP settings in south Auckland (Counties Manukau DHB) or the north shore (Waitemata DHB) could have resulted in a younger and more ethnically diverse study population. However, this could have reduced the probability of recruiting GBM participants, as GBM are known to geographically cluster to the central Auckland districts. This should be considered for a larger study.

Acceptance rates did not vary significantly between SHS and GP. Both settings are attended by a greater proportion of heterosexual male participants compared to the Auckland Hospital ID Outpatient Clinic. Koha for participation may not have been of a monetary value perceived to compensate for time or the invasiveness of study procedures, particularly among heterosexual males, for who an anal swab procedure would rarely be clinically indicated.

### ***Prevalence of infection***

Close to two out of every five (41%) GBM participants tested positive for anal HPV-16 or HPV-18 infection, the most oncogenic HR-HPV types. This was one in ten (13%) among HIV-negative GBM, and one in two (54%) for GBM PLHIV. By comparison, no anal HR-HPV infections were detected among heterosexual men in this sample. Compared to anal HPV infection, oral HPV infection was low among GBM this sample, with 4% testing positive for oral infection any HR-HPV. This was higher among heterosexual males at 11%.

### ***Anal HPV infection prevalence***

No data are published in NZ for a direct comparison of HPV infection prevalence among males. However, consistent with international literature, GBM in this sample experience the burden of anal HPV infection with GBM PLHIV disproportionately over-represented in the prevalence of infection.

One out of every two GBM PLHIV in this study tested positive for anal HPV-16 infection, the most oncogenic HPV type, and one in four tested positive for anal HPV-18 infection. Both are vaccine preventable. The anal HPV infection prevalence results are comparable to those found in the meta-analysis Machalek et al. (73). From the meta-analysis, the prevalence of anal HPV-16 infection among HIV-negative GBM was 13% and 35% among GBM PLHIV, compared to 6% and 46%, respectively, from this feasibility study. However, the prevalence of anal HPV-18 among both HIV-negative GBM (17%) and GBM PLHIV (25%) in the feasibility study is greater than that reported by Machalek et al. (5% and 19%, respectively).

Prevalence of non-HPV-16/-18 HR-HPV types was greater than that of HPV-16 and HPV-18 in this study, consistent with findings from anal HPV infection prevalence studies discussed in Chapter Two, Section Three: Prevalence of HPV infection and related disease among GBM. Prevalence of any HR-HPV type (including HPV-16/-18) among both HIV-negative GBM (40%) and GBM PLHIV (74%) in this feasibility study are greater than that found by Nyitray et al. in their large international study (27%) (168).

GBM in NZ are clustered geographically in urban centres (113). Auckland is the largest urban city in NZ, and therefore the greater availability of potential GBM sexual partners and sexual mixing may partially explain the greater prevalence of anal HPV infection than may be found in a nationally representative sample.

Similarly, recruitment in this study took place at inner-city clinical settings, and as such, GBM recruited from these settings may have greater access to sexual partners and engage in sexual behaviours that place them at a greater risk of acquiring HPV infection. A sample recruited through community settings may find different HPV infection prevalence.

#### *Oral HPV infection prevalence*

Oral HPV infection prevalence among GBM in this study was considerably lower than the prevalence of anal infection, consistent with international literature. GBM PLHIV in this study were found to have the greatest prevalence of oral HR-HPV-16 infection (4.4%). Among HIV-negative GBM and heterosexual males, HPV-16 was not detected. However, a greater prevalence of other non-HPV-16/-18 HR-HPV infection was detected among heterosexual males (11.1%).

International data indicates that the point prevalence of oral HPV infection is low compared to anal HPV infection. However, Kreimer et al. found no significant difference between GBM and heterosexual males when examining oral HPV infection prevalence in their nationally representative sample (155). The limited number of heterosexual males recruited in this feasibility study reduces the ability to generalise findings to the wider heterosexual male population. However, future studies should consider investigating oral HPV infection among

males in NZ, particularly given the increasing incidence of HPV-related oropharyngeal cancers seen among males in this country (267, 268).

### ***HPV-related knowledge and vaccine acceptability***

In brief, among respondents of the HIMS feasibility study, 65.2% reported they had heard of HPV prior to taking part in the study, similar to that found by Chelimo et al. among male participants in a 2008 survey of NZ university undergraduate healthcare students (65.8%) (269).

Vaccine acceptability was high among this sample, with 88.5% of respondents reporting they would receive the HPV vaccine if offered for free, comparable to the 89.7% found among female respondents in the same study by Chelimo et al. in 2008 but greater than the 65.8% among male participants in their study (269). The findings are also greater than the 56% acceptability found by Nadarzynski et al. in their 2014 meta-analysis of HPV vaccine acceptability among GBM (249).

The overall findings from this study suggest a lower level of HPV-related disease awareness among males at higher risk of acquiring HPV but offset with high acceptability of HPV vaccination if provided at no cost. However, men in this sample were recruited while attending healthcare settings; therefore, healthcare interventions may be more acceptable to this group than males recruited from a non-clinical setting.

### ***Future directions***

Future studies are needed to determine study procedures that improve the validity of anal samples. Compared to studies from the published literature, e.g., 10% reported by Nyitray et al. and 14% by Chin-Hong et al., the proportion of invalid anal specimens was greater in this feasibility study (25%) (131, 317). The anal samples found to be invalid in this study were due to insufficient cellular material present in the samples. Therefore, greater training and communication of the sampling procedure for the anal site to either study clinicians or participant (if self-collected) could improve this result for future studies.

There may be potential for the collection of biological specimens through community settings to reduce recruitment bias. Only half of GBM in NZ believe that their GP was aware of their sexuality, which suggests that some GBM are uncomfortable disclosing their sexuality in clinical settings (115). The New Zealand AIDS Foundation (NZAF) partner with ASHS to deliver STI testing at the annual LGBTIQ+ community fair day in Auckland. This includes the self-collection of an anal sample for chlamydia and gonorrhoea and could be utilised for the self-collection of anal samples for HPV testing for either infection or cytological abnormalities. In studies comparing clinician versus patient (self) collected anal samples, there did appear to be a difference in specificity for detecting HR-HPV infection (77, 318). Greater

communication of procedure for collection of samples for HPV would be needed for GBM participants, as this differs from sample collection for chlamydia and gonorrhoea.

Online sexual health services with a mailed self-sampling kit is another study method to explore, and these have been conducted in other countries (319). In 2018, NZAF began home-testing for HIV, with remote follow-up options, with 1774 HIV self-testing kits distributed between June 2018 and June 2019 (320). Combining HIV testing with other STI testing may be an acceptable and feasible method for collecting biological samples from GBM, and other options such as providing pre-paid courier envelopes for participants that could further reduce barriers for returning samples to laboratories for testing.

## Conclusions

The study has demonstrated that comprehensive data relating to HPV infection, knowledge and vaccine acceptability can successfully be collected in a systematic and repeatable manner among males from both outpatient and primary healthcare settings. However, recruitment of males through GP settings is challenging. Increased collaboration and building of partnerships between academic departments, NGOs and GP practices would be required to make a larger study feasible that included these settings.

Anal HPV infection prevalence among GBM was high in this study. One in every two GBM PLHIV and one in eight HIV-negative GBM testing positive for anal infection with HPV-16 or HPV-18, the two most oncogenic HR-HPV types, both of which are vaccine preventable. The high vaccine acceptability if provided for free among GBM indicates that this health burden can be addressed.

# Chapter 5: HPV-related disease knowledge, vaccine awareness and acceptability, and vaccine uptake

## Introduction

It is estimated that HPV vaccination coverage should be 80% of the population to reach a herd immunity threshold, though declines in HPV-related disease may be seen with coverage as low as 20% (216). Maximising vaccine uptake is therefore critical for HPV prevention, disease control and eventual elimination. To achieve this, the health belief model proposes that uptake of a health intervention such as vaccination is dependent on three areas: modifying factors, individual beliefs, and likelihood of action (235).

For the first time in NZ, data on HPV-related disease knowledge, HPV vaccine awareness, and HPV vaccine acceptability and uptake were captured among GBM during the 2014 round of the GAPSS and GOSS behavioural surveillance programme. These data were captured before implementing the publicly funded gender-neutral HPV vaccination programme in NZ in 2017, providing a baseline against which progress can be measured. The candidate helped design the HPV-related items for the survey and coordinated the data collection.

## Purpose

Cross-sectional community and online surveys can provide large and diverse samples of GBM with sufficient numbers to provide statistical power to detect between group differences. The combined GAPSS and GOSS sample captured the first data on HPV-related knowledge and HPV vaccine acceptability and uptake among GBM in NZ. Exploring these data to identify within-population differences can inform the design and development of public health interventions to increase vaccination uptake among GBM.

## Aims

The aims cover the four sections of the chapter:

1. Describe the methods for the Gay Auckland Periodic Survey (GAPSS) and the Gay Online Sex Survey (GOSS).
2. Explore HPV-related disease knowledge among GBM in NZ.
3. Explore HPV vaccination awareness and HPV-vaccine acceptability under two pricing models among GBM in NZ
4. Describe self-reported HPV vaccination uptake among GBM in NZ

## Section One: Methods: Gay Auckland Periodic Sex Survey (GAPSS) and Gay Online Sex Survey (GOSS)

### Introduction

This section describes the methods for the Gay Auckland Periodic Sex Survey (GAPSS) and the Gay Online Sex Survey (GOSS) HIV behavioural surveillance programme. These are repeat, cross-sectional community behavioural surveys, which recruit GBM through community venues and online sites and apps. The analyses using the data collected in these surveys are undertaken in the sections following. Further details of the GAPSS and GOSS methods have been published elsewhere (128).

The surveys meet the WHO and UNAIDS recommendation for second-generation surveillance of HIV/STIs, with the repeated ongoing capture of behavioural data (“behavioural surveillance”) to complement annual epidemiological surveillance (130). They suggest that surveillance systems should be tailored to the epidemic of a country and that country consider the following principles when they design second-generation surveillance:

- to concentrate resources to gather strategic information where they would yield data that is useful to reduce the spread of HIV and in the provision of care for those affected;
- to concentrate data collection in key populations at higher risk of HIV exposure;
- to compare HIV prevalence and HIV-risk behaviours to capture information that informs how the epidemic changes over time.

The two surveys were conducted at the Department of Social and Community Health, Faculty of Medical and Health Sciences, the University of Auckland. The surveys are funded by the Ministry of Health and are conducted in collaboration between the University of Auckland, University of Otago and the New Zealand AIDS Foundation.

The GAPSS and GOSS surveys are cross-sectional behavioural surveillance surveys that monitor changes in HIV-related knowledge, attitudes, sexual practices/behaviour, and sexual health among GBM in NZ. Established in 2002, GAPSS was conducted bi-annually in Auckland in 2002, 2004, and 2008. In 2008, GOSS was introduced to recruit GBM online nationwide across NZ, and both GAPSS and GOSS moved to a tri-annual basis, with recruitment in 2008, 2011 and 2014.

### Consultation and ethics

Both GAPSS and GOSS are voluntary, anonymous, and self-completed surveys. Participants are provided with a PIS (in paper form for GAPSS, and PDF for GOSS) and were considered to provide consent by completing and submitting their questionnaire, either by returning the

paper questionnaire to the dropbox or pressing the “submit” button at the end of the online survey. No koha was provided for participating in GAPSS or GOSS. Ethics approval was provided through University of Auckland Human Participants Ethics Committee (reference#:010738) for both GAPSS and GOSS.

Consultation was undertaken with organisations who work with the NZ GBM population. These included Body Positive (GBM PLHIV) and NZAF (GBM and takātapui). Information and feedback on survey recruitment sites, methods, and questionnaire were incorporated into the final methods for the surveys. Consultation was also undertaken with the owners of venues through which GAPSS recruits. This identified the most suitable times for recruitment to occur at the venues and how best to facilitate recruitment while also allowing patrons to enjoy the venues they came to use.

Information and the organisation of recruitment through online sites and apps used in GOSS were facilitated through NZAF, who employ a social marketing approach to sexual health promotion among GBM and utilise these sites to achieve this.

## GAPSS and GOSS questionnaire

Questions and survey logic were the same in both GAPSS and GOSS. The questionnaire covered sociodemographic variables, knowledge and attitudes related to HIV, engagement with HIV-prevention tools, and sexual partnering and practices related to HIV risk.

### ***Inclusion of HPV-related questions***

In 2013, the candidate considered HPV to be an emerging area of concern for the sexual health of GBM in NZ, particularly for GBM PLHIV. The investigator team for the GAPSS and GOSS surveys agreed to the inclusion of HPV-related questions in the 2014 survey round. The questions sought to cover three topic areas considered necessary to inform and monitor a public health response to HPV among the GBM community:

1. the extent of HPV knowledge,
2. acceptance of the HPV vaccine,
3. and engagement with prevention (vaccination uptake).

The questions were developed to follow the surveys' format in their approach to the exploration of HIV-related variables.

### ***Pilot testing***

Pilot testing was conducted to receive feedback on the novel HPV-related questions, overall questionnaire wording, instructions, and logic. The survey was piloted by a GBM volunteer group from NZAF and was conducted in both paper-based format and an online format to

simulate the two surveys. Volunteers were provided with a feedback form on which they could note any errors or suggestions. The study team then reviewed these forms and considered any feedback to improve the survey for the target population.

### ***Sociodemographic and behavioural variables***

Age was asked as a continuous variable and then grouped into three categories based on eligibility for HPV vaccination. Those eligible for funded vaccination in NZ aged up to and including 26 years, those who are eligible under UK guidelines up to and including the age of 45 years, and those who are not eligible for funded vaccination in any jurisdiction aged 46 years and over.

GAPSS and GOSS participants were able to select multiple ethnic groups that they identify with. A prioritisation system is utilised to group respondents into ethnic groupings based on these responses. StatsNZ level 1 prioritisation was utilised to group participants into the following categories “*European*”, “*Māori*”, “*Pacific*”, “*Asian*”, and “*Other*”.

Participants were given the following options to choose from with regards to their sexual identity: “*gay/homosexual*”, “*bisexual*”, “*takataapu*”, “*fa’afafine*”, “*straight/heterosexual*”, “*queer*”, “*Other (please state)*”. Due to the low number of participants in some groupings, some groups were combined to form the following categorical groupings for the analyses in this thesis: “*gay/homosexual*”, “*bisexual*”, “*other*”.

When participants were asked about the number of male sexual partners in the previous six months, they were presented with the ordinal categorical categories: “*None*”, “*One*”, “*2-5*”, “*6-10*”, “*11-20*”, “*21-50*”, “*50+*”. Due to the small number of participants in some of the groupings, these were combined into the following categories for the analyses in this thesis: “*None*”, “*One*”, “*2-10*”, “*11+*”, in an effort to retain categories that indicated higher and lower levels of sexual partnering.

### **Recruitment and study procedures**

In 2013 and 2014, the candidate was employed as the Research Assistant for the two surveys, with responsibilities that included:

- the hiring, employment administration, and training of survey recruiters,
- piloting of the survey,
- engagement with study venue owners and organisation regarding recruitment,
- and ensuring the logistics and running of survey recruitment over the GAPSS recruitment period,
- the creation of data tables for the basic frequencies report.



### ***GAPSS: Survey recruiters***

A total of 45 recruiters were hired to encourage participants to complete the GAPSS survey. Recruiters hired in the previous round of GAPSS were contacted and invited to work as Senior Recruiters. The recruiter role was also advertised through the Student Job Search website and posted on the NZAF Facebook page. Applicants were invited for interviews and selected based on experience, communication skills, and interest in research.

### ***GAPSS: Survey recruiter training day***

All hired recruiters were required to attend a compulsory training day. Here they learnt about the surveys, the aims, eligibility criteria, recruitment processes and troubleshooting of scenarios that could come up during the recruitment period. The goal of the training was to equip recruiters with sufficient information to engage with potential participants, engage with questions participants may have about the questionnaire, meet other recruiters, be trained in study procedures, and practice their recruitment approach before going into the field.

## Recruitment settings

### ***GAPSS***

Recruitment for the Gay Auckland Periodic Sex Survey (GAPSS) took place at various GBM-associated venues in the greater Auckland area. All recruitment for GAPSS took place over a single week in February commencing with the “Big Gay Out” (BGO) in Auckland, the largest LGBTIQ+ community fair day in New Zealand. This was followed by recruiters being sent to a variety of venues across Auckland city, which included: four sex-on-site (SOS) venues (Centurian, Basement, the Wingate Club, and The Grinder) and two bars (Family, and Legends). Sampling at the bar venues was limited to three evenings (Thursday, Friday, and Saturday), while shifts were allocated at a range of times throughout the week at the SOS venues agreed upon with the venue owners.

### ***GOSS***

Several online dating sites and mobile apps utilised by GBM were used in the recruitment for the Gay Online Sex Survey (GOSS) between February and April 2014. Recruitment was sequential across the various platforms. The process commenced on NZDating.com then moved to Grindr, Manhunt.com, Jack’d, Growlr and Hornet. The recruitment period on NZDating and Grindr was three weeks, as these were considered to be the most popular site and app at the time of recruitment, and two weeks on each of the remaining sites and apps.

## GAPSS: Recruitment and study processes

During the BGO, two tents were set up on either side of Coyle Park where participants could sit in the shade to fill out the survey. Recruiters were positioned near entrances to the park

and areas with high amounts of foot-traffic during the fair day. Recruiters were wearing t-shirts noting them to recruiters for the survey and had a lanyard with a tag provided by the BGO organisers that noted them as official staff. Shifts were allocated to the recruiters throughout the day, which meant they rotated between recruiting participants, providing participants with the study materials, and breaks. Participants were provided with a sticker after completing the survey so that recruiters would not continue to approach those who had already taken part.

GAPSS is a paper-based survey. Participants were provided with a clipboard containing a pen, the questionnaire and a PIS by the recruiter. The participant self-completed the questionnaire, folded it and returned it to a dropbox provided at the venue to maintain confidentiality and anonymity. Upon returning the survey to the dropbox, the participant was provided with a sticker so that recruiters could identify that they had participated in the survey.

At Family Bar and Legend Bar, recruiters were situated in areas where patrons could sit rather than at dance floors. Signs were put outside the venues notifying patrons that GAPSS recruitment was happening at the venue that evening, and recruiters wore the t-shirts that identified them as recruiters for the survey. Recruiters arrived at venues at 9 pm and left at midnight, during which they approached patrons within the quieter area. Participants were provided with a sticker after completing the survey so that recruiters would not approach them again throughout the night.

At SOS venues recruiters were limited to approach patrons of the venue only in communal areas where patrons wore clothing, and no sexual activity could occur. Signs were posted at each venue's entrance to notify patrons that recruiters for GAPSS were at the venue. Recruitment periods varied for each SOS venue but were concentrated around midday and between 6 pm to midnight.

### ***GOSS: Recruitment and study processes***

Participants were recruited into GOSS using banner adverts, messages to user's inboxes, and pop-up adverts. When clicked, users were taken to the survey start page, hosted by Demographix.com. Here they were provided with a brief overview of GOSS and could access the PIS. Participants could then start the survey if they wished and could skip questions they did not wish to answer. They could also exit the survey at any point before submission. Logic skips were built into the online survey so that questions that were not relevant to participants would not be shown. Once completed, participants were asked to submit their surveys and were notified that this would act as consent for their survey data to be used and analysed.

## Data coding and management

### ***GAPSS data coding***

Submitted GAPSS questionnaires were sent to be coded into numerical format by an external service provider. Coding sheets were built and provided to the study investigators for reference. A sample of questionnaires was selected and examined for coding errors against the study investigators' coding sheet. Any discrepancies were followed up with the coding service providers and examined against additional questionnaires to determine the extent of the error.

### ***GOSS data***

Data from GOSS were downloaded from Demographix.com in the form of a Microsoft Excel spreadsheet. Data were converted to categorical numerical values using the coding sheet as provided for GAPSS.

### ***Data cleaning and formatting***

Coded GAPSS and GOSS data were provided in Microsoft Excel spreadsheets and imported into STATA v12.0 and formatted into categorical variables. Data were cleaned by excluding those not eligible for inclusion in the study and those that had provided inconsistent and contradictory responses.

## Combined sample size and respondent characteristics

The combined GAPSS and GOSS sample is shared across the following sections and is explored here to prevent repetition in the sections that follow in this chapter.

The bivariate analysis explored the following variables between the samples and by survey:

- age,
- ethnicity,
- sexual identity,
- HIV status,
- highest qualification,
- perceived GP awareness of respondent's sexual orientation,
- number of male sexual partners in the previous six months,
- and if the respondent reports any UAIC with casual male sexual partners in the previous six months.

Pearson's chi-squared test of association was used to detect significant variance in the above factors between the two survey samples.

Table 27 provides the results of a descriptive analysis of the sociodemographic and key behavioural characteristics of the combined GAPSS and GOSS samples. There are significant differences between the two samples across a range of sociodemographic and behavioural variables. GAPSS participants were significantly more likely than GOSS participants to be older than 27 years, report non-European ethnicity, be gay identified, be living with HIV, hold a degree, believe their GP to be aware of their sexuality, report more male sexual partners, and report less UAIC.

Table 27: Comparison of sociodemographic and behavioural characteristics of participants among GAPSS and GOSS surveys

|                                | Combined    |              | GAPSS       |              | GOSS        |              | p-value          |
|--------------------------------|-------------|--------------|-------------|--------------|-------------|--------------|------------------|
|                                | n           | %*           | n           | %*           | n           | %*           |                  |
| <b>Total</b>                   | <b>3214</b> | <b>100.0</b> | <b>1421</b> | <b>100.0</b> | <b>1793</b> | <b>100.0</b> |                  |
| <b>Age</b>                     |             |              |             |              |             |              | <b>&lt;0.001</b> |
| 16-27                          | 1060        | 33.0         | 405         | 29.7         | 655         | 37.3         |                  |
| 27-45                          | 1270        | 39.5         | 569         | 41.7         | 701         | 40.0         |                  |
| 45+                            | 788         | 24.5         | 390         | 25.6         | 398         | 22.7         |                  |
| NS                             | 96          | -            | 57          | -            | 39          | -            |                  |
|                                |             |              |             |              |             |              |                  |
| <b>Ethnicity</b>               |             |              |             |              |             |              | <b>&lt;0.001</b> |
| European                       | 2230        | 71.2         | 898         | 66.4         | 1332        | 74.9         |                  |
| Māori                          | 308         | 9.8          | 131         | 9.7          | 177         | 10.          |                  |
| Pacific                        | 116         | 3.7          | 63          | 4.7          | 53          | 3.0          |                  |
| Asian                          | 352         | 11.2         | 194         | 14.3         | 158         | 8.9          |                  |
| Other                          | 126         | 4.0          | 67          | 5.0          | 89          | 3.3          |                  |
| NS                             | 82          | -            | 68          | -            | 14          | -            |                  |
|                                |             |              |             |              |             |              |                  |
| <b>Identity</b>                |             |              |             |              |             |              | <b>&lt;0.001</b> |
| Gay                            | 2546        | 79.5         | 1174        | 83.3         | 1372        | 76.6         |                  |
| Bisexual                       | 504         | 15.8         | 158         | 11.2         | 346         | 19.3         |                  |
| Other                          | 151         | 4.7          | 78          | 5.5          | 73          | 4.1          |                  |
| NS                             | 13          | -            | 11          | -            | 2           | -            |                  |
|                                |             |              |             |              |             |              |                  |
| <b>HIV status</b>              |             |              |             |              |             |              | <b>&lt;0.001</b> |
| HIV-negative                   | 2144        | 69.2         | 999         | 74.8         | 1145        | 65.0         |                  |
| HIV-positive                   | 155         | 5.0          | 83          | 6.2          | 72          | 4.1          |                  |
| Never tested/Don't know        | 798         | 25.8         | 254         | 19.0         | 544         | 30.9         |                  |
| NS                             | 117         | -            | 85          | -            | 32          | -            |                  |
|                                |             |              |             |              |             |              |                  |
| <b>Qualification</b>           |             |              |             |              |             |              | <b>&lt;0.001</b> |
| Non-tertiary                   | 1691        | 54.3         | 653         | 48.7         | 1038        | 58.5         |                  |
| Tertiary or higher             | 1423        | 45.7         | 687         | 51.3         | 736         | 41.5         |                  |
| NS                             | 100         | -            | 81          | -            | 19          | -            |                  |
|                                |             |              |             |              |             |              |                  |
| <b>GP aware of orientation</b> |             |              |             |              |             |              | <b>&lt;0.001</b> |
| No/not sure                    | 1569        | 49.5         | 547         | 39.6         | 1022        | 57.2         |                  |
| Yes                            | 1599        | 50.5         | 835         | 60.4         | 764         | 42.8         |                  |
| NS                             | 46          | -            | 39          | -            | 7           | -            |                  |
|                                |             |              |             |              |             |              |                  |

|  | Combined    |              | GAPSS       |              | GOSS        |              | p-value          |
|--|-------------|--------------|-------------|--------------|-------------|--------------|------------------|
|  | n           | %*           | n           | %*           | n           | %*           |                  |
| <b>Total</b>                                     | <b>3214</b> | <b>100.0</b> | <b>1421</b> | <b>100.0</b> | <b>1793</b> | <b>100.0</b> |                  |
| <b>Number of male sexual partners &lt;6mths*</b> |             |              |             |              |             |              | <b>0.045</b>     |
| 20 or less                                       | 2880        | 91.5         | 1230        | 90.4         | 1650        | 92.4         |                  |
| 20+  | 267         | 8.5          | 131         | 9.6          | 136         | 7.6          |                  |
| NS   | 67          | -            | 60          | -            | 7           | -            |                  |
|  |             |              |             |              |             |              |                  |
| <b>Any UAIC &lt;6mths</b>                        |             |              |             |              |             |              | <b>&lt;0.001</b> |
| No   | 2166        | 69.5         | 1079        | 80.0         | 1087        | 61.5         |                  |
| Yes  | 949         | 30.5         | 269         | 20.0         | 680         | 38.5         |                  |
| NS   | 99          | -            | 73          | -            | 26          | -            |                  |

NS = not stated

\* Percentages for NS are separate to the percentages of those responding to the question

## Section Two: Self-reported knowledge of HPV-related disease among a community and online cross-sectional sample of GBM in New Zealand

### Purpose

This section explores the feasibility of using the GAPSS and GOSS surveys to collect behavioural surveillance data on HPV-related disease knowledge among GBM, the prevalence of this knowledge among GBM in NZ, and factors associated with this knowledge, prior to the introduction of funded HPV vaccination for males in 2017. These data provide a baseline measure to inform public health interventions and to monitor change in these data over time.

### Aims

There are three aims that the analyses of this section seek to achieve:

- Demonstrate the acceptability of answering HPV-related disease questions among GBM participating in the GAPSS and GOSS cross-sectional surveys.
- Describe the prevalence of self-reported HPV-related disease knowledge among GBM survey participants.
- Explore HPV-related disease knowledge prevalence by key sociodemographic and behavioural variables.

### Background

Prior to government extending funding for the HPV vaccine to include males up to the age of 27 years in NZ, there had been little active health promotion to males. While MSW were protected through the vaccination of their female sexual partners, GBM received little to no protection as their sexual partners are male. This meant that although GBM were at risk from HPV-related disease, they received little targeted health promotion and were potentially unaware of this risk.

Knowledge of anogenital warts and HPV-related cancers is a key factor in HPV vaccine acceptability for both parents of young women and the young women themselves (231, 321, 322). As the HPV vaccine has been largely framed as a female-only vaccine to date, it is possible that GBM will not perceive the vaccine as relevant for them, in part due to the lack of awareness of HPV-related diseases that affect males.

In the 2014 round of the GAPSS and GOSS repeat behavioural surveillance programme, a series of questions were included that asked GBM participants if they were aware of the HPV-related diseases that affect males. The aim was to achieve a baseline measure of this

knowledge prior to active health promotion among this group, which could then be monitored over time to evaluate the success of health promotion in reaching GBM.

Collection of HPV-related knowledge could inform public health action to increase HPV vaccination rates among this “high-risk” population. The background literature review in Chapter Two: Section Four highlighted that few studies have focussed on the prevalence of HPV-related disease knowledge among GBM and the factors associated with this knowledge (see *Table 16*).

As an existing HIV behavioural surveillance programme among GBM, the GAPSS and GOSS surveys offer a potential tool that can be adapted to monitor changes in key HPV-related variables among GBM.

## Methods

### ***GAPSS and GOSS Recruitment***

Full methods for the GAPSS and GOSS surveys and the participant characteristics are detailed in Chapter Five: Section One. Details on the approach to the analyses of this section are detailed below.

### ***HPV-related disease knowledge questions***

Four questions on HPV-related disease were included in the 2014 GAPSS and GOSS questionnaire. They were preceded by the statement “*The following statements are TRUE*”:

1. *HPV causes anal and genital warts*
2. *HPV can cause anal cancers*
3. *HPV can cause oral cancers*
4. *HPV can cause penile cancers*

Respondent could select one of the following responses to each of the statements above:

- a. *I knew this*
- b. *I wasn't sure*
- c. *I didn't know this*

A respondent was considered to have knowledge of HPV-related disease if they selected “*I knew this*” and not to have knowledge if they selected either “*I wasn't sure*” or “*I didn't know this*”. Those respondents who did not provide a response to a question were assigned a missing value for that question.



### *HPV-related disease knowledge score*

A knowledge score was created by adding the number of self-reported “*I knew this*” to each question, to a maximum total of four. Those who answered either “*I wasn’t sure*” or “*I didn’t know*” were assigned a value of zero for that question. Those who did not provide a response to a question were assigned a missing value for that question. Those who did not provide a response to any of the questions were assigned a missing value for their total knowledge score. A perfect score would be four, a score of zero would indicate they were not aware of any HPV-related disease that affects males or that they provided an answer to one or several questions that was either “*I wasn’t sure*” or “*I didn’t know this*” and did not provide a response to the rest.

### *Grouping knowledge of HPV related disease*

Initially, the bivariate analysis looked at each question separately and identified sociodemographic and behavioural factors associated with each. However, it became clear from the HPV-related disease knowledge score that the majority of respondents who knew that HPV was associated with cancers reported knowing all three of the cancer questions.

This meant that there would be few differences between the sociodemographic and behavioural factors for each of the HPV-related cancer questions due to a shared population. Therefore, the variables were grouped into a combined measure of those reporting any knowledge that HPV can cause cancers in males, resulting in a total of three variable groupings for analysis:

1. Any HPV-related disease knowledge.
  - Respondent selected “*I knew that*” to at least one of the HPV-related knowledge questions.
  - Respondents with missing values for all questions were excluded from analyses using this variable.
2. Knowledge that HPV causes anogenital warts.
  - Respondent selected “*I knew that*” to the question that HPV causes AGWs.
  - Respondents with missing values for this question were excluded from analyses using this variable.
3. Knowledge that HPV causes any HPV-related cancers among males.
  - Responds “*I knew that*” to at least one of the knowledge questions for HPV-related cancers that affect males (anal, oral, penile).
  - Respondents with missing values for all HPV-related cancer questions were excluded from analyses using this variable.

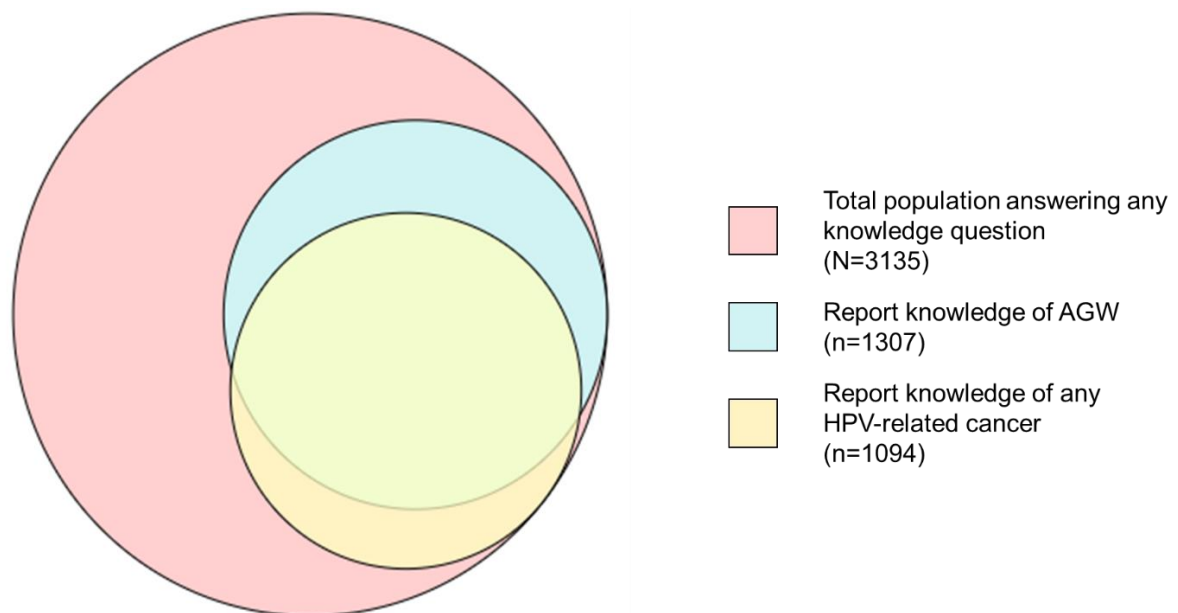
However, the new combined cancer knowledge variable shares a similar issue.

Table 28 highlights that among those who report any knowledge that HPV can cause cancers, there are few who do not also report that HPV causes anogenital warts.

Table 28: Crosstab of “any reported knowledge that HPV causes anogenital warts” and “any reported knowledge that HPV can cause any cancer among males.”

| Knowledge that HPV causes anogenital warts | Knowledge that HPV can cause any cancer among males |   | Total         |
|--|---|---|---------------|
|  | <i>I knew this</i>                                  | <i>I wasn't sure/I didn't know this</i> |               |
| I knew this                                | 881 (80.5%)   | 426 (20.9%)                             | 1307 (41.7%)  |
| I wasn't sure/I didn't know this           | 213 (19.5%)   | 1615 (79.1%)                            | 1829 (58.3%)  |
| Total                                      | 1094 (100.0%)                                       | 2041 (100.0%)                           | 3135 (100.0%) |

Figure 23 visualises the population crossover of HPV-related disease knowledge for AGWs and HPV-related cancers (n=881) reported among the study sample. Therefore, knowledge that HPV causes any cancer was controlled for in the multivariable analyses among the group reporting knowledge that HPV causes anogenital warts and vice versa.



Note: Visualisation of the data was created using the Venn Diagram Plotter software supported by the W.R. Wiley Environmental Molecular Science Laboratory, sponsored by the U.S. Department of Energy's Office of Biological and Environmental Research, and located at PNNL. PNNL is operated by Battelle Memorial Institute for the U.S. Department of Energy under contract DE-AC05-76RL0 1830

Figure 23: Venn diagram of participants reporting knowledge that HPV causes anogenital warts and knowledge that HPV causes any form of cancer among males among the total GAPSS ad GOSS sample.

## ***Statistical analysis***

### *Univariate analysis*

For the univariate analysis, the basic frequencies are presented for each of the HPV-related disease questions included in GAPSS and GOSS and the overall HPV-related disease knowledge score.

### *Bivariate analysis*

In the bivariate analysis, the three knowledge groupings (any HPV-related disease knowledge, knowledge that HPV causes anogenital warts, and knowledge that HPV causes any HPV-related cancers among males) are cross-tabulated with sociodemographic and behavioural factors that include:

- age,
- ethnicity,
- sexual identity,
- HIV status,
- highest qualification,
- amount of free time spent with GBM peers,
- perceived GP awareness of respondent's sexual orientation,
- number of male sexual partners in the previous six months,
- and if the respondent reports any unprotected anal intercourse with casual male partners (UAIC) in the previous six months.
  - Any UAIC was defined as respondents who reported not “*a/ways*” using a condom for anal sex with casual male partners in the previous six months.

Pearson's Chi-squared test was used to identify factors that were significantly associated with disease knowledge groupings. A p-value <0.05 was considered significant.

### *Logistic regression models*

To examine factors independently associated with each knowledge grouping, a logistic regression model was built for both knowledge that HPV causes anogenital warts and knowledge that HPV causes any HPV-related cancers among males to calculate AORs for each factor included in the respective models. Factors that were significantly associated with each knowledge grouping in the bivariate analysis or had a chi-square p-value of less than 0.1 were included in their respective models. Categorical variable groups with the largest population size were primarily chosen as reference groups within the models.

