Copyright Statement

The digital copy of this thesis is protected by the Copyright Act 1994 (New Zealand).

This thesis may be consulted by you, provided you comply with the provisions of the Act and the following conditions of use:

- Any use you make of these documents or images must be for research or private study purposes only, and you may not make them available to any other person.
- Authors control the copyright of their thesis. You will recognise the author’s right to be identified as the author of this thesis, and due acknowledgement will be made to the author where appropriate.
- You will obtain the author's permission before publishing any material from their thesis.

To request permissions please use the Feedback form on our webpage.
http://researchspace.auckland.ac.nz/feedback

General copyright and disclaimer

In addition to the above conditions, authors give their consent for the digital copy of their work to be used subject to the conditions specified on the Library Thesis Consent Form and Deposit Licence.

Note: Masters Theses

The digital copy of a masters thesis is as submitted for examination and contains no corrections. The print copy, usually available in the University Library, may contain corrections made by hand, which have been requested by the supervisor.
Corticosteroid Prescribing in New Zealand Palliative Care Settings

by

Anne Paton Denton

A thesis submitted in partial fulfilment of the requirements for the degree of
Doctor of Pharmacy
The University of Auckland
2012
Abstract

Background
Modern palliative care developed in the 1960s in response to the perceived over-medicalisation and lack of recognition of the plight of the terminally ill patient. The development of evidence-based practice for palliative care has been slow and not without its difficulties because clinical trials involving vulnerable dying patients have been problematic. Prescribing in palliative care does appear to be different from other medical specialities; an example of this is the prescribing of corticosteroids.

Corticosteroids are a potent group of medicines, with many adverse effects, that are widely prescribed as adjuvant drugs in palliative care for both specific and non-specific indications. On initial impression, little of their prescribing appears to be supported by rigorous evidence. This study was commenced with a desire to find out more about these medicines and what influences their prescribing in the palliative care setting.

Aim and objectives
The aim of this study was to explore and clarify the reasons for the prescribing of corticosteroids in New Zealand palliative care settings. Objectives included the identification of which corticosteroids were prescribed, as well as their indications, doses, use of guidelines, and processes for their reviewing and monitoring. The perceptions of those involved in the prescribing of corticosteroids were also sought.

Methods
A mixed methods approach was undertaken to include a quantitative phase (Phase One) and qualitative phase (Phase Two). Phase One was a retrospective review of inpatient use of corticosteroids in a sample of six New Zealand hospices. These hospices were chosen to give a representation of corticosteroid prescribing during the chosen year of 2007. Phase Two consisted of semi-structured interviews with key informants (prescribers and senior nurses) from the six hospices and was intended to elicit information on factors influencing the use of corticosteroids in those hospices.
Results

In Phase One, the case notes of 1179 inpatients in the six hospices were reviewed and data was recorded of those who had been prescribed corticosteroids. There was a marked consistency of between 61% and 69% in the proportion of patients prescribed corticosteroids in the sample hospices. Corticosteroids were prescribed most commonly for non-specific reasons, and despite prescribing being similar in dose range and choice of corticosteroid, it varied in course length, method of stopping, recording of monitoring and reviewing, and recording of adverse effects.

In Phase Two, 18 key informants were interviewed (12 medical practitioners and six senior nurses). Interviewees were shown the data pertaining to their hospice from Phase One of the study. Interviewees agreed that there were a number of challenges associated with these frequently prescribed medicines. They suggested that there was lack of formal evidence behind their corticosteroid prescribing and voiced surprise and disappointment over the amount of non-specific prescribing, methods of stopping corticosteroids, monitoring and reviewing, and lack of recording of adverse effects.

Discussion

As evidenced in this study, corticosteroids are widely prescribed as adjuvant drugs in palliative care, most commonly for non-specific indications. The corticosteroid of choice in this study was dexamethasone. Monitoring and reviewing of these medicines was under-recorded and adverse effects, if recognised, were generally not recorded.

By exploring clinicians’ practice and perceptions of prescribing and comparing this with existing articles and guidelines, it was found that these potent commonly prescribed medicines tended to be used experientially and intuitively. Corticosteroid prescribing appeared not to be supported by rigorous evidence. These findings seem to be consistent with the limited international literature in this area and suggest that it is timely for a reappraisal of their use in palliative care.
Dedication

To Ross, my rock,

Our children and grandchildren

Who are the future
Acknowledgments

It has been a very long journey since I started as a volunteer pharmacist at Cranford Hospice in Hastings in 1984 to the finalising of this thesis. Palliative care became my passion and I would like to acknowledge those with whom I worked through the years.

This thesis could not have been commenced, developed or completed without the advice, help and support of my supervisor, Professor John Shaw, who unstintingly gave time, kindness and encouragement and whom I admire and value greatly.

My gratitude is expressed to the families of Christine and Emily who gave me the impetus to commence this study and have since continued to encourage me.

To all those involved in the six sample hospices thank you for your gracious welcome, your giving of valuable time and your willingness to be interviewed.

My heartfelt thanks to Sue Foggin, of the Philson Library, University of Auckland, who has been a tower of strength since day one.

Thank you to Elizabeth Robinson who performed mathematical miracles and taught me very patiently what I know about statistics.

Thanks to Dr. Lyn Lavery for her invaluable help and guidance with the qualitative phase of this study and to her brother Andrew Lavery for his expertise with the mysteries of Microsoft processes.

I thank Elizabeth Bangera for a difficult job transcribing the semi-structured interviews.

Financial support in the early stages was given by Cranford Hospice (Presbyterian Support East Coast) and the Cancer Society (Central Region).

My thanks to the staff of The Cancer Society Domain Lodge in Grafton, who gave me a home away from home.

Finally, my special thanks to my family and friends for their love, support and patience. I am very privileged.
Table of Contents

Dedication .......................................................................................................................... iv
Acknowledgments ............................................................................................................. v
List of Figures .................................................................................................................... ix
List of Tables ..................................................................................................................... x

Chapter 1: Introduction ....................................................................................................... 1
  1.1: Palliative care ............................................................................................................. 1
    1.1.1: The historical perspective ............................................................................... 1
    1.1.2: The New Zealand perspective ........................................................................... 2
  1.2: Evidence-based medicine (EBM) .............................................................................. 4
  1.3: Research, evidence-based medicine (EBM) and palliative care ......................... 7
  1.4: Prescribing in palliative care ................................................................................... 10
  1.5 Corticosteroids ......................................................................................................... 13
    1.5.1: Corticosteroid prescribing in palliative care ...................................................... 14
  1.6: Review of evidence for the use of corticosteroids .................................................. 24
    1.6.1: Corticosteroids are potent drugs .................................................................... 24
    1.6.2: Corticosteroids are commonly and frequently prescribed in palliative care for non-specific reasons ...................................................... 24
    1.6.3: Corticosteroid benefits may be short-term ...................................................... 26
    1.6.4: Corticosteroid adverse effects ....................................................................... 26
    1.6.5: Corticosteroids and divided doses ................................................................ 28
    1.6.6: Concurrent medicines ..................................................................................... 29
    1.6.7: Withdrawal of corticosteroids ........................................................................ 30
  1.7: The need for more effective corticosteroid guidelines in palliative care ............. 31
  1.8 Summary of introduction ......................................................................................... 35
  1.9 Research aim and objectives ..................................................................................... 37

Chapter 2 Methods: Phase One ...................................................................................... 39
  2.1: Purpose of Phase One ............................................................................................. 39
  2.2: Ethics approval ....................................................................................................... 39
  2.3: Sampling considerations ........................................................................................ 39
    2.3.1: Hospices ........................................................................................................... 39
    2.3.2: Time frame ....................................................................................................... 40
    2.3.3: Numbers of patients ....................................................................................... 40
    2.3.4: Sample size calculations ............................................................................... 41
  2.4: Data recording considerations ................................................................................ 42
    2.4.1: The patient information sheet ........................................................................ 42
    2.4.2: The patient review sheet ................................................................................ 44
  2.5: Data collection ......................................................................................................... 46
    2.5.1: Hospice 1 ........................................................................................................ 47
    2.5.2: Hospice 2 ........................................................................................................ 49
    2.5.3: Hospice 3 ........................................................................................................ 50
    2.5.4: Hospice 4 ........................................................................................................ 51
    2.5.5: Hospice 5 ........................................................................................................ 51
    2.5.6: Hospice 6 ........................................................................................................ 52
4.7: Interview recording and transcribing.................................................................87
4.8: Data analysis ......................................................................................................88

Chapter 5 Results: Phase Two..................................................................................90

  5.1: Palliative care prescribing.................................................................................90
  5.2: Corticosteroid prescribing and associated issues..............................................94
  5.3: Views, knowledge and understanding of corticosteroids.................................97
  5.4: Factors influencing corticosteroid prescribing.................................................102
    5.5.1: Differences in prescribing corticosteroids within hospice, hospital and general practice .................................................................104
    5.5.2: Influences in professional roles within the hospice team............................107
    5.5.3: Differences in corticosteroid prescribing within the hospice team ..........109
  5.6: Perceptions of Phase One data.........................................................................111
    5.6.1: Agreement with individual hospice data presented ..................................111
    5.6.2: General perceptions of hospice data ..........................................................112
    5.6.3: Perceived need to achieve the average .......................................................115
    5.6.4: Changes in prescribing of corticosteroids since 2007 .................................115
  5.7: Guidelines, reviewing and monitoring...............................................................116
    5.7.1: Guidelines ..................................................................................................116
    5.7.2: Lack of recording in patient notes ..............................................................118
    5.7.3: Peer review of corticosteroid prescribing ................................................120
    5.7.4: Review and monitoring .............................................................................121

Chapter 6: Discussion ..............................................................................................125

  Phase One ................................................................................................................126
  Phase Two ...............................................................................................................136
  Mixed methods .......................................................................................................143
  Improvements in clinical practice .........................................................................147
  Future research .......................................................................................................148
  Conclusion .............................................................................................................149

Appendices ..............................................................................................................150

  Appendix A: Example of an International Corticosteroid Guideline, 2008 ..........151
  Appendix B: Example of a New Zealand Corticosteroid Guideline, 2008 ..........153
  Appendix C: Ethics approval ................................................................................155
  Appendix D: Letters of Invitation to Chief Executive Officers and Medical Directors ........157
  Appendix E: Participant Information Sheet ............................................................159
  Appendix F: Participant Consent Form ..................................................................162
  Appendix G: Corticosteroids in Palliative Care Study: Specific Data for Hospice Two ........164

References ..............................................................................................................167
List of Figures