Before the multivariable models were built, an additional step was carried out to test for collinearity of variables using Pearson's correlation coefficient. However, several factors

included in the bivariate analyses were not ordinal categorical nor binary (ethnicity, sexual identity, HIV-status, recruitment site) and could not be tested using this method. The variables, number of male sexual partners and reporting of any UAIC, were also tested for collinearity as they are potentially on the causal pathway for each other but the scores ( $r=0.0304$  and  $r=0.0409$ , respectively) were within the range that could be included in the model without introducing instability. Both the knowledge of anogenital warts and knowledge of any cancer variables had levels of collinearity greater than the  $r=0.5$  value ( $r=0.57$ ). This is not unexpected due to the high number of participants that cross-over both of these groups.

One hypothesis is that the two knowledge variables are on a causal pathway for each other rather than acting as confounders. Inclusion of these variables in their respective models did not lead to wide confidence intervals in any of the included variables with the exception of those with smaller numbers of participants, which would be expected regardless of collinearity, arguing that the inclusion of these knowledge variables did not create undue amounts of instability in their respective models.

Factors that were considered potential confounders were included in the models. These are indicated in the results tables and were included despite not significantly associated at the bivariate level.

## Results

The sample size and characteristics of the combined GAPSS and GOSS samples are described in Chapter Five: Section One.

### ***Response rate to HPV-related disease questions***

The range in response rate for GAPSS is 92.2%—94.4%, while for GOSS this was 98.0%—99.2%. There is a marked difference in response rates between GAPSS and GOSS respondents (see *Table 29*). Of GAPSS respondents, 4.9% did not respond to a single HPV-related disease question compared to 0.6% of GOSS respondents.

Overall, only 2.5% of all participants did not answer a single HPV-related disease question. *Table 29* shows the percentage of non-responders for each of the HPV-related disease questions and the combine non-response rate for all four questions. The non-response rate was lowest for the first question “*HPV can cause penile and anal warts*” (3.0%) and highest for the final question “*HPV can cause penile cancers*” (4.7%). This pattern is similar when we separate respondents by survey (see *Table 29*), with the greatest response rate for the first question and a subsequent decline in rate as the questions progress.

### ***HPV-related disease knowledge in the two surveys***

Table 29 presents the univariate analyses for each HPV-related disease question posed to GAPSS and GOSS participants. Overall, knowledge is low with the majority of participants reporting not knowing or being unsure that HPV could cause the particular disease presented in each question. The greatest proportion of participants reported knowing that “*HPV can cause anal and penile warts*” (41.9%), compared to the least reporting knowing that “*HPV can cause penile cancer*” (24.0%). Self-reported knowledge that HPV could cause each of the three forms of cancer that affect males was noticeably lower than knowledge of HPV causing anogenital warts.

### ***HPV-related disease knowledge score***

Over half (51.5%) of all participants reported not knowing/being unsure of any of the four HPV-related diseases presented (see *Table 29*). Close to a fifth (18.2%) reported knowing that HPV could cause all four diseases. A similar percentage reported only being aware of HPV causing one disease (16.9%), while few reported knowing HPV caused two or three diseases (7.8% and 5.7%, respectively). The HPV-related disease knowledge score highlights that there are three main groupings of respondents, those with no knowledge, those who know at least one disease, and those who have knowledge of all four diseases presented. This differed significantly between the two surveys, with fewer GOSS respondents reporting all knowing all four knowledge items (14.9% vs. 18.2%,  $p < 0.001$ ).

Table 29: Basic frequencies of GBM participant's responses to HPV-related disease knowledge questions in the 2014 round of the GAPSS and GOSS surveys

| Question  | Combined    |              | GAPSS       |              | GOSS        |              | Pearson's Chi-square p-value |
|---|-------------|--------------|-------------|--------------|-------------|--------------|------------------------------|
|   | n           | %*           | n           | %*           | n           | %*           |                              |
| <b>Total</b>  | <b>3214</b> | <b>100.0</b> | <b>1421</b> | <b>100.0</b> | <b>1793</b> | <b>100.0</b> |                              |
| <b>HPV can cause penile and anal warts</b>                |             |              |             |              |             |              | <b>0.050</b>                 |
| I knew that   | 1307        | 41.9         | 589         | 43.9         | 718         | 40.4         |                              |
| I wasn't sure   | 495         | 15.9         | 192         | 14.3         | 303         | 17.0         |                              |
| I didn't know that  | 1317        | 42.2         | 560         | 41.8         | 757         | 42.6         |                              |
| NS  | 95          | (3.0)        | 80          | (5.6)        | 15          | (0.8)        |                              |
| <b>HPV can cause anal cancer</b>                          |             |              |             |              |             |              | <b>&lt;0.001</b>             |
| I knew that   | 916         | 29.6         | 445         | 33.8         | 471         | 26.6         |                              |
| I wasn't sure   | 569         | 18.4         | 236         | 17.9         | 333         | 18.8         |                              |
| I didn't know that  | 1606        | 52.0         | 636         | 48.3         | 970         | 54.7         |                              |
| NS  | 123         | (3.9)        | 104         | (7.3)        | 19          | (1.1)        |                              |
| <b>HPV can cause oral cancer</b>                          |             |              |             |              |             |              | <b>&lt;0.001</b>             |
| I knew that   | 866         | 28.1         | 414         | 31.6         | 452         | 25.6         |                              |
| I wasn't sure   | 559         | 18.2         | 240         | 18.3         | 319         | 18.0         |                              |
| I didn't know that  | 1653        | 53.7         | 656         | 50.1         | 997         | 56.4         |                              |
| NS  | 136         | (4.4)        | 111         | (7.8)        | 25          | (1.4)        |                              |
| <b>HPV can cause penile cancer</b>                        |             |              |             |              |             |              | <b>&lt;0.001</b>             |
| I knew that   | 737         | 24.0         | 363         | 27.7         | 374         | 21.3         |                              |
| I wasn't sure   | 599         | 19.5         | 268         | 20.5         | 331         | 18.8         |                              |
| I didn't know that  | 1731        | 56.4         | 679         | 51.8         | 1052        | 59.9         |                              |
| NS  | 147         | (4.7)        | 111         | (7.8)        | 36          | (2.0)        |                              |
| <b>Total HPV-related disease knowledge score (max. 4)</b> |             |              |             |              |             |              | <b>&lt;0.001</b>             |
| 0   | 1615        | 51.5         | 682         | 50.4         | 933         | 52.3         |                              |
| 1   | 529         | 16.9         | 200         | 14.8         | 329         | 18.5         |                              |
| 2   | 245         | 7.8          | 102         | 7.5          | 143         | 8.0          |                              |
| 3   | 177         | 5.7          | 65          | 4.8          | 112         | 6.3          |                              |
| 4   | 569         | 18.2         | 303         | 22.4         | 266         | 14.9         |                              |
| NS  | 79          | (2.5)        | 69          | (4.9)        | 10          | (0.6)        |                              |

NS = not stated

\* Percentages for NS are separate to the percentages of those responding to the question

### **Knowledge that HPV causes any HPV-related disease in males**

Among participants who provided a response to the HPV-related disease questions, 48.5% reported knowledge of at least one disease (at least one of AGWs, anal cancer, penile cancer, oral cancer).

Table 30 describes factors associated with self-reported knowledge of any of the four HPV-related diseases. Age ( $p=0.040$ ), ethnicity ( $p=0.030$ ), HIV status ( $<0.001$ ), highest level of qualification ( $p=<0.001$ ), perceived GP awareness of sexual orientation ( $p=<0.001$ ), site of recruitment ( $p=0.043$ ), and reporting any UAIC in the previous six months ( $p=0.044$ ) were significantly associated with reporting any HPV-related disease knowledge.

Those groups who reported a greater prevalence of any HPV-related disease knowledge tended to be under the age of 27-45 years, identified as “Other”, were living with HIV, whose highest qualification was tertiary or higher, who believed their GP was aware of their sexual orientation, who were recruited from bars, and who reported no UAIC in the previous six months. No association was found between reporting knowledge of any HPV-related disease and sexual identity, amount of free time spent with GBM peers, or the number of male sexual partners reported in the previous six months.

Ethnicity, HIV status at last test, highest qualification, ever having an STI check, and any UAIC in the previous six months remained significantly associated with reporting knowledge of any HPV-related disease after inclusion in the logistic regression model with other sociodemographic and sexual behavioural variables (see *Table 30*). Compared to those who reported being HIV-negative at last test, those who had never had an HIV test or were unsure of the results of their last test (AOR:0.69, 95% CI:0.54-0.88) were less likely to report knowledge of any HPV-related disease. Three factors were borderline significant, reporting Māori ethnicity (AOR:0.76, 95% CI:0.58-0.995), never having had an STI check (AOR: 0.77, 95% CI:0.59-0.998), and any UAIC in the previous six months (AOR: 0.83, 95% CI:0.70-0.99).

Age, perceived GP awareness of respondent’s sexual orientation, and site of recruitment were no longer significantly associated with reporting any HPV-related disease knowledge after inclusion in the model.

Table 30: Sociodemographic and behavioural characteristics of respondents reporting any knowledge that HPV causes any disease vs. no knowledge of any HPV-related disease.

|                                | N    | "I knew this" |      | Pearson<br>Chi2<br>P-value | AOR         | 95% CI            |
|--------------------------------|------|---------------|------|----------------------------|-------------|-------------------|
|                                |      | n             | %    |                            |             |                   |
| Total                          | 3135 | 1520          | 48.5 | -                          | -           | -                 |
| NS                             | 79   |               |      |                            |             |                   |
| <b>Sociodemographics</b>       |      |               |      |                            |             |                   |
| <b>Age</b>                     |      |               |      | <b>0.040</b>               |             |                   |
| Under 27                       | 1046 | 472           | 45.1 |                            | <i>Ref.</i> | -                 |
| 27-45                          | 1260 | 630           | 50.0 |                            | 0.97        | 0.81-1.17         |
| 45+                            | 782  | 390           | 49.9 |                            | 0.98        | 0.78-1.23         |
| NS                             | 47   |               |      |                            |             |                   |
| <b>Ethnicity</b>               |      |               |      | <b>0.030</b>               |             |                   |
| European                       | 2216 | 1097          | 49.5 |                            | <i>Ref.</i> | -                 |
| Māori                          | 300  | 119           | 39.7 |                            | <b>0.76</b> | <b>0.58-0.995</b> |
| Pacific                        | 114  | 55            | 48.3 |                            | 1.28        | 0.83-1.98         |
| Asian                          | 347  | 172           | 49.6 |                            | 0.84        | 0.65-1.08         |
| Other                          | 126  | 64            | 50.8 |                            | 0.83        | 0.56-1.23         |
| NS                             | 32   |               |      |                            |             |                   |
| <b>Identity</b>                |      |               |      | 0.052                      |             |                   |
| Gay                            | 2491 | 1227          | 49.3 |                            | <i>Ref.</i> | -                 |
| Bisexual                       | 493  | 215           | 43.6 |                            | 0.94        | 0.75-1.17         |
| Other                          | 139  | 72            | 51.8 |                            | 1.21        | 0.82-1.79         |
| NS                             | 12   |               |      |                            |             |                   |
| <b>HIV status</b>              |      |               |      | <b>&lt;0.001</b>           |             |                   |
| HIV-negative                   | 2129 | 1101          | 51.7 |                            | <i>Ref.</i> | -                 |
| HIV-positive                   | 152  | 84            | 55.3 |                            | 1.36        | 0.93-1.99         |
| Never tested/Don't know        | 792  | 300           | 37.9 |                            | <b>0.69</b> | <b>0.54-0.88</b>  |
| NS                             | 62   |               |      |                            |             |                   |
| <b>Qualification</b>           |      |               |      | <b>&lt;0.001</b>           |             |                   |
| Non-tertiary                   | 1676 | 692           | 41.3 |                            | <i>Ref.</i> | -                 |
| Tertiary or higher             | 1415 | 809           | 57.2 |                            | <b>1.83</b> | <b>1.56-2.15</b>  |
| NS                             | 44   |               |      |                            |             |                   |
| <b>GP aware of orientation</b> |      |               |      | <b>&lt;0.001</b>           |             |                   |
| No/not sure                    | 1545 | 698           | 45.2 |                            | <i>Ref.</i> | -                 |
| Yes                            | 1568 | 811           | 51.7 |                            | 1.03        | 0.86-1.23         |
| NS                             | 21   |               |      |                            |             |                   |
| <b>Ever had an STI check</b>   |      |               |      | <b>&lt;0.001</b>           |             |                   |
| Yes                            | 2481 | 1267          | 51.1 |                            | <i>Ref.</i> | -                 |
| No                             | 515  | 192           | 37.3 |                            | <b>0.77</b> | <b>0.59-0.998</b> |
| NS                             | 139  |               |      |                            |             |                   |



|  | N    | "I knew this" |      | Pearson Chi2 P-value | AOR         | 95% CI           |
|--|------|---------------|------|----------------------|-------------|------------------|
|  |      | n             | %    |                      |             |                  |
| <b>Free time spent with GBM*</b>                 |      |               |      | 0.118                |             |                  |
| Little/None                                      | 1229 | 574           | 46.7 |                      | -           | -                |
| A lot/some                                       | 1819 | 902           | 49.6 |                      | -           | -                |
| NS   | 87   |               |      |                      |             |                  |
| <b>Site of Recruitment</b>                       |      |               |      | <b>0.043</b>         |             |                  |
| BGO  | 1037 | 521           | 50.2 |                      | 1.0         | 0.84-1.19        |
| Bars   | 121  | 68            | 56.2 |                      | 1.31        | 0.84-2.05        |
| SOS Venues                                       | 194  | 81            | 41.8 |                      | 0.80        | 0.56-1.14        |
| Online (GOSS)                                    | 1783 | 850           | 47.7 |                      | <i>Ref.</i> | -                |
| NS   | -    |               |      |                      |             |                  |
| <b>Sexual behaviours</b>                         |      |               |      |                      |             |                  |
| <b>Number of male sexual partners &lt;6mths*</b> |      |               |      | 0.136                |             |                  |
| 20 or less                                       | 2811 | 1356          | 48.2 |                      | -           | -                |
| 20+  | 262  | 139           | 53.1 |                      | -           | -                |
| NS   | 62   |               |      |                      |             |                  |
| <b>Any UAIC &lt;6mths</b>                        |      |               |      | <b>0.044</b>         |             |                  |
| No   | 2110 | 1055          | 50.0 |                      | <i>Ref.</i> | -                |
| Yes  | 936  | 431           | 46.1 |                      | <b>0.83</b> | <b>0.70-0.99</b> |
| NS   | 89   |               |      |                      |             |                  |

\* Not included in the logistical regression model

UAIC = unprotected anal intercourse with a casual male partner

GP = general practitioner

GBM = gay, bisexual and other men who have sex with men

BGO = Big Gay Out – annual LBGTIQ community fair day held in Auckland

SOS = sex-on-site venue

NS = not stated

### **Knowledge that HPV causes anogenital warts**

Overall, 41.7% of GBM participants reported knowing that HPV causes AWGs. Table 31 describes the variation in reported knowledge and sociodemographic and behavioural variables. Knowledge that HPV causes anogenital warts varied significantly by age ( $p < 0.001$ ), sexual identity ( $p = 0.017$ ), HIV status at last test ( $p < 0.001$ ), highest qualification gained ( $p < 0.001$ ), perceived GP awareness of respondent's sexual orientation ( $p < 0.001$ ), having ever had an STI check ( $p < 0.001$ ), site of recruitment ( $p = 0.041$ ), and any reported UAIC in the previous six months ( $p = 0.046$ ).

Those groups reporting the lowest prevalence of knowledge were under the age of 27 years, identified as bisexual, had never had an HIV test or were unsure of the result of their last

test, their highest qualification was below tertiary level, had never had an STI check, did not perceive their GP to be aware of their sexual orientation, were recruited from SOS venues, and reported any UAIC in the previous six months. Self-reported ethnicity, the amount of free time spent with GBM peers and the number of casual male sexual partners reported in the previous six months were not significantly associated with reporting knowledge that HPV causes AGWs.

In the multivariable analysis, after including all sociodemographic and behavioural factors and knowledge that HPV causes at least one HPV-related cancer that affects males, those that remained independently associated with knowledge that HPV causes anogenital warts were ethnicity, HIV status at last test, and highest qualification level achieved (*see Table 31*).

Reporting knowledge that HPV causes at least one HPV-related cancer that affects males was strongly independently associated with reporting knowledge that HPV causes AGWs (AOR=14.78, 95% CI:12.08-18.08). Having a tertiary or higher-level qualification was independently associated with reporting knowledge that HPV causes AGWs (AOR=1.38, 95% CI:1.19-1.68). Those who reported being of Asian (AOR=0.60, 95% CI:0.43-0.82) or “Other” ethnicity (AOR=0.59, 95% CI:0.36-0.97), had never tested for HIV or were unsure of the result of their last test (AOR=0.67, 95% CI:0.50-0.90) were less likely to report being aware that HPV caused anogenital warts.

After inclusion in the model, the following factors were no longer significantly associated with reporting knowledge of HPV causing anogenital warts included age, sexual identity, perceived GP awareness of sexual orientation, ever having an STI check, site of recruitment, and any UAIC in the previous six months.

Table 31: Sociodemographic and behavioural characteristics of respondents reporting any knowledge that HPV causes anogenital warts vs. no knowledge of any HPV-related disease

|  | N    | "I knew this" |      | Pearson Chi2 P-value | AOR <sup>β</sup> | 95% CI             |
|--|------|---------------|------|----------------------|------------------|--------------------|
|  |      | n             | %    |                      |                  |                    |
| Total  | 3135 | 1094          | 34.9 | -                    | -                | -                  |
| NS   | 79   |               |      |                      |                  |                    |
| <b>Knowledge HPV causes anogenital warts</b> |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| Yes  | 1307 | 881           | 67.4 |                      | <b>14.70</b>     | <b>11.99-18.02</b> |
| No   | 1828 | 213           | 11.7 |                      | <i>Ref.</i>      | -                  |
| NS   |      |               |      |                      |                  |                    |
| <b>Sociodemographics</b>                     |      |               |      |                      |                  |                    |
| <b>Age</b>                                   |      |               |      | 0.268                |                  |                    |
| Under 27                                     | 1046 | 343           | 32.8 |                      | <i>Ref.</i>      | -                  |
| 27-45  | 1260 | 451           | 35.8 |                      | 0.90             | 0.71-1.15          |
| 45+  | 782  | 279           | 35.7 |                      | 0.85             | 0.63-1.14          |
| NS   | 47   |               |      |                      |                  |                    |
| <b>Ethnicity</b>                             |      |               |      | <b>0.002</b>         |                  |                    |
| European                                     | 2216 | 769           | 34.7 |                      | <i>Ref.</i>      | -                  |
| Māori  | 300  | 78            | 26.0 |                      | 0.77             | 0.53-1.10          |
| Pacific                                      | 114  | 44            | 38.6 |                      | <b>1.93</b>      | <b>1.12-3.32</b>   |
| Asian  | 347  | 140           | 40.4 |                      | <b>1.45</b>      | <b>1.05-2.01</b>   |
| Other  | 126  | 51            | 40.5 |                      | 1.59             | 0.97-2.59          |
| NS   | 32   |               |      |                      |                  |                    |
| <b>Identity</b>                              |      |               |      | 0.218                |                  |                    |
| Gay  | 2491 | 884           | 35.5 |                      | -                | -                  |
| Bisexual                                     | 498  | 155           | 31.4 |                      | -                | -                  |
| Other  | 139  | 50            | 36.0 |                      | -                | -                  |
| NS   | 12   |               |      |                      |                  |                    |
| <b>HIV status</b>                            |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| HIV-negative                                 | 2129 | 788           | 37.0 |                      | <i>Ref.</i>      | -                  |
| HIV-positive                                 | 152  | 69            | 45.4 |                      | <b>1.78</b>      | <b>1.11-2.86</b>   |
| Never tested/Don't know                      | 792  | 212           | 26.8 |                      | 1.05             | 0.77-1.43          |
| NS   | 62   |               |      |                      |                  |                    |
| <b>Qualification</b>                         |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| Non-tertiary                                 | 1676 | 464           | 27.7 |                      | <i>Ref.</i>      | -                  |
| Tertiary or higher                           | 1415 | 617           | 43.6 |                      | <b>1.53</b>      | <b>1.25-1.88</b>   |
| NS   | 44   |               |      |                      |                  |                    |
| <b>GP aware of orientation</b>               |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| No/not sure                                  | 1545 | 476           | 30.8 |                      | <i>Ref.</i>      | -                  |
| Yes  | 1568 | 610           | 38.9 |                      | <b>1.42</b>      | <b>1.25-1.88</b>   |
| NS   | 22   |               |      |                      |                  |                    |

|   | N    | "I knew this" |      | Pearson<br>Chi2<br>P-value | AOR <sup>β</sup> | 95% CI    |
|---|------|---------------|------|----------------------------|------------------|-----------|
|   |      | n             | %    |                            |                  |           |
| <b>Ever had an STI check</b>                    |      |               |      | <b>&lt;0.001</b>           |                  |           |
| Yes   | 2481 | 913           | 36.8 |                            | <i>Ref.</i>      | -         |
| No  | 515  | 135           | 26.2 |                            | 0.93             | 0.67-1.31 |
| NS  | 139  |               |      |                            |                  |           |
| <b>Free time spent with GBM</b>                 |      |               |      | <b>0.025</b>               |                  |           |
| Little/None                                     | 1229 | 400           | 32.6 |                            | <i>Ref.</i>      | -         |
| A lot/some                                      | 1819 | 664           | 36.5 |                            | 0.93             | 0.79-1.21 |
| NS  | 87   |               |      |                            |                  |           |
| <b>Site of Recruitment</b>                      |      |               |      | <b>0.009</b>               |                  |           |
| BGO   | 1037 | 397           | 38.3 |                            | 1.13             | 0.90-1.42 |
| Bars  | 121  | 50            | 41.3 |                            | 1.10             | 0.64-1.90 |
| SOS Venues                                      | 194  | 62            | 32.0 |                            | 0.88             | 0.56-1.40 |
| Online (GOSS)                                   | 1783 | 585           | 32.8 |                            | <i>Ref.</i>      | -         |
| NS  | -    |               |      |                            |                  |           |
| <b>Sexual behaviours</b>                        |      |               |      |                            |                  |           |
| <b>Number of male sexual partners &lt;6mths</b> |      |               |      | 0.073                      |                  |           |
| 20 or less                                      | 2811 | 971           | 34.5 |                            | <i>Ref.</i>      | -         |
| 20+   | 262  | 105           | 40.1 |                            | 1.17             | 0.82-1.67 |
| NS  | 62   |               |      |                            |                  |           |
| <b>Any UAIC &lt;6mths</b>                       |      |               |      | <b>0.001</b>               |                  |           |
| No  | 2110 | 782           | 37.1 |                            | <i>Ref.</i>      | -         |
| Yes   | 936  | 287           | 30.7 |                            | 0.82             | 0.65-1.03 |
| NS  | 89   |               |      |                            |                  |           |

\* Not included in the logistic regression model

α = Adjusted for: age, ethnicity, sexual identity, HIV status at last test, highest qualification, perceived GP awareness of sexual orientation, free-time spent with GBM peers, site of recruitment, number of recent male sexual partners, condom use with recent casual male sexual partners, knowledge that HPV causes AGWs.

UAIC = unprotected anal intercourse with a casual male partner

GP = general practitioner

GBM = gay, bisexual and other men who have sex with men

BGO = Big Gay Out – annual LBGTIQ community fair day held in Auckland

SOS = sex-on-site venue

NS = not stated

### ***Knowledge that HPV can cause any cancers that affect males***

The prevalence of knowledge that HPV causes at least one HPV-related cancer that affects males among the combined sample of GBM was 34.9%. Table 32 presents the bivariate analysis of respondents' self-reported knowledge that HPV can cause at least one of the three cancers presented in the GAPSS and GOSS questionnaires. Factors significantly associated with self-reported cancer knowledge were knowledge that HPV causes AGWs ( $p < 0.001$ ), ethnicity ( $p = 0.002$ ), HIV status at last test ( $p < 0.001$ ), highest qualification reported ( $p < 0.001$ ), perceived GP awareness of respondent's sexual orientation ( $p < 0.001$ ), amount of free time spent with GBM peers (0.025), site of recruitment ( $p = 0.009$ ), and any reported UAIC in the previous six months ( $p = 0.001$ ).

Those who reported Māori ethnicity, had never tested or who were unsure of the result of their last HIV test, who did not hold a tertiary qualification, who did not believe their GP was aware of their sexual orientation, who spent little/no time with their GBM peers, who were recruited from SOS venues, and who reported any UAIC in the previous six months were less likely to report being aware that HPV could cause any cancers in males. Age, sexual identity, and the number of male sexual partners reported in the previous six months did not vary significantly by self-reported knowledge that HPV can cause any cancers in males.

After controlling for the sociodemographic and sexual behavioural factors included in the logistic regression model, ethnicity, HIV status at last test, highest qualification, and perceived GP awareness of sexual orientation were the factors that remained significantly associated with knowledge of any of the HPV-related cancers that can affect males (see *Table 32*). Participants reporting knowledge that HPV causes AGWs had significantly greater odds or reporting knowledge that HPV causes at least one cancer that affects males (AOR=14.70, 95% CI:11.99-18.02). Those who were of Pacific (AOR=1.93, 95% CI:1.12-3.32) or Asian ethnicity (AOR=1.45, 95% CI:1.05-2.01), were living with HIV (AOR=1.78, 95% CI:1.11-2.86), held a tertiary level qualification (AOR=1.53, 95% CI:1.25-1.88), and perceived their GP to be aware of their sexual orientation (AOR=1.42, 95% CI:1.25-1.88) were significantly more likely to report knowledge that HPV caused any cancers in males.

Age, free-time spent with GBM peers, site of recruitment and any reporting any UAIC in the previous six months were no longer significantly associated with knowledge of HPV-related cancers after controlling for the other factors in the logistic regression model.

Table 32: Respondents reporting knowledge that HPV causes any cancer in males vs. no knowledge of any HPV-related disease

|  | N    | "I knew this" |      | Pearson Chi2 P-value | AOR <sup>a</sup> | 95% CI             |
|--|------|---------------|------|----------------------|------------------|--------------------|
|  |      | n             | %    |                      |                  |                    |
| Total                                  | 3135 | 1307          | 41.7 | -                    | -                | -                  |
| NS                                     | 79   |               |      |                      |                  |                    |
| <b>Knowledge HPV causes any cancer</b> |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| Yes                                    | 1094 | 881           | 80.5 |                      | <b>14.78</b>     | <b>12.08-18.08</b> |
| No                                     | 2041 | 426           | 20.9 |                      | <i>Ref.</i>      | -                  |
| NS                                     | 0    |               |      |                      |                  |                    |
| <b>Sociodemographics</b>               |      |               |      |                      |                  |                    |
| <b>Age</b>                             |      |               |      | <b>0.002</b>         |                  |                    |
| Under 27                               | 1046 | 389           | 37.2 |                      | <i>Ref.</i>      | -                  |
| 27-45                                  | 1260 | 548           | 43.5 |                      | 1.08             | 0.86-1.36          |
| 45+                                    | 782  | 346           | 44.3 |                      | 1.14             | 0.87-1.50          |
| NS                                     | 47   |               |      |                      |                  |                    |
| <b>Ethnicity</b>                       |      |               |      | 0.053                |                  |                    |
| European                               | 2216 | 957           | 43.2 |                      | <i>Ref.</i>      | -                  |
| Māori                                  | 300  | 103           | 34.3 |                      | 0.92             | 0.66-1.29          |
| Pacific                                | 114  | 46            | 40.4 |                      | 0.83             | 0.49-1.42          |
| Asian                                  | 347  | 138           | 38.8 |                      | <b>0.60</b>      | <b>0.43-0.82</b>   |
| Other                                  | 126  | 52            | 41.3 |                      | <b>0.59</b>      | <b>0.36-0.97</b>   |
| NS                                     | 32   |               |      |                      |                  |                    |
| <b>Identity</b>                        |      |               |      | <b>0.017</b>         |                  |                    |
| Gay                                    | 2491 | 1067          | 42.8 |                      | <i>Ref.</i>      | -                  |
| Bisexual                               | 493  | 177           | 35.9 |                      | 0.80             | 0.60-1.05          |
| Other                                  | 139  | 59            | 42.5 |                      | 0.96             | 0.60-1.54          |
| NS                                     | 12   |               |      |                      |                  |                    |
| <b>HIV status</b>                      |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| HIV-negative                           | 2129 | 964           | 45.3 |                      | <i>Ref.</i>      | -                  |
| HIV-positive                           | 152  | 73            | 48.0 |                      | 0.86             | 0.54-1.37          |
| Never tested/Don't know                | 242  | 242           | 30.6 |                      | <b>0.67</b>      | <b>0.50-0.90</b>   |
| NS                                     | 62   |               |      |                      |                  |                    |
| <b>Qualification</b>                   |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| Non-tertiary                           | 1676 | 590           | 35.2 |                      | <i>Ref.</i>      | -                  |
| Tertiary or higher                     | 1415 | 700           | 49.5 |                      | <b>1.38</b>      | <b>1.13-1.68</b>   |
| NS                                     | 44   |               |      |                      |                  |                    |
| <b>GP aware of orientation</b>         |      |               |      | <b>&lt;0.001</b>     |                  |                    |
| No/not sure                            | 1545 | 588           | 38.1 |                      | <i>Ref.</i>      | -                  |
| Yes                                    | 1568 | 710           | 45.3 |                      | 0.82             | 0.66-1.02          |
| NS                                     | 22   |               |      |                      |                  |                    |
| <b>Ever had an STI check</b>           |      |               |      | <b>&lt;0.001</b>     |                  |                    |

|   | N    | "I knew this" |      | Pearson<br>Chi2<br>P-value | AOR <sup>α</sup> | 95% CI    |
|---|------|---------------|------|----------------------------|------------------|-----------|
|   |      | n             | %    |                            |                  |           |
| Yes   | 2481 | 1097          | 44.2 |                            | <i>Ref.</i>      | -         |
| No  | 515  | 155           | 30.1 |                            | 0.78             | 0.57-1.08 |
| NS  | 139  |               |      |                            |                  |           |
| <b>Free time spent with GBM*</b>                |      |               |      | 0.162                      |                  |           |
| Little/None                                     | 1229 | 493           | 40.1 |                            | -                | -         |
| A lot/some                                      | 1819 | 776           | 42.7 |                            | -                | -         |
| NS  | 87   |               |      |                            |                  |           |
| <b>Site of Recruitment</b>                      |      |               |      | <b>0.041</b>               |                  |           |
| BGO   | 1037 | 458           | 44.2 |                            | 1.01             | 0.82-1.26 |
| Bars  | 121  | 59            | 48.8 |                            | 1.17             | 0.68-2.00 |
| SOS Venues                                      | 194  | 72            | 37.1 |                            | 0.99             | 0.64-1.53 |
| Online (GOSS)                                   | 1783 | 718           | 40.3 |                            | <i>Ref.</i>      | -         |
| NS  | -    |               |      |                            |                  |           |
| <b>Sexual behaviours</b>                        |      |               |      |                            |                  |           |
| <b>Number of male sexual partners &lt;6mths</b> |      |               |      | 0.060                      |                  |           |
| 20 or less                                      | 2811 | 1162          | 41.3 |                            | <i>Ref.</i>      | -         |
| 20+   | 262  | 124           | 47.3 |                            | 1.16             | 0.82-1.63 |
| NS  | 62   |               |      |                            |                  |           |
| <b>Any UAIC &lt;6mths</b>                       |      |               |      | <b>0.046</b>               |                  |           |
| No  | 2110 | 909           | 43.1 |                            | <i>Ref.</i>      | -         |
| Yes   | 936  | 367           | 39.2 |                            | 0.89             | 0.71-1.10 |
| NS  | 89   |               |      |                            |                  |           |
|   |      |               |      |                            |                  |           |
|   |      |               |      |                            |                  |           |

\* Not included in the logistic regression model

β = Adjusted for: age, ethnicity, HIV status at last test, highest qualification, perceived GP awareness of sexual orientation, free-time spent with GBM peers, site of recruitment, number of recent male sexual partners, condom use with recent casual male sexual partners, knowledge that HPV causes AGWs.

UAIC = unprotected anal intercourse with a casual male partner

GP = general practitioner

GBM = gay, bisexual and other men who have sex with men

BGO = Big Gay Out – annual LBGTIQ community fair day held in Auckland

SOS = sex-on-site venue

NS = not stated

## Discussion

To the candidate's knowledge, this is the first study, internationally, to both describe the prevalence of HPV knowledge and examine sociodemographic and sexual behavioural factors associated with HPV-related disease knowledge among GBM. In this 2014 cross-sectional sample of sexually active GBM, knowledge of HPV being the causal agent for a range of diseases that affect males was low with 51.5% of the combined sample reporting no knowledge of any of the diseases presented. Knowledge that HPV is the causal agent for anogenital warts (41.9%) was greater than that of HPV being the causal agent for anal, oral and penile cancers (29.6%, 28.1%, and 24.0% respectively).

HIV status at last test, highest level of qualification attained, and any reported UAIC in the previous six months were independently associated with each of the three groupings of HPV-related disease knowledge. Other factors found to be independently associated were ethnicity with knowledge of any HPV-related disease, and perceived GP awareness with both knowledge that HPV causes anogenital warts and knowledge that HPV causes any cancers among males. Factors including age, sexual identity, free time spent with GBM peers, and number of male sexual partners in the previous six months were not found to be associated with the three groupings of knowledge in either bivariate or logistic regression analyses.

### **Strengths**

This study utilises the data collected through the GAPSS and GOSS surveys, which recruit a large and diverse sample of GBM from across NZ. Sexual orientation is not routinely asked in datasets collected on a national level, such as in administrative medical records or census. Therefore, a sampling frame cannot be built without a robust denominator estimate, and researchers rely on regular cross-sectional recruitment to gain a sample of GBM large enough to have statistical power to detect both changes over time in key indicators as well as within-population variation.

The GAPSS and GOSS surveys are also periodic surveys with repeatable recruitment, offering the opportunity for the questions to be included in future rounds and compared to these baseline data on HPV-related disease knowledge among GBM prior to the public funding of the HPV vaccine for all males under the age of 27 years.

Other strengths of this study include that participants were asked about the full range of HPV-related disease that can affect males. Previous studies have asked participants awareness of some HPV-related diseases, most commonly anal and oral cancers (see *Table 16*), with only the study by Wheldon et al. found that asked GBM participants about the full range of HPV-related disease (238).



The two surveys collect comprehensive sociodemographic and sexual behavioural data. Linkage of these data to HPV-related disease knowledge allows public health programmes to identify and target groups of GBM who report lower knowledge of HPV-related disease as well as those who may be at greater risk of acquiring and developing HPV-related disease due to reported sexual behaviours. Additionally, this allows an equity lens to be applied to the findings, exploring outcomes for key populations within GBM, such as for Māori.

### ***Limitations***

The HPV-related disease knowledge questions were included in the GAPSS and GOSS surveys opportunistically. The two surveys were not established to measure or monitor these data or factors associated with this knowledge among GBM. Therefore, the factors included in the models are not exhaustive, nor can they fully explain the knowledge variables. Other studies have found gender, income, and relationship status to be explanatory factors associated with HPV-related disease knowledge, which were not collected in this analysis (323).

Participants were presented with a “true” statement, making the knowledge of HPV-related disease prompted in this study. Other studies identified have asked respondents to identify if a statement is true or false and sought to build a knowledge scale, which was beyond the scope and capacity of the GAPSS and GOSS surveys.

A limitation of cross-sectional studies is that it is not possible to attribute temporal causality, to determine which came first, knowledge or the factor related to it (such as sexual behaviours, testing, HIV-status). Directly asking respondents to recall where they believed acquired their knowledge of HPV-related disease would be subject to recall bias but could be a potential avenue to explore further opportunities for public health promotion and education.

As previously noted in the Chapter Five: Section One recruitment for the surveys is not random but opportunistic. Therefore, the results from these analyses cannot be generalised to the GBM population of NZ, yet as there few opportunities to capture a representative sample of GBM in NZ, the cross-sectional recruitment method is appropriate to study this population and provides insight that could inform public health programmes and larger studies.

There are few data to compare these results for HPV-related disease knowledge to other populations in NZ, such as women who have sex with women, heterosexual women and MSW. This lack of a comparison group makes interpreting the level of knowledge held by this population of GBM difficult, and therefore, international comparisons must be utilised.

## **Discussion**

### *Feasibility of using GAPSS/GOSS to monitor HPV-related knowledge among GBM*

It is feasible to use GAPSS and GOSS as tools to provide estimates of HPV knowledge among GBM in NZ. The response rate to HPV-related disease questions among those participating in the survey was high, with 97.5% of respondents answering at least one question. However, a decline in response rate was observed as the questions progressed (range: 97.0% - 95.3%). While the aim was to consider the feasibility of using the GAPSS and GOSS surveys to gain an estimate of HPV-related disease knowledge among GBM in NZ, the robustness of these estimates of knowledge must also be considered. Participation bias will affect these results and therefore the response rate, with those who participate in the surveys being more likely to respond to the questions compared to those who do not participate. Participants who do not submit their questionnaire were also excluded from the final study population for both GAPSS and GOSS. While a participant could submit an incomplete questionnaire, particularly in GAPSS, this restriction would lead to a bias towards a higher response rate being recorded.

Of those who did not provide a response to HPV-related disease questions, the majority were GAPSS participants (see *Table 29*). The method of completion for the two surveys may enable or facilitate greater ability to skip questions. GAPSS is pen and paper, while for GOSS online, each question is posed individually with automated logic skips. Site of recruitment may also explain some of this variation, GAPSS recruits from venues where GBM are socialising and may not be inclined to fully participate in a survey, while GOSS they may be in a moment of free time, facilitating greater focus on completing the survey. However, while there is a difference between the response rates of the two surveys, the rate does not drop below 90% in either survey. Furthermore, the pattern of decline in response rate was similar across both, with the greatest number of participants responding to the first question and numbers declining with subsequent questions. This suggests that it is the survey method rather than the questions that influence non-response for the HPV-related questions.

### *Prevalence of HPV-related disease knowledge among GBM.*

The level of HPV-related disease knowledge among this cross-sectional sample of GBM in NZ was low, with 48.5% of GBM reporting being aware of at least one form of HPV-related disease that affects males. Self-reported knowledge was greater for HPV being the causal agent for anogenital warts compared to HPV-related cancer knowledge.

Knowledge of the causal relationship between HPV and anogenital warts has been established for longer compared to knowledge of HPV being the causal agent for HPV-

related cancers that affect males. Among the general population, HPV-related cancers that affect males are also less prevalent compared to cervical cancer and anogenital warts, making the investment in public health interventions and health promotion programmes unlikely to be cost-effective for these cancers. The GAPSS and GOSS surveys were carried out in early 2014 when there had been little to no promotion of the HPV vaccine or HPV-related cancers that affect males in NZ. Furthermore, the quadrivalent HPV vaccine had only been publicly funded and targeted to females. These factors combined could explain the difference seen between AGW and HPV-related cancer knowledge in this study. This may also partially explain why the vast majority of those who are aware of any HPV-related cancer are also aware of HPV causing anogenital warts, but not vice versa.

Overall, GBM in the combined GAPSS and GOSS sample had a lower knowledge of HPV-related disease compared to international studies. Differences in recruitment methods, sample size, sample demographics and survey approach can explain some of these differences. As identified in the background literature review (see *Table 16*), a number of studies have examined knowledge of various HPV-related diseases among GBM internationally. Wheldon et al. recruited 179 young GBM through snowball methods at education providers in South-Eastern USA (238). Among these GBM, 57% reported being aware HPV caused warts, 43% anal cancer, 39% oral cancer, and 31% penile cancer. The findings are comparable to the combined GAPSS and GOSS sample of which, 42% report knowing HPV causes AGWs, 30% knowing HPV causes anal cancer, 28% knowing HPV causes oral cancer, and 24% knowing HPV causes penile cancer. Brewer et al. recruited males online across the USA in 2010, aged between 18 and 59. Of the 312 GBM recruited in the Brewer study, 46% reported knowledge that HPV causes genital warts, 32% anal cancer, and 25% oral cancer. In 2014, Fenkl et al. recruited 163 GBM at GBM-associated venues and community events in Florida USA, with 69% of respondents reporting knowledge that HPV causes genital warts and 56% anal cancer (and pre-cancers) (241). Closer to NZ, Zou et al. recruited 200 young GBM in 2012 through community media and attending various university groups, venues and events, but required them to physically attend a Melbourne SHC, of which 89% reported being aware that HPV caused genital warts (324). While the proportion of those reporting AGW knowledge is higher than found in the combined GAPSS and GOSS sample, the difference is likely to be a result of recruitment methods (clinic attendance vs. community settings).

Comparison to other studies carried internationally is difficult due to differences in recruitment, populations sampled, sample size, and heterogeneity in questions asked limiting generalisability and direct comparison to the GAPSS and GOSS findings. There are also differences in HPV vaccination recommendations, funding and promotion to consider. In the USA, HPV vaccine had been approved by the FDA for use in boys since October 2009 for

the prevention of genital warts and in December 2010 for the prevention of anal cancer and precancers (207). These approvals and funding (through health insurance) were generally ahead of other countries and certainly NZ. Several of the studies carried out in the USA recruited GBM after either the recommendation or funding of HPV vaccination for males, and therefore, this could have implications for the levels of knowledge expected among their samples. This also affects comparability to the GAPSS and GOSS findings.

Between 16%-20% of GBM respondents reported “*I wasn’t sure*” to the HPV-related knowledge questions (see *Table 29*). In the analysis, those selecting this response have been classified as not having knowledge of HPV-related disease, but this could be an oversimplification and changing this classification could bring results in line with international comparisons mentioned above. However, many of the studies above made use of an HPV knowledge scale in which many of the questions were either “true” or “false” with the majority also providing a “do not know” or “unsure” option. Therefore, the other possible explanations of differences in recruitment methods, population size and state of national HPV vaccination recommendations or funding are more likely to influence differences in the results as compared to question design.

#### *Factors associated with HPV-related disease knowledge among GBM*

From the three logistic models, factors that were independently associated with any form of HPV-related disease knowledge build a picture of those GBM who have limited access to healthcare or healthcare-related knowledge in NZ; being those who are of Māori ethnicity, who do not have a tertiary qualification, who have never accessed sexual health testing services, and who engage in higher-risk sexual behaviours for HIV. These factors are widely accepted as being markers of vulnerable or marginalised populations. More positively, those who do have a higher education, access sexual healthcare services and disclose their sexual orientation to their healthcare provider are significantly more likely to report any form of HPV-related disease knowledge even after controlling for other factors.

Differences between models allude to channels for HPV-related disease knowledge acquisition among GBM in NZ, as well as gaps where certain GBM populations are not being reached with health promotion. This is particularly clear in the model for knowledge that HPV causes any cancers in males, with reporting living with HIV and having a healthcare provider who is aware of participants’ sexual orientation being independently associated with reporting this knowledge. Both of these factors could be perceived as proxy measures for being engaged with culturally appropriate healthcare for the GBM population, providing healthcare and knowledge that is specific to GBM healthcare needs.

Despite a number of variables being significantly associated with HPV-related disease knowledge at the bivariate level, some lost this significance once included in a logistic

regression model. Decisions made during the analyses could have impacted this, namely the inclusion of knowledge of HPV being the causal agent for anogenital warts or any cancers among males in their respective models. These knowledge factors were included in the models as they are considered to be on the causal pathway in these analyses. They could also be considered explanatory variables if a different approach were to be taken. Due to the cross-sectional nature of the data used for these analyses and without having directly asked participants, directionality nor the timeline in which knowledge of either warts or cancers was gained can be ascertained. Future studies could include questions asking participants to recall where and when they gained knowledge of HPV-related diseases.

Reporting of being of Māori ethnicity and having any UAIC in the previous six months were negatively associated with reporting knowledge of any HPV-related diseases. However, these factors are not independently associated with either knowledge of HPV causing anogenital warts or any HPV-related cancers. Smaller group sizes of both Maori and those reporting any UAIC in the separate anogenital wart and cancer knowledge models could explain these differences. Ethnicity was independently associated with anogenital wart knowledge and HPV-related cancer knowledge, but the associations were different in both models. Reporting being of Asian or “Other” ethnicity was negatively independently associated with knowledge that HPV causes anogenital warts. Conversely, reporting being of Asian or Pacific ethnicity was positively associated with knowledge that HPV causes any cancers in males.

In a 2012 study by Colón-López et al. sought to determine factors independently associated with HPV-related knowledge among “high risk” males (N=202), including HPV-related disease knowledge. (325). Thirty per cent of their sample reported being of GBM identity. A scale comprised of 15 true or false questions was posed to participants, and the authors considered a participant to have an “adequate” knowledge score if they responded correctly to 70% of the questions or more. Participants were asked about their sociodemographics and sexual and other HPV risk behaviours. At a bivariate level, only sexual identity and self-reported history of herpes or genital wart diagnosis were associated with an “adequate” HPV-related knowledge score. Factors that were not associated with an “adequate” score included age (though this was included in their logistic regression models), education, income, employment, number of sexual partners and self-reported history of other STI diagnoses. From the regression analysis, only self-reported history of a herpes diagnosis remained independently associated with an “adequate” HPV-related disease knowledge score after controlling for age, sexual identity and history of a genital wart diagnosis. Similar to the findings in the study presented in this chapter, this could be considered a proxy measure for engagement with sexual healthcare to gain knowledge. However, this association was not

seen with a history of other STIs in their study, potentially indicating confusion between HPV and HSV among participants.

The study by Fenkl et al. reported on HPV knowledge and associated sociodemographic factors, sexual behaviours associated with anal HPV infection, and health screening practices among GBM (241). Recruitment for this study was similar to the GAPSS study, through GBM-associated venues and events, but there was no additional online recruitment component comparable to GOSS. Using one-way ANOVA, the authors found HIV status and having previously had an anal Pap-smear were significantly associated with reporting HPV-related knowledge. This is consistent with the study presented here and the study by Colón-López et al., which found that engagement with sexual health care is associated with greater knowledge of HPV. However, both of these studies had a much smaller sample size compared to the combined GAPSS and GOSS sample, and Fenkl et al. did not use logistic regression to control for other factors that could be confounding association with HPV-related knowledge.

## Conclusion

GAPSS and GOSS surveys present an acceptable method for obtaining HPV-related knowledge data among GBM in NZ. In 2014, the majority of GBM participants reported being unaware of HPV-related diseases that can affect males. Knowledge gaps were identified among those who report limited engagement with sexual healthcare and concentrated among populations potentially experiencing intersectional minority statuses.

Findings from the analyses carried out in this section are encouraging, in that those who have a higher level of qualification and believe their GP to be aware of their sexuality are more likely to report knowledge of HPV-related disease. Similarly, those GBM living with HIV, who are more vulnerable to these diseases, are more likely to report awareness of HPV-related diseases.

Future studies could build on this work by including questions specifically related to HPV-risk behaviours and knowledge acquisition. These data could be utilised by public health promotion programmes to build on existing knowledge transfer pathways and find ways to address the gaps that have been identified here.

## Section Three: HPV-vaccine knowledge and acceptability among a cross-sectional community and online sample of GBM in Aotearoa, New Zealand

### Purpose

Understanding the prevalence and factors associated with vaccine acceptability is key to informing and developing vaccination programmes that are targeted and responsive. A vaccine can be highly effective, safe and cost-effective but it will not have the desired impact if those who are most at risk do not know that it is available, and the vaccine is not an acceptable intervention to them.

### Aims

- Describe GAPSS and GOSS study participant response rates to the HPV vaccine awareness and acceptability questions included in the 2014 survey round.
- Describe HPV vaccine awareness among the GBM participants of GAPSS and GOSS.
- Explore HPV vaccine acceptability among GBM participants of the 2014 GAPSS and GOSS rounds under the two pricing conditions presented.
- Determine sociodemographic and sexual behavioural factors that are independently associated with HPV vaccine awareness and acceptability under the two pricing conditions.

### Background

GBM are a population group that experiences a disproportionate burden of HPV-related disease. It is estimated that 85% of anal cancers are caused by HPV and that GBM experience a 20-fold greater incidence of anal cancer compared to heterosexual males, an incidence rate which has continued to increase over time (274, 326). Among HIV-negative GBM, the rate of anal cancers was found to be 5.1 per 100,000 person-years among and for GBM PLHIV 46 per 100,000 person-years (275). These rates among HIV-negative GBM are comparable to the incidence of cervical cancers in the UK prior to the introduction of screening programmes (2).

Studies examining factors associated with HPV vaccine acceptability among GBM include a number of questions relating to an individual's knowledge of HPV and their perception of the risks and benefits of the vaccine (327). Few examine a participant's sexual behaviours related to the risk of HPV-acquisition as potential factors associated with knowledge or acceptability (see *Table 17*). Of those that have included questions relating to sexual

behaviours, a greater number of lifetime sexual partners and a history of STIs are two factors that appear significantly associated with HPV vaccine acceptability.

In NZ, there have been no studies examining HPV acceptability among GBM. In 2010, Chelimo et al. conducted a small study of university students' acceptability of the HPV vaccine, which included male students (272). They found that male university students were less willing to be vaccinated compared to their female peers, with 65.8% of males compared to 89.7% of females willing to accept free vaccination.

Vaccination has been shown to not only prevent HPV-related disease but also infection and carriage (328). Therefore, increasing uptake among GBM HPV could have a herd immunity impact (216). Furthermore, anogenital warts are a predictor for HIV acquisition among GBM (329), who are also over-represented among HIV diagnoses in NZ (316). Therefore, targeting GBM engaging in higher-risk sexual practices with HPV vaccination could have a disproportionate network impact on HIV incidence.

## Methods

The GAPSS and GOSS surveys are repeat, cross-sectional behavioural surveys designed to collect data on sociodemographics, knowledge and attitudes, testing and sexual behaviours related to HIV risk among sexually active GBM. The methods provided below describe the approach taken to the analyses of this Section.

### ***GAPSS and GOSS Recruitment***

The recruitment methods for both these studies are covered in more detail in Chapter Five: Section One and are published elsewhere in greater detail (128).

### ***HPV Vaccine Knowledge and Acceptability Questions***

In the 2014 survey round, questions were included that sought to collect baseline data on GBM knowledge of HPV-related disease, HPV vaccine awareness and acceptability, and HPV vaccine uptake.

Participants were provided with a statement explaining the existence of the Gardasil4 vaccine and that it provides protection against anogenital warts and HPV-related cancers in males: "*Gardasil – the vaccine used to protect girls against cervical cancer – also protects men against other cancers and genital warts*". They were asked if they were aware of this prior to taking part in the survey. Possible responses included:

- "*I knew this*"
- "*I didn't know this*"
- "*I wasn't sure*"



Participants were informed, that to provide the best protection, the vaccine required three doses: *“The next questions are about the Gardasil vaccine that requires three injections to give the best protection against HPV”*. Given the information provided, participants were asked if they would be willing to be vaccinated under two different conditions. Firstly, they were asked if they would consider being vaccinated if the three-dose course was fully funded). Secondly, they were asked if they would be willing to be vaccinated if they would be required to pay the 2014 price in NZ for the vaccine course, which was rounded to NZ\$500.00 (NZ\$167.00/dose). Possible responses to both questions included:

- “Yes”
- “No”
- “I’m not sure”

### **Statistical Analyses**

The analyses consist of three steps: firstly, basic frequencies for each of the three questions (HPV-vaccine knowledge, acceptability at \$500.00, and acceptability if fully funded); secondly, bivariate analyses for the two acceptability questions cross-tabulated with sociodemographic, knowledge, testing and sexual behavioural factors, and those factors potentially associated or considered confounders; thirdly, logistic regression modelling for each acceptability question to determine independently associated factors.

The response options to the questions were dichotomised for these analyses. For knowledge of HPV-vaccine, the responses were grouped “*I knew this*” and “*I didn’t know this/I wasn’t sure*”. For the acceptability questions, the responses were grouped “Yes” and “*No/I’m not sure*”.

Where possible, factors for inclusion in the bivariate and logistic regression analyses were chosen based on those found to be independently associated with HPV vaccine acceptability among GBM and sexual risk behaviours known to be associated with HPV acquisition risk in the literature. These included:

- age
- ethnicity
- highest level of qualification achieved
- knowledge of HPV-related disease
- HPV vaccine awareness
- number of male sexual partners in the previous six months
- reporting any UAIC in the previous six months

Factors included that are specific to the GAPSS/GOSS questionnaire include:

- sexual identity
- result of last HIV test
- free time spent with GBM
- having ever had a check-up or treatment for an STI
- perceived GP awareness of sexual orientation

Site of recruitment was included in logistic regression analyses to control for potential recruitment bias.

#### *Logistic regression models*

A logistic regression model was constructed for each acceptability condition, fully funded and at full price. For each model, those variables found to be significantly associated (Chi-square p-value of 0.05 or less) with each condition in bivariate analysis were included in their respective models. Variables with a p-value of 0.01 or less were also included in the respective models. Factors that were not significant or had a p-value greater than 0.01 were included in the models if they were hypothesised to be potential confounders or explanatory factors. These include age and site of survey recruitment.

Where possible and appropriate, independent variables have been dichotomised to aid in model stability and to add statistical power where sample sizes are limited.

All data analyses were conducted using STATA version 13.1 (Stata Corporation, College Station, TX, US).

## Results

Awareness of the HPV vaccine and the protection it offers against HPV-related diseases that affect males was 17.1% among the combined sample of GBM (see *Figure 24*). Vaccine acceptability was 78.1% under the pricing condition of fully funded, with few respondents (4.1%) indicating they would not be willing to receive the vaccine under this condition. In comparison, vaccine acceptability was 12.5% under the pricing condition of NZ\$500.00, with the majority of participants (54.8%) responding that they would not be willing to be vaccinated under this pricing condition.

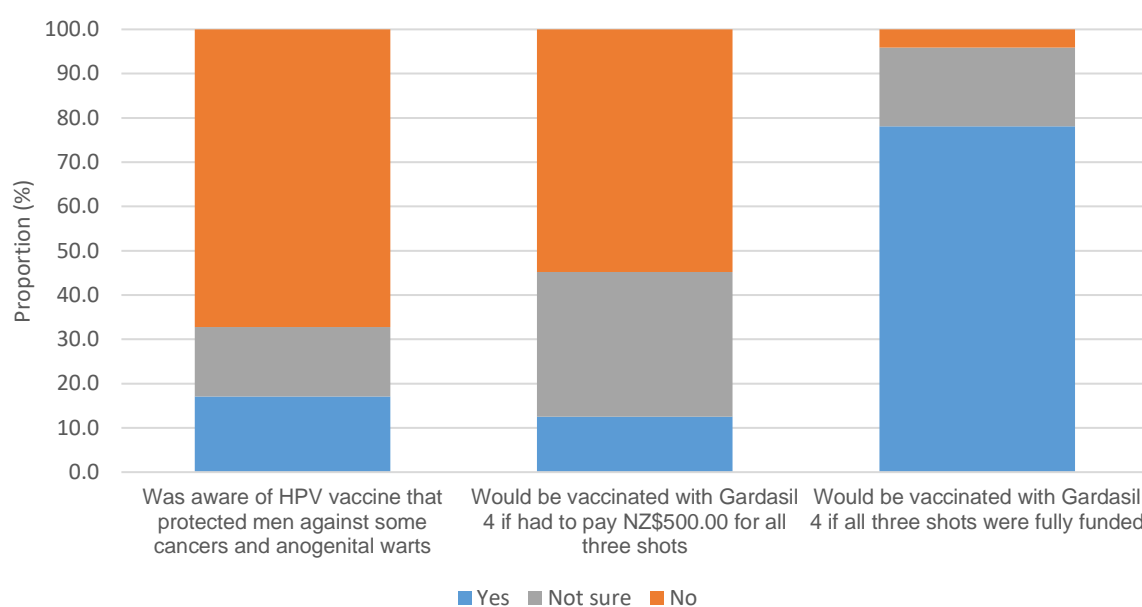


Figure 24: Participants responses to HPV vaccine knowledge and acceptability questions, among the combined GAPSS and GOSS sample.

Table 33 shows that of the combined GAPSS and GOSS sample, across all three vaccine-related questions, between 3.1%—3.3% of participants did not provide a response to any one question. Overall, a greater proportion of GOSS participants responded to all vaccine questions (range:1.1%—1.3%) compared to GAPSS respondents (range:5.5%—6.1%). Among both surveys, the response rate was similar for the HPV vaccine awareness question and vaccine acceptability under the price condition of fully funded. Similarly, in both surveys, the response rate was lowest for the vaccine acceptability question with the price condition of \$500.00.

Table 33: Basic frequencies of GBM participant's responses to HPV-vaccine knowledge and acceptability questions in the 2014 round of the GAPSS and GOSS surveys

| Question   | Combined    |              | GAPSS       |              | GOSS        |              | P-value          |
|--|-------------|--------------|-------------|--------------|-------------|--------------|------------------|
|  | n           | %*           | n           | %*           | n           | %*           |                  |
| <b>Total</b>   | <b>3214</b> | <b>100.0</b> | <b>1421</b> | <b>100.0</b> | <b>1793</b> | <b>100.0</b> |                  |
| <b>Was aware that Gardasil 4 vaccine protected men against some cancers and anogenital warts</b> |             |              |             |              |             |              | <b>&lt;0.001</b> |
| I knew this  | 531         | 17.1         | 279         | 20.8         | 252         | 14.2         |                  |
| I didn't know this   | 2092        | 67.2         | 804         | 59.9         | 1288        | 72.8         |                  |
| I wasn't sure  | 490         | 15.7         | 260         | 19.4         | 230         | 13.0         |                  |
| NS   | 101         | (3.1)        | 78          | (5.5)        | 23          | (1.3)        |                  |
| <b>Would be vaccinated with Gardasil 4 if all three shots were fully funded</b>                  |             |              |             |              |             |              | <b>&lt;0.001</b> |
| Yes  | 2433        | 78.1         | 931         | 69.4         | 1502        | 84.7         |                  |
| No   | 127         | 4.1          | 76          | 5.7          | 51          | 2.9          |                  |
| Don't know   | 555         | 17.8         | 335         | 25.0         | 220         | 12.4         |                  |
| NS   | 99          | (3.1)        | 79          | (5.6)        | 20          | (1.1)        |                  |
| <b>Would be vaccinated with Gardasil 4 if had to pay NZ\$500.00 for all three shots</b>          |             |              |             |              |             |              | <b>&lt;0.001</b> |
| Yes  | 388         | 12.5         | 202         | 15.1         | 186         | 10.5         |                  |
| No   | 1702        | 54.8         | 623         | 46.7         | 1079        | 60.9         |                  |
| Don't know   | 1017        | 32.7         | 510         | 38.2         | 507         | 28.6         |                  |
| NS   | 107         | (3.3)        | 86          | (6.1)        | 21          | (1.2)        |                  |

NS = not stated

\* Percentages for NS are separate to the percentages of those responding to the question

### **HPV vaccine awareness**

Table 33 shows that of the combined GAPSS and GOSS sample, 96.9% of participants answered this question. A greater proportion of GOSS participants answered this question (98.7%) as compared to GAPSS participants (94.5%).

Awareness of the HPV vaccine and its protection of men against HPV-related disease was 17.1% among this sample (see Table 33). When the sample was split into the two surveys, there was a greater proportion reporting "I knew this" among GAPSS participants (20.8%) as compared to GOSS participants (14.2%). Similarly, there was a greater proportion reporting "I wasn't sure" among GAPSS participants (19.4%) compared to GOSS participants (13.0).

### ***Acceptability of HPV vaccination if fully funded***

The response rate to this question was 96.9% among the combined sample (see Table 33). Fewer GAPSS participants provided a response (94.4%) compared to GOSS participants (98.9%).

Among the combined sample, 78.1% of all participants reported they would be willing to be vaccinated if it were provided for free. Acceptability under this condition was greater among GOSS participants compared to those in GAPSS (84.7% and 69.4%, respectively), with a greater proportion of GAPSS participants (25.0%) reporting that they were not sure if they would receive the vaccine under this condition compared to GOSS participants (12.4%).

Table 34 shows those factors significantly associated with HPV vaccine acceptability if the vaccine were provided for free. For sociodemographic factors, age ( $p=0.001$ ), sexual identity ( $p=0.006$ ), HIV status at last test ( $p=0.005$ ), and being recruited online ( $p<0.001$ ) were significantly associated with acceptability under this pricing condition, while ethnicity, highest level of qualification and free time spent with GBM were not found to be associated.

Both reporting knowledge of HPV-related diseases that affect males ( $p<0.001$ ), and knowledge that of the HPV vaccine protects males against HPV-related disease ( $p<0.001$ ), were strongly associated with acceptability if the vaccine were provided for free.

Testing and sexual behavioural factors associated with acceptability under this condition included having ever been tested or treated for an STI ( $p=0.014$ ) and reporting any UAIC in the previous six months ( $p<0.001$ ). Perceived GP awareness of participant's sexual orientation and number of male sexual partners in the previous six months were not associated.

Factors included in the logistic regression model that remained independently associated with greater odds of reporting HPV vaccine acceptability if fully funded, included those who report a sexual identity "Other" than gay or bisexual (AOR=0.52, 95% CI:0.34-0.81), had never tested for HIV or were unsure about the result of their last test (AOR=0.73, 95% CI:0.55-0.97), who were recruited online (AOR=2.64, 95% CI:2.13-3.27), who reported knowledge of any HPV-related disease that affects males (AOR=1.70, 95% CI:1.38-2.10), who reported knowledge that the HPV vaccine protects males against HPV-related disease (AOR=2.12, 95% CI:1.52-2.97), and who reported any UAIC in the previous six months (AOR=1.42, 95% CI:1.13-1.78).

Age and reporting ever having a check-up or treatment for an STI were no longer significant once included in the model. Ethnicity was included in the model due to its  $p$ -value of 0.097 at the bivariate level, but no significance was seen once included in the logistic regression model.

Table 34: Respondents reporting they would receive all three vaccinations if fully funded vs. would not or were unsure

|                                  | N    | "Yes" |      | Pearson<br>Chi2<br>P-value | AOR         | 95% CI           |
|----------------------------------|------|-------|------|----------------------------|-------------|------------------|
|                                  |      | n     | %    |                            |             |                  |
| Total                            | 3115 | 2433  | 78.1 | -                          | -           | -                |
| NS                               | 99   |       |      |                            |             |                  |
| <b>Sociodemographics</b>         |      |       |      |                            |             |                  |
| <b>Age</b>                       |      |       |      | <b>0.001</b>               |             |                  |
| Under 27                         | 1044 | 842   | 80.7 |                            | <i>Ref.</i> | -                |
| 27-45                            | 1250 | 985   | 78.8 |                            | 0.71        | <b>0.56-0.91</b> |
| 45+                              | 776  | 569   | 73.3 |                            | 0.53        | <b>0.40-0.70</b> |
| NS                               | 45   |       |      |                            |             |                  |
| <b>Ethnicity</b>                 |      |       |      | 0.097                      |             |                  |
| European                         | 2206 | 1744  | 79.1 |                            | <i>Ref.</i> | -                |
| Māori                            | 300  | 239   | 79.7 |                            | 1.35        | 0.94-1.93        |
| Pacific                          | 111  | 80    | 72.1 |                            | 0.78        | 0.47-1.29        |
| Asian                            | 344  | 265   | 77.0 |                            | 0.93        | 0.68-1.28        |
| Other                            | 124  | 88    | 71.0 |                            | 0.78        | 0.50-1.22        |
| NS                               | 30   |       |      |                            |             |                  |
| <b>Identity</b>                  |      |       |      | <b>0.006</b>               |             |                  |
| Gay                              | 2474 | 1959  | 79.2 |                            | <i>Ref.</i> | -                |
| Bisexual                         | 490  | 369   | 75.3 |                            | 0.80        | 0.61-1.04        |
| Other                            | 140  | 97    | 69.3 |                            | <b>0.52</b> | <b>0.34-0.81</b> |
| NS                               | 11   |       |      |                            |             |                  |
| <b>HIV status</b>                |      |       |      | <b>0.005</b>               |             |                  |
| HIV-negative                     | 2114 | 1685  | 79.7 |                            | <i>Ref.</i> | -                |
| HIV-positive                     | 154  | 117   | 76.0 |                            | 0.78        | 0.50-1.21        |
| Never tested/Don't know          | 791  | 587   | 74.2 |                            | <b>0.73</b> | <b>0.55-0.97</b> |
| NS                               | 56   |       |      |                            |             |                  |
| <b>Qualification</b>             |      |       |      | 0.548                      |             |                  |
| Nontertiary                      | 1669 | 1301  | 78.0 |                            | -           | -                |
| Tertiary or higher               | 1404 | 1107  | 78.9 |                            | -           | -                |
| NS                               | 42   |       |      |                            |             |                  |
| <b>GP aware of orientation</b>   |      |       |      | 0.138                      |             |                  |
| No/not sure                      | 1534 | 1182  | 77.1 |                            | -           | -                |
| Yes                              | 1562 | 1238  | 79.3 |                            | -           | -                |
| NS                               | 19   |       |      |                            |             |                  |
| <b>Ever had an STI check</b>     |      |       |      | <b>0.014</b>               |             |                  |
| Yes                              | 2468 | 1966  | 79.7 |                            | <i>Ref.</i> | -                |
| No                               | 512  | 383   | 74.8 |                            | 0.84        | 0.62-1.13        |
| NS                               | 135  |       |      |                            |             |                  |
| <b>Free time spent with GBM*</b> |      |       |      | 0.702                      |             |                  |

|  | N    | "Yes" |      | Pearson<br>Chi2<br>P-value | AOR         | 95% CI           |
|--|------|-------|------|----------------------------|-------------|------------------|
|  |      | n     | %    |                            |             |                  |
| Little/None                                      | 1224 | 960   | 78.4 |                            | -           | -                |
| A lot/some                                       | 1810 | 1409  | 77.9 |                            | -           | -                |
| NS   | 81   |       |      |                            |             |                  |
| <b>Site of Recruitment</b>                       |      |       |      | <b>&lt;0.001</b>           |             |                  |
| BGO  | 1032 | 722   | 70.0 |                            | <i>Ref.</i> | -                |
| Bars   | 117  | 79    | 67.5 |                            | 0.97        | 0.60-1.58        |
| SOS Venues                                       | 193  | 130   | 67.4 |                            | 1.34        | 0.89-1.99        |
| Online (GOSS)                                    | 1773 | 1502  | 84.7 |                            | <b>2.64</b> | <b>2.13-3.27</b> |
| NS   | -    |       |      |                            |             |                  |
| <b>HPV-related knowledge</b>                     |      |       |      |                            |             |                  |
| <b>Knowledge of any HPV-related disease</b>      |      |       |      | <b>&lt;0.001</b>           |             |                  |
| Any knowledge                                    | 1505 | 1257  | 83.5 |                            | <b>1.70</b> | <b>1.38-2.10</b> |
| No knowledge                                     | 1602 | 1171  | 73.1 |                            | <i>Ref.</i> | -                |
| NS   | 7    |       |      |                            |             |                  |
| <b>Knowledge of Gardasil vaccine</b>             |      |       |      | <b>&lt;0.001</b>           |             |                  |
| I knew that                                      | 527  | 462   | 87.7 |                            | <b>2.12</b> | <b>1.52-2.97</b> |
| I didn't know/ I wasn't sure                     | 2565 | 1951  | 76.1 |                            | <i>Ref.</i> | -                |
| NS   | 23   |       |      |                            |             |                  |
| <b>Sexual behaviours</b>                         |      |       |      |                            |             |                  |
| <b>Number of male sexual partners &lt;6mths*</b> |      |       |      | 0.280                      |             |                  |
| 20 or less                                       | 2794 | 2187  | 78.3 |                            | -           | -                |
| 20+  | 260  | 211   | 81.2 |                            | -           | -                |
| NS   | 61   |       |      |                            |             |                  |
| <b>Any UAIC &lt;6mths</b>                        |      |       |      | <b>&lt;0.001</b>           |             |                  |
| No   | 2097 | 1596  | 76.1 |                            | <i>Ref.</i> | -                |
| Yes  | 930  | 777   | 83.6 |                            | <b>1.42</b> | <b>1.13-1.78</b> |
| NS   | 88   |       |      |                            |             |                  |

\* Not included in the logistical regression model

UAIC = unprotected anal intercourse with a casual male partner

GP = general practitioner

GBM = gay, bisexual and other men who have sex with men

BGO = Big Gay Out – annual LBGTIQ community fair day held in Auckland

SOS = sex-on-site venue

NS = not stated

### **Acceptability of HPV vaccination at the cost of NZ\$500.00**

Overall, 96.7% of GAPSS and GOSS participants answered this question (see *Table 33*). Similar to other HPV-related questions in these surveys, a greater proportion of GOSS participants answered this question compared to GAPSS participants (98.8% and 93.9%, respectively).

Acceptability of the HPV at full price among this sample of GBM was 12.5%. GAPSS participants reported greater acceptability of the HPV vaccine at the 2014 price (15.1% vs. 10.5%, respectively), but also greater uncertainty compared to GOSS participants (38.2% vs. 28.6%, respectively).

Factors significantly associated at the bivariate level with HPV vaccine acceptability at the price of NZ\$500.00 are shown in *Table 35*. Of the sociodemographic factors, those who were 27 years or older ( $p < 0.001$ ), knew the result of their last HIV test ( $p = 0.001$ ), and had a tertiary level or higher-level qualification ( $p = 0.008$ ), and were recruited in bars ( $p < 0.001$ ) were significantly more likely to report acceptance of the HPV vaccine at the cost of \$500.00. Ethnicity, sexual identity, and free time spent with GBM were not found to be associated with acceptability under this price condition.

Both knowledge of HPV-related diseases that affect males ( $p < 0.001$ ), and of the HPV vaccine and its protective effect for males ( $p < 0.001$ ), were significantly associated with acceptability at NZ\$500.00.

In terms of testing and sexual behaviours, those significantly more likely to report HPV vaccine acceptability at this price condition were those who believed their GP to be aware of their sexual orientation ( $p = 0.002$ ), had ever had an STI test or treatment ( $< 0.001$ ), and reported no UAIC in the previous six months ( $p = 0.002$ ). Number of male sexual partners reported in the previous six months was not significantly associated.

After controlling for all sociodemographic, knowledge, and testing and sexual behaviours that were significant at the bivariate level, factors that remained independently associated with HPV vaccine acceptability at full price included are shown in *Table 35*. Being aged 27 years or older and reporting knowledge that there is an HPV vaccine that protects males against HPV-related disease (AOR=2.47, 95% CI:1.84-3.31) were independently associated with greater odds of reporting vaccine acceptability at the price of NZ\$500.00. While having never had an STI check or treatment (AOR=0.58, 95% CI:0.37-0.92) was independently associated with lower odds of reporting acceptability.

Those factors from the bivariate analyses that were no longer significant after inclusion in the logistic regression model included HIV status at last test, highest level of qualification achieved, perceived GP awareness of sexual orientation, site of survey recruitment, reporting



knowledge of any HPV-related diseases that affect males, and reporting any UAIC in the previous six months.