Figure 1: Practical and ethical challenges to palliative care research, applied to a model randomised controlled trial ................................................................. 10
Figure 2: The World Health Organization Analgesic Ladder .................................................. 12
Figure 3: How corticosteroids reduce inflammation ............................................................ 14
Figure 4: The chemical structures of hydrocortisone, prednisone, methylprednisolone and dexamethasone ................................................................. 21
Figure 5: Christine before corticosteroids ........................................................................... 27
Figure 6: Christine seated left ......................................................................................... 27
Figure 7: Christine after corticosteroids ............................................................................ 27
Figure 8: Emily before corticosteroids ............................................................................... 27
Figure 9: Emily after corticosteroids .................................................................................. 27
Figure 10: Proportion of patients prescribed corticosteroids .............................................. 56
Figure 11: Proportion of patients prescribed corticosteroids for non-specific indications .... 57
Figure 12: Proportion of patients prescribed corticosteroids for neurological symptoms .... 58
Figure 13: Proportion of patients prescribed corticosteroids for soft tissue infiltration symptoms . 58
Figure 14: Proportion of patients prescribed corticosteroids for the balance of the recorded indications .............................................................................. 59
Figure 15: Proportion of patients who had adverse effects recorded .................................. 65
Figure 16: Proportion of patients with adverse effects to corticosteroid prescribing ........ 66
Figure 17: Proportion of patients where corticosteroids were stopped abruptly ............... 66
Figure 18: Proportion of patients co-prescribed corticosteroids and omeprazole .............. 67
Figure 19: Proportion of patients co-prescribed corticosteroids and NSAIDs ................... 68
Figure 20: Proportion of patients co-prescribed corticosteroids with phenytoin ............... 68
Figure 21: Proportion of patients co-prescribed corticosteroid with zopiclone ................... 69
Figure 22: Corticosteroid reviews recorded across the sample hospices ............................ 71
Figure 23: Tree nodes identifying the research themes ...................................................... 89
List of Tables

Table 1: Some historical drivers for the development of evidence-based medicine .................................. 5
Table 2: Patient needs: Clinical trial considerations ................................................................. 9
Table 3: Proposed solutions to address the clinical trial considerations ................................... 9
Table 4: Indications for corticosteroids in palliative care ......................................................... 15
Table 5: Controlled clinical trials or meta-analyses or randomised controlled trials of corticosteroids in palliative care .............................................................................................................. 16
Table 6: Systematic reviews of corticosteroids in palliative care ............................................. 16
Table 7: Relative potencies and equivalent doses of representative corticosteroids ............. 18
Table 8: Showing clinically important drug-drug interactions involving P450 dexamethasone and prednisolone ........................................................................................................................................................... 20
Table 9: Prednisone availability in New Zealand ........................................................................ 22
Table 10: Methylprednisolone availability within New Zealand ............................................. 22
Table 11: Dexamethasone availability within New Zealand ................................................... 23
Table 12: Indications for the use of corticosteroids as adjuvant therapies .............................. 23
Table 13: Examples of these inducers, and substrates of the CYP 450 group of iso-enzymes .... 30
Table 14: Doses above which adrenal suppression is possible ................................................ 31
Table 15: Gannon’s indications and suggested doses ................................................................. 33
Table 16: Indications and suggested doses from a New Zealand corticosteroid guideline ....... 34
Table 17: Precision estimates based on sample sizes .............................................................. 41
Table 18: An example of the patient information database sheet for one of the sample hospices 43
Table 19: An explanation of the patient information database sheet by column ...................... 44
Table 20: An example of the patient review sheet database for one of the sample hospices ...... 45
Table 21: An explanation of the patient review database sheet by column .............................. 46
Table 22: Patient characteristics .............................................................................................. 55
Table 23: Description of indications ......................................................................................... 56
Table 24: Proportion of patients prescribed prednisone by indication ..................................... 60
Table 25: Proportion of patients prescribed methylprednisolone by indication .................... 61
Table 26: Proportion of patients prescribed dexamethasone by indication ............................ 61
Table 27: Prednisone by dose range by indication by hospice ................................................ 62
Table 28: Methylprednisolone by dose range by indication by hospice ................................... 63
Table 29: Dexamethasone by dose range by indication by hospice ....................................... 64
Table 30: Duration of corticosteroid courses (in days) .............................................................. 70
Table 31: Duration of corticosteroid courses by indication- all hospices combined ............. 70
Table 32: Phase Two: Semi-structured interview frame ............................................................. 82
Table 33: Interviewees by number and designation ................................................................. 84
Table 34: Interviewees perceptions of their hospice graph results ......................................... 113
Table 35: A comparison of the literature findings, actual usage of corticosteroids, and practitioner perceptions as revealed by this research study .......................................................... 145
Chapter 1: Introduction

This research investigates aspects of the use of corticosteroids in palliative care. Corticosteroids are potent medicines and are commonly prescribed in this field. The researcher has observed many cases of adverse effects with corticosteroid use, and whilst the intention of their use is to achieve beneficial results, the consequences may render this questionable.

The introduction of this thesis starts with the historical and international perspectives of palliative care. The focus of this introduction is on the prescribing of drugs within the palliative care field and the effects resulting from the use of corticosteroids in particular. Issues will be discussed in the context of the development of the evidence-based and palliative care movements.

1.1: Palliative care

Palliative care has been defined and described by the World Health Organization as:

An approach that improves the quality of life of patients and their families facing the problems associated with life threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual. (World Health Organization, 2007, para. 1).

Specialised palliative care teams are multidisciplinary and holistic in their care of dying patients. The team may include a range of medical, nursing and allied health professionals and volunteers (Maddocks, 1997).

1.1.1: The historical perspective

Until the early 20th century, death was seen to be a natural part of the process of living rather than a medical event (Randall & Downie, 2006). With the improvements in technology and effective life-saving medications cure, instead, became the focus. Because of this, during the first half of the 20th century, dying patients became neglected in mainstream medicine since by dying, these patients represented a failure (Randall & Downie, 2006; 2004). However, by the 1950s and 1960s there was a renewed awareness that this did not serve dying patients well and that they deserved better (Woodruff, 2004). From this point, the modern hospice movement developed.
In 1967, Cicely Saunders opened St Christopher’s Hospice in South London. While this was not the first hospice, it became recognised as the cornerstone of the modern hospice movement. It became one of the early palliative care training hospices (Eti, 2011). In those days, the hospices frequently operated separately from the hospital system (Doyle, Hanks, & MacDonald, 1993). Because the term ‘hospice’ in French speaking Canada denotes custodial care, in 1975, Balfour Mount (Canada) introduced the term ‘palliative care’ to describe a programme for patients with advanced disease (Doyle et al., 1993; Eti, 2011).

The terms hospice, terminal care and palliative care are interchangeable. ‘Hospice’ is used to refer to the philosophy and practice of hospice care, which is in effect the same as the philosophy and principles of palliative care. It can also refer to a hospice unit (Ministry of Health, 2001). Hospital systems now recognise the need for multidisciplinary palliative care teams within their system, so intra-hospital teams are emerging. ‘Palliative care’ is now considered the umbrella term for a new medical speciality although palliation has in fact been practised for centuries (Doyle et al., 1993).

Modern palliative care has developed rapidly through Europe, North America and Australasia and is starting to be seen as a basic right when curative care is no longer possible (Doyle et al., 1993).

1.1.2: The New Zealand perspective

New Zealand’s development of palliative care closely followed the United Kingdom. Ivan Lichter set up the first New Zealand palliative care unit at Waikari Hospital, Dunedin in 1974. Mary Potter Hospice in Calvary Hospital, Wellington was opened in 1975, followed by St Joseph’s in the Mercy Hospital (Auckland) and Te Omanga, the first stand-alone unit, (Lower Hutt) in 1979. In 1986, Hospice New Zealand, the national body representing hospices was founded. At that time its purpose was to monitor standards, review education and share information (Denton, 1995). The Australian and New Zealand Society of Palliative Medicine (ANZSPM) was established in 1993 (Lewis, 2007).

New Zealand hospices were slow to pick up the term ‘palliative care’. It was felt that much energy and effort had gone into promoting the term ‘Hospice Movement’, not as bricks and mortar but as a philosophy. The community gave their local hospices enormous support. However, when the Ministry of Health
introduced the New Zealand Palliative Care Strategy in 2001, the words ‘palliative care’ were used throughout and the term ‘Hospice’ was seldom used in that document (Ministry of Health, 2001).

In 2007, Mary Schumacher, Chief Executive of Hospice New Zealand, stated that there were 38 full members of Hospice New Zealand, 32 of which were hospices. The other six were palliative care teams within the hospital system. That same year, ‘Palliative Care Nurses New Zealand’ was formed. The Palliative Care Council was established in 2008, as an independent body representing the palliative care sector, which provides strategic advice to the Minister of Health about palliative and end-of-life care (Palliative Care Council of New Zealand, 2010).

By 2010, Hospice New Zealand’s membership was 29 full members and six associate members. None of these member services are hospital based. Hospital Palliative Care is a separate organisation with nine members. (Information supplied by Hospice New Zealand 2011).

The practice of palliative or hospice care has changed over the years in response to the developing demands and expectations of government, clinicians, patients and carers. Initially, palliative care was developed in response to the perceived over-medicalisation and lack of recognition of the plight of the terminally ill patient. In the early days, hospices were set up in local communities by inspired individuals and committees, who by community action funded and acquired buildings and staffed them often with volunteers and other dedicated individuals (Denton, 1995). Medical professionals were drawn from the local community, and although not trained in this specialised area, achieved excellent results.

Hospices eventually overran the local communities’ ability to fund them, so Ministry of Health driven agencies e.g. local District Health Boards (DHBs) increasingly became more involved (Denton, 1995). This assured the continuing existence of the hospice, but with that came a loss of control of policy, since the funding agencies did not necessarily recognise the input by, and therefore ownership of, the local community.

In 1999, the Australasian Chapter of Palliative Medicine was established and palliative care became a recognised medical speciality (Australasian Chapter of
Palliative Medicine, 2009). Some New Zealand medical practitioners, in recognition of their considerable hospice experience, were grand-parented into that specialty. This was a needed development for the improvement and standardisation of practice, but it has been felt by some that the spectre of over-medicalisation with the loss of some intangible spiritual and emotional aspects of traditional palliative care may perhaps be becoming evident.

1.2: Evidence-based medicine (EBM)

There have been two broad parallel conceptual models running within the application of palliative care. These are the ‘palliative care model’ and the ‘evidence-based model’, in turn facilitated by the development of the World Wide Web.

In the early 1990s, a group of clinicians and epidemiologists from McMaster University in Ontario, Canada presented the medical world with a new concept, “evidence-based medicine” (Sackett, Straus, Richardson, Rosenberg, & Haynes, 2000).

Sackett and his co-workers defined evidenced-based medicine as follows: “The conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research” (Lipman, Jackson, & Tyler, 2000).

Some authors have argued that evidence-based medicine is not a new concept. Jenicek and Hitchcock for example have stated that:

Evidence-based medicine is the newest name for a very old idea. The best physicians have always sought the best empirical evidence available on which to base diagnoses and therapeutic decisions. What is new is the availability of a much broader array of empirical data and far more sophisticated methods of validation and interpreting them (Jenicek & Hitchcock, 2005).