Table 35: Respondents who report they would have all three vaccinations doses for the cost of NZ\$500.00 vs. would not or were unsure

|                                | N    | "Yes" |      | Pearson<br>Chi2<br>P-value | AOR         | 95% CI           |
|--------------------------------|------|-------|------|----------------------------|-------------|------------------|
|                                |      | N     | %    |                            |             |                  |
| Total                          | 3107 | 388   | 12.5 | -                          | -           | -                |
| NS                             | 107  |       |      |                            |             |                  |
| <b>Sociodemographics</b>       |      |       |      |                            |             |                  |
| <b>Age</b>                     |      |       |      | <b>&lt;0.001</b>           |             |                  |
| Under 27                       | 1039 | 80    | 7.7  |                            | <i>Ref.</i> | -                |
| 27-45                          | 1249 | 180   | 14.4 |                            | <b>1.81</b> | <b>1.33-2.47</b> |
| 45+                            | 115  | 115   | 14.9 |                            | <b>1.75</b> | <b>1.23-2.48</b> |
| NS                             | 45   |       |      |                            |             |                  |
| <b>Ethnicity</b>               |      |       |      | 0.727                      |             |                  |
| European                       | 2202 | 274   | 12.4 |                            | -           | -                |
| Māori                          | 301  | 35    | 11.6 |                            | -           | -                |
| Pacific                        | 110  | 10    | 9.1  |                            | -           | -                |
| Asian                          | 344  | 48    | 14.0 |                            | -           | -                |
| Other                          | 123  | 15    | 12.2 |                            | -           | -                |
| NS                             | 27   |       |      |                            |             |                  |
| <b>Identity</b>                |      |       |      | 0.237                      |             |                  |
| Gay                            | 2471 | 320   | 13.0 |                            | -           | -                |
| Bisexual                       | 485  | 53    | 10.9 |                            | -           | -                |
| Other                          | 140  | 13    | 9.3  |                            | -           | -                |
| NS                             | 11   |       |      |                            |             |                  |
| <b>HIV status</b>              |      |       |      | <b>0.001</b>               |             |                  |
| HIV-negative                   | 2115 | 290   | 13.7 |                            | <i>Ref.</i> | -                |
| HIV-positive                   | 152  | 20    | 13.2 |                            | 0.84        | 0.49-1.46        |
| Never tested/Don't know        | 784  | 67    | 8.6  |                            | 1.14        | 0.78-1.66        |
| NS                             | 56   |       |      |                            |             |                  |
| <b>Qualification</b>           |      |       |      | <b>0.008</b>               |             |                  |
| Non-tertiary                   | 1665 | 183   | 11.0 |                            | <i>Ref.</i> | -                |
| Tertiary or higher             | 1400 | 198   | 14.1 |                            | 1.05        | 0.82-1.35        |
| NS                             | 42   |       |      |                            |             |                  |
| <b>GP aware of orientation</b> |      |       |      | <b>0.002</b>               |             |                  |
| No/not sure                    | 1533 | 162   | 10.6 |                            | <i>Ref.</i> | -                |
| Yes                            | 1555 | 223   | 14.3 |                            | 1.10        | 0.85-1.43        |
| NS                             | 19   |       |      |                            |             |                  |
|                                |      |       |      |                            |             |                  |
| <b>Ever had an STI check</b>   |      |       |      | <b>&lt;0.001</b>           |             |                  |
| Yes                            | 2466 | 333   | 13.5 |                            | <i>Ref.</i> | -                |

|  | N    | "Yes" |      | Pearson Chi2 P-value | AOR         | 95% CI           |
|--|------|-------|------|----------------------|-------------|------------------|
|  |      | N     | %    |                      |             |                  |
| No   | 507  | 38    | 7.5  |                      | <b>0.58</b> | <b>0.37-0.92</b> |
| NS   | 134  |       |      |                      |             |                  |
| <b>Free time spent with GBM*</b>                 |      |       |      | 0.210                |             |                  |
| Little/None                                      | 1220 | 140   | 11.5 |                      | -           | -                |
| A lot/some                                       | 1807 | 235   | 13.0 |                      | -           | -                |
| NS   | 80   |       |      |                      |             |                  |
| <b>Site of Recruitment</b>                       |      |       |      | <b>&lt;0.001</b>     |             |                  |
| BGO  | 1027 | 141   | 13.7 |                      | <i>Ref.</i> | -                |
| Bars   | 117  | 24    | 20.5 |                      | 1.27        | 0.70-2.28        |
| SOS Venues                                       | 191  | 37    | 19.4 |                      | 1.56        | 0.97-2.51        |
| Online (GOSS)                                    | 1772 | 186   | 10.5 |                      | 0.89        | 0.68-1.17        |
| NS   | -    |       |      |                      |             |                  |
| <b>HPV-related knowledge</b>                     |      |       |      |                      |             |                  |
| <b>Knowledge of any HPV-related disease</b>      |      |       |      | <b>&lt;0.001</b>     |             |                  |
| Any knowledge                                    | 1501 | 238   | 15.9 |                      | 1.24        | 0.95-1.62        |
| No knowledge                                     | 1598 | 149   | 9.3  |                      | <i>Ref.</i> | -                |
| NS   | 8    |       |      |                      |             |                  |
| <b>Knowledge of Gardasil vaccine</b>             |      |       |      | <b>&lt;0.001</b>     |             |                  |
| I knew that                                      | 522  | 122   | 23.4 |                      | <b>2.47</b> | <b>1.84-3.31</b> |
| I didn't know/ I wasn't sure                     | 2561 | 262   | 10.2 |                      | <i>Ref.</i> | -                |
| NS   | 24   |       |      |                      |             |                  |
| <b>Sexual behaviours</b>                         |      |       |      |                      |             |                  |
| <b>Number of male sexual partners &lt;6mths*</b> |      |       |      | 0.555                |             |                  |
| 20 or less                                       | 2789 | 343   | 12.3 |                      | -           | -                |
| 20+  | 258  | 35    | 13.6 |                      | -           | -                |
| NS   | 60   |       |      |                      |             |                  |
| <b>Any UAIC &lt;6mths</b>                        |      |       |      | <b>0.002</b>         |             |                  |
| No   | 2091 | 284   | 13.6 |                      | <i>Ref.</i> | -                |
| Yes  | 929  | 89    | 9.6  |                      | 0.79        | 0.60-1.04        |
| NS   | 87   |       |      |                      |             |                  |

\* Not included in the logistical regression model

UAIC = unprotected anal intercourse with a casual male partner

GP = general practitioner

GBM = gay, bisexual and other men who have sex with men

BGO = Big Gay Out – annual LBGTIQ community fair day held in Auckland

SOS = sex-on-site venue

NS = not stated

## Discussion

These data are the first to be collected on GBM HPV vaccine knowledge and acceptability in NZ. Among this large and diverse national cross-sectional sample of GBM, knowledge that the HPV vaccine also protects males from HPV-related disease was 17.1%. There was also a stark difference in HPV vaccine acceptability between the two conditions presented to participants, with 78.1% acceptance rate for a vaccine provided for free and 12.5% acceptance rate for a vaccine at the 2014 price.

Knowledge that the HPV vaccine provides protection to males against HPV-related disease was the only shared independent predictor of acceptability under both conditions. Being aged 27 years or older and having ever had a check-up or treatment for an STI were also independently associated with willingness to be vaccinated if required to pay. Whereas a sexual identity “Other” than gay or bisexual, never having tested for HIV or a participant not knowing the result of their last HIV test, being recruited through online channels, knowledge of any HPV-related disease that affects males, and reporting any UAIC in the previous six months were factors independently associated with acceptance of the HPV vaccine if provided for free.

### ***Study strengths***

A strength of this study is that it is a large and diverse, national, cross-sectional sample of GBM in NZ. Compared to studies examining HPV vaccine acceptability among GBM, the sample size of this study is considerably larger. Though not generalisable to the GBM population of NZ or globally, it provides the statistical power to show differences between groups and provide a robust estimate for vaccine acceptability among GBM in NZ.

The study methods are repeatable and can control for recruitment bias or changes in sociodemographic variables between survey rounds. Additionally, the anonymous and self-completed nature of the survey reduces reporting and social desirability biases.

Examining sexual risk behaviours allows the exploration of HPV acceptability among those most at risk of acquiring HPV and/or HIV through sexual contact. This is important for the design and implementation of HPV vaccination programmes and particularly in NZ where there is a catch-up programme in place for GBM who have previously missed out on school-based programmes and where HPV has been framed only to cause of cervical cancer.

### ***Study limitations***

A limitation of the study is that the survey was not designed to determine factors related to vaccine acceptability among GBM. Other studies designed for this purpose have examined associations with perceptions of the personal benefits and possible side-effects of the

vaccine, as well as an individual's perceived risks of acquiring HPV or developing HPV-related disease based on health belief or behavioural change theory models. Perception of the effectiveness of the HPV vaccine for males, anticipatory regret, and perceived risk of acquiring HPV or HPV-related disease have been shown to be associated with HPV vaccine acceptability in a number of studies (281). In this study, these could not be examined due to limited space in an existing survey. However, the inclusion of sexual behaviours known to be associated with HPV acquisition allows the examination of HPV vaccine acceptability among those potentially most at risk of developing HPV-related disease, regardless of personal perception of risk.

Due to the wording of the HPV vaccine knowledge question, it would not be possible to know that the vaccine protects men from HPV-related disease without knowledge of HPV-related disease, meaning these two questions potentially have a high level of collinearity or share the same causal pathway to vaccine acceptability. It may be that this is a staged process, first acquiring knowledge of either the HPV vaccine or HPV-related disease then finding out the next stage. An improvement would be to change the question to be two separate questions, firstly regarding knowledge or awareness of the HPV vaccine and secondly knowledge that it also protects males from HPV-related disease.

Willingness to be vaccinated is different from vaccine uptake. Though this study asks participants if they would be willing to be vaccinated under hypothetical conditions, this is not a measure of current or future vaccine uptake should either condition be available to GBM. While vaccine uptake is explored in Chapter Three, it is worth noting that there will be factors affecting vaccine uptake that are not explored when examining vaccine acceptability, such as barriers to accessing healthcare, health literacy and household income.

The difference in response rate to questions between GAPSS and GOSS highlights some possibilities and raises questions. The online questionnaire design of GOSS, where questions are posed individually and had skips and logic built-in, may have led to greater completion compared to participants being confronted with the questionnaire in its entirety (GAPSS). However, the response or completion rate for both GAPSS and GOSS is not available for comparison, so while single question completion rate might have been higher, overall survey completion rate may have been lower, resulting in a biased sample.

### ***Discussion of results***

In this sample, the vaccine acceptability rate if offered for free of 71% was comparable to a similar study by Rank et al. in 2012 with a 67% acceptance rate among Canadian MSM (N=1169) (254).

The study by Rank et al. reports a similar study methodology to GAPSS and also use an existing survey designed to measure factors of interest for HIV prevention and control among GBM, making it comparable to GAPSS. The question relating to HPV vaccine acceptability was framed as a willingness to be vaccinated if the vaccine were available for GBM, which could be interpreted by participants in a number of ways and does not specify it is fully funded. However, as most healthcare in Canada is publicly funded, it is likely that this was interpreted as being funded.

Among wider studies of HPV vaccine acceptability in GBM, acceptance rates vary widely from 6% to 86% (255, 300). Comparison to other studies is limited by sample size, recruitment methods, sociodemographic composition of samples, year of study recruitment, the questions posed and the response options available. Reiter et al. and Lau et al. explore HPV vaccine acceptability among GBM under different cost conditions, similar to this study, finding an acceptance rate of 6% and 29% (Reiter et al. and Lau et al., respectively) if the vaccine cost the full price and a rate of 74% and 79% (Reiter et al. and Lau et al., respectively) if the vaccine were provided for free (256, 300). Though not directly comparable due to differences in the studies, the marked differences in vaccine acceptability under different price conditions are shared with the GAPSS and GOSS results.

In a 2013 meta-analysis of HPV vaccine acceptability among males, Newman et al. found that there was no significant difference in vaccine acceptability among GBM as compared to heterosexual males (GBM n=986, 58% acceptance, heterosexual males n=1713, 51% acceptance;  $p=0.81$ ) (281). While there may be no significant difference in acceptability rates, it is possible that factors related to acceptability are different for GBM and heterosexual males, but these factors are not separated in their analyses. However, results from this analysis found similar factors related to HPV vaccine acceptability to this study, including HPV awareness, knowledge of HPV, cost, and a history of STIs.

A factor found to be associated with greater vaccine acceptability in studies among GBM and other populations is healthcare provider recommendation, particularly in the USA (251). In these analyses, perceived GP awareness of participant's sexual orientation could be a similar variable. This factor was found to be significant in the bivariate analysis under the condition of the participant being required to pay the full price. However, it was not found to be independently associated when included in the logistic regression model for acceptability under this condition.

Health seeking behaviour and engagement with sexual healthcare was positively associated with HPV vaccine acceptability in this study. Participant's knowledge of the result of their last HIV test and ever having had a check-up or treatment for an STI (both of which were independently associated with acceptability) shows a level of engagement in healthcare that

could have a similar effect on HPV vaccine acceptability as healthcare provider recommendation as seen in other studies (330). Similarly, having a history of STIs has been found to be associated with HPV vaccine acceptability, and this is reflected in this study with having ever had a check-up or treatment for an STI being independently associated (281).

Reassuringly, reporting any UAIC in the previous six months is independently associated with increased vaccine acceptability under the condition of it being offered for free. This could have significant implications for the current situation in NZ where the HPV vaccine is available fully funded to all persons under the age of 27 years, as individuals engaging in UAIC are more likely to acquire HPV and therefore suffer from HPV-related disease. However, the possible positives of vaccinating those at highest risk may be mitigated by the potential of this group to have already been exposed to HPV strains covered by the vaccine and therefore reduce the efficacy of the vaccine. The same independent association is not seen under the condition where the individual must pay the full price for the HPV vaccine, and indeed the association at the bivariate level is in the opposite direction. This may be due to the small numbers of individuals willing to be vaccinated under this condition and limiting statistical power to show differences within groups. While not independently associated, the negative correlation with the requirement to pay for vaccination could have a potential impact on the effectiveness of HPV vaccination programmes in countries where the vaccine is not funded for males.

The number of recent male sexual partners was not independently associated with HPV vaccine acceptability under either condition, despite being a risk factor for acquiring HPV. A possible explanation is that reporting any UAIC may be confounding the result with a level of collinearity between the two variables, though this has not been explored further. Similarly, other variables such as ever having a check-up or treatment for an STI or perceiving their GP to be aware of their sexual orientation may have explained some of the difference, as these variables could also be associated with having a greater number of sexual partners.

Knowledge of the HPV-related disease and the HPV vaccine's protection of males against these are independently associated with willingness to be vaccinated for free among GBM in NZ, doubling the odds of willingness to be vaccinated in the case of HPV vaccine knowledge. These are two key areas that could be readily translated into health promotion messages and campaigns. With the extension of school-based HPV vaccination programmes to cover all persons aged 9-12 years, it is probable that the rates of vaccination among GBM will be similar to their heterosexual peers, building with each year and each new generation coming through. However, to maximise on the potential benefit offered by the catch-up programme, GBM already beyond these ages must be empowered to seek vaccination on their own volition. With a vaccine acceptability rate of 80.7% among those under the age of 27 years if

offered for free, health promotion campaigns that are targeted and culturally appropriate to GBM could bridge this gap.

Being over the age of 27 years was independently positively associated with acceptance of the vaccine at full price. Currently, those over the age of 27 years must pay the full cost if they wish to receive the HPV vaccine. Vaccine acceptability among this age cohort is relevant due to the potential individual and GBM community-level benefits offered by vaccination. The UK extended HPV vaccination in a staged progression to all self-identifying GBM under the age of 45 years through sexual health clinics as of April 2018 upon the recommendation of the Joint Committee on Vaccination and Immunisation after receiving a positive cost-benefit analysis and a feasibility study was successfully conducted between 2016 and March 2017 (331, 332). Should the modelling of the cost-benefit and targeted vaccination approach be translatable to GBM in NZ, there could be potential benefits to the extension of the vaccine to those GBM under the age of 45 years.

## Conclusions

The GAPSS and GOSS programme provides ongoing behavioural surveillance that can be utilised to explore HPV-related variables among GBM. The acceptability of HPV vaccination among this large and diverse cross-sectional sample is heavily affected by cost.

Participants over the age of 27 years have almost twice the odds of reporting willingness to pay for the HPV vaccine compared to those under 27 years. This has relevance for the consideration of offering or marketing the HPV vaccination to those no longer eligible for funded HPV vaccination in NZ.

Those who report engaging in UAIC, a risk factor for HPV acquisition, have 1.4 greater odds to report being willing to be vaccinated for free compared to those who report no UAIC. This may relate to results from other studies around perceived personal risk and benefits of vaccination and is an encouraging result, despite the potential for decreased vaccine efficacy among this group due to potential early acquisition of HPV.

Finally, knowledge of HPV-related disease and HPV vaccination benefits are independently associated with willingness to be vaccinated. Chapter Five: Section Two highlights that HPV-related disease knowledge is low among GBM in NZ, as is knowledge of the benefits of HPV vaccination for males as seen in this analysis. These findings have important implications for health promotion campaigns aiming to increase vaccination coverage among this population.

## Section Four: Self-reported HPV vaccine uptake among a community and online sample of GBM in Aotearoa, New Zealand

### Purpose

There have been no estimates of HPV vaccine uptake among GBM in NZ. The data provided in this 2014 combined GAPSS and GOSS sample provides the first baseline estimate of HPV vaccine uptake among GBM, prior to the change in eligibility for the funded vaccine in NZ in 2017. In this chapter, the prevalence of HPV vaccine uptake and sociodemographic variables associated with uptake will be explored among the GAPSS and GOSS sample of GBM.

### Aims

- Describe the response rate to the HPV vaccine uptake question among GAPSS and GOSS participants
- Describe the prevalence of self-reported HPV vaccine uptake among GAPSS and GOSS participants
- Explore HPV vaccine uptake prevalence by sociodemographic variables among the GAPSS and GOSS sample

### Background

Vaccination against the HPV is the most effective prevention tool available to reduce the HPV-related health inequities experienced by GBM. In Chapter Two, the review of the literature revealed that condoms do not provide significant benefit in preventing anal HPV infection and there is limited robust evidence available to indicate the clinical benefit of treating high-grade anal disease for the prevention of HPV-related anal cancers (194, 201).

Chapter Three conducted a systematic review of the literature to identify and collate published literature of HPV vaccination uptake among GBM. A limited number of studies were identified, with none found that examined HPV vaccination uptake among GBM prior to the extension of funding (including through healthcare insurance providers in the USA). This places NZ in a unique position to explore HPV vaccination prevalence and associated factors among this population prior to public funding, with the potential to monitor

In the 2014 round of the GAPSS and GOSS repeat cross-sectional surveys, a question relating to HPV vaccine uptake was included. The HPV vaccine was not funded for males at this point in time in NZ, relying on males to pay for the vaccine themselves after seeking it out or it being recommended to them by their healthcare provider. Prior to the 2017 change in eligibility for funded HPV vaccination, the vaccine had been promoted as a cervical cancer vaccine and therefore could have been deemed as irrelevant to gay males in particular, who do not have female sexual partners.



Monitoring HPV vaccine uptake among GBM through targeted and repeat behavioural surveillance is essential in lieu of sexual orientation data being collected in administrative health databases in NZ such as the National Health Index (NHI) and the National Immunisation Register (NIR). Current estimates of HPV vaccine coverage from the NIR among eligible male age cohorts since 2017 place coverage at 67% (217). With an estimated 3.6% of males in NZ identifying as non-heterosexual, it is possible that GBM may be overrepresented in the one-third of eligible males that did not receive the HPV vaccine (108).

## Methods

The methods detailed below relate to analyses undertaken in this Section. Detailed methods of the GAPSS and GOSS behavioural surveillance programmes are covered in greater detail in Chapter Five: Section One

### ***GAPSS and GOSS recruitment***

The recruitment methods for both GAPSS and GOSS are covered in Chapter Five: Section One and have been published elsewhere (128).

### ***HPV vaccine uptake question***

A single question was posed to both GAPSS and GOSS participants relating to HPV vaccine uptake. Participants were provided with the statement “*I have already been vaccinated with Gardasil*” with the possible responses of:

- “No”
- “Yes, 1 shot”
- “Yes, 2 shots”
- “Yes, 3 shots”

This question was in a group of questions relating to the HPV vaccine that was preceded with the statement “The NEXT questions are about the Gardasil vaccine that requires three injections to provide the best protection against HPV”.

### ***Statistical analysis***

The response rate was calculated as the proportion of respondents providing an answer to the HPV vaccine uptake question. The proportion of those not providing an answer is also reported. The univariate analysis describes the responses to the HPV vaccine uptake question in the combined GAPSS and GOSS sample and for each survey individually.

For the bivariate analysis, the question relating to HPV vaccine uptake has been dichotomised into the following response groupings:

- “No”,
- “Yes, 1 shot”/“Yes, 2 shots”/“Yes, 3 shots”.

The candidate took this step to increase statistical power to detect variance between groups due to the limited number of GAPSS and GOSS respondents self-reporting having any number of “shots”. With the low number of respondents to each of the “Yes” groupings, there is limited statistical power to show meaningful differences between these groups. Combined GAPSS and GOSS HPV vaccine uptake prevalence is explored with sociodemographic, HPV-related knowledge, and sexual behavioural variables, including:

- age,
- ethnicity,
- sexual orientation,
- HIV status at last test,
- highest qualification achieved,
- site of survey recruitment,
- perceived GP awareness of sexual orientation,
- knowledge that HPV causes at least one disease in males,
- knowledge there is an HPV vaccine that is effective in preventing HPV-related disease among males,
- ever had an STI check-up or treatment,
- number of male sexual partners in the previous six months,
- reporting any UAIC in the previous six months.

Fisher’s exact test of association was used to determine significant variations among groups within the bivariate analyses due to reduced numbers present in some of the groupings (under 20 participants). In the bivariate analysis, an additional sensitivity analysis was undertaken due to the number of respondents with missing data for the uptake question being similar to the number of respondents who answered (*see Table 37*). Here, missing data were recoded so that they were included in the bivariate analysis test for association to explore whether the characteristics of those respondents with missing data differ to those that answered the uptake question.

Multivariable analyses were not conducted due to the low numbers of participants self-reporting HPV vaccine uptake.

All data analyses were conducted using STATA version 13.1 (Stata Corporation, College Station, TX, US).

## Results

Vaccine uptake among GBM in this community sample was three per cent (n=92/3107). Self-reported uptake was greater among GAPSS participants (4.5%) than among GOSS participants (1.8%) ( $p < 0.001$ ) (see *Figure 25*). Of those reporting having received any number of vaccine doses, over half report having received all three doses (n=47/92) and this pattern was similar among both GAPSS and GOSS samples (see *Table 36*).

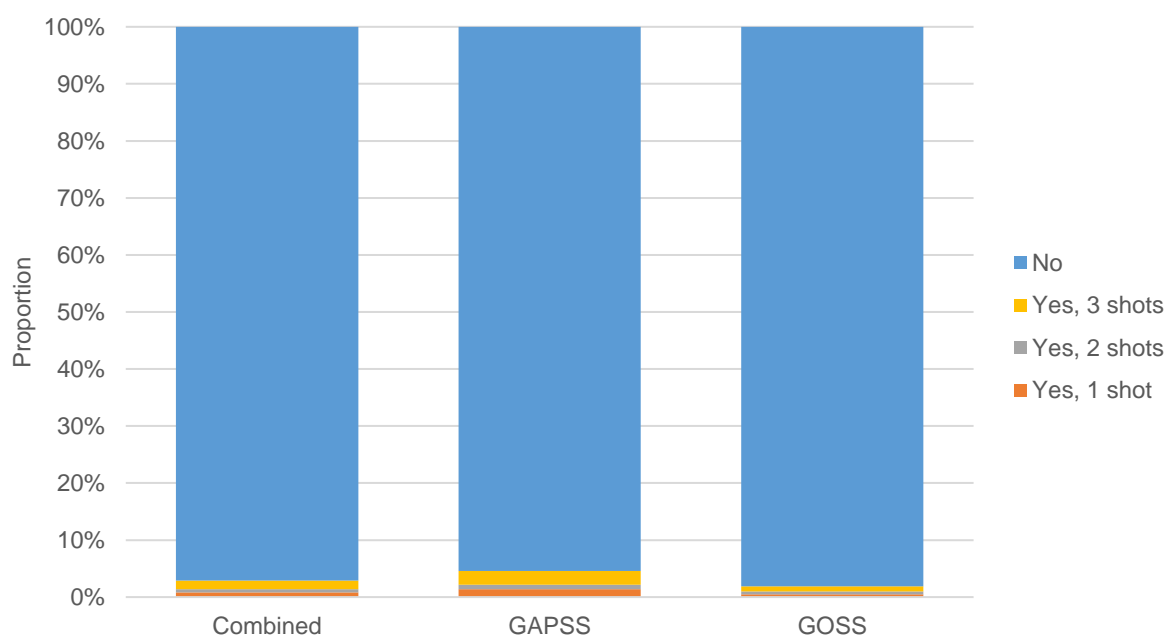


Figure 25: Self-reported HPV vaccine uptake and course completion among GBM by sample

### ***Question acceptability***

Of the 3214 participants that submitted their questionnaire, a total of 3107 (96.7%) participants answered the question relating to HPV vaccine uptake. As seen in the majority of HPV-related questions explored in this thesis, there was a lower response rate among GAPSS (92.9%) participants as compared to GOSS participants (98.4%) (see *Table 36*).

Table 36: Basic frequencies of GBM participant's responses to HPV-vaccine uptake question in the 2014 round of the GAPSS and GOSS surveys

| Question  | Combined    |              | GAPSS       |              | GOSS        |              | Fishers Exact<br>p-value |
|---|-------------|--------------|-------------|--------------|-------------|--------------|--------------------------|
|   | n           | %*           | n           | %*           | n           | %*           |                          |
| <b>Total</b>  | <b>3214</b> | <b>100.0</b> | <b>1421</b> | <b>100.0</b> | <b>1793</b> | <b>100.0</b> |                          |
| <b><i>"I have already been vaccinated with Gardasil."</i></b> |             |              |             |              |             |              | <b>&lt;0.001</b>         |
| No  | 2992        | 97.0         | 1260        | 95.5         | 1732        | 98.2         |                          |
| Yes, 1 shot   | 26          | 0.8          | 18          | 1.4          | 8           | 0.5          |                          |
| Yes, 2 shots  | 19          | 0.6          | 10          | 0.8          | 9           | 0.5          |                          |
| Yes, 3 shots  | 47          | 1.5          | 32          | 2.4          | 15          | 0.9          |                          |
| NS  | 130         | (4.0)        | 101         | (7.1)        | 29          | (1.6)        |                          |
| <b>Dichotomised</b>   |             |              |             |              |             |              | <b>&lt;0.001</b>         |
| No  | 2992        | 97.0         | 1260        | 95.5         | 1732        | 98.2         |                          |
| Yes ( <i>any shot</i> )                                       | 92          | 2.9          | 60          | 4.5          | 32          | 1.8          |                          |
| NS  | 130         | (4.0)        | 101         | (7.1)        | 29          | (1.6)        |                          |

NS = not stated

Percentages for NS are separate to the percentages of those responding to the question

### ***Bivariate analyses***

Table 37 shows that of the sociodemographic variables included in the bivariate analysis, ethnicity ( $p=0.002$ ) and site of recruitment ( $p<0.001$ ) were significantly associated with HPV vaccine uptake among the combined GAPSS and GOSS sample, with those who report their ethnicity as Asian (6.1%) and those recruited in GBM-associated bars (6.2%) being more likely to report receiving the vaccine. A non-significant variance in vaccine uptake was seen for sexual identity ( $p=0.067$ ) and for perceived GP awareness of participant's sexual orientation ( $p=0.072$ ). Other variables including age, HIV status, highest qualification, and free time spent with GBM peers were not significantly associated with HPV vaccine uptake among this sample.

Knowledge of reporting knowledge of any HPV-related disease and knowledge that the HPV vaccine provides protection to males were both significantly associated with HPV vaccine uptake ( $p<0.001$ ). Those reporting a higher number of sexual partners ( $p=0.001$ ) and those reporting having no UAIC ( $p=0.007$ ) in the previous six months were significantly more likely to report receiving the HPV vaccine. However, there was no significant variance in vaccine uptake between those who report having ever had a check-up or treatment for an STI compared to those who have not.

Table 37: Respondents reporting they have received a dose of the HPV vaccine and those with missing data for the same question, among GBM respondents of the combined GAPSS and GOSS samples

|                                | N    | “Yes, 1/2/3 shots” |     | Fisher’s exact P-value <sup>a</sup> | “Missing” |      | Fisher’s exact P-value <sup>b</sup> |
|--------------------------------|------|--------------------|-----|-------------------------------------|-----------|------|-------------------------------------|
|                                |      | n                  | %   |                                     | n         | %    |                                     |
| Total                          | 3107 | 92                 | 3.0 | -                                   | 130       | 4.0  | -                                   |
| <b>Sociodemographics</b>       |      |                    |     |                                     |           |      |                                     |
| <b>Age</b>                     |      |                    |     | 0.248                               |           |      | 0.303                               |
| Under 27                       | 1037 | 32                 | 3.1 |                                     | 23        | 2.2  |                                     |
| 27-45                          | 1240 | 39                 | 3.2 |                                     | 30        | 2.4  |                                     |
| 45+                            | 763  | 15                 | 2.0 |                                     | 25        | 3.2  |                                     |
| NS                             | 44   |                    |     |                                     | 44        | -    |                                     |
| <b>Ethnicity</b>               |      |                    |     | 0.002                               |           |      | *                                   |
| European                       | 2184 | 48                 | 2.2 |                                     | 46        | 2.1  |                                     |
| Māori                          | 297  | 12                 | 4.0 |                                     | 11        | 3.6  |                                     |
| Pacific                        | 108  | 2                  | 1.9 |                                     | 8         | 6.9  |                                     |
| Asian                          | 342  | 21                 | 6.1 |                                     | 10        | 2.8  |                                     |
| Other                          | 124  | 4                  | 3.2 |                                     | 2         | 1.6  |                                     |
| NS                             | 29   |                    |     |                                     | 29        | -    |                                     |
| <b>Identity</b>                |      |                    |     | 0.067                               |           |      | 0.004                               |
| Gay                            | 2456 | 69                 | 2.8 |                                     | 90        | 3.5  |                                     |
| Bisexual                       | 480  | 14                 | 2.9 |                                     | 24        | 4.8  |                                     |
| Other                          | 138  | 9                  | 6.5 |                                     | 13        | 8.6  |                                     |
| NS                             | 10   |                    |     |                                     | 10        | -    |                                     |
| <b>HIV status</b>              |      |                    |     | 0.127                               |           |      | 0.391                               |
| HIV-negative                   | 2096 | 69                 | 3.3 |                                     | 48        | 2.2  |                                     |
| HIV-positive                   | 152  | 5                  | 3.3 |                                     | 3         | 1.9  |                                     |
| Never tested/Don’t know        | 781  | 15                 | 1.9 |                                     | 17        | 2.1  |                                     |
| NS                             | 55   |                    |     |                                     | 55        |      |                                     |
| <b>Qualification</b>           |      |                    |     | 0.592                               |           |      | 0.656                               |
| Non-tertiary                   | 1650 | 46                 | 2.8 |                                     | 41        | 2.4  |                                     |
| Tertiary or higher             | 1394 | 44                 | 3.2 |                                     | 29        | 2.0  |                                     |
| NS                             | 40   |                    |     |                                     | 40        |      |                                     |
| <b>GP aware of orientation</b> |      |                    |     | 0.072                               |           |      | 0.146                               |
| No/Not sure                    | 1522 | 37                 | 2.4 |                                     | 47        | 3.0  |                                     |
| Yes                            | 1544 | 55                 | 3.6 |                                     | 55        | 3.4  |                                     |
| NS                             | 10   |                    |     |                                     | 10        | -    |                                     |
| <b>Site of Recruitment</b>     |      |                    |     | <0.001                              |           |      | <0.001                              |
| BGO                            | 1021 | 43                 | 4.2 |                                     | 67        | 6.2  |                                     |
| Bars                           | 113  | 7                  | 6.2 |                                     | 19        | 14.4 |                                     |
| SOS Venues                     | 186  | 10                 | 5.4 |                                     | 15        | 7.5  |                                     |
| Online (GOSS)                  | 1764 | 32                 | 1.8 |                                     | 29        | 1.6  |                                     |
| NS                             | -    |                    |     |                                     | -         |      |                                     |
|                                |      |                    |     |                                     |           |      |                                     |
|                                |      |                    |     |                                     |           |      |                                     |
| <b>Knowledge</b>               |      |                    |     |                                     |           |      |                                     |

|  | N    | “Yes, 1/2/3 shots” |     | Fisher’s exact P-value <sup>α</sup> | “Missing” |     | Fisher’s exact P-value <sup>β</sup> |
|--|------|--------------------|-----|-------------------------------------|-----------|-----|-------------------------------------|
|  |      | n                  | %   |                                     | n         | %   |                                     |
| <b>Knowledge of any HPV-related disease</b>      |      |                    |     | <b>&lt;0.001</b>                    |           |     | <b>&lt;0.001</b>                    |
| Any knowledge                                    | 1495 | 67                 | 4.5 |                                     | 25        | 1.6 |                                     |
| No knowledge                                     | 1583 | 24                 | 1.5 |                                     | 32        | 2.0 |                                     |
| NS   | 6    |                    |     |                                     | 6         |     |                                     |
| <b>Knowledge of Gardasil vaccine</b>             |      |                    |     | <b>&lt;0.001</b>                    |           |     | <b>&lt;0.001</b>                    |
| I knew that                                      | 519  | 48                 | 9.3 |                                     | 12        | 2.3 |                                     |
| I didn’t know/ I wasn’t sure                     | 2542 | 43                 | 1.7 |                                     | 40        | 1.6 |                                     |
| NS   | 23   |                    |     |                                     | 23        |     |                                     |
| <b>Sexual Behaviours</b>                         |      |                    |     |                                     |           |     |                                     |
| <b>Ever had an STI check</b>                     |      |                    |     | 0.121                               |           |     | <b>0.003</b>                        |
| Yes  | 2444 | 80                 | 3.3 |                                     | 63        | 0.6 |                                     |
| No   | 512  | 10                 | 2.0 |                                     | 3         | 2.5 |                                     |
| NS   | 128  |                    |     |                                     | 128       |     |                                     |
| <b>Number of male sexual partners &lt;6mths*</b> |      |                    |     | <b>0.001</b>                        |           |     | <b>0.002</b>                        |
| 20 or less                                       | 2770 | 74                 | 2.7 |                                     | 110       | 3.8 |                                     |
| 20+  | 255  | 18                 | 7.1 |                                     | 12        | 4.5 |                                     |
| NS   | 59   |                    |     |                                     | 8         | -   |                                     |
| <b>Any UAIC &lt;6mths</b>                        |      |                    |     | <b>0.007</b>                        |           |     | <b>0.004</b>                        |
| No   | 2076 | 73                 | 3.5 |                                     | 90        | 4.2 |                                     |
| Yes  | 923  | 16                 | 1.7 |                                     | 26        | 2.7 |                                     |
| NS   | 85   |                    |     |                                     | 85        |     |                                     |

NS = not stated

<sup>α</sup> Fisher’s exact not including those with missing data for HPV vaccination uptake question.

<sup>β</sup> Fisher’s exact including those with missing data for HPV vaccination uptake question.

\* Fisher’s exact unable to be calculated due to enumerations exceeding memory limits due to multiple categories within the ethnicity variable creating cells.

### **Sensitivity analyses**

Table 37 shows the results of the additional sensitivity analyses that included those with missing data for the HPV vaccination uptake question. Two additional variables were found to differ significantly when those respondents with missing data were included. These were identity ( $p=0.004$ ), with a greater proportion of bisexual and respondents identifying with an identity “Other” than gay or bisexual also not responding to the HPV vaccination uptake question, and reporting ever having had an STI check ( $p=0.003$ ), with a lower proportion of respondents who report having had an STI check not responding to the HPV vaccine uptake question. The significance of the remaining variables in the bivariate analyses did not differ compared to the analyses where missing data were included.

## Discussion

To the candidate's knowledge, this is the first study to examine HPV-vaccine uptake among GBM in New Zealand and one of the first to examine HPV-vaccine uptake among GBM outside of the USA. Vaccine uptake is low among this 2014 community sample of GBM recruited offline and online in NZ, with 3% of respondents reporting having received at least one dose of the HPV vaccine.

Self-reported HPV vaccine uptake was significantly greater among those of Asian ethnicity, recruited from GBM-associated bars, those who reported knowledge of at least one HPV-related disease that affects males, those who report knowledge of the HPV vaccine and its effectiveness against HPV-related disease, those who report a greater number of recent male sexual partners, and report any recent UAIC.

### ***Strengths***

The strengths of the GAPSS and GOSS recruitment and study design methods are reported in previous chapters and published elsewhere (128). In brief, the surveys recruit a large and diverse sample of GBM in NZ reflecting a similar sociodemographic composition of the wider NZ male population, the anonymous and self-completed nature of the surveys reduces the potential for reporting bias due to social desirability,

Specific to this analysis, the inclusion of HPV vaccination uptake into the GAPSS and GOSS surveys allows the exploration of these data with a range of sexual health testing and sexual risk behaviour questions.

The question relating to HPV vaccination required participants to specify the number of vaccine dose they believed they received. Though vaccine uptake was low among the 2014 round of GAPSS and GOSS, limiting the use of these groupings in analyses, future rounds could monitor trends in vaccine schedule completeness and identify sociodemographic or behaviours factors associated with non-completion.

### ***Limitations***

Limitations inherent to the GAPSS and GOSS recruitment and study design methods are covered in previous chapters and published elsewhere (128). In brief, the cross-sectional design of the surveys limit generalisability of the results to the wider GBM population of NZ. Additionally, due to the anonymous and self-reported nature of the surveys it would be possible for the same individual to undertake the surveys multiple times and provide different responses. Lastly, testing and sexual behaviours are subject to recall bias as participants are asked to recall over the period of six to twelve months or in their lifetimes.

Specific to these analyses, the GAPSS and GOSS surveys were built to detect changes in knowledge and attitudes, testing, and sexual behaviours related to HIV risk among GBM. Variables found to be associated with HPV vaccine uptake in other studies have not been included, nor have those known to be associated with wider vaccine uptake or willingness to be vaccinated.

The ability to detect significant differences in vaccine uptake between groups in this study was limited by the number of participants reporting receiving the HPV vaccine. The overall low number of participants reporting HPV vaccine uptake alludes to the larger concern that GBM are not being vaccinated against HPV, despite being a population that experiences a disproportionate burden of HPV-related disease.

The additional sensitivity analysis demonstrated that there are significant differences in characteristics between those who responded to the HPV vaccination uptake question and those who did not. However, the majority of non-respondents were recruited through the GAPSS survey (*see Table 36*) and differences in sociodemographic and behavioural characteristics between the two survey populations are a known limitation demonstrated in Section One: Methods: Gay Auckland Periodic Sex Survey (GAPSS) and Gay Online Sex Survey (GOSS). These factors could be controlled for in a multivariable model but due to the low proportion of respondents reporting receiving the vaccine, this analysis could not be undertaken.

Vaccination uptake is self-reported, and there is a likelihood that some participants may have incorrectly reported receiving the vaccine, particularly with the significantly higher coverage among Asian GBM, where the vaccine is not funded for males in a number of countries covered by this ethnicity grouping. There could also be a language barrier or a misconception of having been vaccinated under NZ immigration rules, in which all migrants to NZ, including those on a student visa, are required to have a number of specific vaccinations, though HPV is not one these.

### ***Comparison to other studies***

At the time of writing, and as reported in the systematic literature review in Chapter Three, vaccination uptake among GBM has not been reported by any countries other than the USA and the UK (156, 257, 290, 296, 300, 333). Interpreting results is difficult both due to the limited analyses that could be performed with a low HPV vaccine prevalence in this sample and due to the lack of studies reporting HPV vaccination prevalence among GBM globally.

The most robust estimates come from the National HIV Behavioral Surveillance (NHBS) survey in the USA, of which 17.2% of GBM participants self-report having received at least one dose of the HPV vaccine in 2014, the same year GAPSS and GOSS were conducted



(299). Vaccination uptake among GBM in the USA was greater than that found in this sample. Interpreting the reasons for this difference in uptake is complex. It is possible that much of the variation seen in HPV vaccine prevalence among GBM within these USA samples reflect variation in healthcare access and socioeconomic status. The in NZ vaccination is delivered primarily thorough public healthcare systems and school-based vaccination programmes, which over the long term deliver a more equitable outcome. By comparison, the majority of provision in the USA is via private healthcare and private insurance, with individuals being able to choose their healthcare provider and for GBM criteria of choice might be that the provider is either GBM or “GBM friendly”. In addition, HPV vaccination was recommended and available to males earlier in the USA due to FDA approval in 2010, but uptake has been lower compared to that seen among eligible males in countries that provide a school-based vaccination programme such as Australia.

Oliver et al. also explored factors associated with reporting having received at least one dose of HPV vaccination among GBM aged 18-26 years in the 2014 NHBS (299). Similar to that found in the 2014 GAPSS and GOSS samples, they report that HPV vaccine uptake was greater among GBM who reported a greater number of recent sexual partners (among those reporting >5 sexual partners in the last 12 months, Prevalence Ratio=1.34, 95% CI: 1.03-1.75, comparison group was those reporting one sexual partner), though they used a lower partner number threshold as their upper limit compared to that in GAPSS and GOSS (20+ partners) as well as using a younger sample. In contrast to the findings of the GAPSS and GOSS sample analysis, they found vaccine uptake was greater among those reporting a higher level of qualification, who were living with HIV, who disclosed their sexual orientation to their healthcare provider, and who had tested for an STI in the previous 12 months. Differences in the sample age and recruitment methods may partially explain the differences in findings, as well as the differences in the provision of HPV vaccination between the USA and NZ at the time of recruitment as detailed previously.

Nadarzynski et al. report an HPV vaccination uptake prevalence of 3.2% among British GBM aged 18-26 years recruited online in 2015 in their supplementary material (298), comparable to the 3.1% reported among GBM aged 16-26 years in this combined sample. In 2015, the UK and NZ both had female-only school-based vaccination programmes in place, with little to no health promotion of the vaccine for GBM or other males, making the comparison more relevant. However, GBM in the combined GAPSS and GOSS sample were recruited through venues, dating websites and mobile apps, which could result in a different sample demographic compared to one recruited solely through a social and networking site such as that used by Nadrzynski et al.

Targeted HPV vaccination programmes have been discussed as a possible and more cost-effective method for meeting the HPV-related health inequity experienced by this population (334). Using this approach would require GBM to disclose their sexual orientation to healthcare providers to access vaccination. However, perceived GP awareness of participant's sexual orientation was not significantly associated with uptake in the analysis presented in this Chapter. Nadarzynski et al. comment in their study examining factors associated with HPV vaccine acceptability in the UK, that a recommendation by a healthcare provider was significantly associated with HPV vaccine acceptability but that just over half the sample of GBM had disclosed their sexual orientation to a healthcare provider, similar to findings in the GAPSS and GOSS sample (115, 298). In the 2015 study among younger GBM by Reiter et al., HPV vaccine uptake was significantly associated with sexual orientation disclosure to healthcare providers (300). Healthcare provider recommendation has been found to be significantly associated with HPV vaccine uptake among GBM (290, 299, 300). As noted, all of these studies are from the USA, and this association is likely largely due to the lack of a school-based vaccination programme in the USA, relying on patients to be vaccinated opportunistically when attending their healthcare provider.

## Conclusion

GAPSS and GOSS are existing behavioural surveillance programmes targeting the GBM population of NZ, the inclusion of a question on HPV vaccine uptake is a simple and acceptable way to estimate HPV vaccination coverage among this population.

Prevalence of HPV vaccination among GBM recruited in the 2014 round of GAPSS and GOSS was extremely low. To ensure the extension of HPV vaccination funding closes the HPV-related health inequity experienced by GBM, these data are a baseline against which uptake should continue to be monitored following the extension of funding to males in 2017.

# Chapter 6: Changes in HPV-related variables among GBM over time

## Introduction

Public health professionals monitoring programmes need to measure change over time to make evidence-based decisions and ensure effective public health programmes and interventions. From 1<sup>st</sup> of January 2017, males under the age of 27 years became eligible for publicly funded HPV vaccination in NZ (273). The vaccine is primarily provided through a school-based vaccination programme but is also available through primary and outpatient healthcare. The HPV-related health inequity experienced by GBM was one factor that contributed to the extension of funding to include males in NZ (335).

To the candidate's knowledge, the first data on HPV-related knowledge and vaccine acceptability and uptake among GBM were captured through the GAPSS and GOSS behavioural surveillance programme in 2014 (*see Chapter Five*). Data collection for the next round of the GAPSS and GOSS HIV behavioural surveillance programme was expected to occur in 2017; however, this was not purchased by MoH (336). In response to this surveillance gap, these same HPV-related variables and HPV vaccine uptake questions were included in the 2018 round of the Ending HIV Evaluation Survey (EHIV Survey) led by the candidate and conducted by the New Zealand AIDS Foundation (NZAF). These 2018 data are the first collected among GBM after the extension of publicly funded HPV vaccination to males in January 2017 and can help assess changes over time (i.e., pre- and post-HPV vaccine extension to males, and therefore GBM).

## Purpose

In lieu of capturing sexual orientation data in sustainably funded, nationally representative behavioural surveillance or administrative health datasets, estimates of changes over time in HPV-related variables and HPV vaccine uptake among GBM can be gained opportunistically from repeat cross-sectional community sampling studies.

## Aims

The aims cover the two sections of the chapter:

1. Describe the methods for the Ending HIV Evaluation Survey
2. Compare HPV-related disease knowledge, HPV vaccine awareness and HPV vaccine uptake among GBM recruited through online channels in NZ in 2014 and 2018.

## Section One: Methods: New Zealand AIDS Foundation Ending HIV Evaluation Survey

### Introduction

In August 2016, NZAF commenced a series of online surveys targeted to GBM in NZ to track progress towards their goal of ending new HIV infections in NZ by 2025 (337). The surveys have a dual purpose, firstly to track progress on the strategic goals of NZAF and secondly to evaluate the “Ending HIV” social marketing campaign. In 2018, NZAF chose to repeat HPV-related questions that had been included in the 2014 GAPSS and GOSS surveys to determine if GBM were aware of, and had made use of, the 2017 change in funding for HPV vaccination. NZAF had made several submissions to Pharmac on GBM’s access to HPV vaccination and had an interest in monitoring progress.

### Role of the candidate

The EHIV Surveys are the intellectual property of the New Zealand AIDS Foundation. The candidate is the named Primary Investigator of the EHIV Survey studies through their role with NZAF as the Policy and Science Manager. The candidate is responsible for the study conception, consultation, design, questionnaire production, piloting, ethics application, data collection, data cleaning and processing, data analysis, and reporting. For the 2018 EHIV Survey round, the candidate was assisted by Mr Danyon Petousis-Harris, the Scientific Officer of NZAF, who aided in survey design and piloting, data analysis, and reporting. Recruitment was facilitated by Mr Anthony Walton, the Marketing Coordinator, who was responsible for online advertisement development and placement.

The candidate provides access to the dataset in their role as the Policy and Science Manager with NZAF. Additional permission has been sought for the use of the EHIV Survey data in this thesis and was granted by Dr Jason Myers, the Chief Executive of NZAF (see *Appendix*).

### Ethical considerations and consultation

The questionnaire for each survey round is developed in consultation with the teams that make up NZAF. Teams are consulted on the topics to be covered in the questionnaire and the potential wording of the questions. Where it is considered necessary, additional consultation with key populations, such as GBM PLHIV and takātapui Māori, is conducted on the scope and wording of questions that specifically target these populations.

Ethical approval of the study was gained through the New Zealand Ethics Committee (reference: 2016\_21).

On clicking through an online link to the EHIV Survey, participants are presented with a landing page that explains the scope, purpose, who is running the survey, contact details, and the key ethical considerations of participation in the survey, which include:

- its voluntary nature,
- anonymous data collection and reporting,
- data storage and access,
- and that submission will be considered consent to the data being used.

Participants are provided with a link to a PDF of the PIS, which can be downloaded and provides a more in-depth explanation of study's purpose and the ethical considerations.

## Questionnaire

The EHIV Surveys track trends in core variables related to NZAF's strategic goals and contractual measures agreed with the MoH. These include:

- knowledge and attitudes,
- engagement with HIV prevention tools,
- testing for HIV and STIs,
- perceived barriers and benefits to testing and prevention tool use,
- sexual risk behaviours related to HIV and STIs,
- and engagement with Ending HIV social marketing campaigns.

The surveys are also responsive, including emerging areas of interest or concern within the wider HIV and sexual health fields, such as acceptability of home testing for HIV and sexualised drug use.

The survey was created and hosted through the SurveyMonkey® website. Questions posed are largely single-choice categorical questions, though a small number allow multiple choices or are continuous (e.g., age and number of sexual partners).

Internal survey logic allows participants to skip questions that are not relevant to their experiences based on the answers they provide. Each question is posed individually, and for those questions where a response is required (those of strategic importance to NZAF), participants are provided with a "*Prefer not to say*" option. Definitions of key concepts or abbreviations are provided to participants when they are included or relevant to a question.

Where possible, the wording of questions on topics covered by the GAPSS and GOSS surveys (e.g., sociodemographics, sexual partnering, and condom use measures) are utilised to allow for direct comparability and identifying potential trends over time.

### ***Questionnaire piloting***

Prior to the start of online recruitment, the EHIV Survey questionnaire was piloted with volunteers attending a condom packing evening held every Wednesday at the Auckland office of NZAF. Volunteers were asked if they wish to participate, up to a maximum of 15 volunteers in total. Desktop computers were provided with the online survey open at the landing page. Volunteers were provided with a feedback form to record any errors they encounter, and then an open comments section to provide any additional feedback. Each volunteer self-completed the questionnaire after being asked to complete as they would for themselves or pick a “persona”. Participation in the pilot was voluntary and responses to the questionnaire were not recorded.

Volunteer feedback forms were collated, and the necessary changes made. Additional feedback in the open text box was considered and changes made if thought relevant and required.

### ***Inclusion of HPV-related questions***

The candidate’s decision to repeat the HPV-related questions included in the 2014 GAPSS and GOSS questionnaires was made in consultation with the current NZAF Executive Director Dr Jason Myers, and Operations Manager Mr Joe Rich. The questions were deemed relevant to the NZAF Strategic Goal to prevent HIV and STI transmission and overarching aim to improve the sexual health of GBM in NZ (337). The exact wording of the HPV-related questions included in the 2014 round of GAPSS and GOSS was preserved.

### **ENDING HIV Survey sample**

Participants were eligible to participate if they were 16 years or older and can read and comprehend English. The survey is voluntary, anonymous, and self-completed. The survey aims to recruit 2,000 participants, with a minimum of 100 participants from each of the following ethnic groups: Māori, Pacific, and Asian, to provide sufficient statistical power to determine differences within these ethnic groups. However, these recruitment goals were not met in the 2018 round of the EHIV Survey for Pacific and Asian GBM (*see Table 38*).

While participants are eligible to participate regardless of their gender or sexual orientation, recruitment for the EHIV Surveys is heavily targeted to GBM in terms of the language used in advertisements and recruitment sites. Those participants who do not identify as GBM or do not report recent sexual contact with a male are provided with a logic skips to reach the questions relating to the Ending HIV social marketing campaign evaluation.

GBM in the EHIV Survey were defined as participants who:

- Identify as male,
- Do not identify as heterosexual or identify as heterosexual and report ever having sex with a male.

Table 38 provides an overview of the responses to sociodemographic variables by GBM participants recruited into the 2018 EHIV Survey.

Table 38: Sociodemographic and behavioural characteristics of GBM participants recruited into the 2018 EHIV Survey round

|   | <b>n</b>    | <b>%</b>     |
|---|-------------|--------------|
| <b>Total</b>                                | <b>1031</b> | <b>100.0</b> |
| <b>Age</b>                                  |             |              |
| Under 27                                    | 358         | 34.7         |
| 27-45                                       | 416         | 40.4         |
| 45+   | 257         | 24.9         |
| NS  | -           |              |
| <b>Ethnicity</b>                            |             |              |
| European                                    | 794         | 77.0         |
| Māori                                       | 103         | 10.0         |
| Pacific                                     | 23          | 2.2          |
| Asian                                       | 53          | 5.1          |
| Other                                       | 58          | 5.6          |
| NS  | -           |              |
| <b>Sexual identity</b>                      |             |              |
| Gay   | 794         | 77.3         |
| Bisexual                                    | 188         | 18.3         |
| Other                                       | 45          | 4.4          |
| PNS/NS                                      | 4           |              |
| <b>HIV status at last test</b>              |             |              |
| HIV-negative                                | 753         | 73.5         |
| HIV-positive                                | 62          | 6.1          |
| Never tested/Don't know                     | 210         | 20.4         |
| PNS/NS                                      | 6           |              |
| <b>Source of online recruitment</b>         |             |              |
| Social media                                | 494         | 47.9         |
| Dating app                                  | 474         | 46.0         |
| Internet banner ad                          | 63          | 6.1          |
| NS  | -           |              |
| <b>Had an STI test/treatment &lt;12mths</b> |             |              |
| Yes   | 470         | 46.0         |
| No  | 369         | 36.1         |

|  | n   | %    |
|--|-----|------|
| Never had an STI test/Can't remember             | 183 | 17.9 |
| PNS/NS   | 9   | -    |
| <b>Number of male sexual partners &lt;6mths*</b> |     |      |
| 20 or less                                       | 830 | 90.1 |
| 20+  | 91  | 9.9  |
| PNS/NS   | 3   | -    |
| <b>Any UAIC &lt;6mths‡</b>                       |     |      |
| No   | 196 | 29.2 |
| Yes  | 476 | 70.8 |
| PNS/NS   | 359 | -    |

\* = only asked of those who report any sexual contact with a man in the previous six months.

UAIC = unprotected (condomless) anal intercourse with a casual male partner

‡ = only asked of those who report any anal sex with casual male partners in the previous six months

PNS = prefer not to state

NS = not stated/missing value

## Recruitment settings

Participants were recruited over five weeks through various online and mobile app sites. Participants were recruited through online banners, pop-up messages, and messages in individuals' inboxes that link to the online survey. Recruitment takes place on mainstream and GBM-specific online social media and mobile dating apps, with geo-targeting limiting respondents to those currently in NZ. These sites and channels used for the 2018 EHIV Survey round included:

1. Social Media:
  - Facebook
2. GBM targeted dating apps:
  - Grindr
  - Squirt
  - Growlr
  - Scruff
  - Hornet
3. Website and banner advertisement:
  - TrafficJunky

## Study recruitment

Study recruitment commenced on Friday 3<sup>rd</sup> August 2018 and took place over five weeks. Throughout the five weeks, recruitment took place across all sites simultaneously. Where available on the platform, broadcasts and messages to user inboxes were sent out only once



during the study period (mobile dating apps only). Upon clicking on the advert or link for the survey, participants are taken to the landing page of the EHIV Survey and presented with information on the survey and a link to the PIS. Those who consented to participate clicked the start button to commence the survey.

Participants were presented with each question individually and could skip questions or select "*Prefer not to state*". As the survey is voluntary, participants were able to exit the survey at any point. Those who completed and submitted the survey were considered to have given consent for their responses to be analysed by NZAF. At the end of the survey, participants were provided with links and information to support and testing services related to sexual health, HIV, and LGBTIQ+ should the questions have raised any concerns.

### Data management and coding

The candidate downloaded data from SurveyMonkey in Microsoft Excel format. The data were converted into categorical numerical format using a coding sheet. Data were then imported into STATA v13.0 statistical software. In STATA, the numerical categorical data were formatted to include variable descriptions and text reflecting the variable response options. Incomplete surveys (those who had not completed the required questions) were removed. Under the ethics agreement, these participants had not submitted their surveys and therefore consented to their data being stored and used for analyses. Participants were also excluded where data were obviously fabricated or contradictory.

### Strengths

Research targeted to specific populations disproportionately affected by a disease provides data to develop and inform public health interventions and programmes to address such health inequities. Chapter Two, Section Two: Part Two described the WHO guidelines on secondary surveillance for HIV and explored how this can be applied to other communicable diseases such as HPV (130). The use of repeat, periodic sampling to estimate shifts in behaviours that can facilitate the transmission of communicable disease and use of prevention tools among GBM has previously been utilised by the GAPSS and GOSS surveys in NZ (128).

The EHIV Survey collects HPV-related variables that measure three topic areas: HPV-related knowledge, HPV vaccine acceptability, and HPV vaccine uptake. Knowledge and acceptability are demonstrated factors associated with HPV vaccine uptake (231, 232). Inclusion of these topics aligns with WHO recommendations for secondary surveillance to monitor behaviours and predictors of epidemic spread, including predictors and the use of prevention tools. These, in turn, can be used to inform the targeting and evaluation of programmes that promote or provide these prevention tools to the GBM population.

Recruitment includes a mixture of mainstream and GBM-specific channels. This provides a greater cross-section of the GBM population in NZ, including GBM who are younger and may not be sexually active as compared to those recruited from dating sites and apps alone. For programmes that seek to address the burden of HPV among GBM the experience of both these populations are important to capture; vaccines are targeted to those who are newly or not yet sexually active, while prevention, screening, and treatment tools target to those who are sexually active and ineligible for publicly funded vaccination.

## Limitations

Due to the cross-sectional design and recruitment methodology used, it can be assumed that the survey population is not representative of the total GBM population of NZ. However, the analyses aim to determine if there has been a change in HPV-related variables over time among a defined population of GBM recruited online. This does not require a representative sample.

Measures of HPV vaccination uptake are self-reported, which are subject to recall bias. This is particularly true for the number of doses received, however, as GBM are not identifiable within the NIR, it would not be possible to test for validity between recall and actual vaccination completeness among this population. Future studies could explore this among a subset of GBM and request NHI numbers from these men to assess vaccination recall.

For both surveys, the recruitment rate was not calculated. Recruitment occurred online for both surveys, with participants recruited through a range of methods such as banner advertisements and private messages in user inboxes, at each step of the recruitment process there is likely to be participant drop-off. There is potential to record participation rate based on two steps, the number of individuals who view the study landing page and the completion rate of those who started the survey. However, there are limitations to both of these approaches and limited information to determine if those who participated are significantly different to those who completed the surveys.

## Section Two: Changes in HPV-related knowledge, vaccine acceptability and vaccine uptake among online cross-sectional samples of sexually active GBM aged 16 to 26 years, pre- and post-public funding for HPV vaccination for males in Aotearoa, New Zealand

### Purpose

This section seeks to explore the opportunistic inclusion of self-reported HPV-related variables in online behavioural surveys to provide estimates for these variables over time among GBM in NZ. These estimates provide insight into whether GBM, who experience a greater burden of HPV-related disease, are benefitting from the extended funding policy, and provide information to inform public health programmes seeking to increase HPV vaccination uptake among this population.

### Aims

1. Examine differences in HPV-related variables between the two survey populations of the 2014 GOSS and the 2018 Ending HIV Survey.

### Background

As of January 2017, all NZ males under the age of 27 years became eligible for funded HPV vaccination with the nonavalent HPV vaccine (Gardasil9<sup>®</sup>) (273). While this change in funding eligibility was in-part driven by the inequity experienced by GBM, the effect of the change has been to deliver a gender-neutral HPV vaccination programme to school children during school year eight (aged 11—12 years) (335). This leaves the majority of the eligible male cohorts in an informal “catch-up” programme delivered through primary care and outpatient settings. Catch-up vaccination requires patient or healthcare provider initiation of HPV vaccination, creating an additional barrier to vaccine uptake. As demonstrated in the previous chapter, knowledge of the HPV vaccine was low (18%) among GBM in NZ in 2014, acting a further barrier to initiating vaccination among this population.

Coverage of HPV vaccination among females in NZ remains below the 75-80% target set by the MoH National HPV Immunisation Programme in 2015 (218). In 2017, coverage of HPV vaccination among the 2003 age cohort of females was estimated to be 67% according to NIR data (338). Uptake among males of the same age cohort is believed to be equivalent, though these data are yet to be published (217).

In NZ, an estimated 2.3% of men identify as gay or bisexual (108). Without data on sexual orientation collected in administrative health datasets such as the NHI and NIR, HPV vaccination coverage cannot be reported for GBM in NZ, and it cannot be known whether coverage among GBM is reaching the herd immunity threshold. Therefore, estimates of HPV

vaccination coverage among GBM over time must be estimated through other methods. This section explores the inclusion of shared HPV-related variables in online cross-sectional sexual behavioural surveys targeted at GBM in NZ over time.

The GAPSS and GOSS surveys, explored in earlier chapters, sought to capture HPV-related knowledge, and vaccine acceptability and uptake among GBM in NZ in 2014. An expected 2017 round of the GAPSS and GOSS was not funded by MoH (336). At this time, the New Zealand AIDS Foundation (NZAF) implemented online data collection targeting GBM through the EHIV Surveys to evaluate its behavioural change social marketing campaigns. In the 2018 round of the EHIV Surveys, the same set of HPV-related questions from the 2014 round of the GAPSS and GOSS surveys were included.

## Methods

For this analysis, only the 2018 EHIV Survey and 2014 GOSS survey data will be used rather than the combined 2014 GAPSS and GOSS sample. This is to improve comparability with the EHIV Survey, as both GOSS and the EHIV Survey targeted and recruited GBM through online channels.

Figure 26 provides an overview of the process followed for the methods of this chapter. The process is explained in further detail in the following sections, but is outlined in brief below:

1. Limit the survey datasets to only those shared variables across the two surveys.
2. Limit the two survey populations based on a shared eligibility criterion.
3. Combine the two datasets.
4. Limit populations based on NZ HPV vaccine age eligibility criteria (under 27 years).
5. Explore differences between the samples based on the shared variables.
6. Compare HPV-related variables across the two datasets.
7. Control for significant differences in shared variables across the two datasets to examine differences in HPV-related variables between the two surveys.

All processes and analyses were conducted in Stata.IC v.13.1.

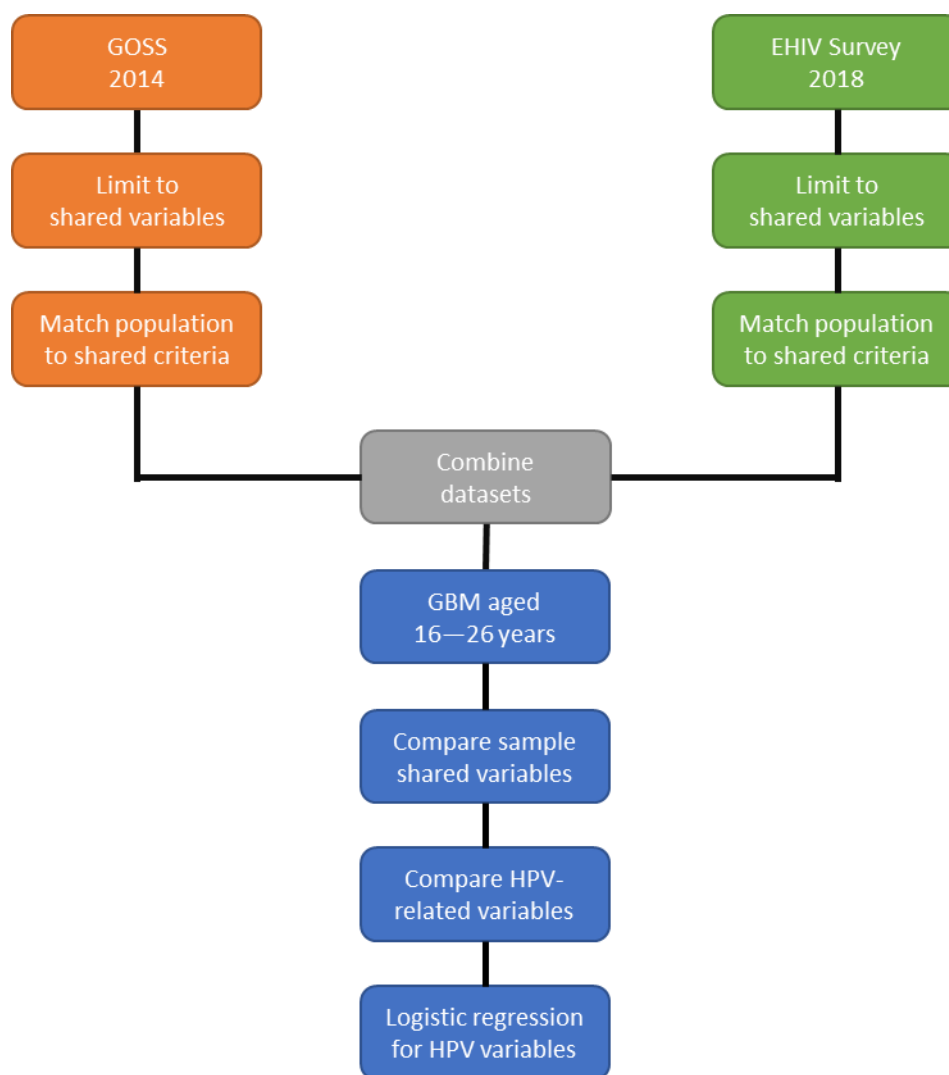


Figure 26: Diagrammatic representation of the approach taken for the analyses, consisting of dataset preparation and merging, and identification and separation of study populations.

### ***Survey recruitment***

#### *Gay Online Sex Survey (GOSS) recruitment*

Methods for the GOSS survey are covered in Chapter Five: Section One and have been published elsewhere (128).

#### *Ending HIV Survey: Stay Safe 2018 recruitment*

The methods for the 2018 round of the EHIV Survey are reported in Chapter Six: Section One.

### ***Shared questions across the two surveys***

The GOSS and EHIV Survey shared questions where possible and appropriate to improve the comparability and constancy of data for GBM and HIV. For the analyses in this Chapter,

the sociodemographic, sexual health, and some sexual behavioural variables that have been used in previous analyses in this thesis will be used here. These include:

- Sociodemographic variables:
  - Age.
  - Ethnicity.
  - Sexual orientation.
  - HIV status at last HIV test.
- Sexual health and behavioural variables:
  - Perceived GP awareness of sexual orientation.
  - Self-reported check-up or treatment for an STI in the previous 12 months.
  - Number of male sexual partners in the previous six months.

Definitions of “sex” and “casual sexual partners” remained the same between surveys and were described to participants when asked about sexual behaviours and partnering.

*Any reported unprotected anal intercourse with casual male partners*

Condom use over the previous six months in both survey questionnaires was ranked on a five-point Likert-like scale: “*Always*”, “*Almost always*”, “*Half the time*”, “*Rarely*”, and “*Never*”. However, the variable constructed to identify participants who reported any unprotected (condomless) anal intercourse with casual male partners in the previous six months differed between the two surveys.

In the GOSS dataset, the variable describing a respondent’s engagement in any UAIC in the previous six months is a composite variable made up of two questions relating to their self-reported condom use over the previous six months with casual male sexual partners and the sexual positions they took with those partners during anal sex. That is:

- Overall condom use during anal sex with casual male partner(s) in the previous six months.
  - When they were the top/insertive partner.
    - “*Always*”, “*Almost always*”, “*Half the time*”, “*Rarely*”, and “*Never*”.
  - When they were the bottom/receptive partner.
    - “*Always*”, “*Almost always*”, “*Half the time*”, “*Rarely*”, and “*Never*”.

The measure of any UAIC was then created based on the respondent’s answers to the two questions. A participant who answered anything but “*Always*” to at least one of the above questions were coded as reporting any UAIC.

- Any reported UAIC with a casual male partner in the previous six months?
  - “Yes” = self-reported at least one of the following:

- When insertive partner: “*Almost always*”, “*Half the time*”, “*Rarely*”, and “*Never*” /OR/ No insertive anal sex with casual male sexual partners.
- When receptive partner: “*Almost always*”, “*Half the time*”, “*Rarely*”, and “*Never*” /OR/ No receptive anal sex with casual male sexual partners.
- “No” = self-reported to both or one of the following:
  - When insertive partner: “*Always*” /OR/ No insertive anal sex with casual male sexual partners.
  - When receptive partner: “*Always*” /OR/ No receptive anal sex with casual male sexual partners.

The 2018 EHIV Survey did not have separate questions for different sexual positioning during anal sex with casual male partners but instead asked participants to report their overall condom use during all anal sex acts in the previous six months with casual male partners. Participants were coded as reporting any UAIC in the previous six months if they answered anything other than “*Always*” to this question.

### ***Combining datasets***

The EHIV Surveys include questions taken or adapted from the GAPSS and GOSS surveys to allow for cross-survey comparability. The datasets for both the August 2018 round of EHIV Survey and the February 2014 round of GOSS were refined to only included the variables utilised in these analyses. Before combining the two datasets, all variables were coded with the same numerical values to avoid errors when combined. Figure 26 provides a flow diagram overview of the process for combining the GOSS and EHIV Survey datasets.

### ***Limiting study population based on HPV vaccination funding eligibility in NZ***

For the analyses, the survey respondents will be limited to those aged 16 to 26 years at the time of the survey to reflect the NZ HPV vaccination funding criteria. The GBM in this age range are eligible for publicly funded HPV vaccination in NZ. The age range does not capture the full cohort of GBM eligible for funded HPV vaccination in NZ (ages nine to twenty-six years), this is due to the eligibility criteria and ethical issue with ability to provide informed consent for participation in the study surveys. However, over time, those age cohorts that are now being vaccinated through the school-based vaccination programmes will meet the eligibility criteria for the surveys. A similar approach has been used by Meites et al. and Oliver et al. using the USA HIV behavioural surveillance programme (NHBS), using repeat sampling of this population over time to identify changes in HPV vaccination uptake (296, 299).

### ***Matching study populations: Eligibility criteria for analyses***

Eligibility criteria for the two surveys used in this chapter differ. Chapter Five: Section One describes the eligibility criteria for the GOSS study. This includes being aged 16 years or older, identifying as male and reporting sexual contact with a male in the previous five years. By comparison, Chapter Six: Section One, provides the eligibility criteria for the EHIV Survey, which is being aged 16 years or older. Participants in the EHIV Survey are then provided with sociodemographic and sexual behavioural questions. Reporting recent (within six months prior to survey) sexual contact with a male is a shared variable between the two surveys.

To ensure greater comparability, the study population for the analyses in this chapter were restricted to those participants:

- Aged 16 to 26 years.
- Self-identify as male.
- Report sexual contact with another male in the previous six months.

### ***Bivariate analyses: Comparing shared variables and HPV-related variables***

The bivariate analyses for this chapter are split into two parts. Firstly, the two study populations were compared based on the shared sociodemographic, sexual health, and sexual behavioural variables. Secondly, the HPV-related questions included in the two surveys are compared: HPV-related disease knowledge, HPV-vaccine knowledge, HPV-vaccine acceptability, and HPV vaccine uptake.

Pearson's chi-squared test of trend was used to identify significant differences between the two study populations, with a p-value of 0.05 or less being considered significant. Where the number of participants in a variable category was less than 20, Fisher's exact test was used to identify significant differences between the two surveys, with a p-value of 0.05 or less being considered significant.

### ***HPV-related variables: Logistic regression models***

Adjusted odds ratios (AOR) were calculated for each HPV-related variable being investigated, using logistic regression to determine if changes between the datasets were independent of differences in population characteristics of the survey populations. Sociodemographic and behavioural variables that were found to be significantly different between the survey population at the bivariate level were included in the logistic regression models.

HPV-related variables were coded into dichotomous variables for use in their respective logistic regression models:



- HPV-related knowledge variables (including HPV vaccine knowledge) were coded
  - “*I knew this*” vs. “*I didn’t know this/I wasn’t sure*”,
- HPV-vaccine acceptability questions were coded
  - “*I would*” vs. “*I wouldn’t/I’m not sure*”,
- HPV-vaccine uptake was coded
  - “*One shot/ two shots/ three shots*” vs. “*No shots*”

Due to the low number of participants in some sociodemographic and behavioural variables, categories were condensed where possible and appropriate to increase the number of participants in each category and improve model stability. These include:

- ethnicity,
- sexual identity,
- and number of male sexual partners reported in the previous six months.

Sexual behaviour and healthcare engagement variables were deemed to be potential confounders to HPV-related variables, and as such, were included in the logistic regression models. Sensitivity analyses were undertaken for each logistic regression model comparing controlling for sociodemographic variables only and the second model controlling for both sociodemographic and sexual behaviour and healthcare engagement variables.

## Results

A combined total of 2817 participants were eligible and completed either GOSS 2014 (n=1793, 63.7%) or EHIV Survey 2018 (n=1024, 36.4%). After the removal of those participants who did not identify as male and reported no recent sexual contact with another male in the previous six months, a combined total of 2337 participants were included in the analyses. Of these, 1625 (69.5%) had been recruited for the 2014 GOSS survey and 712 (30.5%) recruited into the 2018 EHIV Survey.

Limiting to those aged between 16 and 26 years of age, a total of 821 participants were eligible for the analysis, 595 (72%) from the GOSS survey and 226 (28%) from the EHIV Survey.

### *Sociodemographic and sexual behavioural variables*

Table 39 shows that among GBM aged 16 to 26 years at the time of recruitment, self-reported HIV status at last test ( $p < 0.001$ ), perceived GP awareness of participant’s sexual orientation ( $p = 0.001$ ), and reporting any UAIC in the previous six months ( $p < 0.001$ ) varied significantly between datasets. EHIV Survey participants were significantly more likely to

report being HIV-negative, perceiving their GP to be aware of their sexual orientation and report any UAIC in the previous six months.

No significant differences between survey populations were found for self-reported ethnicity ( $p=0.107$ ), sexual orientation ( $p=0.332$ ), reporting a recent STI check or treatment in the 12 months prior to the survey ( $p=0.608$ ), and reported number of male sexual partners in the six months prior to the survey ( $p=0.412$ ).