There are those to whom evidence-based methods are irrelevant and who place great faith in their own perceptions or anecdote. The complementary/alternative medicine movement developed alongside the evidence-based medicine movement and the question may be asked: “Is this related or coincidental?” An absence of evidence does not mean a treatment or practice is ineffective or of no
value, it just means there is an absence of recognised published evidence (Higginson, 1999; Kerridge, Lowe, & Henry, 1998). If funders do not consider alternative strategies when it comes to supporting or funding, is a bias being created?

Nevertheless, health costs have been escalating and are of rising concern and evidence-based practice offers a means of allocating available resources. But evidence-based medicine is broader than the financial and medical implications, it also affects philosophy, ethics and politics (Lockett, 1997).

Over the past two decades, evidence-based practice has developed in momentum, strength and credibility. Evidence-based medicine and practice has become a useful tool for clinicians and managers alike. It assists clinicians to validate and direct their practice and health funders to prioritise their expenditure (Lockett, 1997).

Table 1 traces the development of the ‘modern’ evidence-based movement from the thalidomide disaster, which led to clinical trials being a requirement before a marketing licence for a drug would be granted. This was followed by Archibald Cochrane’s influence on the development of evidence-based practice, which led to the Cochrane Collaboration, an international endeavour in which specialists from different countries systematically find, appraise and review available evidence from randomised controlled trials and other sources of information (Belsey & Snell, 2007).

**Table 1**: Some historical drivers for the development of evidence-based medicine

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961</td>
<td>Thalidomide disaster</td>
</tr>
<tr>
<td>1963</td>
<td>Clinical trials prior to a marketing licence being granted</td>
</tr>
<tr>
<td>1979</td>
<td>Cochrane asserted physicians should have access to reliable evidence</td>
</tr>
<tr>
<td>1980s</td>
<td>The birth of clinical guidelines</td>
</tr>
<tr>
<td>1992</td>
<td>The British National Health Service named a centre after Cochrane</td>
</tr>
<tr>
<td>1990s</td>
<td>Sackett and colleagues named ‘evidence-based medicine’ concept</td>
</tr>
<tr>
<td>1993</td>
<td>The Cochrane Collaboration became a reality</td>
</tr>
<tr>
<td>1998</td>
<td>Pain, Palliative Care Supportive Group (PaPaS), a Cochrane Group was instituted</td>
</tr>
<tr>
<td>2010</td>
<td>Formation of the Palliative Care Research Cooperative Group</td>
</tr>
</tbody>
</table>

Adapted from Lipman et al. (2000)
“Evidence-based medicine is not a purely academic or financial exercise ... its implementation has major clinical implications that can save lives” (Belsey & Snell, 2007).

Evidence-based medicine makes clinicians question their own practice and for some clinicians this can be threatening. There is still a certain amount of resistance particularly from older, more traditional clinicians for whom formal evidence-based medicine critiques were not part of their previous experiences (Lockett, 1997).

The proposition for evidence-based medicine gave rise to considerable discussion. While accepting the value of randomised controlled trials, it has been suggested by some that trials are often narrow in their construction. Studies can be biased by the requirements of the initiators of the study and the results can only be as good as the evidence critiqued (Montori et al., 2005).

A selected group recruited for a trial may not be relevant to a medical practitioner confronted by an individual patient with his/her unique set of co-morbidities, expectations and life context. It is argued that the correct application of intuition can only come with experience and knowledge of the particular circumstances of the patient rather than by the results of clinical trials and can defy logical sequences of explanation while still being correct in outcome, that is the art of medicine as opposed to science. Use of intuition avoids the well documented problem of being ‘evidence burdened’ as compared to ‘evidence advised’. It does not deny the value of evidence, but it places it in the context of experience, expertise and situational knowledge (Greenhalgh, 2002).

Tricia Greenhalgh suggests “Intuition is not unscientific. It is a highly creative process, fundamental to hypothesis-generation in science. The experienced practitioner should generate and follow clinical hunches as well as (not instead of) applying the deductive principles of evidence-based medicine” (Greenhalgh, 2002).

Randall and Downie comment that sitting quietly and listening is being replaced by task-orientated clinicians, protocols and pathways, and that the art of listening is being taken over by the scientific approach (Randall & Downie, 2006).
The idea of evidence-based medicine has gained traction because there is a perceived gap between practice and the evidence for that practice. Expert opinion and intuition are not necessarily quantifiable and are not denied by Sackett et al.’s 2000 definition. There is an increasing requirement for education, accountability and compliance along with a new ability to access data with modern information technology. In the meantime managers and funders, with capped budgets want to disperse available resources more efficiently.

1.3: Research, evidence-based medicine (EBM) and palliative care

Palliative care in the earlier days did not follow evidence-based parameters and was often seen as ‘fringe’ medicine, and a ‘soft option’ to mainstream medicine. The choices of medicines used in palliative care were dictated by pharmacological knowledge, experience, intuition and anecdote. There was little evidence-based practice at this time (Doyle, 2004).

In the early 1980s, there were few known randomised controlled trials (RCTs) in palliative care. Evidence and practice were drawn from other medical specialities but often this evidence was not formalised. Despite this, clinicians generally prescribed effectively, achieving good symptom management (Doyle, 2004). For the credibility of the palliative care movement, it is important to produce high quality research (Kutner, 2005; Lipman et al., 2000). Randomised controlled trials (RCTs) are the gold standard for evidence in mainstream medicine. Palliative care must achieve these standards but this goal may be challenging because of the nature of palliative care patients, most of whom are in the last stages of life (Higginson, 1999).

In 2010, The International Association of Hospice and Palliative Care website listed 38 journals but, despite this, there are still few clinical trials in palliative care. Palliative care research is underfunded because the development of services has, until recently, been of higher priority. To work effectively within palliative care, the process, aims and outcomes of evidence-based medicine must sit comfortably with the palliative care community (Higginson, 1999).

Whilst randomised controlled trials (RCTs) may not be the answer for palliative care research because of the setting, robust research is essential to ensure
reliable symptom management. The barriers to research that surround this specialised practice that need to be overcome include lack of funding resources, ethical issues around a vulnerable population base and practical issues of small community based provider sites (Abernethy et al., 2010).

The care of patients in palliative care is by a multidisciplinary team, and individual to the patient’s needs. Palliative care teams pride themselves on caring for the individual physically, emotionally, socially, intellectually and spiritually. A patient’s disease progression is unpredictable, and to assemble large groups of palliative care patients for a study is not easy. Good quality effective research in palliative care is difficult to conduct because the subjects are dying and their lifespan is not predictable (Jubb, 2002).

The patient and his/her family are vulnerable and for some being part of a research trial is not a priority. There are some individuals who take comfort and satisfaction from being able to assist future outcomes; somehow it makes their death more worthwhile so they volunteer to be part of a clinical trial (Janssens & Gordijn, 2000; Shelby-James, Abernethy, & Currow, 2006). A minority group of palliative care patients stay in randomised controlled drug trials, looking for a cure as they die.

There can be a tension between clinicians, family members and carers who see research and researchers as not being attuned to the dying patient’s needs and block him/her from being part of the research project. This appears to have arisen because the physician and family are seen to meet the individual patient’s needs and suffering, while the research goal is more general with no expectation that the results will meet the needs of the individual dying patient (Abernethy et al., 2010; Agrawal & Danis, 2002).

Clinical trials must therefore meet the needs of palliative care patients, families and carers. By choosing to be part of a trial, a patient must not be disadvantaged in any way. Agrawal and Danis suggest there are six areas, which must be addressed; these suggestions are included in Table 2 and 3.
Table 2: Patient needs: Clinical trial considerations

<table>
<thead>
<tr>
<th>The patient’s physical symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Their psychological and cognitive symptoms</td>
</tr>
<tr>
<td>Economic demands and care giving needs</td>
</tr>
<tr>
<td>Social relationships and support</td>
</tr>
<tr>
<td>Spiritual and existential beliefs</td>
</tr>
<tr>
<td>Hope and expectations</td>
</tr>
</tbody>
</table>

Adapted from Agrawal and Danis (2002)

Table 3: Proposed solutions to address the clinical trial considerations

| To modify the informed consent discussion, so that participants do not join the study with false hopes of cure |
| To build a palliative care component into clinical trials, so palliation continues alongside the research |
| To attend to the needs of family caregivers of terminally ill research subjects, so they alongside the palliative care patient are treated as a unit |
| To arrange for continuity of care, so that dropping out of the trial does not jeopardise medical care. A patient may because of the progression of their disease need to pull out of a trial or may decide the trial is not for them |
| To train clinical investigators in end of life care so they are able to recognise and talk to the patient about what is happening |
| To develop a counselling strategy for terminally ill participants in clinical research |

Adapted from Agrawal and Danis (2002)

Research in health can be either quantitative or qualitative or may be a mixture of both methodologies (Pope & Mays, 2006). Grande and Todd suggest: “That further randomised controlled trials in palliative care require a blend of qualitative and quantitative methods as well as measuring both process and outcome of care” (Grande & Todd, 2000).

The ethics of the situation justifying research in the terminally ill can be challenging for clinicians and researchers alike (Keeley, 2008), but as long as ethical challenges and principles are addressed carefully there seems to be no justification for not improving the quality of palliative care research (Jubb, 2002).

The following framework Figure 1 from Jubb identifies the practical and ethical challenges to palliative care research when it is applied to a model randomised controlled trial.
The development of appropriate assessment tools and frameworks for palliative care research is essential for palliative care to develop credibility and useful strategies in this particular end of life environment. These tools and frameworks must meet the needs of patient, family and palliative care provider (Aoun & Kristjanson, 2005). Funders need to be assured that funding is used efficiently while clinicians must be confident their practices are appropriate for their patients needs.

1.4: Prescribing in palliative care

All medical specialties attempt to prescribe the smallest number of drugs for the best gain and the fewest adverse effects. The philosophy of medicine use in palliative care may be encapsulated by the well-known injunction: ‘Primum non nocere’ – ‘first do no harm.’ Palliative care prescribers respect this intention but their prescribing differs from other specialities in many ways.
A medicine may be prescribed off-registration for a helpful side-effect rather than its registered indication, frequently for symptoms that are difficult to control. The prescribing of these medicines off-registration is often supported by literature (Atkinson & Kirkham, 1999; Verhagen et al., 2008). In palliative care the least invasive parenteral route is considered to be the subcutaneous route, and this tends to be the route chosen by most palliative care clinicians. But palliative care medications given subcutaneously are often not registered or supported by published clinical evidence for this route (Toscani et al., 2009).

For a medicine to be distributed in New Zealand, it must have the consent of the Minister of Health about its therapeutic claims. It may be promoted and distributed only according to the data included with the application made for registration and consent to distribute. While funding criteria can determine whether the state pays for a medicine, an authorised prescriber may in accordance with Section 25 of the Medicines Act ("Medicines Act," 1981), unless restricted for instance by the Misuse of Drugs Act, prescribe the medicine any way they see fit.