Table 39: Frequencies of sociodemographic and behavioural variables among GOSS and EHIV Survey participants eligible for funded HPV vaccination in NZ (aged 16-26 years)

|                                       | GOSS 2014  |              | EHIV Survey 2018 |              | Chi2<br>p-value     |
|---------------------------------------|------------|--------------|------------------|--------------|---------------------|
|                                       | n          | %*           | N                | %*           |                     |
| <b>Total</b>                          | <b>595</b> | <b>100.0</b> | <b>226</b>       | <b>100.0</b> | <b>-</b>            |
| <b>Sociodemographic variables</b>     |            |              |                  |              |                     |
| <b>Ethnicity</b>                      |            |              |                  |              | 0.107 <sup>a</sup>  |
| European                              | 409        | 69.0         | 168              | 74.3         |                     |
| Māori                                 | 74         | 12.5         | 25               | 11.1         |                     |
| Pacific                               | 24         | 4.1          | 8                | 3.5          |                     |
| Asian                                 | 71         | 12.0         | 15               | 6.6          |                     |
| Other                                 | 15         | 2.5          | 10               | 4.4          |                     |
| NS                                    | 2          | (0.3)        | 0                | -            |                     |
| <b>Sexual Orientation</b>             |            |              |                  |              | 0.332 <sup>a</sup>  |
| Gay                                   | 438        | 73.6         | 175              | 77.4         |                     |
| Bisexual                              | 127        | 21.3         | 38               | 16.8         |                     |
| Other                                 | 30         | 5.0          | 13               | 5.8          |                     |
| NS                                    | 0          | -            | 0                | -            |                     |
| <b>HIV Status at last test</b>        |            |              |                  |              | <0.001 <sup>a</sup> |
| HIV-negative                          | 308        | 51.9         | 164              | 72.6         |                     |
| HIV positive                          | 7          | 1.2          | 2                | 0.9          |                     |
| Never tested/not sure of result       | 279        | 47.0         | 60               | 26.6         |                     |
| NS                                    | 1          | (0.2)        | 0                | -            |                     |
| <b>Sexual health</b>                  |            |              |                  |              |                     |
| <b>GP aware of sexual orientation</b> |            |              |                  |              | <b>0.001</b>        |
| Yes                                   | 192        | 32.3         | 100              | 44.6         |                     |
| No                                    | 281        | 47.3         | 76               | 33.9         |                     |
| Not sure                              | 121        | 20.4         | 48               | 21.4         |                     |

|  | GOSS 2014 |        | EHIV Survey 2018 |        | Chi2<br>p-value |
|--|-----------|--------|------------------|--------|-----------------|
|  | n         | %*     | N                | %*     |                 |
| NS   | 1         | (0.2)  | 2                | (0.9)  |                 |
| <b>Respondent had an STI check in &lt;12mths</b>           |           |        |                  |        | 0.608           |
| Yes  | 291       | 50.0   | 116              | 52.0   |                 |
| No   | 291       | 50.0   | 107              | 48.0   |                 |
| NS   | 13        | (2.2)  | 3                | (1.3)  |                 |
| <b>Sexual behaviours</b>                                   |           |        |                  |        |                 |
| <b>Number of male sexual partners &lt;6mth<sup>b</sup></b> |           |        |                  |        | 0.412           |
| 20 or less   | 563       | 94.6   | 217              | 96.0   |                 |
| 21+  | 32        | 5.4    | 9                | 4.0    |                 |
| NS   | 0         | -      | 0                |        |                 |
| <b>Any UAIC &lt;6mths<sup>b</sup></b>                      |           |        |                  |        | <0.001          |
| Yes  | 226       | 47.8   | 136              | 70.1   |                 |
| No   | 207       | 52.2   | 58               | 29.9   |                 |
| NS   | 162       | (27.2) | 32               | (14.2) |                 |

NS = not stated

\* Percentages for NS are separate to the percentages of those responding to the question

a = Fisher's exact test for association used due to low numbers in some categories

b = only asked of those who reported having anal sex with casual male sex partners in last six months

UAIC = unprotected (condomless) anal intercourse with casual male sexual partners

### HPV-related variables

Compared to 2014 GOSS participants, 2018 EHIV Survey participants were significantly more likely to report knowledge of each of the three types of HPV related cancers that affect males ( $p < 0.001$ ) (see Table 40). They were also significantly more likely to report being aware of the HPV vaccine ( $p < 0.001$ ), and to report receiving at least one dose of the HPV vaccine ( $p < 0.001$ ).

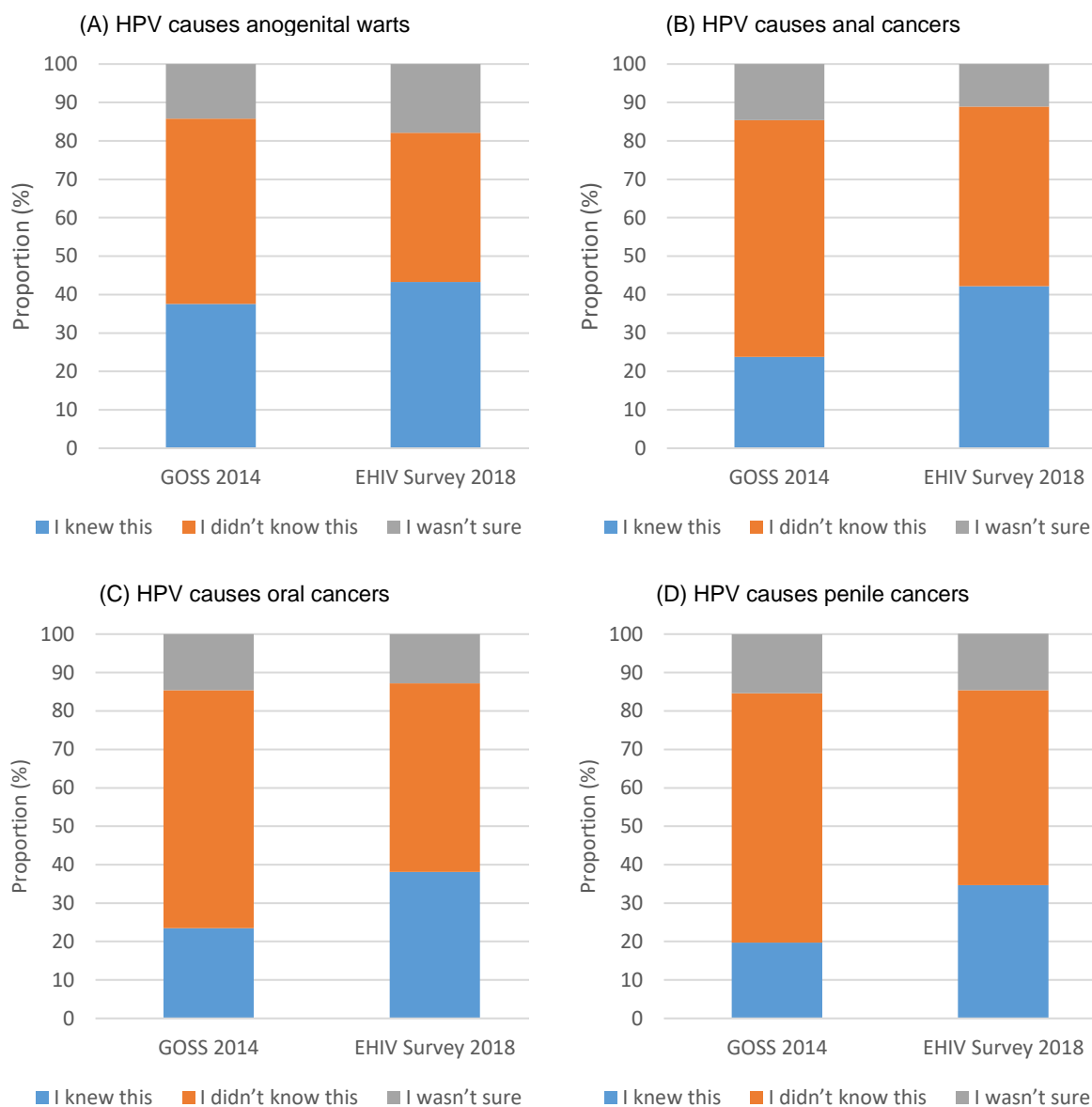


Figure 27: Changes in knowledge of HPV-related disease among GBM aged 16 to 26 years recruited online pre- and post-public funding of HPV vaccination for males, by survey round.

Self-reported knowledge that HPV caused anogenital warts did not vary significantly between the two survey populations (see Figure 27). Similarly, HPV vaccine acceptability under either price condition, if the full course was fully funded ( $p = 0.171$ ) or if offered at the price of NZ\$500.00 ( $p = 0.568$ ), did not differ significantly between the two surveys (see Figure 28).

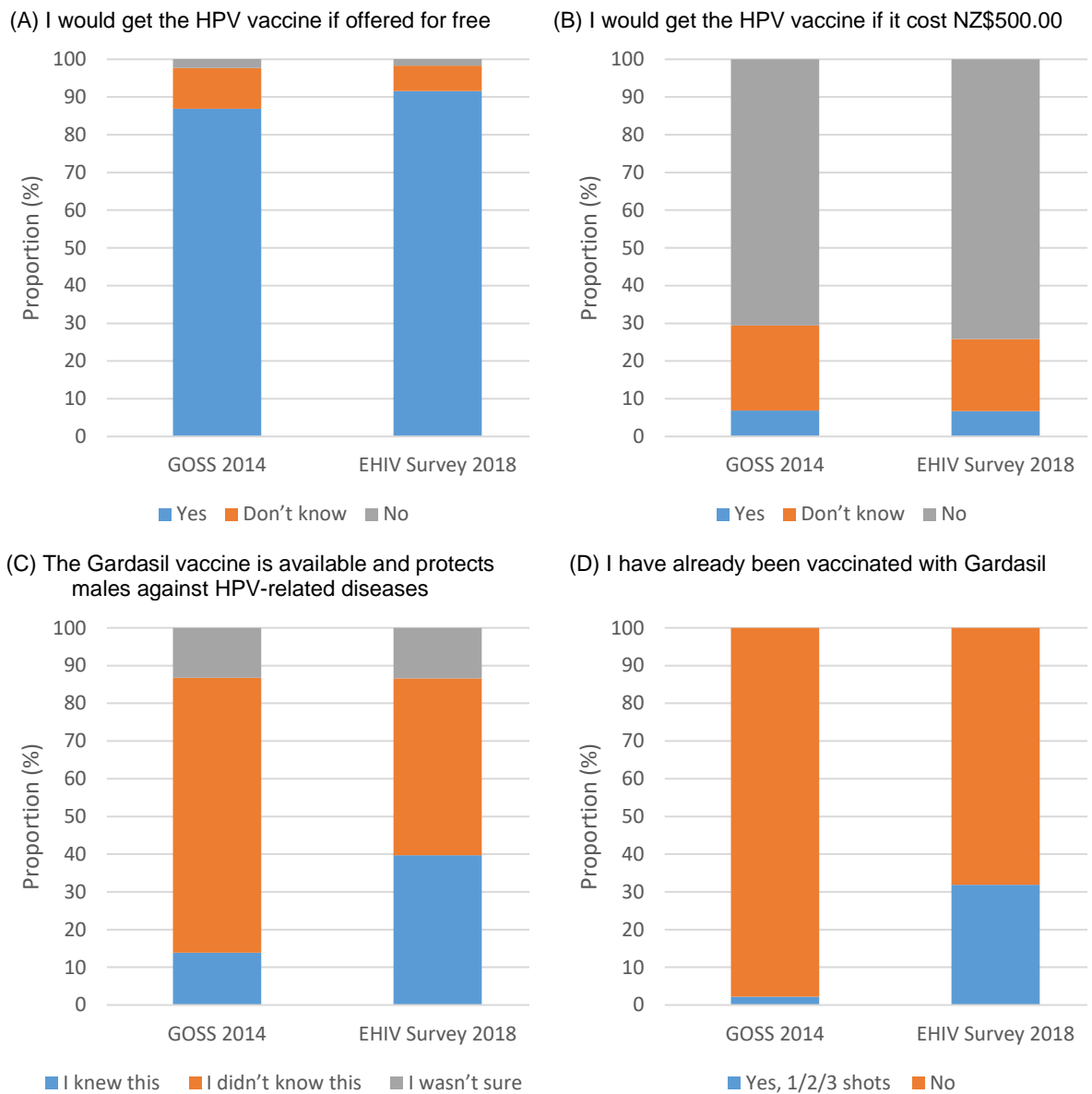


Figure 28: Changes in HPV vaccination acceptability, knowledge and uptake among GBM aged 16 to 26 years recruited online pre- and post-public funding of HPV vaccination for males, by survey round.

Table 40: Responses to HPV-related questions in the GOSS 2014 and 2018 EHIV Survey among GBM participants eligible for funded HPV vaccination in ANZ (aged 16- 26 years)

|  | GOSS 2014  |              | EH Survey 2018 |              | Chi2<br>p-value    |
|--|------------|--------------|----------------|--------------|--------------------|
|  | n          | %*           | n              | %*           |                    |
| <b>Total</b>   | <b>595</b> | <b>100.0</b> | <b>226</b>     | <b>100.0</b> | -                  |
| <b>HPV-related Disease Knowledge</b>   |            |              |                |              |                    |
| <b>HPV causes anogenital warts</b>   |            |              |                |              | 0.052              |
| I knew this  | 222        | 37.6         | 97             | 43.3         |                    |
| I didn't know this   | 285        | 48.2         | 87             | 38.8         |                    |
| I wasn't sure  | 84         | 14.2         | 40             | 17.9         |                    |
| NS   | 4          | (0.7)        | 2              | (0.9)        |                    |
| <b>HPV causes anal cancers</b>   |            |              |                |              | <0.001             |
| I knew this  | 140        | 23.8         | 95             | 42.2         |                    |
| I didn't know this   | 363        | 61.6         | 105            | 46.7         |                    |
| I wasn't sure  | 86         | 14.6         | 25             | 11.1         |                    |
| NS   | 6          | (1.0)        | 1              | (0.4)        |                    |
| <b>HPV causes oral cancers</b>   |            |              |                |              | <0.001             |
| I knew this  | 138        | 23.5         | 86             | 38.1         |                    |
| I didn't know this   | 364        | 61.9         | 111            | 49.1         |                    |
| I wasn't sure  | 86         | 14.6         | 29             | 12.8         |                    |
| NS   | 7          | (1.2)        | 0              | -            |                    |
| <b>HPV causes penile cancers</b>   |            |              |                |              | <0.001             |
| I knew this  | 116        | 19.7         | 78             | 34.7         |                    |
| I didn't know this   | 383        | 64.9         | 114            | 50.7         |                    |
| I wasn't sure  | 91         | 15.4         | 33             | 14.7         |                    |
| NS   | 5          | (0.8)        | 1              | (0.4)        |                    |
| <b>Vaccine Awareness</b>   |            |              |                |              |                    |
| <b>Gardasil is available and protects males against HPV-related diseases</b> |            |              |                |              | <0.001             |
| I knew this  | 82         | 13.9         | 89             | 39.7         |                    |
| I didn't know this   | 430        | 72.9         | 105            | 46.9         |                    |
| I wasn't sure  | 78         | 13.2         | 30             | 13.4         |                    |
| NS   | 5          | (0.8)        | 2              | (0.9)        |                    |
| <b>Vaccine Acceptability</b>   |            |              |                |              |                    |
| <b>I would get vaccinated with Gardasil if offered for free</b>              |            |              |                |              | 0.171 <sup>a</sup> |
| Yes  | 515        | 86.9         | 206            | 91.6         |                    |
| No   | 14         | 2.4          | 4              | 1.8          |                    |
| Don't know   | 64         | 10.8         | 15             | 6.7          |                    |
| NS   | 2          | (0.3)        | 1              | (0.4)        |                    |

|  | GOSS 2014 |       | EH Survey 2018 |       | Chi2<br>p-value     |
|--|-----------|-------|----------------|-------|---------------------|
|  | n         | %*    | n              | %*    |                     |
| <b>Would get vaccinated with Gardasil if cost NZ\$500.00</b> |           |       |                |       | 0.568 <sup>a</sup>  |
| Yes  | 41        | 6.9   | 15             | 6.7   |                     |
| No   | 417       | 70.6  | 167            | 74.2  |                     |
| Don't know   | 133       | 22.5  | 43             | 19.1  |                     |
| NS   | 4         | (0.7) | 1              | (0.4) |                     |
| <b>Vaccine Uptake</b>  |           |       |                |       |                     |
| <b>Already been vaccinated with Gardasil</b>                 |           |       |                |       | <0.001 <sup>a</sup> |
| Yes, 1 shot  | 0         | 0.0   | 11             | 4.9   |                     |
| Yes, 2 shots   | 4         | 0.7   | 17             | 7.5   |                     |
| Yes, 3 shots   | 9         | 1.5   | 44             | 19.5  |                     |
| No   | 579       | 97.8  | 154            | 68.1  |                     |
| NS   | 3         | (0.5) | 0              | -     |                     |
|  |           |       |                |       | <0.001 <sup>a</sup> |
| Yes, 1/2/3 shots   | 13        | 2.2   | 72             | 31.9  |                     |
| No   | 579       | 97.8  | 154            | 68.1  |                     |
| NS   | 3         | (0.5) | 0              | -     |                     |

NS = not stated

\* Percentages for NS are separate to the percentages of those responding to the question

a = Fisher's exact test for association used due numbers below n=20 in some categories

Table 41 shows the results for the logistic regression analyses of HPV-related variables between the two surveys. Unadjusted odds ratios indicate that greater knowledge and vaccine uptake are significantly associated with the 2018 EHIV Survey. With the exception of knowledge that HPV caused some oral cancers, all those HPV-related variables found to be significant at a bivariate level remained significant after controlling for sociodemographic and both sociodemographic and behavioural variables.

After controlling for both sociodemographic and behavioural variables that differed significantly between survey populations, knowledge that HPV cause some anal cancers (AOR=2.57, 95% CI:1.32-5.01) and penile cancers (AOR=2.40, 95% CI:1.26-4.56), being aware of the HPV vaccine (AOR=2.45, 95% CI:1.26-4.76), and receiving any dose of the HPV vaccine (AOR=28.49, 95% CI:12.22-66.43) all remained independently associated with the 2018 EHIV Survey round.

Knowledge that HPV causes oral some cancers was not independently associated with survey round after controlling for significant sociodemographic and behavioural differences between the two surveys (AOR=1.65, 95% CI:0.87-3.13). Knowledge that HPV causes anogenital warts (AOR=0.96, 95% CI:0.56-1.67), and HPV vaccine acceptability under the two price conditions were not found to be independently associated with survey rounds.



Table 41: Results of logistic regression analyses of HPV-related questions comparing responses in GOSS 2014 and EHIV Survey 2018 among GBM participants eligible for funded HPV vaccination in NZ (aged 16-26), using three models.

|                                      | Unadjusted   |                      | Sociodemographic Variables Only <sup>α</sup> |                     | Sociodemographic and behaviour variables <sup>β</sup> |                      |
|--------------------------------------|--------------|----------------------|--|---------------------|---|----------------------|
|                                      | OR           | 95% CI               | AOR*   | 95% CI              | AOR*  | 95% CI               |
| <b>HPV-related disease Knowledge</b> |              |                      |  |                     |   |                      |
| <b>Anogenital warts</b>              |              |                      |  |                     |   |                      |
| I didn't know/I wasn't sure          | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| I knew that                          | 0.92         | 0.59 – 1.43          | 0.89   | 0.56 – 1.41         | 0.96  | 0.56 – 1.67          |
| <b>Anal cancers</b>                  |              |                      |  |                     |   |                      |
| I didn't know/I wasn't sure          | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| I knew that                          | <b>2.33</b>  | <b>1.39 – 3.91</b>   | <b>2.04</b>                                  | <b>1.17 – 3.55</b>  | <b>2.57</b>   | <b>1.32 – 5.01</b>   |
| <b>Oral cancers</b>                  |              |                      |  |                     |   |                      |
| I didn't know/I wasn't sure          | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| I knew that                          | <b>1.84</b>  | <b>1.12 – 3.05</b>   | 1.66   | 0.98 – 2.82         | 1.65  | 0.87 – 3.13          |
| <b>Penile cancers</b>                |              |                      |  |                     |   |                      |
| I didn't know/I wasn't sure          | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| I knew that                          | <b>1.85</b>  | <b>1.13 – 3.03</b>   | <b>1.69</b>                                  | <b>1.00 – 2.85</b>  | <b>2.40</b>   | <b>1.26 – 4.56</b>   |
| <b>HPV vaccine knowledge</b>         |              |                      |  |                     |   |                      |
| <b>Gardasil vaccine</b>              |              |                      |  |                     |   |                      |
| I didn't know/I wasn't sure          | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| I knew that                          | <b>2.82</b>  | <b>1.68 – 4.73</b>   | <b>2.63</b>                                  | <b>1.49 – 4.64</b>  | <b>2.45</b>   | <b>1.26 – 4.76</b>   |
| <b>HPV vaccine acceptability</b>     |              |                      |  |                     |   |                      |
| <b>Fully funded</b>                  |              |                      |  |                     |   |                      |
| No/Not sure                          | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| I would                              | 1.71         | 0.95 – 3.06          | 1.33   | 0.73 – 2.45         | 1.33  | 0.66 – 2.68          |
| <b>NZ\$500.00</b>                    |              |                      |  |                     |   |                      |
| No/Not sure                          | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| I would                              | 1.13         | 0.57 – 2.24          | 0.99   | 0.49 – 2.00         | 1.50  | 0.66 – 3.40          |
| <b>HPV vaccine uptake</b>            |              |                      |  |                     |   |                      |
| <b>Received HPV vaccine</b>          |              |                      |  |                     |   |                      |
| None                                 | <i>Ref.</i>  | -                    | <i>Ref.</i>                                  | -                   | <i>Ref.</i>   | -                    |
| Yes, 1/2/3 shots                     | <b>20.82</b> | <b>11.24 – 38.58</b> | <b>17.75</b>                                 | <b>9.44 – 33.38</b> | <b>28.49</b>  | <b>12.22 – 66.43</b> |

<sup>α</sup> = Adjusted for: ethnicity and HIV status at last test.

<sup>β</sup> = Adjusted for: ethnicity, HIV status at last test, perceived GP awareness of sexuality, number of recent male sexual partners, condom use with recent casual male sex partners.

## Discussion

To the candidate's knowledge, this is the first study internationally among GBM to examine changes in HPV-related knowledge, vaccine acceptability and vaccine uptake pre- and post-expansion of public HPV vaccination funding to include males.

The findings indicate that there has been a significant increase in self-reported HPV vaccination uptake among sexually active GBM aged 16 to 26 years recruited online between 2014 and 2018 in NZ, from 2% to 32%, ( $p < 0.001$ ). The increase in uptake is independent of sociodemographic and behavioural differences between the two samples (AOR=28.49, 95% CI:12.22—66.43).

Significant increases in self-reported knowledge of HPV-related cancers that can affect males and knowledge of the HPV vaccine itself were also found among GBM, independent of sociodemographic and behavioural factors. The proportion of GBM reporting knowledge that HPV causes some anal cancers almost doubled from 24% in 2014 to 42% in 2018 (AOR=2.57, 95% CI:1.32—5.01) and knowledge that HPV causes some penile cancers was also found to have increased over time (AOR=2.40, 95% CI:1.26—4.56). Awareness of the HPV vaccine and its efficacy for males more than doubled between survey years from 14% to 40% (AOR=2.45, 95% CI:1.26—4.76).

No change was found for some HPV-related variables. Knowledge that HPV causes anogenital warts did not significantly differ between the 2014 and 2018 survey rounds ( $p = 0.052$ ). Similarly, HPV vaccine acceptability if offered for free or at NZ\$500.00 was not found to be significantly associated with survey year ( $p = 0.171$  and  $p = 0.568$ , respectively). However, knowledge that HPV causes some oral cancers was found to significantly differ between survey years ( $p < 0.001$ ), but this association did not remain after controlling for sociodemographic and behavioural factors (AOR=1.65, 95% CI:0.87—3.13).

### **Strengths**

The strengths associated with individual study methods are presented for GOSS in Chapter Five: Section One and for EHV Survey in Chapter Six: Section One. Here, the strengths associated with the approach taken in this analysis are explored below.

The analysis used data collected pre- and post-extension of public funding to include males. Data collected prior to the extension of funding to include males can be considered baseline data to monitor the coverage of HPV vaccination over time among GBM in NZ. Repeat cross-sectional sampling through online channels track changes in HPV related variables among this population of GBM who are at risk of acquiring and developing HPV-related disease. These data can be used to inform public health programmes designed to address the HPV-related health inequity experienced by GBM.

Both surveys recruited using a similar methodology, repeat cross-sectional recruitment, to monitor changes over time among GBM. In addition, the 2018 EHIV Survey repeated the questions used in the 2014 GOSS survey round, allowing the HPV-related data to be directly comparable across surveys. Through repeat cross-sectional sampling and repeat use of HPV-related questions, the data collected can be compared and tracked over time among this at-risk population of GBM.

For the analysis, survey populations were limited to those aged 16 to 26 years and report sexual activity with a male in the previous six months. Limiting both survey populations to these criteria further increase the comparability between the population samples. This population also stand to gain the most benefit from HPV vaccination, being eligible for funded vaccination and at-risk of acquiring HPV infection through recent sexual activity.

Both surveys collect a range of sociodemographic and behavioural data that are potentially associated with or act as confounding variables to the HPV-related variables. Additionally, differences found between the populations in these analyses in terms of sociodemographic and behavioural variables could reflect population-level shifts among GBM or related to shifts in the user base of the social media and dating app platforms used to recruit the for the surveys. Identifying and adjusting for these differences are therefore important and have been incorporated into the analyses.

The use of repeat cross-sectional surveys to recruit a population not reflected in administrative health datasets offers a complementary narrative to evaluate the impact of public health policy change on this population. Without measures of sexual orientation captured in administrative health datasets, GBM are an invisible population, limiting the ability to identify health inequities experienced by this population. Additional data collection methods such as those used in this analysis are required to identify health inequities experienced by GBM, inform public health interventions to address them, and monitor progress towards health equity.

### ***Limitations***

The biases associated with the recruitment methods for each survey are explored in the methods chapter for GOSS (*see Chapter Five: Section One*) and the EHIV Survey (*see Chapter Six: Section One*). Explored below are limitations in relation to the approach and analyses undertaken in this Section.

Ethnicities other than European are underrepresented in the survey populations for both GOSS and the EHIV Survey compared to census ethnicity data, particularly for Pacific and Asian populations (339). Online recruitment is one likely contributor to this outcome, alongside language and cultural barriers to participating in a survey related to sexual

behaviours among GBM. In the 2013 NZ Census, 82% of households reported that they had internet access, and this varied considerably by region and socioeconomic variables with Maori (67%) and Pacific (65%) reporting the lowest access to the internet as well as those in Gisborne (68%) and Northland (73%) (340). Additionally, much of the recruitment was mobile app-based for both surveys in this analysis, further biasing the sample to those who have access to mobile devices and either household internet or a mobile data plan.

Causality between time and changes in HPV-related knowledge and HPV-vaccination acceptability and uptake cannot be inferred due to the cross-sectional nature of the surveys. GBM who report receiving any dose of the HPV vaccine may have started the course at a younger age prior to the change in funding. It cannot be inferred that the expansion of funding for the HPV vaccine to include males was the independent cause for the increase in HPV vaccine uptake seen between the two survey populations. Similarly, increases seen between the two surveys for HPV-related knowledge and vaccine acceptability cannot be attributed solely to the change in funding eligibility for the HPV vaccine.

Respondents were asked to self-report HPV-related knowledge, acceptability, and vaccine uptake as well as sociodemographic, healthcare engagement and sexual behavioural questions. This is subject to recall and social-desirability biases. Both surveys were anonymous and voluntary, which could reduce reporting of socially desirable behaviours and knowledge. The anonymous nature of the surveys means that it is not possible to follow-up confirmation of vaccination status through medical records.

Compared to GOSS participants, EHIV Survey participants reported greater engagement with healthcare and greater engagement in sexual risk practices. Differences in sociodemographic and behavioural variables between surveys may also result from differences in recruitment settings and techniques, further confounding true trends in HPV-related variables. While these analyses were not seeking to find factors associated with HPV-related variables, it has been demonstrated that socio-demographic and behaviours are associated with HPV vaccine uptake, knowledge, and acceptability (249, 251, 299). Inclusion of these variables in the regression models will have reduced the influence of these differences, though future studies should aim to further minimise differences through recruitment methods.

Statistical power for detection of between group differences was reduced as a result of restricting the study population to only those aged 16 to 26 years, who identify as male, and reported sexual contact with at least one male in the six months prior to the survey. Several bivariate analyses required the use of Fisher's exact test due to fewer than 20 participants being present in some groupings. Where possible and appropriate this was mitigated by grouping categories within variables together to increase the number of participants within

category groupings. The wide confidence interval for the adjusted odds ratio for HPV vaccine uptake (AOR=28.49, 95% CI:12.22—66.43) is partially explained by the limited number of participants reporting receiving the vaccine in the 2014 GOSS sample (n=13/595). Future surveys exploring HPV vaccine uptake among GBM should consider over-recruiting GBM under the aged of 27 years to increase statistical power to detect between group differences (such as ethnicity and region of residence).

This study examines those GBM who are eligible for the catch-up programme only. It does not capture those GBM who receive the vaccine through school-based programmes as these males will have been aged between 11 and 14 years of age at the time the survey was implemented. Future studies will need to be able to identify between those who have received the vaccine through school-based programmes, those through catch-up programmes, and those not eligible for the funded vaccine but have self-funded to receive it.

### ***Discussion of findings***

The significant increases in HPV vaccination uptake were seen among those GBM eligible for funded vaccination, independent of differences in sociodemographic and behavioural factors. Despite the significant increase in HPV vaccine uptake among these GBM, the self-reported vaccine uptake of 32% remains less than the 75-80% HPV vaccination coverage target set by the MoH in 2015 (218). Levels of self-reported HPV-related knowledge also remain consistently below a 50% majority among the study sample (see *Table 40*), potentially acting as a contributor to the sub-optimal prevalence of HPV vaccination uptake.

Compared to changes in HPV vaccination uptake, relatively modest increases were seen in HPV-related knowledge. No increases were found for knowledge that HPV causes anogenital warts and that HPV causes some oral cancers, despite these two being the most common HPV-related diseases to affect the general male population (267, 274, 341).

Though the extreme increase is a result of self-reported vaccination uptake among GBM in the GOSS sample being exceptionally low, evident in the wide confidence interval for the AOR, it demonstrates a potential gap in health promotion to males and could result in even greater vaccination uptake if addressed.

There are additional environmental and systemic factors that could have impacted HPV vaccine uptake among GBM outside of the school-based vaccination programmes in NZ. Firstly, there have been shortages in the nonvalent HPV vaccine supply to NZ, with a call for available vaccines to be prioritised to school-based vaccination delivery programmes (342). Secondly, there has been limited funding provided for health promotion of the HPV vaccine to males outside of school-based vaccination programmes and no GBM-specific health promotion programmes or materials created (see *Figure 29*) (343).



Figure 29: Screenshot of BestShot campaign website by Seqirus™, the supplier for Gardasil® 9 in NZ. Each “couple” featured in the campaign consists of a male and female pair. Available from: <https://www.bestshot.co.nz/#hpv>

### ***Comparison to other studies***

As described throughout this thesis, sexual orientation data are not routinely collected or reported in administrative health databases in NZ and globally. Data on healthcare uptake and outcomes among GBM must therefore be captured through other means of surveillance of purposeful studies. In the published literature, two studies explored changes in HPV vaccine uptake among GBM, both recruiting in the USA.

Oliver et al. estimate HPV vaccination uptake to be 17.2% among GBM recruited in 2014 compared to 4.9% in 2011. They used the 2011 and 2014 rounds of the NBHS behavioural surveillance programme to identify an increase in HPV vaccination uptake among GBM age 18—26 years, with 2011 being the year that HPV vaccination was approved for use in males by the FDA (207). Oliver et al. do not explore differences in sociodemographic and behavioural variables between the two NHBS rounds that may have influenced HPV vaccination uptake, though they do explore factors associated with HPV vaccination uptake among the vaccine eligible GBM in the 2014 sample.

Loretan et al. used the American Men’s Internet Survey online survey to described changes among GBM who have ever been eligible for HPV vaccination in the USA between 2014 and 2017 (344). The study methods were similar to the GOSS and EHIV Survey in that they recruited GBM through online dating sites, apps, and banner advertisements. They estimate self-reported HPV vaccination uptake among GBM to be 37.6% in 2017, compared to 22.5% in 2014. The 2017 estimate is four years after HPV vaccination was recommended for GBM in the USA, and six years after the recommendation for males (207). Similar to NZ, the 37.6% coverage estimate for 2017 is lower than the coverage for all 13—17-year-old males in the USA, which is estimated to be 62.6% in 2017 (217, 345).

In contrast, the United Kingdom implemented a targeted and publicly funded HPV vaccination programme for GBM up to the age of 45 years in 2018, delivered through sexual

health outpatient clinics. Data from pilot surveillance of this approach have indicated that among GBM who attended clinics and were eligible for HPV vaccination, less than half received the vaccine (46%) (331). Edelstein et al. did not report data on those eligible GBM who did not receive the HPV vaccine at visit, for example, whether the vaccine was offered and declined, which could be used to inform health promotion messages. Moreover, these data do not capture the experience of GBM who are not engaging with sexual health services and few GBM attending the clinics for the first time reported that they were attending solely with the intention to receive the HPV vaccine (11%).

Cross-sectional uptake data explored in this analysis indicate that HPV vaccination coverage is increasing among GBM, both in NZ and internationally. Repeat sampling studies such as GOSS, EHIV Survey, NBHS, and American Men's Internet Survey can provide an indication of changes in vaccination uptake over time among populations that are not captured through national administrative datasets. Future research should seek to explore between group differences to determine if increases in HPV-related variables have been observed equally among all GBM populations, such as those identifying with Māori ethnicity and those who reside outside of urban centres.

In lieu of national health records that capture sexual orientation and vaccination status, alternative data collection methods are required to accurately monitor vaccination uptake among populations whose experiences are not reflected. GBM are a population disproportionately affected by HPV-related disease and therefore capturing data for this population should be considered a priority in HPV vaccination programme evaluation to assess equitable health outcomes.

## Conclusion

Vaccination uptake has increased significantly post-funding of HPV vaccination to include males among online samples of GBM in NZ. Significant increases in HPV-related knowledge have also been observed over this same period. Opportunistic inclusion of HPV-related measures in online cross-sectional surveys targeting GBM is feasible and offers complimentary data to administrative health datasets that do not capture sexual orientation information.

All GBM eligible for publicly funded HPV vaccination should have the opportunity to receive it. These data can be used to track changes in HPV vaccination uptake among GBM and determine if this population is receiving benefit from the extension of HPV vaccination funding or continues to experience health inequities. Sociodemographic and behavioural differences associated with lower HPV-related knowledge or vaccine uptake can be used to inform public health programmes targeting these groups with the aim to address these gaps.

# Chapter 7: Comfort with having sexual orientation confidentially recorded on official databases among a community and online sample of GBM in Aotearoa, New Zealand

*“The greatest threat to the health of lesbian, gay, and bisexual...[communities]... is the lack of scientific information about their health.” – Sell et al. 2014 (346).*

## Purpose

Would GBM in NZ feel comfortable having their sexual orientation recorded confidentially on government or healthcare databases to monitor public health needs, inequities and progress?

## Aims

1. Describe GBM comfort with having sexual orientation recorded confidentially on official databases.
2. Explore differences in comfort by key sociodemographic and behavioural variables associated with sexual health.
3. Identify variables independently associated with comfort disclosing sexual orientation.

## Introduction

One goal of public health is to identify and eliminate health inequities experienced by groups through the systematic collection of data to inform decision making, programme and intervention development, and monitoring and evaluation (347). As has been highlighted throughout this thesis, in NZ and the majority of countries around the world, sexual orientation data is not routinely collected in a manner that provides a high-quality evidence base on which decisions can be made regarding health priorities and expenditure that affect LGBTIQ+ populations (*see Chapter Two, Section Two: Part Two*). This includes data that could be used to monitor HPV-related outcomes, including vaccination coverage and HPV-related disease prevalence.

Inequities have been revealed for GBM and other LGBTIQ+ populations beyond sexual health and HIV. These include mental health, suicidality, cancers, cardiovascular disease, ageing, weight, income, smoking, and drug and alcohol abuse (348-354). Bränström et al. demonstrated that sexual orientation minorities, while experiencing no difference in the prevalence of “non-preventable” disease, experienced a greater burden of “preventable disease” compared to the heterosexual population (355). The authors explained this using a



“fundamental causality” theory, in which disadvantaged or minority populations, are less able than the majority to leverage resources and privilege to access preventative care, tools or programmes that would result in better health outcomes.