Section 29 of the Medicines Act allows for medicines as yet unlicensed to be prescribed provided certain processes are followed ("Medicines Act," 1981). Prescribers, however, are often uncomfortable about prescribing ‘off registration’ for a variety of reasons. This can lead to a sub-optimal standard of symptom management for the patients whose symptoms have been unable to be controlled by registered usages (Atkinson & Kirkham, 1999).

Physical symptoms most frequently seen in palliative care patients with progressive disease include: pain, nausea and vomiting, weight loss, anorexia, cough, dyspnoea, effusion/ascites/oedema, weakness and constipation (Maddocks, 1997). Not all patients have pain (Faull, Carter, & Woof, 1998), which is the most feared symptom compared to some other symptoms such as nausea and vomiting, but is often easier to manage.

Opioid prescribing for pain is common in palliative care. These medicines sit on Step Three of the World Health Organization (WHO) analgesic ladder and are used for severe pain. Figure 2 illustrates the three steps of the World Health Organization analgesic ladder.
Figure 2: The World Health Organization Analgesic Ladder

Adapted from Woodruff (2004)

**Step 1**: Bottom rung of ladder (mild pain): Non opioid (e.g. Paracetamol) +/- adjuvant (e.g. NSAID or corticosteroid).

**Step 2**: Middle rung of ladder (mild to moderate pain): mild opioid (codeine) +/- non opioid +/- adjuvant.

**Step 3**: Highest rung of ladder (moderate to severe pain): strong opioid (morphine) +/- non opioid +/- adjuvant.

The frequency of prescribing of opioids and the doses used are peculiar to palliative care and seldom seen in other medical specialities. Palliative care prescribers become very familiar with the prescribing of these drugs and their use at the end of life is well supported by rigorous evidence (Portenoy et al., 2006). In contrast, corticosteroids are prescribed with little evidence-based rigour (see section 1.5). Opioids, though helpful for pain relief, are not without adverse effects. It is common for a patient to experience transient nausea and require an anti-emetic short term, after being prescribed an opioid. Because opioids and constipation go hand in hand, the prescribing of a laxative is essential. A patient who enters the palliative care service on few medications may find, on discharge, they are on many more.

In palliative prescribing, drugs may be given in doses higher than the usual recommended dose, for instance docusate and senna for constipation. The normal dose is one or two tablets a night, but doses of four tablets, twice daily, are common in palliative care (Denton, 2007). Often there is a ‘layering’ of medicines. The medicines prescribed depend on the symptom needing to be treated and often more than one class of drug will be used for the management of...
a symptom. For instance, opioids, such as morphine, are commonly used in palliative care for severe soft tissue and visceral organ pain. Adjuvant drugs such as anticonvulsants, non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids may be given if nerve or bone is involved (Denton, 2007; Woodruff, 2004).

Modern palliative care encompasses many diagnoses, not cancer alone (Eti, 2011). As a result, the range of symptoms treated is widening. The initial task of palliative care is the relief of physical symptoms (Randall & Downie, 2006). This does not discount psychosocial aspects, however these are difficult to address if the patient is not physically comfortable. With the broadening of palliative care to include patients with long-term conditions, there are an expanding number of wide-ranging medications now being prescribed. At the end of life, non-essential medicines tend to be reduced to the key drugs required. Additional medicines may be added to the key drugs to maintain effective terminal symptom management (Denton, 2007).

The New Zealand Palliative Care Strategy (Ministry of Health, 2001) states that palliative care aims neither to hasten nor to postpone death. The reality is that either might happen. Some drugs, for example corticosteroids, may extend life, while sedation for extreme terminal restlessness may shorten life. Dosages and usages of medicines are frequently atypical. The comfort and quality of remaining life becomes the focus of care but the need to prolong existence at all costs may no longer necessarily be paramount (Twycross & Wilcock, 2001).

1.5 Corticosteroids

The adrenal cortex secretes two classes of steroid hormones: corticosteroids and androgens. The principal adrenal steroids are those with mineralocorticoid and glucocorticoid activity. Glucocorticoids affect carbohydrate and protein metabolism while mineralocorticoids affect water and electrolyte balance (Brunton, 2006; Rang, Dale, Ritter, & Moore, 2003; Richter, Neises, & Clar, 2002). These hormones inhibit the production of prostaglandins and thus reduce inflammation and oedema associated with tumours. Corticosteroids may be used as adjuvant analgesics. In addition, they have a central action, evident in the effect on mood and appetite (Woodruff, 2004).
A proposed mechanism of action of corticosteroids is demonstrated in Figure 3: It is proposed that:

Steroids enter the tissue cell and are carried by a transporter molecule into the nucleus, where they activate segments of DNA to produce mRNA. This results in the production of mediator proteins at cellular ribosomes, and these proteins block the arachidonic acid cascade at its earliest point blocking the production of all the eicosanoid inflammatory mediators (McGavock, 2003).

**Figure 3**: How corticosteroids reduce inflammation

Corticosteroids, as indicated in Table 4 are a class of drugs prescribed commonly in palliative care as adjuvant medicines to help alleviate both specific and non-specific debilitating symptoms (Kiani, Yip, Tuffin, Roberts, & Clifford, 2011; Lundstrom & Furst, 2006; Matsuo, Morita, & Iwase, 2011; S Mercadante, Berchovich, Casuccio, Fulfarò, & Mangione, 2007; Nauck et al., 2004; Twycross, Bergl, John, & Lewis, 1994).
**Table 4: Indications for corticosteroids in palliative care**

<table>
<thead>
<tr>
<th>Specific Indications</th>
<th>Non-specific Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Raised intracranial pressure</td>
<td>• Improvement in ‘wellbeing’</td>
</tr>
<tr>
<td>• Spinal cord compression</td>
<td>• Mood</td>
</tr>
<tr>
<td>• Lymphangitis carcinomatosis</td>
<td>• Fatigue/weakness</td>
</tr>
<tr>
<td>• Bowel obstruction</td>
<td>• Anorexia</td>
</tr>
<tr>
<td>• Superior vena cava obstruction</td>
<td>• Pain relief</td>
</tr>
<tr>
<td>• Obstructive lymphadenopathy</td>
<td>• Dyspnoea</td>
</tr>
<tr>
<td>• Ureteric obstruction</td>
<td>• Nausea/vomiting</td>
</tr>
<tr>
<td>• Chemotherapy</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Hardy (1998)

Corticosteroids are potent medicines and their prescribing has been commonplace for fifty years in palliative care therapy (Kaal & Vecht, 2004; Popiela, Lucchi, & Giongo, 1989; Weissman, 1988). Literature searches have been and continue to be conducted by the author on various electronic databases, which include MEDLINE, EMBASE, AMED, CINHAL and Cochrane. It appears currently there have been few randomised controlled trials conducted on the use of corticosteroids in palliative care (Bruera et al., 2004; Bruera, Roca, Cedaro, Carraro, & Chacon, 1985; Della Cuna, Pellegrini, & Piazzi, 1989; S Mercadante et al., 2007).

The lack of published robust literature for corticosteroids is illustrated by a MEDLINE search conducted in May 2010 (years 2005-2010) for controlled clinical trials, meta-analyses or randomised controlled trials, that found four entries for corticosteroids and 20 entries for opioids. A further search for systematic reviews found only one review for corticosteroids, while there were 14 opioid reviews. The search was repeated in July 2011 (see Table 5 and 6) the corticosteroid entries remained unchanged while the opioid entries for the trials and meta-analyses had increased to 25, and the entries for systematic reviews had increased to 23.
Table 5: Controlled clinical trials or meta-analyses or randomised controlled trials of corticosteroids in palliative care

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Palliative care / or terminal care / or hospice care /or terminally ill/</td>
<td>53889</td>
</tr>
<tr>
<td>2</td>
<td>exp analgesics, opioid/</td>
<td>82802</td>
</tr>
<tr>
<td>3</td>
<td>exp adrenal cortex hormones/</td>
<td>307985</td>
</tr>
<tr>
<td>4</td>
<td>1 and 2</td>
<td>1848</td>
</tr>
<tr>
<td>5</td>
<td>1 and 3</td>
<td>402</td>
</tr>
<tr>
<td>6</td>
<td>limit 4 to (English language and yr = “2005–2010”)</td>
<td>501</td>
</tr>
<tr>
<td>7</td>
<td>limit 5 to (English language and yr = “2005–2010”)</td>
<td>70</td>
</tr>
<tr>
<td>8</td>
<td>limit 6 to (controlled clinical trial or meta-analysis or randomised controlled trial)</td>
<td>25</td>
</tr>
<tr>
<td>9</td>
<td>limit 7 to (controlled clinical trial or meta-analysis or randomised controlled trial)</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 6: Systematic reviews of corticosteroids in palliative care

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Palliative care / or terminal care / or hospice care /or terminally ill/</td>
<td>53889</td>
</tr>
<tr>
<td>2</td>
<td>exp analgesics, opioid/</td>
<td>82802</td>
</tr>
<tr>
<td>3</td>
<td>exp adrenal cortex hormones/</td>
<td>307985</td>
</tr>
<tr>
<td>4</td>
<td>1 and 2</td>
<td>1848</td>
</tr>
<tr>
<td>5</td>
<td>1 and 3</td>
<td>402</td>
</tr>
<tr>
<td>6</td>
<td>limit 4 to (English language and yr = “2005–2010”)</td>
<td>501</td>
</tr>
<tr>
<td>7</td>
<td>limit 5 to (English language and yr = “2000 –2010”)</td>
<td>70</td>
</tr>
<tr>
<td>8</td>
<td>limit 6 to (controlled clinical trial or meta-analysis or randomised controlled trial)</td>
<td>23</td>
</tr>
<tr>
<td>9</td>
<td>limit 7 to (controlled clinical trial or meta-analysis or randomised controlled trial)</td>
<td>1</td>
</tr>
</tbody>
</table>

While trials, meta-analyses and systematic reviews of corticosteroids are few, there are articles and editorials written since the early 1970s, which make consistent recommendations. For instance, literature suggests that there are advantages for using these drugs short-term, but long-term use may be questionable because of the adverse effect profile (Wooldridge, Anderson, Perry, & Smith, 2001). While individual areas of practice have improved, the approaches to rationalising therapy in this area have been ad hoc. Edwards and Elwyn
comment in “Evidence-based Patient Choice” that clinical practice and service delivery varies between countries, between services within those countries depending on geographical areas, and between clinicians within one team (Edwards & Elwyn, 2001).

Corticosteroids have been considered for the palliative therapy of terminal cancer since the late 1950s (Kaal & Vecht, 2004; Popiela et al., 1989; Weissman, 1988). Sweeney and Bruera suggest they were used anecdotally for many years as ‘general comfort drugs’, without real evidence to substantiate this use (Sweeney & Bruera, 2001). The evidence for actual doses of steroid use is poor and is often a matter of local practice and opinion (Ross, Walker, & Woods, 2005). Lockett’s book describing traditional medicine, uses the expression “Muddling through elegantly” and this may well apply to corticosteroid prescribing (Lockett, 1997).

Glucocorticosteroids (glucocorticoids), as mentioned above, affect carbohydrate and protein metabolism while mineralocorticosteroids (mineralocorticoids) affect water and electrolyte balance (Brunton, 2006; Rang et al., 2003). The prolonged use of glucocorticoids may induce diabetes, osteoporosis and mental disturbances, while the prolonged use of mineralocorticoids results in hypertension, sodium and water retention and potassium loss. The long term administration of glucocorticoids can lead to Cushing’s syndrome, a metabolic disorder, the effects of which may be central obesity, round ‘moon face’, supraclavicular, chest and abdominal fat pads, buffalo hump, muscle atrophy, oedema, decreased glucose tolerance, minor infections, which become systemic and long lasting, thinned skin, and a degree of emotional change (British Medical Association & Royal Pharmaceutical Association of Great Britain, 2006; Rang et al., 2003).

The consequences of Cushing’s syndrome can be of such significance, with respect to changes in physical appearance and emotional state, that patients and families suggest the results from long term use of corticosteroids are worse than the original indication the corticosteroid was prescribed for (Abbas, 2004; Hardy, 1998; Shafford, 2006; Sweeney & Bruera, 2001).

With synthetic corticosteroids it is possible to separate the mineralocorticoid adverse effects from the desirable glucocorticoid effects. However, the dilemma is to separate the wanted anti-inflammatory glucocorticoid effects from the
unwanted adverse effects (Rang et al., 2003). The drugs with the higher anti-inflammatory effects appear likely to have higher secondary adverse effect profiles with long-term use (Fernandez del Vallado, Gijonbanos, & Beltrangutierrez, 1964; Fuenfer, Olson, & Polk, 1975; Goodman & Gilman, 1975).

In Table 7 the equivalent doses of different corticosteroids, their glucocorticoid (anti-inflammatory potency) and mineralocorticoid (sodium retaining potency) activity and their duration of action are shown.

### Table 7: Relative potencies and equivalent doses of representative corticosteroids

<table>
<thead>
<tr>
<th>Compound</th>
<th>Anti-inflammatory Potency</th>
<th>Sodium Retaining Potency</th>
<th>Duration of Action</th>
<th>Equivalent Dose – ìmg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>1</td>
<td>1</td>
<td>S*</td>
<td>20</td>
</tr>
<tr>
<td>Prednisone</td>
<td>4</td>
<td>0.8</td>
<td>I*</td>
<td>5</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4</td>
<td>0.8</td>
<td>I*</td>
<td>5</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>5</td>
<td>0.5</td>
<td>I*</td>
<td>4</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>25</td>
<td>0</td>
<td>L*</td>
<td>0.75</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>25</td>
<td>0</td>
<td>L*</td>
<td>0.75</td>
</tr>
</tbody>
</table>

*S*: short biological half-life, 8 to 12 hours.
I*: intermediate biological half-life, 12 to 36 hours.
L*: long biological half-life, 36 to 72 hours.
Ø These dose relationships apply only to oral and intravenous administration, as glucocorticoid potencies may differ greatly following intramuscular or intra-articular administration.

Within the palliative care field internationally, when a corticosteroid is initiated, one of the following four corticosteroids tend to be prescribed: prednisone, methylprednisolone, dexamethasone or betamethasone. In the early international literature, the two drugs most commonly prescribed were the synthetic corticosteroids dexamethasone and methylprednisolone (Watanabe & Bruera, 1994). Currently, the medicine of preference internationally appears to be dexamethasone (Bruera et al., 2004; Davis, Khoshknabi, & Yue, 2006; Klepstad et al., 2005; Pilkey & Daeninck, 2008; Rajer & Kovac, 2008; Shafford, 2006; Shih & Jackson, 2007; Sturdza et al., 2008; Watanabe & Bruera, 1994).
Methylprednisolone in 2000 appeared to remain the corticosteroid of choice in France (Laval et al., 2000), while betamethasone is the drug of choice in Sweden and Japan (Lundstrom & Furst, 2006; Okishiro, Tanimukai, Tsuneto, & Ito, 2009). Although betamethasone is known to be more expensive than dexamethasone, its glucocorticoid action is identical and like dexamethasone it has no mineralocorticoid action (Brunton, 2006; Lundstrom & Furst, 2006).

For this study, the drugs researched were prednisone, methylprednisolone and dexamethasone as these medicines are the agents prescribed in palliative care in New Zealand and were those used in the sample hospices studied. Prednisone (a pro-drug) differs from methylprednisolone and dexamethasone as it is biologically inert. It is, however, readily and rapidly absorbed from the gastrointestinal tract and converted in the liver to its active metabolite, prednisolone (Sweetman, 2007). Prednisone and prednisolone are metabolically interconvertible (Begg, Atkinson, & Gianarakis, 1987).

All three corticosteroids are readily absorbed from the gastrointestinal tract and have similar plasma-half lives ranging from two to five hours (Ontjes, 1995). The term plasma half-life (drug half-life) refers to the time necessary to reduce the level of the drug in the plasma to half its initial value. The plasma half-life is different to the biological half-life, which is the time required for half the quantity of a drug deposited in a living organism to be metabolised or eliminated by normal biological process. From a treatment perspective, it is the biological half-life, which is considered of more importance. Whilst prednisone and methylprednisolone have similar biological half-lives of 12 to 36 hours dexamethasone has a longer biological half-life of 36 to 72 hours (Brunton, 2006).

It was previously common practice to give these medications in divided doses (up to four times daily) because of their short plasma half-life of only two to five hours. Evidence-based literature has since shown that the effective half-life is the considerably longer biological half-life and a single daily dose is sufficient (Palliative Care Expert Group, 2010; Turner & Elson, 1993; Twycross, 1994).

Martindale suggests, “The slower metabolism of the synthetic corticosteroids with their lower protein binding affinity may account for their increased potency compared with the natural corticosteroids.” Dexamethasone has a plasma protein
binding of 68 ± 3%, prednisone of 75 ± 2% and methylprednisolone 78 ± 3% (Hardman, Gilman, & Limbird, 1995).

These drugs are metabolised in the liver by the cytochrome P450 (CYP) group of enzymes and excreted renally (Sweetman, 2007; Wilcock et al., 2005). Their metabolism may be increased by drugs that induce (CYP) hepatic enzymes such as phenytoin, carbamazepine and phenobarbitone (Back, 2001; McGavock, 2003) and decreased by drugs that inhibit (CYP) hepatic enzymes, for example the fluconazole and fluoxetine (McGavock, 2003; Twycross & Wilcock, 2007). In 2005 a multicentre audit was conducted across palliative care centres in the United Kingdom, to study the potential drug-drug interactions involving cytochrome P450 enzymes. Twenty four interactions were discussed in this study and, of those, twelve were associated with corticosteroids (dexamethasone and prednisolone) (Wilcock et al., 2005).

Table 8 shows twelve potentially concerning drug-drug interactions of dexamethasone and prednisolone.

**Table 8:** Showing clinically important drug-drug interactions involving P450 dexamethasone and prednisolone

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug Combination</th>
<th>Drug Effects Decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important</td>
<td>Dexamethasone and phenytoin</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Potentially important</td>
<td>Dexamethasone and temazepam</td>
<td>Temazepam</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone and amitriptyline</td>
<td>Amitriptyline</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone and fentanyl</td>
<td>Fentanyl</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone and quinine</td>
<td>Quinine</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone and simvastatin</td>
<td>Simvastatin</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone and tacrolimus</td>
<td>Tacrolimus</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone and zopiclone</td>
<td>Zopiclone</td>
</tr>
<tr>
<td></td>
<td>Prednisolone and diazepam</td>
<td>Diazepam</td>
</tr>
<tr>
<td></td>
<td>Prednisolone and amlodipine</td>
<td>Amlodipine</td>
</tr>
<tr>
<td></td>
<td>Prednisolone and fentanyl</td>
<td>Fentanyl</td>
</tr>
<tr>
<td></td>
<td>Prednisolone and trazadone</td>
<td>Trazadone</td>
</tr>
<tr>
<td></td>
<td>Prednisolone and zopiclone</td>
<td>Zopiclone</td>
</tr>
</tbody>
</table>

Adapted from Wilcock et al. (2005)
Figure 4 shows the chemical structures of hydrocortisone, prednisone, methylprednisolone and dexamethasone. This figure shows the basic similarity of the molecules and indicates the points where they differ.

**Figure 4:** The chemical structures of hydrocortisone, prednisone, methylprednisolone and dexamethasone

- **Hydrocortisone**
- **Prednisone**
- **Methylprednisolone**
- **Dexamethasone**

Adapted from Sweetman (2007)

Hydrocortisone, the first of these structures, is a naturally occurring corticosteroid with glucocorticoid and, to a lesser extent, mineralocorticoid activity. It is the most important of the predominantly glucocorticosteroids secreted by the adrenal cortex (Sweetman, 2007). Prednisone, methylprednisolone and dexamethasone are synthetic derivatives of hydrocortisone (Ontjes, 1995).

Prednisone has an additional double bond at C1, 2 leading to a four-fold increase in glucocorticoid activity relative to hydrocortisone and decreased sodium-retaining activity. Methylprednisolone has a double bond at C 1, 2 and an additional 6 alpha methyl group, which enhances the glucocorticoid activity five-fold and further decreases the mineralocorticoid activity. Dexamethasone has the double bond, a 16 alpha methyl group and an additional fluoride atom at C9 giving it approximately 25 times the glucocorticoid activity of hydrocortisone with no sodium-retaining effects (Brunton, 2006; Ontjes, 1995; Rang et al., 2003; Sweetman, 2007). These changes in structure give rise to the differences in their anti-inflammatory action.
In the 1990s, methylprednisolone was widely used in palliative care but dexamethasone later became the drug of choice (Kiani et al., 2011; Watanabe & Bruera, 1994). Possible reasons for this may include the availability of an oral preparation of dexamethasone and lower cost. However, the more likely reasons were its longer duration of action, lack of mineralocorticoid effect and the observation that its glucocorticoid activity was considerably higher than methylprednisolone. Therefore, the anti-inflammatory effect was enhanced (Brunton, 2006; Watanabe & Bruera, 1994).

Some palliative care centres continue to use methylprednisolone when patients are unable to swallow and a high dose parenteral form is required in the short term. A swap is then made to dexamethasone once the patient is able to ingest oral medications. The main reason for using parenteral methylprednisolone appears to be the smaller injection volume.

Table 9, 10 and 11 demonstrate the availability of these agents in New Zealand and the level of subsidy they attract.