Legal protections exist in NZ against discrimination based on sexual orientation through the Human Rights Act 1993 (356). Similar protections exist in the majority of more economically developed countries and a number of other countries (357, 358). Inclusion of sexual orientation measures across government and state-owned data collection is essential to ensure anti-discrimination protections are addressing the inequitable experience of LGBTIQ+ populations because it is data that inform funding and policies. However, despite these protections, previous research by the candidate showed that only half of GBM sampled in the combined GAPSS and GOSS 2014 round reported believing their GP to be aware of their sexual orientation (115).

Sexual orientation is a construct of multiple dimensions that include sexual identity, sexual behaviour, and sexual attraction (*see Figure 8*). In spite of legal protections in a number of countries, there remain few examples of a recognised standard definition of sexual orientation within or across countries. Australia and NZ have both developed a statistical standard for sexual orientation that is recommended for use whenever sexual orientation is measured (359, 360). NZ has also recently confirmed that sexual identity will be included in the 2023 Census (361). The USA and UK have made a public commitment to collect, analyse and report sexual orientation and gender identity (SOGI) data to tackle health inequities experienced by LGBTIQ+ populations, though this has limited the scope of SOGI data collection to only health-related surveys or datasets (120, 362).

Globally, the absence of sexual orientation data results in a lack of understanding and evidence to support research and public health responses for the health inequities experienced by LGBTIQ+ populations. Funding for research on health issues experienced by GBM beyond HIV and AIDS is rare. Carefully designed non-representative surveys do provide a reliable basis for public health decision making for these populations, and the thesis has discussed the limitations for recruiting GBM through random and probability-based sampling methods (*see Chapter Two, Section Two: Part Two*).

In NZ, recording sexual orientation as a demographic field in the NHI is a potential way to improve the quality of evidence relating to quantifying health inequities experienced by LGBTIQ+ populations by providing total population data. Arguments against the inclusion of sexual orientation data in total population “administrative” datasets or surveillance have included similar arguments that have historically been made against ethnicity data collection (276, 346). These include:

1. Sexual orientation data are not perceived as relevant to the purpose of data collection.
2. Adding a variable would be costly or alter the survey length or require another question to be deleted.
3. A standardised, valid, and reliable measure of sexual orientation does not exist.
4. Respondents would refuse to answer sexual orientation questions or stop interviews when asked their sexual orientation.
5. Sexual orientation minorities represent a small proportion of the general population; therefore, there would not be enough power to analyse data related to sexual orientation.
6. Sexual orientation is a “proxy” for other variables, and these should be measured instead (e.g., stigma and discrimination).
7. If sexual minorities are found to be at greater risk for certain health concerns, this could be used to further stigmatise these populations.

Systematic and linked data collection by the government or government organisations have been met with caution from the general population. In early 2014, the prospect of having personal data recorded and stored electronically by government and healthcare institutions remained a novel concept in NZ. The NZ government announced plans to move to electronic health records in 2015 and in 2019 this plan has been replaced with a “Health Information Platform” that links together information provided by the individual across different datasets (363). The movement to electronic health records and online platforms for sharing of patient health information for monitoring and wider research purposes, particularly by private organisations, has been controversial with concerns over privacy and data security from the general public (364).

No studies were found that explored community acceptability of having sexual orientation recorded in routine data collection among sexual orientation minorities, and GBM specifically. Published literature has explored the acceptability of disclosing sexual orientation under research, healthcare, and government surveillance settings (see *p.260*). An argument could be made that disclosure of sexual orientation under these settings implies that the data will be recorded and held on official database and comfort with having these data recorded is one of many perceived barriers to disclosure of sexual orientation in these settings.

The emergent and growing field of “big data”, the global movement to electronic data records for individuals interacting with institutions and organisations, and recent ethical and privacy breaches of user data held by large corporations make comfort with personal data being held

by a separate party a complex and multifaceted concept worthy of investigation. The analyses conducted in this chapter seeks to explore if GBM in NZ would be comfortable with having their sexual orientation recorded in government or clinical “official” databases.

## Methods

### GAPSS and GOSS methods

The methods for GAPSS and GOSS are described Chapter Five: Section One. Detailed below are details that are specific to the analyses and approach taken in this Chapter.

### Measure of comfort

At the time of questionnaire development, no examples of survey questions were found that sought to measure comfort with having sexual orientation recorded in administrative databases. Therefore, the research team developed an original question. To determine comfort with having sexual orientation recorded confidentially on official databases, participants were asked “*Would you be comfortable for your sexuality to be recorded in official health databases, so long as it was confidential?*” with possible responses including: “Yes”, “No” or “Not sure”.

### Study population

Participants were included in the analyses if they were eligible to participate in GAPSS and GOSS: they were aged 16 years or older, identified as “male”, had been sexually active with another “male” in the previous five years, and were able to read and understand English.

Non-responses to the sociodemographic and behavioural variables have been recorded in the results tables (*see Table 43*). Participants that provided a response to the comfort of having sexual orientation recorded in databases were included in the logistic regression model, those with missing data for this question were excluded from the model.

### Statistical analyses

A three-step analysis was conducted to answer the research aims for this chapter. The basic frequencies of combined responses to the comfort question were reported, including missing data for those who did not respond, then reported individually for each of the two questionnaires, GAPSS and GOSS.

Associations with sociodemographic and behavioural variables considered to have a potential impact on comfort were explored through bivariate analyses. Variables for the bivariate analyses included: age, ethnicity, sexual identity, highest qualification attained, survey recruitment method (offline vs. online), HIV status at last test, perceived GP awareness of participant’s sexual orientation, number of male sexual partners in the previous

six months, any reported unprotected (condomless) anal sex with casual male partners in the previous six months.

For logistic regression modelling, comfort was coded into a binary variable with responses grouped as “Yes and “No/Not sure”. Adjusted odds ratios were calculated with a 95% confidence interval. Reference groups were selected based on the size of the subgroup within the variable, with those that had the greatest number being the reference group or selected as the lowest value category within an ordinal categorical variable. Age and the method by which participants were recruited into the survey were included as a potential predictor (age) or confounding (recruitment) variable in the model. Other variables included in the logistic regression model were those sociodemographic and behavioural variables found to be associated with reporting comfort in the bivariate analyses or with a p-value equal to or less than 0.01.

All statistical analyses were conducted in STATA IC version.13.1 (Stata Corporation, College Station, TX, USA).

## Results

A total of 3214 GBM took part in the GAPSS and GOSS surveys, of these men 98.7% (n=3173) completed the question relating to the comfort of having their sexual orientation recorded on, while 1.3% (n=41) did not. Almost all the participants not completing the question were found in the GAPSS survey sample (n=38).

### Comfort with having sexual orientation recorded confidentially in official databases

Table 42 shows that the majority (63.1%) of GBM in the combined sample indicated that they would be comfortable with having their sexual orientation recorded in official databases. Comfort varied significantly by survey, with greater comfort reported among GAPSS participants compared to GOSS participants, 71.8% vs. 56.4% respectively.

Table 42: Comfort with having sexuality recorded confidentially in official health databases among GBM by survey

|  | Combined |       | GAPSS    |       | GOSS     |       | Chi2 p-value     |
|--|----------|-------|----------|-------|----------|-------|------------------|
|  | <i>n</i> | %     | <i>n</i> | %     | <i>n</i> | %     |                  |
| <b>Comfortable having sexuality recorded</b> |          |       |          |       |          |       | <b>&lt;0.001</b> |
| Yes  | 2002     | 63.1  | 993      | 71.8  | 1009     | 56.4  |                  |
| No   | 766      | 24.1  | 235      | 17.0  | 531      | 29.7  |                  |
| Not Sure                                     | 405      | 12.8  | 155      | 11.2  | 250      | 14.0  |                  |
| Total  | 3173     | 100.0 | 1383     | 100.0 | 1790     | 100.0 |                  |
| Mi   | 41       | (1.3) | 38       | (2.7) | 3        | (0.2) |                  |

Mi = missing. Proportion not included as part of the total.

### Comfort by sociodemographic and behavioural variables

In the bivariate analyses, comfort varied significantly by almost all sociodemographic and behavioural variables included in the analyses, with the exception of age ( $p=0.422$ ) and any reported UAIC ( $p=0.112$ ) (see *Table 43*).

Significantly greater levels of comfort were reported among those who report being gay identified ( $p<0.001$ ), holding a non-tertiary qualification ( $p=0.004$ ), recruited in the GAPSS survey ( $p<0.001$ ), self-reported as being HIV-negative at last test ( $p<0.001$ ), believe their GP to be aware of their sexual orientation ( $p<0.001$ ), and who report 11 or more male sexual partners in the previous six months ( $p<0.001$ ). Significantly lower comfort was reported among participants who self-identified as an ethnicity “Other” than European, Maori, Pacific or Asian ( $p=0.004$ ).

### Factors associated with comfort of having sexual orientation recorded

The majority of sociodemographic variables remained significantly associated with comfort after inclusion in the logistic model (see *Table 43*). Those reporting an “other” ethnicity had lower odds of reporting comfort (AOR:0.64, 95%CI:0.43—0.96) compared to those identifying as European. Similarly, participants identifying as bisexual (AOR:0.45, 95%CI:0.35—0.56) or an “other” sexual identity (AOR:0.58, 95%CI:0.40—0.86) were less likely to report comfort compared to those identifying as gay/homosexual. Highest qualification achieved was found to be independently associated, with participants who hold a tertiary qualification having lower odds of reporting comfort (AOR:0.67, 95%CI:0.57—0.80) compared to participants who reported holding a non-tertiary qualification.

Of the sociodemographic variables included in the model, two variables altered significance after controlling for other variables. Age became independently associated, with participants having lower odds of reporting comfort if they were aged 27—45 years (AOR: 0.68,

95%CI:0.55—0.83) or 46 years and older (AOR:0.57, 95%CI:0.45—0.72) compared to those aged 16—26 years. While self-reported HIV status at last test was no longer associated with comfort after inclusion in the model.

Which survey participants took part in was independently associated with reporting comfort. Compared to participants in GOSS, those participating in GAPSS had 1.75 times the odds of reporting comfort (95%CI:1.47—2.09).

Perceived GP awareness of participant's sexuality remained significantly associated with comfort, with lower odds of reporting comfort found among those participants who did not believe their GP to be aware (AOR:0.32, 95%CI:0.26—0.40) and those who were not sure (AOR:0.53, 95%CI:0.42—0.67), compared to those who believed their GP was aware.

No sexual behaviours included in these analyses were found to be associated with reporting comfort with having sexual orientation recorded in official databases. The reported number of male sexual partners in the previous six months was no longer associated with reporting comfort after inclusion in the logistic model.

Table 43: Comfort with having sexuality recorded confidentially in official health databases among GBM by sociodemographic and sexual behavioural variables

|  | N    | Yes  |      | Chi-square       | OR          | 95% CI             | AOR         | 95% CI             |
|--|------|------|------|------------------|-------------|--------------------|-------------|--------------------|
|  |      | n    | %    |                  |             |                    |             |                    |
| <b>Sociodemographics</b>                     |      |      |      |                  |             |                    |             |                    |
| <b>Age</b>                                   |      |      |      | 0.422            |             |                    |             |                    |
| 16-26  | 1056 | 686  | 65.0 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| 27-45  | 1263 | 792  | 62.7 |                  | 0.91        | 0.76 – 1.08        | <b>0.68</b> | <b>0.55 – 0.83</b> |
| 46+  | 784  | 489  | 62.4 |                  | 0.89        | 0.74 – 1.08        | <b>0.57</b> | <b>0.45 – 0.72</b> |
| Mi   | 70   |      |      |                  |             |                    |             |                    |
| <b>Ethnicity</b>                             |      |      |      | <b>0.004</b>     |             |                    |             |                    |
| European                                     | 2221 | 1408 | 63.4 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| Māori  | 307  | 211  | 68.7 |                  | 1.27        | 0.98 – 1.64        | 1.28        | 0.96 – 1.71        |
| Pacific                                      | 115  | 72   | 62.6 |                  | 0.97        | 0.66 – 1.42        | 0.96        | 0.62 – 1.49        |
| Asian  | 349  | 222  | 63.6 |                  | 1.01        | 0.80 – 1.28        | 1.24        | 0.95 – 1.63        |
| Other  | 125  | 61   | 48.8 |                  | <b>0.55</b> | <b>0.38 – 0.79</b> | <b>0.64</b> | <b>0.43 – 0.96</b> |
| Mi   | 56   |      |      |                  |             |                    |             |                    |
| <b>Sexual identity</b>                       |      |      |      | <b>&lt;0.001</b> |             |                    |             |                    |
| Gay/homosexual                               | 2518 | 1718 | 68.2 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| Bisexual                                     | 499  | 197  | 39.5 |                  | <b>0.30</b> | <b>0.25 – 0.37</b> | <b>0.45</b> | <b>0.35 – 0.56</b> |
| Other  | 145  | 80   | 55.2 |                  | <b>0.57</b> | <b>0.41 – 0.80</b> | <b>0.58</b> | <b>0.40 – 0.86</b> |
| Mi   | 11   |      |      |                  |             |                    |             |                    |
| <b>Highest qualification</b>                 |      |      |      | <b>0.004</b>     |             |                    |             |                    |
| Non-tertiary                                 | 1683 | 1103 | 65.5 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| Tertiary                                     | 1416 | 858  | 60.6 |                  | <b>0.81</b> | <b>0.70 – 0.94</b> | <b>0.67</b> | <b>0.57 – 0.80</b> |
| Mi   | 74   |      |      |                  |             |                    |             |                    |
| <b>Recruitment method</b>                    |      |      |      | <b>&lt;0.001</b> |             |                    |             |                    |
| Offline: GAPSS                               | 1383 | 993  | 71.8 |                  | <b>1.97</b> | <b>1.70 – 2.29</b> | <b>1.75</b> | <b>1.47 – 2.09</b> |
| Online: GOSS                                 | 1790 | 1009 | 56.4 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| Mi   | -    |      |      |                  |             |                    |             |                    |
| <b>HIV status at last test</b>               |      |      |      | <b>&lt;0.001</b> |             |                    |             |                    |
| HIV-negative                                 | 2137 | 1397 | 65.4 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| HIV positive                                 | 154  | 113  | 73.4 |                  | <b>1.46</b> | <b>1.01 – 2.11</b> | 1.10        | 0.73 – 1.64        |
| Never tested/Not sure                        | 795  | 436  | 54.8 |                  | <b>0.64</b> | <b>0.55 – 0.76</b> | 1.02        | 0.82 – 1.26        |
| Mi   | 87   |      |      |                  |             |                    |             |                    |
| <b>GP aware of sexual orientation</b>        |      |      |      | <b>&lt;0.001</b> |             |                    |             |                    |
| Yes  | 1596 | 1188 | 74.4 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| No   | 1030 | 476  | 46.2 |                  | <b>0.30</b> | <b>0.25 – 0.35</b> | <b>0.32</b> | <b>0.26 – 0.40</b> |
| Not sure                                     | 535  | 332  | 62.1 |                  | <b>0.56</b> | <b>0.46 – 0.69</b> | <b>0.53</b> | <b>0.42 – 0.67</b> |
| Mi   | 12   |      |      |                  |             |                    |             |                    |
| <b>Sexual Behaviours</b>                     |      |      |      |                  |             |                    |             |                    |
| <b>Number of male sex partners &lt;6mths</b> |      |      |      | <b>&lt;0.001</b> |             |                    |             |                    |
| None   | 213  | 115  | 54.0 |                  | <i>Ref.</i> | -                  | <i>Ref.</i> | -                  |
| One  | 690  | 459  | 66.5 |                  | <b>1.69</b> | <b>1.24 – 2.31</b> | 1.17        | 0.82 – 1.66        |
| 2-10   | 1651 | 1010 | 61.2 |                  | <b>1.34</b> | <b>1.01 – 1.79</b> | 1.12        | 0.80 – 1.54        |
| 11+  | 558  | 369  | 66.1 |                  | <b>1.66</b> | <b>1.21 – 2.29</b> | 1.23        | 0.85 – 1.79        |

|                            | N    | Yes  |      | Chi-square | OR          | 95% CI      | AOR | 95% CI |
|----------------------------|------|------|------|------------|-------------|-------------|-----|--------|
|                            |      | n    | %    |            |             |             |     |        |
| Mi                         | 61   |      |      |            |             |             |     |        |
| <b>Any UAIC &lt;6mths*</b> |      |      |      | 0.112      |             |             |     |        |
| None                       | 2137 | 1325 | 62.0 |            | <i>Ref.</i> | -           | -   | -      |
| Any                        | 943  | 613  | 65.0 |            | 1.14        | 0.97 – 1.34 | -   | -      |
| Mi                         | 93   |      |      |            |             |             |     |        |

\* = Omitted from the logistic regression model

OR = odds ratio

AOR = Adjusted odds ratio. Adjusted for age, ethnicity, sexual identity, education level, site of recruitment, HIV status, GP awareness of sexual orientation, and number of male sexual partners in the previous six months.

UAIC = unprotected (condomless) anal sex with casual male partner

## Discussion

To the candidate’s knowledge, this is the first study to explore self-reported comfort with having sexual orientation data recorded confidentially on official databases among a large cross-sectional sample of NZ GBM, of which 63% of participants reported being comfortable with this potential scenario. Greater comfort was independently associated with having been recruited offline. While lower levels of comfort were independently associated with being aged older than 26 years, identifying as an ethnicity “other” than European, Māori, Pacific or Asian, having a bisexual or “other” sexual identity, holding a tertiary qualification, and believing their GP to be unaware of their sexual orientation

## Strengths and limitations

Strengths and limitations of the GAPSS and GOSS methodology have been covered in Chapter Five: Section One. Covered below are those associated with the analysis approach used in this chapter.

Sexuality is broadly understandable by diverse participants. The question posed in the survey covers a number of facets of sexual orientation. The focus of the question was on “sexuality”, covering sexual identity, attraction, and behaviours (see *Chapter Two, Section Two: Part Two*). The broad focus captures the full cross-section of GBM, including those who may identify as heterosexual but have male sexual partners, and participants who may identify as GBM but not yet be sexually active.

The large and diverse sample of GBM recruited through the GAPSS and GOSS behavioural surveillance programme permits between group analysis within the GBM sample. The analyses sought to identify differences within the GBM population through sociodemographic and behavioural factors associated with comfort, allowing future research to explore and build on these findings.



The question did not specify which aspect of “sexuality” would be recorded. Participants may have different levels of comfort depending on aspect, i.e. sexual behaviour compared to sexual identity. The question also did not specify what was meant by “official” databases (e.g. clinical, government, or justice) and who would have access to the data even if considered “confidential”. Future research should seek to differentiate between these factors to determine which may play a greater role in determining comfort.

The question consisted of multiple concepts, including disclosure, sexual orientation, acceptability, privacy, and trust in official institutions. When asked about “comfort” with having data recorded, the question did not differentiate between comfort with disclosure of sexuality in an “official” setting and comfort with having sexual orientation recorded. However, the question did specify “confidentiality”, removing a potential barrier due to concerns with privacy.

The analyses were limited to variables measured in relation to HIV risk as the survey was not designed to measure and explore factors associated with comfort with having sexual orientation recorded in official databases. Therefore, other factors that were not recorded may have a greater association, such as trust in government/medical institutions, attitudes towards privacy, experience of homophobia or discrimination, acceptability under different scenarios such as reasons for collection.

No follow-up questions were posed relating to perceived barriers or benefits of having sexuality recorded in databases. The analysis presented in this chapter identifies differences in comfort within the GBM population but is unable to provide insight into the reasons why comfort or discomfort was reported. Future studies should include measures of perceived barriers and benefits to the provision of sexuality to official health databases.

Compressing the responses into a binary variable during analysis removed some of the nuance captured in the responses to the question. There were 13% of respondents who selected “*Not sure*”. These participants may consider it to be acceptable but dependent on the purpose of the database, security measures, and who has access. Moss et al. call for greater research into the public concerns and understanding of who has or will have access to their health data and what it will be used for (364).

## Discussion of results

Close to two out of three (63%) GBM participants report comfort with having their sexuality recorded in official databases. Sexual identity was independently associated with comfort, with those who report an identity other than “*gay/homosexual*” being less likely to report comfort (“*bisexual*” AOR: 0.45, 95% CI: 0.35-0.56, “*other*” AOR: 0.58, 95% CI: 0.40-0.86).

Greater comfort was found among participants recruited through venue-based community venue-based sampling compared to those recruited online (GAPSS AOR: 1.75, 95% CI:1.47-2.09). There is potential that men recruited into the GAPSS survey, who were in public and attending venues that were GBM-associated, demonstrate a level of comfort with others being aware of their sexual orientation. By comparison, men recruited online into GOSS have a level of anonymity when visiting a GBM-targeted website or app, as this can be done in private. Populations of GBM recruited online have shown to differ to those recruited through venue-based sampling in terms of age, levels of GBM community connection, and sexual behaviours, which may be associated with comfort disclosing sexual identity (128).

Comfort was independently associated with highest qualification achieved, with those higher qualified being less comfortable (Tertiary qualification AOR: 0.81, 95% CI: 0.57-0.80). This is an unexpected finding and contrasts with other studies that have explored “trust” in government and healthcare institutions, where educational attainment is often positively correlated with trust (365).

Self-reported ethnicity was found to be independently associated with comfort. Those GBM reporting an ethnicity “Other” than European, Māori, Asian or Pacific reported less comfort compared to those identifying as European (“Other” AOR: 0.64, 95% CI: 0.43-0.96). The category of “*Other*” ethnicity includes Middle Eastern, Latin American, and African populations. Distrust in healthcare institutions has been found among Latin and African Americans as a result of historic and ongoing institutional racism within Western institutions (366, 367). In NZ, health inequities and discrimination are well documented in for the Māori population, but this has not resulted in a reduced level of comfort in this study, therefore other explanations may be required (8, 368). Disclosure of sexual orientation among GBM was associated with ethnicity, with Asian GBM being less likely to disclose their sexual orientation to healthcare providers, however, an association was not identified for Asian GBM in this study (115).

Associations with HIV status and testing were no longer associated when included in the logistic model. Initially, PLHIV were found to report greater comfort, which may be a result of already having data recorded in administrative health databases due to the regular engagement with healthcare. Those who report having never tested will include those who may not be comfortable accessing healthcare in relation to their sexual orientation or behaviour, while also including those who may not be recently sexually active or have not engaged in behaviours that place them at risk of HIV acquisition.

Drawing on the framework of the health belief model, comfort with having sexual orientation recorded on official databases can be viewed as a potential barrier to the disclosure of sexual orientation in healthcare and other data collection scenarios (235). This is potentially

confirmed with the difference within the same sample (GAPSS and GOSS) between comfort of having sexual orientation recorded (63%) and perception that their GP was aware of their sexual orientation (51%) (115). This indicates that there are likely to be further barriers to disclosure in practice that have not been measured here. Perceived self-efficacy or willingness to disclose sexual orientation to healthcare providers could also be explored in future research.

## Comparison to other studies

No studies were found in the published literature that explored acceptability among GBM of having sexual orientation recorded in official databases specifically. However, literature was identified related to the acceptability of being asked and the willingness to disclose sexual orientation and gender identity (SOGI) in healthcare settings. Disclosure of sexual orientation is a necessary step for the recording of sexual orientation data on official databases.

### ***Aotearoa New Zealand***

Henrickson et al. asked LGBTIQ+ participants of the Lavender Islands 2004 survey in NZ (n=1233/2269 male) if they would be willing to accurately answer a question on sexual identity if it were to be included in the NZ census, of which 86.8% reported that they would be. Data were not disaggregated for GBM, nor were factors associated with willingness explored. However, the census represents an “official database” on which identifiable information alongside SOGI measures would be “confidentially” recorded, offering a specific example in which the theme of the question posed in this chapter would be implemented. Willingness to provide sexual orientation data in the census was greater than comfort with a more general concept of disclosure found among the 2014 GAPSS and GOSS participants (63%), indicating that comfort or willingness to disclose sexual orientation data are potentially context or instrument specific.

In NZ, just over half (50.5%) of the GBM participants from the same 2014 GAPSS and GOSS studies report that they perceive their GP to be aware of their sexuality (115). Perceived awareness was independently associated with age, ethnicity, number of male sexual partners, HIV and STI testing, and STI diagnosis. The estimate of GP awareness of sexuality was lower than that found by Neville et al. in 2004, with an estimated 64.7% (n=729/1218) of GBM in their national cross-sectional sample reporting they had disclosed their sexuality to their healthcare provider, and older participants being significantly more likely to report disclosure (369).

### ***Other studies***

In 2016, Bjarnadottir et al. conducted an integrative review of the literature covering these related aspects of sexual orientation disclosure in healthcare settings, with a focus on the

patient perspective, organising the 21 studies identified in the literature across two thematic categories (370):

1. Acceptability of being asked SOGI questions (n=6).
2. Willingness to disclose or respond to SOGI questions in healthcare settings (n=17).

Of the 21 identified papers, 17 reported LGBTIQ+ participants recruited from a range of healthcare settings that included primary care, cancer care, and counselling. Of these studies, six explored the acceptability of being asked SOGI questions using surveys, response rates and qualitative interviews. Overall, the response rate to SOGI questions was greater than other sociodemographic questions such as highest qualification achieved. In the study by Cahill et al. included in the review, the majority of participants (83%) recruited from healthcare centres agreed that they would answer a question on sexual orientation upon registration with a healthcare centre, with acceptability significantly greater among non-heterosexual participants ( $p=0.007$ ) (371). Additionally, 78% agreed it was important information for their healthcare professionals to be aware of their patients' sexual orientation, with no significant differences found by ethnicity, age, or recruitment site.

In the review by Bjarnadottir, 17 studies explored disclosure of sexual orientation in healthcare settings, of which eight exclusively recruited lesbian or bisexual women who have sex with women. There were 12 studies that explored the belief that it was important for a healthcare provider to be aware of a patient's sexual orientation to be able to provide the best and most appropriate care, particularly in terms of sexual health (370). Nine of the 17 studies reported on participant's concern about disclosure, these included fear of being treated poorly, receiving worse care, or being met with discrimination.

Compared to the findings of this chapter, a lower proportion of the general population reported they would be willing to disclose their sexual orientation in emergency department settings (52%), even if assured confidentiality, in a 2017 study by Haider et al. (372). The study investigated the difference in acceptability between a random sample of the population (both heterosexual and LGBT+) and a panel of healthcare providers; with the population sample asked if they would be willing to disclose and healthcare providers asked if they believed patients would be willing to disclose. Clear differences between the population sample and the perceptions held by the healthcare professionals emerged. Greater proportions of healthcare professionals reporting they believed patients would be willing to disclose sexual orientation if assured confidentiality (88%) but also that patients would be offended (80% providers vs. 10% patients) and refuse to answer (78% providers vs. 10% patients). Age, race and education were not associated with refusing to disclose in bivariate analyses, and after adjustment for age, educational level, race, marital status, rental status, head of household, work status, and income, only bisexual patients had increased odds of

refusing to provide sexual orientation compared with heterosexual patients (AOR: 2.40; 95%CI: 1.26-4.56). This finding supports the association found in this analysis that those reporting a bisexual identity and those reporting an “other” sexual identity were less likely than those identifying as gay/homosexual to report comfort.

In the 2018 systematic review of the literature of disclosure to healthcare providers among GBM, Qiao et al. noted that disclosure rates among GBM ranged from 16%—90% (373, 374), with a median value of 61% and noticeable variation by country of study (375). Factors associated with disclosure included: sociodemographic factors (age, ethnicity, socioeconomic status), sexual identity, and sexual behaviours, as well as healthcare provider-related factors (being known as “gay-friendly”, patient trust, and communication) (375). The median reported rates of disclosure of sexual orientation to healthcare providers and associated factors were similar to those found with comfort found in the study presented in this chapter.

Collection and reporting of SOGI measures are required in US health centres that provide primary care funded by the Health Resources and Services Administration (primarily serving isolated and economically vulnerable communities) since March 2016 (376). Grasso et al. pooled data reported by 1367 US health centres caring for 25,860,296 patients (376). The majority of patients were missing sexual orientation and gender identity data (77.1% and 62.8% of patients, respectively). Among the 22.9% (n=5,919,236) patients with sexual orientation data, 68.8% identified as straight, 3.7% identified as lesbian, gay, bisexual, or “something else”, and 27.5% did not disclose their sexual orientation. Grasso et al. comment that the lack of complete data should be viewed in the context of imperfect implementation, that providers were informed of the requirement in late March (the year begins in January) and data were required to be reported from systems that did not have an existing data field for recording of SOGI measures. In future years when these systems are in place, more reliable data will emerge from these settings and reports. However, the populations served by the centres are not representative of the US population as a whole and are already subject to inequitable healthcare access that would result in poorer health outcomes.

#### *Implications for future research*

Close to two out of three GBM participants (63%) reported being comfortable with the idea of having their sexual orientation recorded on official databases. The findings from these analyses add to the literature challenging some of the widely held concerns that GBM, LGBTIQ+ and wider heterosexual population would not be willing to engage with data collection regarding their sexual orientation. However, there is a history of discrimination and persecution of LGBTIQ+ populations by the government both in NZ and globally, which is still ongoing. Therefore, it should not be surprising that there is caution from a proportion of the GBM population regarding the collection and storage of data that has been used to

discriminate against them. Identifying and addressing health inequities experienced by GBM (and other LGBTIQ+ populations) is one benefit to the collection of SOGI, but there will also be harms.

The creation and use of standardised measures of SOGI are needed as well as consensus as to where it is meaningful to collect and analyse these measures. Examples of standardised measures for sexual orientation exist globally, the USA, NHS: England, Australia and NZ have each published a measure, and examples from other countries may also exist (359, 360). The measures created by Australia and NZ were created as “statistical standards”, that is they are to be used in all data collection tools that seek to collect sexual orientation data. The European Council provides advice on where it is appropriate to collect data on sexual orientation to its member countries, in that they “...*should ensure that personal data referring to a person’s sexual orientation or gender identity are not collected, stored or otherwise used by public institutions including in particular within law enforcement structures, except where this is necessary for the performance of specific, lawful and legitimate purposes; existing records which do not comply with these principles should be destroyed.*” (377). Addressing health inequities experienced by LGBT+ populations would be viewed as “necessary” and “lawful and legitimate purposes” and as such collection and storage of SOGI data by public institutions including government and healthcare organisations would be an exception to this broad recommendation. However, clear ethics and governance policies to avoid the use of the data for purposes outside of this scope would be needed and enforced.

The question posed in this study was multi-layered combining sexual orientation, disclosure, data being held by third party institutions, and privacy. Future studies, ideally led by government in partnership with rainbow communities, should seek to disaggregate these concepts to identify reasons for acceptability and hesitancy. Questions should specify characteristics of sexual orientation being recorded, the type of database, potential uses of the data, and reasons for acceptance and concerns that could result in hesitancy.

Further research should seek to examine the understanding of what data collection and recording in official databases means for the community and the individual, for example, are individuals aware of the benefits and risks of having these data recorded on databases for themselves and for their communities? Studies could also explore comfort under different scenarios and settings, such as primary and outpatient healthcare versus hospitalisation. The finding from the study presented in this chapter and the 2017 study by Haider et al. indicate that assurance of confidentiality does not appear to be as powerful a factor at removing barriers to disclosure of sexual orientation as would be anticipated. Future

research could explore patient understanding, concerns, and beliefs regarding confidentiality of sexual orientation in healthcare settings.

An additional opportunity now exists in NZ through the Integrated Data Infrastructure. The Integrated Data Infrastructure would allow the collection of sexual orientation in one government-collected dataset to be linked based on identifiable information from that same individual across datasets on a probability basis, i.e., how many common variables match (378). This means that sexual orientation would only be required to be collected on one such dataset, and it could be linked to entries across others, which includes the NHI dataset.

To encourage and facilitate disclosure of sexual orientation in healthcare settings, patients must feel safe to do so. Future sexual orientation data collection efforts in these settings would benefit from increased training for staff and improved messaging on the clinical benefits of SOGI data collection and reporting. Previous research by the Stonewall organisation in the UK highlights negative experiences of the LGBT+ population and confidential patient information in healthcare settings, with only 40% of GBM reporting they believe their GP to have a clear policy on patient confidentiality (379).

These findings relate to overarching themes of ethical considerations of agency, consent and beneficence that have been slow to be realised and fully addressed in digital technologies (380, 381). The fast-moving pace and new developments mean that it is often difficult to fully explain or predict the future consequences of having these data recorded could be. The “terms and conditions” or online “consent” pages are often legally focused rather than in a framework that is accessible and understood by the public. Participants providing these data to an agency or organisation should be provided with information to be able to make an informed choice, such as examples of what these data will be used for and who will have access. There will also be consequences for those not providing the information, whether directly or indirectly, and these too should be made as transparent as possible.

## Conclusion

Three out of four GBM participants are comfortable with the concept of having their sexual orientation recorded on official databases, when assured confidentiality. Comfort was independently associated with a range of sociodemographic and behavioural variables indicating that differences in comfort levels exist within the GBM population.

Collection of sexual orientation data on administrative health datasets facilitates the disaggregation of clinical surveillance data for HPV-related disease and vaccination coverage for GBM, allowing changes in these variables to be tracked over time.

Future research should narrow the focus to explore the implementation of SOGI data collection in healthcare settings using StasNZ suggested standard for sexual orientation. Additional research should seek to include healthcare provider perceptions and experience to inform the design and implementation of training programmes for staff to ensure culturally appropriate care for GBM are available once disclosure occurs in these settings.



## Chapter 8: Synopsis and conclusions

Intersecting biological, network, behavioural, and structural factors make gay, bisexual and other men who have sex with men (GBM) vulnerable to HPV infection and developing HPV-related diseases. Mounting international evidence indicates that the incidence of HPV-related anal cancer among males continues to increase. This is a significant public health concern among GBM, with rates of anal cancers among GBM PLHIV estimated to be greater than rates of cervical cancers prior to the introduction of cervical screening programmes, and rates among GBM PLHIV being greater still (2, 73).

The early introduction of female-only HPV vaccination programmes to reduce cervical cancer, and its demonstrated success in doing so, have increased the HPV-related health inequity experienced by GBM. Vaccination impact data show declines in anogenital wart incidence among vaccinated female cohorts and protective herd immunity effects extending to their heterosexual male partners, but no declines were observed among GBM in the same period (4). The HPV vaccine has demonstrated efficacy in reducing anal precancerous lesions among GBM and has been recommended for GBM up to the age of 26 years for the prevention of anal cancers and anogenital warts by the USA FDA since 2011, and all men up to the age of 45 years since 2018, yet few countries have extended HPV vaccination programmes to cover males or offered targeted programmes for GBM (213, 382).

In January 2017, NZ became one of the few countries to extend public funding for HPV vaccination to males through school-based vaccination programmes and a catchup programme up to the age of 26 years, providing an opportunity to address the HPV-related health inequities experienced by GBM. However, GBM are an “invisible” population in Aotearoa NZ as sexual orientation data are not routinely collected in administrative health datasets nor in nationally representative health surveys. This results in a lack of data available to inform, monitor and evaluate public health interventions seeking to address the HPV-related health inequities experienced by GBM in NZ.

The thesis sought to improve understanding of HPV among GBM in NZ to inform public health programming and identify areas for future research.

## Summary of findings

### HPV-related health inequity experienced by GBM

The paucity of high-quality evidence in the published literature on GBM's experience of HPV prevention, infection and related disease was highlighted as a recurring theme throughout the background literature review and thesis. Robust and generalisable data are required to identify health inequities and inform the design and evaluation of public health interventions to address them. Due to limitations with random sampling methodology and of capturing of sexual orientation data in administrative health datasets for this population, cross-sectional studies were identified as an appropriate method for capturing a large and diverse sample of GBM with sufficient statistical power to detect within-group differences.

Chapter Two used a narrative literature review approach to explore the biological determinants for the observed vulnerability of GBM to anal HPV-infection and related disease. As a population group, GBM are particularly vulnerable to HPV infection and related disease for several reasons:

1. **Biological vulnerability:** The anal compartment contains an epithelial "transformation zone" that is particularly vulnerable to HPV infection due to the availability of basal epithelial cells (13). Penetrative anal sex is a common sexual behaviour among GBM in ANZ, with 82.6% of GBM in the 2014 GAPSS and GOSS sample reporting anal sex with a casual male sex partner in the previous six months (34).
2. **Underlying prevalence:** Anal HPV infection is common among GBM. Prevalence drives incidence. The greater the underlying prevalence of infection in a population, the greater the likelihood of encountering an infected individual is.
3. **Dense sexual networks:** It is estimated that 2.3% of the NZ male population identify as GBM (108). This results in a smaller pool of sexual partners to draw upon in comparison to the heterosexual majority, meaning that chains of HPV transmission are much shorter.
4. **Sexual partner turnover:** Sexual behavioural surveys indicated that, in general, a greater proportion of GBM report greater numbers of recent sexual partners as compared to their heterosexual peers (34, 35).

The limitations of existing prevention tools, screening and treatments for HPV infection and related disease were explored, confirming that prophylactic HPV vaccination offered the most effective intervention for the prevention of HPV-related disease among GBM despite the lack of long-term evidence in the prevention of anal cancers for this population. HPV vaccine acceptability was found to be high among GBM in those studies that investigated it, but awareness of the HPV-related diseases that affect males and of the HPV vaccine itself were

identified as potential barriers to vaccine uptake. Limited published HPV-related data were identified in NZ for GBM, related only to disease notification data for AGWs.

Chapter Three is the first systematic literature review to examine the prevalence of HPV vaccination among GBM. The review revealed limited published literature, with the majority coming from the USA. The review also highlighted that, despite the inclusion of grey-literature, published country reporting of HPV vaccination coverage was not disaggregated by sexual orientation, reinforcing the need for cross-sectional studies to estimate HPV vaccination uptake among GBM. The key finding from the review was that among the studies identified, the prevalence of HPV vaccination uptake among GBM (range: 2.6% to 58.8%) was unlikely to meet a possible herd immunity threshold for HPV (286, 289).

Chapter Four presented the first data collected on oral and anal HPV infection prevalence among GBM in NZ, to the candidate's knowledge. The data demonstrate the benefit that GBM in NZ would receive from HPV vaccination. The findings aligned with the international literature, identifying that HR-HPV-16/-18 anal infection among GBM is prevalent (41%), particularly among GBM PLHIV (54%), while oral HR-HPV-16/-18 infection is less prevalent (3%). Among participants who identified as "gay" and had a valid anal specimen, 42% tested positive for anal HR-HPV-16/-18 infection, the two HPV types that are responsible for 93% of all anal HPV-related cancers (171). Future studies are needed to explore the impact of the gender-neutral HPV vaccination programme in NZ on the prevalence of HR-HPV infection among GBM over time.

### Informing programmes to increase HPV vaccine uptake among GBM

Despite over two decades of mounting evidence that GBM are disproportionately impacted by HR-HPV types and the creation of a safe and effective vaccine to prevent both infection and development of HPV-related disease, GBM remain a population that continue to experience HPV-related health inequities due to few countries funding or promoting HPV vaccination to males, and fewer still directly to GBM. With rising rates of anal HPV-related cancers and a lack of efficacy data for the screening and treatment of high-grade anal disease for the prevention of anal cancers, increasing vaccination uptake among GBM must be prioritised.

To the candidate's knowledge, Chapter Five presents the first data collected on HPV-related disease knowledge, HPV vaccine awareness, and HPV vaccine uptake among GBM prior to an extension of public funding for HPV vaccination to include males. Chapter Six presents the first follow-up HPV-related data captured among GBM after the extension of public funding for HPV vaccination to include males, repeating the same questions to provide an insight into potential changes over time.

In combination, the two chapters demonstrated the feasibility and value of adding questions that seek to collect data on potential barriers and facilitators of HPV vaccination uptake into existing cross-sectional surveillance tools that target GBM. These tools collect a large and diverse sample of GBM, powered to detect between group differences and identify factors associated with HPV-related variables of interest to aid the design, targeting and evaluation of public health interventions seeking to improve HPV vaccination uptake for this population.

Awareness of the risk posed by HPV among GBM participants in 2014 was low, with almost half (49%) of GBM participants reporting knowledge of any HPV-related disease that affects males, and less than one in three (30%) reporting knowledge that HPV causes some anal cancers, the HPV-related cancer that is most common among GBM. After controlling for sociodemographic and behavioural variables, lower reporting of knowledge of any HPV-related disease was independently associated with never having tested for HIV, reporting Māori ethnicity, and reporting any UAIC in the previous six months. In 2018, after controlling for sociodemographic and behavioural differences between the two online samples, knowledge that HPV causes some anal cancers had significantly increased compared to 2014 among vaccine-eligible GBM (AOR=2.57, 95% CI:1.32-5.01). Increasing the prevalence of self-reported knowledge of HPV-related disease among GBM remains an area for future research and target for public health promotion.

A key driver of HPV vaccination uptake is awareness of the vaccine and of its benefits, facilitating active health-seeking rather than relying on passive recommendation when accessing the healthcare system. Self-reported awareness of the HPV vaccine and its protective effect for males was lower than knowledge of HPV-related diseases among the 2014 sample of GBM (17% and 49%, respectively). Awareness of the vaccine increased significantly between 2014 and 2018 among NZ GBM recruited online (15% vs. 35%,  $p < 0.001$ ). After adjusting for sociodemographic and behavioural variables, vaccine eligible GBM in the 2018 round had 2.45 greater odds of reporting awareness of the HPV vaccine and its benefits for males compared with those in the 2014 survey round (AOR=2.45, 95% CI:1.26-4.76). Increases in HPV vaccine awareness indicate that this is a modifiable target for health promotion. Targeted and culturally relevant campaigns developed in partnership with GBM community organisations can have a disproportionate impact on increasing HPV vaccination awareness and potentially uptake.

The HPV vaccine carries a considerable cost per dose, being one of the most expensive vaccines on the market at the time this thesis was commenced, though this price has subsequently dropped (383). Prior to the extension of public funding to include males in NZ and for those who remain ineligible for funding post-the extension, cost presents a barrier to HPV vaccine uptake. This was reflected in the results from the 2014 baseline data, in which

13% of GBM reported willingness to pay the full price of three doses, while 78% reported willingness to receive the three doses if provided at no cost. In 2018, among both vaccine eligible GBM, HPV-vaccine acceptability had not significantly changed from baseline in 2014 for either cost condition.

Self-reported HPV vaccine uptake among GBM in NZ was rare (3%) in 2014, prior to the extension of public funding to include males. Encouragingly, compared to the baseline 2014 data, vaccine eligible GBM in the 2018 survey were significantly more likely to report having received at least one dose of the HPV vaccine (2.2% vs 31.9%,  $p < 0.001$ ). After controlling for sociodemographic and sexual behavioural differences between the two survey rounds, greater vaccine uptake was found to be independently associated with the 2018 survey round (AOR=28.49, 95% CI:12.22-66.43). The self-reported prevalence of HPV vaccination uptake among these GBM do not approach the herd immunity threshold but may be sufficient to see population-level impacts (216, 299). Factors associated with HPV vaccine uptake in 2014 included ethnicity, knowledge of HPV-related disease, awareness of the HPV vaccine, number of recent sexual partners, and reporting recent condomless anal sex with casual male partners. Future research should seek to examine if these factors remain associated after the change in public funding for HPV vaccination in NZ.

Overall, the data presented in Chapters Five and Six have demonstrated that HPV-related variables of interest to public health programmes and decision-makers can not only be measured and analysed for GBM in NZ, but the reported prevalence of these indicators can be modified with strong public health interventions and messages. Future research should determine the various channels through which GBM are receiving their public health messages to further increase the effectiveness and reach of future interventions and health promotion for this population.

### Informing public health responses to HPV-related disease among GBM in the future

The greatest barrier to addressing health inequities faced by GBM is the ability to identify and quantify these inequities in an accurately timely manner. Sexual orientation minority populations including GBM are not identified in routine health statistics and reporting collected by government institutions, despite mounting evidence that a wide range of health inequities exist for these populations (276, 352). Recording of sexual identity in healthcare and other public health statistics has been identified and considered as a possible solution to overcoming these obstacles.

Chapter seven explored factors associated with the comfort of having sexuality confidentially recorded on “official” databases. The majority of participants (63%) reported comfort with their sexuality being confidentially recorded. However, close to one in three participants were

unsure or not comfortable. Lower levels of comfort were independently associated with sociodemographic and healthcare engagement factors that allude to reduced comfort with disclosing sexuality. Addressing concerns with comfort requires greater research on this topic to be conducted on the perceived barriers and benefits of providing sexual orientation data in healthcare settings.

## Implications for public health

The opportunistic inclusion of HPV-related questions in existing HIV behavioural surveillance surveys that target GBM in NZ demonstrate the feasibility of adapting second generation surveillance (SGS) for HPV. The SGS guidelines for HIV from the WHO and UNAIDS have been implemented successfully within NZ (384). The relationships between government (MoH), crown research institutes (ESR), tertiary research groups (AIDS Epidemiology Group and Gay Men's Sexual Health Research Group) and community NGOs (NZAF), have been a strong model to use SGS data to deliver timely and evidence-based public health programmes to control and prevent HIV among GBM (337). However, the capture of sexual orientation in administrative health datasets would be required for the realisation of clinical surveillance for HPV.

Figure 30 provides a diagrammatic concept overview of SGS clinical and behavioural surveillance endpoints for HPV among GBM. Reporting of these endpoints should be disaggregated by sociodemographic variables, in particular by ethnicity, to identify differences within the GBM population.

Continued monitoring of HPV vaccination uptake among GBM is required to ensure that the policy change to extend funded HPV vaccination to males is achieving health equity for this group. In NZ, GBM are not reflected in immunisation coverage data. The low proportion of males that identify as GBM (2.3%) mean that a non-significant change in HPV vaccination coverage among all males in NZ could disproportionately affect coverage among GBM.

The consistent and high vaccine acceptability among GBM eligible for funded HPV vaccination demonstrated in Chapter Six indicates that the anal HPV-related disease health inequities experienced by GBM can be addressed through the provisions of HPV vaccination. Increasing HPV vaccination uptake among eligible GBM is achievable through partnerships with existing NGOs, such as NZAF, that deliver behavioural change health programmes to GBM in NZ. However, there may be additional barriers to HPV vaccination uptake that have not been identified in this thesis, which will require further research.

There will continue to be rising rates of HPV-related disease before coverage among vaccinated age cohorts reaches a population level of herd immunity. Chapter Two: Section Four highlighted the lack of effective treatments available for anal HPV-related cancers and

the high level of recession for this cancer. Similar to cervical cancer screening for women, GBM may require regular testing to detect persistent anal HR-HPV infection. However, the natural progression from anal infection with HR-HPV to malignant anal cancer is not clear and much of the anal lesions spontaneously clear making the clinical relevance, ethical considerations, and cost-effectiveness of such a screening programme uncertain.

In light of these concerns, the provision of funded HPV vaccination to GBM aged up to 45 years may be required to achieve health equity for HPV-related anal cancers. The low acceptability of self-funding the HPV vaccine at cost did not significantly change over time between the GOSS 2014 study (11%) and the 2018 EHIV Survey (12%), making it unlikely that GBM are willing to seek and self-fund HPV vaccination (*see Chapter Six*). In the USA, the FDA recommended HPV vaccination for both females and males up to the age of 45 years in 2018 (382). The UK has funded HPV vaccination for GBM up to the age of 45 years through sexual health clinics, stating that statistical modelling had indicated cost-effectiveness up to this age group (332).

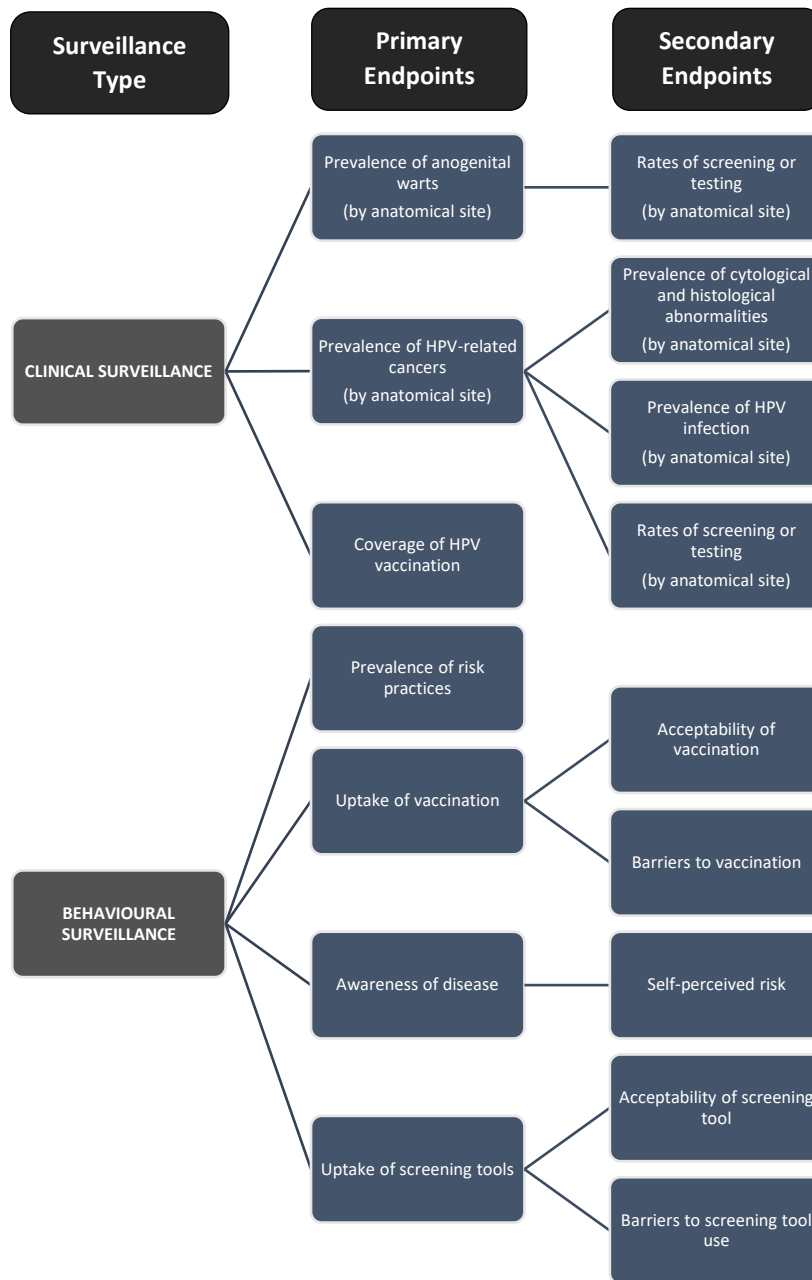


Figure 30: Diagrammatic representation of clinical and behavioural surveillance endpoints for HPV.



## Informing future research

In addition to those areas of future research identified previously as directly related to the continuation of work undertaken in this thesis, three focused avenues of future research are explored in this section.

### Biological specimen collection for HPV-related research among GBM

Alternative study designs should be explored for estimating HPV infection prevalence among GBM in NZ than that utilised by the HIMS study. Chapter Four demonstrates recruiting GBM, collecting and analysing biological specimens for HPV, and behavioural data capturing are feasible through outpatient and primary healthcare settings in NZ. However, the high cost, low recruitment rate, low validity rate of anal specimens and limited generalisability of the study question the appropriateness of the methods for answering the research question.

Biological specimen collection through community settings has been demonstrated for estimating HIV infection prevalence among GBM in NZ (314). The study collected oral samples for HIV testing, and it is feasible that a similar method would translate for estimating oral HPV infection prevalence, such as has been conducted in the USA (385). Anal HPV infection and related disease are growing health inequities experienced by GBM, and the collection of anal specimens through community settings would require a more complex approach than oral specimens. The ManCount study by Gilbert et al. demonstrated the feasibility and acceptability for GBM to be recruited and self-sample for anal HPV infection through community settings in Canada, though, similar to the HIMS study in Chapter Four, they report a large proportion of invalid anal specimens that would need to be factored into power calculations (386). However, there appears to be some difference between self-collected and clinician collected anal specimens for HPV testing, for HR-HPV types in particular, which may negatively impact the research despite the potential for removing barriers to participation (77).

A practical and cost-effective way to conduct biological specimen collection for HPV could be to include the HPV-specific elements into an existing surveillance tool. Both Natsal and the USA Health Survey have included specific biological specimen collection in randomised population surveillance (161). In NZ, biological specimen collection could be included in the sexual and reproductive health module of the NZHS. However, as highlighted in Chapter Two, nationally representative random sampling surveillance programmes do not recruit a sample of GBM with sufficient statistical power to detect within-group differences that are needed to inform responses. The method for collection of anal HPV specimens also lends itself for the collection of samples for rectal STIs such as chlamydia and gonorrhoea, though separate swabs would be required for each, increasing the burden on the participant.

This secondary usage approach could also be extended to existing biological specimens that have already been collected through these surveillance tools and clinical testing purposes. This method has been employed by Chow et al. in Australia to monitor the decline in the prevalence of HPV infection among young women attending SHCs (387). Ethical concerns in relation to the consent given by participants as to what the specimens can be used for would need to be considered if seeking a retrospective analysis. The HIMS study presented in this thesis specified that samples would be stored for potential future use and testing for HPV and other STIs.

Pre-exposure prophylaxis for HIV and the routine engagement in healthcare to access this prevention tool offers an option to recruit a clinical cohort of GBM and collect repeat biological samples and survey data for HPV-related research. GBM eligible for publicly funded pre-exposure prophylaxis in NZ present a cohort that engages in condomless anal sex with other men, and as such places them at greater risk of HPV acquisition than other populations of GBM (388, 389). This makes this group of GBM of particular interest, being a group that is more likely to be repeatedly exposed to HPV infection and therefore develop HPV-related anal cancers. These men can be readily identified in clinical datasets without the need for collection of sexual orientation data and can be tracked over time. Additionally, vaccinating this population could potentially have a disproportionate network effect on HPV transmission among GBM, as these men report greater number of sexual partners and therefore are more connected across the dense GBM sexual network. Exploring HPV infection, HPV vaccination uptake, and associated barriers among this group of GBM who are routinely engaged with sexual healthcare is an avenue for future research.

### Improving national HPV-related data quality for GBM to inform public health programming

Collection of sexual orientation data in medical records would allow disaggregation of HPV-related cancer diagnosis and outcomes by sexual orientation and therefore monitoring of changes in these diagnoses and outcomes among GBM. In NZ, a statistical standard for sexual orientation exists but to date is not widely implemented outside of government-led surveillance surveys. Capturing of sexual orientation measures in administrative healthcare datasets has been proposed, most recently in 2018, but remains contentious with only 35% of submissions from healthcare providers (including DHBs and associations) in support of changes (112). The support of healthcare providers for the implementation of sexual orientation data collection is essential as they are the ones responsible to the solicitation and accurate recording of this information from patients accessing their services.

The ACCESS project in Australia presents another model to improve clinical surveillance among GBM (119). The project conducts enhanced sentinel surveillance for key populations

by utilising partnerships with settings that include laboratories, primary healthcare clinics, sexual health clinics and community health services. These settings collect sexual orientation measures in a variety of ways at these settings, which are then extracted by the ACCESS project alongside de-identified patient data for consultations, tests, results, and treatments. Setting up a similar network would be possible in NZ. However, relative to Australia, NZ has a small population and it may be more effective to focus efforts on improving and standardising data collection through including sexual orientation measures in administrative health datasets.

In NZ, the inclusion of sexual identity measures in administrative health datasets would also facilitate linkage of sexual identity data to other government collected data through the Integrated Data Infrastructure on a probability basis through shared identifiers (e.g. name, age, date of birth, sex, ethnicity) (390). While this would allow for greater identification of not only health inequities but also social and economic determinants of health among GBM and other sexual orientation minority populations, future research should also seek to determine GBM awareness, understanding, and concerns and consequences with such data linkage.

## Concluding remarks

This thesis took a systematic public health approach to generate evidence that can inform public health interventions and health promotion aimed at eliminating HPV-related inequities for GBM.

A high prevalence of HR-HPV anal infection drives the prevalence of HPV-related anal disease among GBM. Anal HR-HPV infection is common among GBM attending primary and outpatient healthcare settings in Auckland, NZ. These prevalence data confirm rationale to ensure HPV vaccination uptake among GBM is at least equal to that of the wider population, with the goal of reaching a herd immunity threshold over time.

Identifying sociodemographic and behavioural differences in barriers and facilitators to HPV vaccine uptake among GBM are essential to the targeting and design of interventions and health promotion campaigns for this population. Sociodemographic, healthcare engagement and sexual behavioural factors are associated with differences in HPV-related disease knowledge, HPV vaccine awareness and acceptability, and HPV vaccine uptake among GBM in NZ.

Changes in HPV-related variables and associated factors can be monitored opportunistically over time through incorporation into existing surveillance programmes targeted to GBM. This thesis demonstrates the feasibility and the value of capturing HPV-related data in existing surveillance targeted to GBM populations to inform public health approaches and monitor these variables over time.

Finally, as has been highlighted throughout this thesis, the greatest barrier to achieving health equity for GBM is the lack of data available about their health. A majority of GBM reported comfort with having their sexuality recorded confidentially on official datasets. Sexual orientation data collection in administrative healthcare databases, with appropriate legal and privacy safeguards, are urgently needed to identify and quantify the full extent of HPV-related and other health inequities experienced by GBM in NZ and globally.

# Appendices

## Appendix A: NZAF Memorandum



New Zealand AIDS Foundation  
Te Tuāpapa Māte Āraikore o Aotearoa

### MEMORANDUM

**DATE:** 13/01/2021

**TO:** Adrian Ludlam

**FROM:** Dr Jason Myers | Chief Executive, NZAF

**RE:** Permission for use of data collected in the Ending HIV Evaluation Survey

**TITLE:** PhD Thesis: Human Papillomavirus Infection, Awareness, and Vaccine Acceptability and Uptake among Gay, Bisexual, and Other Men who have Sex with Men in Aotearoa, New Zealand

Mr. Adrian Ludlam is the named Primary Investigator of the Ending HIV Evaluation Survey.

I (Dr Jason Myers), in my role of Chief Executive of NZAF, hereby grant Adrian Ludlam permission to analyse the data and present the findings of these analyses using the data collected in the *“Ending HIV Evaluation Survey”*, expressly for the thesis titled *“Human Papillomavirus Infection, Awareness, and Vaccine Acceptability and Uptake among Gay, Bisexual, and Other Men who have Sex with Men in Aotearoa, New Zealand”*.

There are no personal identifiers collected within these data due to the anonymous nature of the survey.

The Ending HIV Evaluation Survey research program has been granted ethics approval by the New Zealand Ethics Committee (#2016\_21). The scope of the research undertaken by Adrian Ludlam within his PhD thesis is deemed to fall within the aims and objectives of the study.

SIGNATURE: \_\_\_\_\_

A handwritten signature in blue ink, appearing to read 'J. Myers', written over a horizontal line.

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NZAF National Office  
31 Hargreaves St, St Mary's Bay, Auckland 1011  
PO Box 6663 Wellesley St, Auckland 1141

+64 9 303 3124  
[contact@nzaf.org.nz](mailto:contact@nzaf.org.nz)  
[www.nzaf.org.nz](http://www.nzaf.org.nz)

# Appendix B: HIMS Feasibility Study PIS

Participant Information Sheet: HPV in Men Feasibility Study

SCHOOL OF POPULATION HEALTH



## Participant Information Sheet

### Study title

The human papillomavirus in men study (HIMS)

### Names of researchers

Dr Helen Petousis-Harris  
Associate Professor Mark Thomas  
Associate Professor Nikki Turner  
Mr Adrian Ludlam  
Dr Peter Saxton

Department of General Practice  
and Primary Health Care  
School of Population Health  
Cnr Morrins and Merton Rd  
Glen Innes  
[www.health.auckland.ac.nz](http://www.health.auckland.ac.nz)

The University of Auckland  
Private Bag 92019  
Auckland  
New Zealand,

Helen Petousis-Harris  
Telephone: 64 9 373 7599  
extrn B2078  
Email: [h.petousis-harris@auckland.ac.nz](mailto:h.petousis-harris@auckland.ac.nz)

Hello, Kia ora, Talofa lava, 您好,

We are a multi-disciplinary group of researchers from the University of Auckland conducting a scientific study at this clinic. The study is being run by Dr Helen Petousis-Harris, Director of Immunisation Research and Vaccinology at the Immunisation Advisory Centre (IMAC), the University of Auckland.

We are investigating human papillomavirus (HPV) infection among New Zealand males. Currently there is very little information on HPV infection among men, men's awareness about HPV. This study aims to change this and we would like your help.

### In summary:

- This study is voluntary.
- This study is anonymous.
- We will ask you to complete: an oral rinse, an anal swab, and a short questionnaire.
- Results of the HPV testing conducted in this study will not be provided to you or your healthcare provider.
- You will be compensated with a NZ\$20 Westfield shopping voucher for completing all study procedures.

### This study is voluntary

Participation is entirely voluntary. If you decide to take part, you can withdraw at any point before all procedures are completed and you will not be required to undertake any procedures you do not wish to. You will be asked to provide verbal consent to participate in the study and at the start of each procedure. You may revoke your consent at any point during the study procedures.

Participation or non-participation in this study will not affect the care you receive from your healthcare provider in any way.

### This study is anonymous

Your name will not be on any study material or forms, and any specimens or information you provide will not be traceable to you. The results of your HPV testing and the information provided on your questionnaire will not be given to your healthcare provider, nor will it be put on your medical records.

Upon completion of the study the information and samples you provided cannot be traced back to you, therefore if you wish to withdraw your information and data from the study at a later date this will not be possible. Data will only be presented as grouped sets; no data from a single individual will be presented.

**Who can participate?**

If you identify as male and were born biologically male, are aged between 16 and 49 years, are able to speak and read English, and live in Auckland then we invite you to participate in this study.

If you agree to take part today, you will be offered a \$20 Westfield shopping voucher as compensation for your time once you have finished the study procedures.

**Disclosure of Sexual Orientation**

We aim to recruit equal numbers of both heterosexual men and gay, bisexual and takatāpui men, therefore the healthcare provider will also ask you about the sex of your recent sexual partners to gain this information.

If you do not wish to disclose this information to your healthcare provider then you may not wish to participate in this study. You do not have to provide a reason for not participating in this study to your healthcare provider. Participating or not participating will not affect the care you receive from your healthcare provider. Furthermore, any information that you disclose to your provider will be treated confidentially and will not adversely affect the care you receive in any way.

**What is human papillomavirus (HPV)?**

HPV is a virus that is sexually transmitted. In males it can infect the mouth and throat, the penis and the anus. It is easily transmitted by direct skin-to-skin contact.

The majority of HPV infections are transient and go away without causing any health problems or symptoms. HPV is the cause of genital warts and some people with HPV will develop these. In rare cases, after ongoing and persistent infection with certain types of HPV, infection can result in the development of cancer at the site of infection (head and neck, penis, and anus).

**Who is at risk from HPV?**

HPV is the most common sexually transmitted infection worldwide. Most men become infected with HPV at some point in their lives. Anyone who has had sexual contact or plans to at some point in their lives is at risk of acquiring HPV infection. Increasing numbers of partners increases the risk of getting HPV, but the virus is so common it may be acquired after having only a single lifetime partner. The levels of HPV infection have also been found to vary between certain groups of men and also between countries.

**What will I be asked to do?**

We will ask you to complete three study procedures:

*Oral rinse and gargle:* your healthcare provider will provide you with a measure of mouthwash and ask you to rinse it in your mouth for 30 seconds; they will then ask you to gargle it for 5 seconds and expel it into the collection vial. The mouthwash used will contain a very small amount of alcohol.

*Anal swab:* your healthcare professional or practice nurse will insert a wet swab 3-5cm into the anal passage and rotate it as it is withdrawn for about 10-15 seconds, placing pressure onto the walls of the anal passage. This should not feel uncomfortable nor be painful.

*Questionnaire:* we will ask you to self-complete a short 5 minute questionnaire and then return it to a secure drop-box. The questionnaire will ask you about your knowledge of HPV prior to the study and your feelings about some statements.

All specimens collected from the procedures will be sent directly to the laboratory for testing.

**Study compensation**

By taking part in this study you will be offered compensation for your time in the form of a NZ\$20 equivalent voucher (Westfield). This compensation will only be provided upon the completion of all study procedures as stated above.



**Where will the findings be published?**

The research team will report the overall proportion ("prevalence") of participants found to have certain types of HPV infection, and whether this varied by groups of respondents such as by age group or by sexuality. We will also report how many individuals agreed to take part in this study as a proportion of all those who were invited (the "response rate"). The research team will report these findings in academic presentations and journal articles. The overall findings will also be discussed with groups who were consulted about this study, such as HIV and sexual health clinicians, GPs, the New Zealand AIDS Foundation and Body Positive.

**Will I get my results?**

We will not be able to give you back the results of the HPV test. This is due to two reasons: firstly the HPV test we are using is still new and not clinically validated and therefore is not accurate enough to be able to say a test is positive beyond doubt. Secondly the study is anonymous and we are unable to link the result from the laboratory back to you. It is not possible to determine whether you are at risk of developing HPV-related cancer from a single positive HPV test.

**Can I get my samples returned to me for disposal?**

We will not be able to return specimens collected in the study to participants. The study is anonymous and therefore we are unable to link a specimen back to the participant it was taken from. If you have cultural concerns regarding the collection, storage and destruction of specimens that you provide, you may wish to discuss this with your family, whanau, hapu and iwi before consenting to this study.

**Data storage and destruction**

After the specimens are tested for HPV, they will be stored at LabPlus laboratory for a period of up to 6 years for further testing of HPV types and sexually transmitted infection if funding for this is later acquired. The laboratory will then destroy the specimens by incineration. The anonymous questionnaires will be stored securely at the Department of General Practice and Primary Health Care at the University of Auckland and will only be accessible by the research team. These will be stored for 6 years and then destroyed. Information from the questionnaires will be electronically stored for a minimum of 6 years for future analysis. The electronic data will be stored securely with password protection and firewalled.

**Risks**

It is possible that the health professional may notice other medical conditions affecting your oral or anogenital area during the specimen collection process, for example anal warts. You may then be referred for examination and treatment for any suspected abnormalities. However it is important to understand that you are not being medically examined. If you are concerned about a health issue affecting your oral or anogenital areas, or would like a routine health screen for these areas, please make an appointment with your healthcare provider.

**Who paid for this research?**

Funding for this research was provided by the Health Research Council (HRC) of New Zealand. Funding for staff time was also provided by the University of Auckland and the NZAF Fellowship.

**Where can I get more information about HPV?**

If this study has raised questions or concerns about HPV you can find extra information on the NZ HPV Project website: <http://npv.org.nz> . Your healthcare provider has also been given pamphlets and other material with information regarding HPV, please take some copies for your reference.

Participant Information Sheet: HPV in Men Feasibility Study

**Who can I contact if I have concerns about the research?**

For queries regarding concerns with the research or its procedures, please contact:

*Principle investigator:*

Dr Helen Petousis-Harris,  
Dept. General Practice and Primary Health Care,  
Faculty of Medical and Health Sciences  
University of Auckland  
Private Bag 92019, Auckland 1142.  
Ph: 64 9 373 7599 extn 82078  
Email: [h.petousis-harris@auckland.ac.nz](mailto:h.petousis-harris@auckland.ac.nz)

*Head of department:*

Professor Felicity Goodyear-Smith  
Dept. General Practice and Primary Health Care,  
Faculty of Medical and Health Sciences  
University of Auckland  
Private Bag 92019, Auckland 1142.  
Ph: 64 9 923 2357  
Email: [f.goodyear-smith@auckland.ac.nz](mailto:f.goodyear-smith@auckland.ac.nz)

For any queries regarding ethical concerns you may contact:

The Chair  
Health and Disability Ethics Committees  
Ministry of Health  
Freyberg House  
20 Aitken Street  
PO Box 5013  
Wellington  
6011  
Ph: 0800 4 ETHICS

Email: [hdecs@moh.govt.nz](mailto:hdecs@moh.govt.nz) - please include the study reference number 15/NTB/5 in your email

PROVISIONALLY APPROVED BY THE NORTHERN B HEALTH DISABILITY ETHICS COMMITTEE  
ON 11/02/2015 for (3) years, Reference Number 15/NTB/5

# Appendix C: HIMS Feasibility Study FUR

Participant Information Sheet: HPV in Men Feasibility Study

SCHOOL OF POPULATION HEALTH



## Storage of Specimens for Future Research

### Study title

Human papillomavirus (HPV) in men (HIMS)

### Names of researchers

Dr Helen Petousis-Harris  
Associate Professor Mark Thomas  
Associate Professor Nikki Turner  
Mr Adrian Ludlam  
Dr Peter Saxton

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The University of Auckland  
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Auckland  
New Zealand,

Helen Petousis-Harris  
Telephone: 64 9 373 7599  
extn 82078  
Email: h.petousis-harris@auckland.ac.nz

## Additional Participant Information Sheet

As part of the HIMS study we ask that you provide two specimens – an oral rinse and an anal swab – that will be tested for the presence of HPV. During the testing not all of the specimen will be used and we would like to ask your permission to store the remainder for future research.

### Who will ask me if I consent for them to be stored?

You will be asked by your healthcare provider if you understand what we are asking of you when we request for your specimens to be stored for future research. You will have a chance to ask any questions about this that you may have. We will also ask you again on the HIMS questionnaire. Here we ask that you tick the box if you do NOT consent to your specimens being stored for future research.

### Why store your specimens for future research?

Collection of specimens is an expensive and time consuming process for participants, researchers and research funders. If we are able to collect samples from one study and make use of them for a different study later, this makes the whole process more efficient and less costly, allowing public funding for research to be stretched further.

### What will the specimens be used for?

No future research or studies have been confirmed that will make use of the specimens collected here. However, we will be proposing they be used to test for other types of HPV that we are not able to test for in this current study, and also for other sexually transmitted infections (STIs).

### Storage of your samples is voluntary

Participation is entirely voluntary. You will be asked to provide verbal consent to participate in the study and to verbally consent to your samples being stored for future use. You may revoke your consent at any point during the study procedures. You will not be able to revoke your consent once the study procedures are complete due to the anonymous nature of the study as we cannot link you to your specimens or questionnaire once they have been submitted.

Participation or non-participation in this study or the storage of specimens will not affect the care you receive from your healthcare provider in any way.

**Your specimens are anonymous**

Your name will not be on any study material or forms, and any specimens or information you provide will not be traceable to you. The results of your HPV testing, of any future testing and the information provided on your questionnaire will not be given to your healthcare provider, nor will it be put on your medical records.

Upon completion of the study the information and specimens you provided cannot be traced back to you, therefore if you wish to withdraw your information and data from the study at a later date this will not be possible. Data will only be presented as grouped sets; no data from a single individual will be presented.

**Where will the specimens be stored and for how long?**

Specimens will be stored by the University of Auckland at the Tamaki Innovation Campus in a secure freezer facility. Specimens will be stored for a period of six years and then be destroyed.

**Who will have access to the specimens?**

Only the researchers named on this study and those at the University of Auckland who have access to the secure freezer facility who are party to a strict code of conduct agreement will have direct access to the specimens while in storage.

Future studies may include other researchers or laboratory staff, however each study will need to pass rigorous ethical committee standards before it is approved. Researchers from other institutions may collaborate on future studies, but the specimens will remain stored with the University of Auckland until sent to a laboratory for testing.

**Will the specimens be sent overseas?**

Where feasible, transportation and testing of specimens overseas will be avoided. However, currently Australia offer the most comprehensive testing for HPV available and it is possible that we will employ their laboratory services for this end.

**Will I get my results from any future testing?**

We will not be able to give you back the results of any future testing. The study is anonymous and we are unable to link the result from the laboratory back to you.

**Can I get my specimens returned to me for disposal?**

We will not be able to return specimens collected in the study to participants. The study is anonymous and therefore we are unable to link a specimen back to the participant it was taken from. If you have cultural concerns regarding the collection, storage and destruction of specimens that you provide, you may wish to discuss this with your family, whanau, hapu and iwi before consenting to this study.

**Risks**

There are no foreseeable risks to you participating in future research by providing your anonymous samples. However, during their collection your healthcare provider may notice some anomaly in your oral or anal region that may require further medical investigation. Your healthcare provider will inform you of this and refer you for a further appointment if necessary.

**Who paid for this research?**

Funding for this research was provided by the Health Research Council (HRC) of New Zealand. Funding for staff time was also provided by the University of Auckland and the NZAF Fellowship.

**Where can I get more information about HPV?**

If this study has raised questions or concerns about HPV you can find extra information on the NZ HPV Project website: <http://hpv.org.nz>

Participant Information Sheet: HPV in Men Feasibility Study

**Who can I contact if I have concerns about the research?**

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APPROVED BY THE NORTHERN B HEALTH DISABILITY ETHICS COMMITTEE ON 11/02/2015 for  
(3) years, Reference Number 15/NTB/5

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