**Table 9: Prednisone availability in New Zealand**

<table>
<thead>
<tr>
<th>Prednisone</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet 1mg</td>
<td>Fully funded</td>
</tr>
<tr>
<td>Tablet 2.5mg</td>
<td>Fully funded</td>
</tr>
<tr>
<td>Tablet 5mg – Also available up to 30 tablets on a Practitioners Supply Order (PSO)</td>
<td>Fully funded</td>
</tr>
<tr>
<td>Tablet 20mg</td>
<td>Fully funded</td>
</tr>
</tbody>
</table>

Reproduced from PHARMAC Schedule August 2011

**Table 10: Methylprednisolone availability within New Zealand**

<table>
<thead>
<tr>
<th>Methylprednisolone</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet 4mg 100mg</td>
<td>Fully funded</td>
</tr>
<tr>
<td>Injection (Methylprednisolone Sodium Succinate) 40mg/ ml, 1ml, 62.5mg/ml, 2ml, 500mg, 1g</td>
<td>Fully funded</td>
</tr>
</tbody>
</table>

Tablets and injections must be recommended by a specialist.

Reproduced from PHARMAC Schedule August 2011
Table 11: Dexamethasone availability within New Zealand

<table>
<thead>
<tr>
<th>Dexamethasone</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet 1mg and 4mg</td>
<td>Fully funded</td>
</tr>
<tr>
<td>Oral liquid 1mg/ml</td>
<td>Fully funded</td>
</tr>
<tr>
<td>Injection Dexamethasone Sodium Phosphate 4mg/ml 1ml, 2ml</td>
<td>Fully funded</td>
</tr>
</tbody>
</table>

Tablets must be recommended by a specialist.

Liquid must be written by a paediatrician or paediatric cardiologist or on the recommendation of a paediatrician or paediatric cardiologist.

The Injection is only available on a Medical Practitioner’s Supply Order (MPSO).

Dexamethasone can be administered by the subcutaneous route, which is an effective and convenient alternative route.

Reproduced from PHARMAC Schedule August 2011

Table 12 shows the main indications for dexamethasone prescribing in palliative care. Recommended doses are included in this table

<table>
<thead>
<tr>
<th>Indications</th>
<th>Dexamethasone Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-specific / ‘general wellbeing’</td>
<td></td>
</tr>
<tr>
<td>Appetite stimulation</td>
<td>2-4mg daily</td>
</tr>
<tr>
<td>Increase sense of well being</td>
<td></td>
</tr>
<tr>
<td>Anti-emetic</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>Shortness of breath</td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td></td>
</tr>
<tr>
<td>Raised intracranial pressure</td>
<td>Up to 16mg daily</td>
</tr>
<tr>
<td>Cerebral tumours</td>
<td>Up to 16mg daily</td>
</tr>
<tr>
<td>Spinal cord compression</td>
<td>Up to 16mg daily</td>
</tr>
<tr>
<td>Nerve compression or infiltration</td>
<td>4-8mg daily</td>
</tr>
<tr>
<td>Capsular stretching</td>
<td></td>
</tr>
<tr>
<td>Liver metastases</td>
<td>4-8mg daily</td>
</tr>
<tr>
<td>Other visceral metastases</td>
<td>4-8mg daily</td>
</tr>
<tr>
<td>Soft tissue infiltration</td>
<td></td>
</tr>
<tr>
<td>Head and neck tumours</td>
<td>4-8mg daily</td>
</tr>
<tr>
<td>Abdominal and pelvic tumours</td>
<td>4-8mg daily</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>4-8mg daily</td>
</tr>
</tbody>
</table>

Adapted from Ross et al. (2005) p. 21

‘General wellbeing’ is a traditional term used for corticosteroid prescribing for non-specific indications. Throughout this study, the terms non-specific and ‘general wellbeing’ are interchangeable and describe the group of symptoms placed under these headings. ‘General wellbeing’ should not be perceived as a perception of the reduction of the severity of the reasons why a corticosteroid is prescribed for these symptoms.
1.6: Review of evidence for the use of corticosteroids

1.6.1: Corticosteroids are potent drugs

Goodman and Gilman suggest that with the exception of replacement therapy in deficiency states, the use of glucocorticoids is largely empirical and based only on extensive clinical experience. Because of the number and the severity of side-effects, the decision to start corticosteroids needs to be carefully considered. Some authors suggest that an appropriate dose is achieved by trial and error (Brunton, 2006). The adverse effects from the use of corticosteroids, such as muscle weakness, insomnia and oral candidiasis, may mirror the symptoms of cancer patients with advanced disease, and are therefore not always recognised (Bruera, 1993).

Internationally, the percentage of palliative care patients prescribed corticosteroids ranges from as low as 32%, to a high, in one study of 80% (Gannon & McNamara, 2002; Hanks, Trueman, & Twycross, 1983; Hardy, 1998; Kiani et al., 2011; Klepstad et al., 2005; Lundstrom & Furst, 2006; Matsuo et al., 2011; S Mercadante, Fulforo, & Casuccio, 2001a; Nauck et al., 2004; Needham, Daley, & Lennard, 1992; Pilkey & Daeninck, 2008; Shafford, 2006). Concern has been raised that the prescribing of corticosteroids in palliative care has become casual rather than their use being closely monitored for specific indications (Lundstrom & Furst, 2006).

The Palliative Care Formulary Edition Three (PCF3) points out in a table of indications for the use of corticosteroids in advanced cancer, that inclusion does not necessarily mean that a corticosteroid is the treatment of choice (Twycross & Wilcock, 2007).

1.6.2: Corticosteroids are commonly and frequently prescribed in palliative care for non-specific reasons

Corticosteroid use for specific reasons short-term such as spinal cord compression or bowel obstruction is supported by weak though sometimes inconclusive evidence (Loblaw, Perry, Chambers, & Laperriere, 2005; Sebastiano Mercadante, Casuccio, & Mangione, 2007). However, controversy has been expressed about their non-specific use (Lundstrom & Furst, 2006), the most common indication for their prescribing, since there appears to be little robust
evidence to support this use, although some earlier studies suggest some positive results.

When a corticosteroid is prescribed for non-specific reasons, it appears that the consequences of prescribing it are often not considered. Robert Twycross asks in ‘Pain relief in advanced cancer’: “Is using a corticosteroid a fashion rather than a science?” (Twycross, 1995). The choice of using a corticosteroid can be arbitrary: is it habit, cost, availability or a case of not knowing what else to try? An example is the long-term use of potent glucocorticoids for cachexia and anorexia when there is a well documented alternative in megestrol acetate, which although a corticosteroid, has only slight glucocorticoid properties (Lipman et al., 2000; McHugh & Miller-Saultz, 2011; Sweetman, 2007). Twycross goes on to say that a study by Wilcox et al. in 1986 showed there was a 50% response to placebo.

By 2006, the view was held that the use of corticosteroids for non-specific symptoms (e.g. appetite loss, nausea, fatigue, pain, shortness of breath or poor wellbeing) had clinical experiential support with positive short-term results but this benefit seldom lasted more than four weeks.

This was not a new view – Bruera in 1993 had written that corticosteroids were able to produce an increase in appetite but the effect was short-lived. His paper commented that Moertel et al. in 1974 found in their study a significant difference in appetite and strength after two weeks of dexamethasone but the improvement was no longer there after four weeks (Bruera, 1993; Moertel, Schutt, Reiteneier, & Hahn, 1974). In contrast, Lundstrom & Furst claim that patients in their surveys of the use of corticosteroids in palliative care in Sweden had positive results beyond four weeks (Lundstrom & Furst, 2006).

It could be argued there are alternatives to corticosteroids in treating cachexia and anorexia, which may include treating the underlying cause, giving dietary advice and perhaps a glass of wine prior to meals (Lipman et al., 2000). A Cochrane review published in 2010: “Pharmacological treatments for fatigue associated with palliative care” remarked that although corticosteroids were frequently prescribed for fatigue in palliative care there was a lack of research studies supporting this use (Peuckmann, Elsner, Krumm, Trottenberg, & Radbruch, 2010).
1.6.3: Corticosteroid benefits may be short-term

A clear plan is needed when corticosteroids are being administered. Regular monitoring of response leading on to dose adjustment is essential. The suggested prescribing of these medicines is for the shortest time frame, and at the lowest effective dose, although some would suggest starting with a high dose to prevent missing a beneficial response, then adjusting the dose down when this is achieved (Twycross, 1992). If corticosteroids are of no benefit, then they should be discontinued (Matsuo et al., 2011; Wooldridge et al., 2001).

The benefits of the use of high dose corticosteroids in the dying patient is perhaps controversial, but may have a profound effect on the end of life symptoms and perceptions of both patient and family in terms of hope and psychological wellbeing even if short term. Lundstrom and Furst suggest that: “Reduced symptoms contribute to feelings of normalising life, symbolising hope. This should be addressed when communicating goals of treatment and care with the patient and family” (Lundstrom, Furst, Friedrichsen, & Strang, 2009).

1.6.4: Corticosteroid adverse effects

The following page (p. 27) contains photographs of two palliative care patients before and after the commencement of high-dose corticosteroids. Both show adverse effects from long-term use. These two patients are representative of many seen by the researcher and a catalyst for this study to be undertaken. The photographs have been included with the permission of their families.
**Figure 5:** Christine before corticosteroids

**Figure 6:** Christine seated left

**Figure 7:** Christine after corticosteroids

**Figure 8:** Emily before corticosteroids

**Figure 9:** Emily after corticosteroids
The literature suggests that 50 to 75% of patients prescribed corticosteroids for more than three weeks will have adverse effects (Kiani et al., 2011; Shafford, 2006; Weissman, 1988).

In long-term therapy, the adverse effects of treatment may be greater than the disease symptoms being treated (Berman, 2011; British Medical Association & Royal Pharmaceutical Association of Great Britain, 2006). Prescribers should be aware of these adverse effects and have a plan in place (Abbas, 2004; Shafford, 2006).

With the increasing malaise of the palliative care patient, adverse effects from the use of corticosteroids may not be recognised, seen as a problem or recorded but, instead, considered part of the dying process (Bruera, 1993; Hardy, 1998; Lundstrom & Furst, 2006).

The literature suggests adverse effects are not necessarily due to long-term use (Batchelor, Taylor, Thaler, Posner, & DeAngelis, 1997). These adverse effects of corticosteroids appear to be underestimated. Lundstrom and Furst commented that two-thirds of the respondents in a survey on the use of corticosteroids in Swedish palliative care did not perceive adverse-effects related to the treatment of corticosteroids as a problem, which raised a question of those physicians’ ability to judge adverse effects. In addition, the different medical specialties in this review responded differently (Lundstrom & Furst, 2006).

Vecht et al. in their randomised study in 1994 on the treatment of brain tumour oedema suggested that adverse effects were dose-related: the higher the dose given the more adverse effects. In this study, the same symptom relief was obtained by a lower dose and the necessity to use a high dose was questionable (Vecht, Hovestadt, Verbiest, van Vliet, & van Putten, 1994). A further paper supporting this study suggested a low dose corticosteroid should be prescribed where possible for brain oedema, to minimise adverse effects and that high doses should be used in emergencies only (Kaal & Vecht, 2004).

1.6.5: Corticosteroids and divided doses

Patients are often still administered divided daily doses (more than one dose in a 24 hour period) of corticosteroids despite literature showing that the long biological half-lives of these drugs allows a once a day dose (Palliative Care
Expert Group, 2010; Turner & Elson, 1993; Twycross, 1994). Sleeplessness can be the result of a patient receiving a final dose of corticosteroids in the evening.

A hypnotic may then be administered to counteract this effect. Zopiclone or temazepam are often prescribed despite literature suggesting corticosteroids render these sedatives less effective (Hesse, Von Moltke, & Greenblatt, 2003; Wilcock et al., 2005).

1.6.6: Concurrent medicines

Three medicines commonly prescribed in palliative care with corticosteroids are omeprazole, a proton pump inhibitor prescribed to protect the gastrointestinal tract from haemorrhage, phenytoin an anticonvulsant and zopiclone a hypnotic.

*Omeprazole/Corticosteroid co-prescribing*

Omeprazole is frequently prescribed for gastrointestinal tract protection when a patient is commenced on a corticosteroid. The literature suggests there is no valid reason for this. Conversely, the literature does advocate that if the same patient has an NSAID added to a corticosteroid regime, gastrointestinal tract protection is essential (Shafford, 2006). The prescribing of the combination of corticosteroid and NSAID is frequent in palliative care and has a four to fifteen fold increased risk of peptic ulcer (Abbas, 2004; Kiani et al., 2011; Twycross & Wilcock, 2007).

*Phenytoin/Corticosteroid co-prescribing*

In palliative care, phenytoin is one of the most commonly prescribed anticonvulsants for patients newly diagnosed with primary or secondary brain tumours. It is often co-prescribed with a corticosteroid (particularly dexamethasone). As discussed previously on pages 16 and 17, corticosteroids are metabolised in the liver by the cytochrome P450 (CYP) group of enzymes (Sweetman, 2007; Wilcock et al., 2005). Their metabolism may be increased by drugs that induce (CYP) hepatic enzymes or decreased by drugs that inhibit CYP enzymes.

Phenytoin is widely known as an enzyme inducer, accelerating the metabolism of the dexamethasone it is co-prescribed with, resulting in reduced dexamethasone levels and suboptimal dose (Back, 2001; Twycross, 1994; Wilcock et al., 2005). In more recent years, there has been added evidence suggesting phenytoin and
dexamethasone may mutually lower each other’s efficacy, thus it is not only the corticosteroid dose that may be suboptimal (Baxter, 2008; Rossi, 2009; Ruegg, 2002). These drugs though frequently co-prescribed are not considered optimal in combination and an alternative anticonvulsant should be initiated (Ruegg, 2002).

Table 13 identifies the specific CYP 450 enzymes that can affect the relative metabolism of corticosteroids and phenytoin when they are co-prescribed.

**Table 13: Examples of these inducers, and substrates of the CYP 450 group of isoenzymes**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Inducer</th>
<th>Substrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenytoin</td>
<td>CYP3A4</td>
<td>CYP2C19</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>CYP3A4</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td></td>
<td>CYP3A4</td>
</tr>
<tr>
<td>Prednisone</td>
<td>CYP2C19</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Australian Medicines Handbook (2009)

**Zopiclone/Corticosteroid co-prescribing**

Zopiclone, mentioned in section 1.6.6, is one of the hypnotics of choice in palliative care but like corticosteroids is also metabolised in the liver by the cytochrome P450 (CYP) group of enzymes, CYP3A4 substrate. Zopiclone’s potency is reduced when prescribed concurrently with dexamethasone (Wilcock et al., 2005).

**1.6.7: Withdrawal of corticosteroids**

Withdrawal of corticosteroids should be decided on a case-by-case basis. The use of corticosteroids suppresses the natural function of the adrenal cortex, which requires time to return to normal function. If a patient has been on corticosteroids for more than three weeks, the corticosteroid must be reduced gradually to allow the adrenal glands to recover and not cause an adrenal crisis. Severe adrenal crisis can result in death (Kaal & Vecht, 2004; Swartz & Dluhy, 1978; Twycross, 1994). When the reducing medication reaches physiological doses (equivalent to prednisone 7.5mg) the reduction needs to be slower still e.g. 1 to 2mg per week (British Medical Association & Royal Pharmaceutical Association of Great Britain, 2006; Twycross & Wilcock, 2007).

Table 14 illustrates the doses above which adrenal suppression is likely.
Table 14: Doses above which adrenal suppression is possible

<table>
<thead>
<tr>
<th>Drug</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>20 to 30mg</td>
<td>15 to 25mg</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>7.5 to 10mg</td>
<td>7.5mg</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>1 to 1.15mg</td>
<td>1mg</td>
</tr>
</tbody>
</table>

Source: Twycross & Wilcock (2007)

There is confusion in the literature around stopping corticosteroids when a patient is in the terminal phase of life and is no longer swallowing. The Palliative Care Formulary (PCF3) advocates that if a patient is dying and can no longer swallow, it is generally acceptable to stop corticosteroids abruptly (Twycross & Wilcock, 2007). The length of time the patient has been on the corticosteroid appears not to be a consideration. In contrast, others would suggest that though ‘unnecessary’ drugs may be discontinued when a patient is dying, key drugs should be switched to a parenteral route and continued. Corticosteroids can be regarded as key drugs and cessation may cause adrenal crisis.

There are parenteral formulations for both commonly used corticosteroids, therefore stopping for the reason given ‘there is no longer an oral route’ is not justifiable and could be considered unethical. Abrupt cessation of a corticosteroid could exacerbate terminal restlessness and in turn may hasten death (Anonymous, 1995; British Medical Association & Royal Pharmaceutical Association of Great Britain, 2006; Gannon, 2001; Hardy et al., 2001; Rousseau, 2004). Gannon would suggest that instead of stopping these medicines. “There is a rationale for increasing corticosteroids in the terminal phase (to match physiological response)” (Gannon, 2001).

1.7: The need for more effective corticosteroid guidelines in palliative care

Corticosteroids are potent medicines and have been commonly prescribed in palliative care without guidelines. It is important to develop corticosteroid prescribing guidelines to curb the potential for haphazard prescribing (Shafford, 2006). These guidelines need to be evidence-based to ensure the best outcome for the patient with minimum adverse effects (Lundstrom & Furst, 2006). The guidelines must to be easy to follow, clinically relevant, comprehensive, and
flexible for busy clinicians. It appeared that, until recently, few guidelines in circulation were evidence-based (Greenhalgh, 2006).

Guidelines for corticosteroids have been slow to develop. In 2007 when this study commenced, there were only two sets of guidelines for corticosteroid use in palliative care listed at www.palliativedrugs.com a website that provides comprehensive and independent information for health professionals about drug usage in palliative care.

These were:

1. Guidelines written in 2002 by Gannon, The Princess Alice Hospice, Esher, UK. These guidelines were unreferenced.

2. Guidelines written in 2004 by Jerram, St Barnabas Hospice, Worthing, UK. These included: audit results, a draft revised steroid guidelines sheet and revised steroid guidelines. These guidelines were referenced.

Although there were variations, both sets of guidelines recommended doses of dexamethasone (the stated medicine of choice) within the range of doses recommended in most standard palliative care texts of the time (Back, 2001; Twycross & Wilcock, 2001).

In practice internationally at that time corticosteroid guidelines were few, and decisions on doses appeared to be empirical (British Medical Association & Royal Pharmaceutical Association of Great Britain, 2006).

As of 2009, there were four sets of referenced corticosteroid guidelines listed on palliative drugs.com, two of which have additional steroid proforma charts:

1. Guidelines updated in 2008 by Gannon, The Princess Alice Hospice, Esher, UK. They include a proforma sheet endorsed by Harris Hospice Care, The Princess Alice Hospice, Guy’s and St Thomas’ NHS Foundation Trust and St. Christopher’s Hospice (Appendix A).

2. Guidelines written in 2004 by Jerram, St Barnabas Hospice, Worthing, UK. These include: audit results, a draft revised steroid guidelines sheet and revised steroid guidelines. They are the same guidelines as listed in 2007. Gannon’s and Jerram’s choice of dexamethasone, indications for use and dose remain the same as listed in 2007.
3. Undated guidelines written by Murray, Wigan and Leigh Hospice, Lancashire: UK. They include a proforma sheet.

4. Guidelines written in 2008 by Husbands, Pan Birmingham Palliative Care Network UK.

Gannon’s indications and suggested doses for the prescribing of dexamethasone are summarised in Table 15 as an example of the four sets of United Kingdom guidelines found on the palliativedrugs.com website.

**Table 15: Gannon’s indications and suggested doses**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Starting daily dose of dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>2mg to 4mg</td>
</tr>
<tr>
<td>To improve wellbeing/mood</td>
<td></td>
</tr>
<tr>
<td>Weakness</td>
<td></td>
</tr>
<tr>
<td>Non-specific pains</td>
<td></td>
</tr>
<tr>
<td>Nerve compression pain</td>
<td>4mg to 8mg</td>
</tr>
<tr>
<td>Liver capsule pain</td>
<td></td>
</tr>
<tr>
<td>As an anti-emetic</td>
<td></td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td></td>
</tr>
<tr>
<td>To combat post radiation inflammation</td>
<td></td>
</tr>
<tr>
<td>Raised intracranial pressure</td>
<td>12mg to 16mg</td>
</tr>
<tr>
<td>Superior vena cava obstruction</td>
<td></td>
</tr>
<tr>
<td>Carcinomatosis lymphangitis</td>
<td></td>
</tr>
<tr>
<td>Malignant spinal cord compression</td>
<td></td>
</tr>
</tbody>
</table>

From the Corticosteroid Guidelines: The Princess Alice Hospice, Esher, United Kingdom

Table 16 is an extract from a New Zealand corticosteroid guideline. It appears on the www.healthpoint.co.nz website for general practitioners and health professionals and is a resource provided (for guidance only) by The Mercy Hospice in Auckland, New Zealand (Appendix B).
Table 16: Indications and suggested doses from a New Zealand corticosteroid guideline

<table>
<thead>
<tr>
<th>Indications</th>
<th>Suggested daily dose of dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved general wellbeing and appetite (say, two week course)</td>
<td>4mg (Equivalent to 25mg of prednisone)</td>
</tr>
<tr>
<td>Maintenance of symptoms controlled initially on higher doses</td>
<td></td>
</tr>
<tr>
<td>Nerve compression pain (at times may warrant a higher dose)</td>
<td>8mg</td>
</tr>
<tr>
<td>Bone pain (at times may warrant a higher dose)</td>
<td></td>
</tr>
<tr>
<td>Spinal cord compression</td>
<td>16mg</td>
</tr>
<tr>
<td>Raised intracranial pressure</td>
<td></td>
</tr>
<tr>
<td>Superior vena cava obstruction</td>
<td></td>
</tr>
<tr>
<td>Tracheal/bronchial compression</td>
<td></td>
</tr>
<tr>
<td>Pulmonary lymphangitis</td>
<td></td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td></td>
</tr>
</tbody>
</table>

From the www.healthpoint.co.nz website

Although there are variations, the New Zealand guideline indications and suggested doses for dexamethasone do not differ greatly from those found on palliative drugs.com. This is not surprising as many of the New Zealand guidelines have been adapted from those found on this website.

Guidelines advise that a corticosteroid should be stopped after five to seven days if there is no symptomatic relief, and that patients must be monitored and reviewed regularly and watched closely for adverse effects (Hardy et al., 2001; S Mercadante, Fulfaro, & Casuccio, 2001b; Needham et al., 1992; Twycross, 1992). Treatment, which is longer than three weeks (some guidelines state two weeks) with doses over 4mg of dexamethasone (or an equivalent dose of an alternative corticosteroid) must be titrated down carefully to avoid withdrawal symptoms and the threat of adrenal crisis (Shafford, 2006). When prescribed long-term, these medicines must not be stopped abruptly.

Despite the presence of guidelines, patients are frequently started on a corticosteroid without knowing why it has been commenced or knowing how long it is to be continued. Equally, a patient may be continued on a corticosteroid long-term, without review, and the prescribing questioned only on the renewal of a prescription, if at all (Abbas, 2004; Twycross, 1994).
Patients’ lack of compliance or misunderstanding can lead to an abrupt cessation of treatment when a prescription runs out. There may be an assumption that the course finishes with an empty bottle. It is important that patients are counseled about their corticosteroid use and are aware of, and able to recognise, adverse effects (Shafford, 2006). This situation can be worsened by inadequate communication between a specialist service and the patient’s general practitioner. Unsupervised maintenance doses should be avoided where possible as their reviewing may then be easily missed (Gannon & McNamara, 2002).

It is important to record in a patient’s notes the reason for starting a corticosteroid and the doses used. This is not always the case, as was found in one hospice ‘snapshot’ of corticosteroid prescribing conducted by Helman in 2007 (personal correspondence). There appeared to be no guidelines for the choice of corticosteroid. Doses seemed to be chosen based on uncontrolled anecdotal reports, and clinical experience, to meet what appeared to be the individual patient’s needs.

Ineffective reviewing and monitoring, with no stop date for a corticosteroid, is common. Lack of, or inadequate documentation in patient notes, may lead to confusion as to why a corticosteroid is started and why a particular dose is prescribed (Gannon & McNamara, 2002).

Hardy and colleagues suggested in 2001 that if steroids were prescribed according to guidelines, and patients were closely monitored, the beneficial effects of corticosteroids would outweigh the adverse effects (Hardy et al., 2001).

1.8 Summary of introduction

The introduction of this thesis deals with the historical and international perspectives of palliative care, evidence-based practice and ‘modern’ palliative care. Issues have been discussed in the context of the development of the evidence-based and palliative care disciplines. To work effectively within palliative care, the processes, aims and outcomes of evidence-based medicine must sit comfortably with the palliative care community.

There has been tension between those in the palliative care field who insist that rigorous research is essential for the credibility of the speciality moving forward, and those who believe that the dying patient must be protected at all costs.
Because of the vulnerability of the population involved, clinical trials have been few. Clinical trials must meet the needs of the palliative care patient, families and carers to be acceptable.

Corticosteroids are ‘old’ medicines, they have been prescribed since the late 1950s. Corticosteroids are commonly prescribed as adjuvant analgesics for patients in palliative care. They are potent medicines with frequent adverse effects and while the intent is to achieve beneficial results for the patient, the consequences of long-term use may deny this objective. Currently there have been few randomised controlled trials of corticosteroids in palliative care, nevertheless there are numerous publications voicing caution and concern about the haphazard use of these medicines.

The synthetic corticosteroids principally used in palliative care internationally are prednisone, dexamethasone, methylprednisolone and betamethasone. Because of their different chemical structures, some corticosteroids have stronger glucocorticoid properties than others. The stronger the glucocorticoid properties the more effective the anti-inflammatory effect, but the greater likelihood of adverse effects.

They all have long biological half-lives, particularly dexamethasone and betamethasone, so they may be given as a once a day dose, early in the day. The corticosteroid of choice internationally appears to be dexamethasone, which, like betamethasone, has the highest anti-inflammatory properties. There is literature supporting this choice and suggesting that 32% to 80% of all patients in a palliative care service will have at least one course of corticosteroids.

A number of studies and guidelines advise that if corticosteroids show no benefit they should be stopped before adverse effects occur, but a course taken for longer than three weeks (some guidelines suggest two weeks) should be reduced gradually and not stopped abruptly. A patient still on long-term corticosteroids in their terminal phase of life and no longer able to swallow should have a route change to continue these essential medicines. An abrupt cessation at this time may lead to adrenal suppression with an increase in terminal restlessness.

Because of their metabolism by the CYP 450 enzymes, they are involved in a significant number of drug-drug interactions. Adverse effects are not always
recognised as corticosteroid in origin but instead the assumption may be that they are part of the dying process.

The researcher, as a clinician working in palliative care, was alarmed at the concerns voiced by several palliative care patients who became Cushingoid after the prescribing of corticosteroids. The Cushingoid effects were sometimes considered worse than the reason the corticosteroid was prescribed for initially. Some dying patients and their families struggled to cope with these additional physical and mental changes.

These concerns prompted the researcher to consider a research study examining the current use of corticosteroids in palliative care. Initially, an international study was felt to be desirable, to compare and contrast New Zealand practice with that of other countries. After considering the pros and cons of this approach, a study based in New Zealand hospices emerged as being more feasible. In the context of the findings from international literature, the study sought to examine not only the current practices concerning the prescribing of these medicines, but also the influences on that prescribing. The following aims and objectives for the study were determined.

1.9 Research aim and objectives

The overall aim of this study is to explore and clarify the reasons for the prescribing of corticosteroids in palliative care in New Zealand. The aim can be summarised in the following research questions:

- Why are corticosteroids prescribed in palliative care?
- How are corticosteroids prescribed in palliative care?
- How are corticosteroids monitored and reviewed in palliative care?

Specific objectives include the identification of which corticosteroids are most commonly prescribed and the indications and doses for their use. In addition, the research seeks to determine whether guidelines are being followed, and to evaluate how these medicines are reviewed and monitored. This will be achieved by exploring clinicians’ practice and expectations of the use of corticosteroids in the palliative care setting, and by measuring the extent, type and perceptions of corticosteroid use in palliative care and comparing this with existing literature.
The research was conducted in two ‘Phases’. Phase One was a retrospective review of corticosteroid prescribing in selected New Zealand hospices, while Phase Two consisted of semi-structured interviews with key informants to determine influences on prescribing.
Chapter 2 Methods: Phase One

2.1: Purpose of Phase One
The overall purpose of Phase One of this study was to elucidate how corticosteroids are prescribed in New Zealand. The specific objectives were to record the choice of corticosteroid, the duration of corticosteroid course, and the doses prescribed. In addition, the study sought to document the factors considered when stopping these medicines, to determine if adverse effects were recorded, and to document whether their prescribing was monitored and reviewed. This was accomplished by undertaking a retrospective review of corticosteroid prescribing and the management of corticosteroid usage in a selected number of New Zealand hospices over a defined period. The calendar year 2007 was chosen as the defined period.

2.2: Ethics approval
Because this research was to be conducted over more than one region in New Zealand, ethics approval was required to be given by the Multi-regions Ethics Committee. This was applied for and granted in July 2008 (Appendix C).

2.3: Sampling considerations
2.3.1: Hospices
Throughout New Zealand, in 2007, there were 32 hospices. In consultation with a biostatistician, a sample of six hospices (approximately one hospice in five) was considered sufficient to give a credible representation and an accurate ‘snapshot’ of the corticosteroid prescribing of the time. The rationale for choosing the particular sample hospices was to have a balance of larger urban and smaller rural hospices thus gaining a cross section of corticosteroid prescribing across New Zealand hospices. In choosing the particular hospices, consideration was also given to how much travelling was realistic in the timeframe available. Of the six hospices chosen, two were large city hospices, two served a large city and regional areas, and two were smaller city hospices with a rural catchment, all in the North Island of New Zealand.

Once Ethics approval was received the selected hospices were sent two letters of invitation, one to the Chief Executive Officer, a second to the Medical Director
This correspondence was followed by a phone call to the hospices from the researcher a week later. All hospices accepted the invitation and each was allocated a number from one to six for confidentiality purposes. Individual patient consent forms were not required for this research.

2.3.2: Time frame

A one-year period was considered a reasonable and sufficient time frame for data collection. The year 2007 (January 1st to December 31st) was chosen as the most recent full year of patient data.

2.3.3: Numbers of patients

Initially, the plan was to include all patients from the sample of six hospices who had been prescribed a course of the corticosteroids in the defined period. A trial was conducted to ascertain whether there were sufficient numbers to make an acceptable sample size. The hospice chosen for this trial was the researcher's home hospice. This hospice also went on to be used as a trial of the database for the retrospective study but was excluded from the six sample hospices because of the close working relationship the researcher had with this hospice.

The trial hospice had 450 patients both as inpatients and outpatients, for the year 2007. The plan was to check every third set of notes (150 in total) to find the proportion of patients who had been prescribed corticosteroids. Of the 150 patients, 74 had been prescribed corticosteroids (49%). During this trial, obtaining information on patients who had never had an in-house hospice admission was very time consuming. The accuracy of the information was doubtful because outside practitioners had treated these patients off-site and their records were not always available. The plan moved to only include those patients who had been admitted in to a hospice, 250 in total in the case of the trial hospice.

In consultation with the biostatistician, a further study was completed to confirm the percentage of in-patients on corticosteroids in the overall investigation. One in three inpatient notes were reviewed, and those on corticosteroids were separated. Thirty-nine (47%) of these patients had been prescribed corticosteroids. Once the trial was completed, the resultant figures were sent to the biostatistician for consideration of what was an acceptable sample size for the research project to continue, however a decision on sample size was not made at
this time. Discussion continued on a credible sample size, and included whether all inpatients on corticosteroids should be reviewed, or whether a one in two or one in three sample was sufficient.

Hospice 1 was chosen as the first hospice to be visited to obtain an understanding of the required sample size. The plan as stated in the trial prospectus was to isolate the patients who had had hospice admissions for that year (January 1\textsuperscript{st} to December 31\textsuperscript{st} 2007), then to check every third patient’s medication charts to discover if they had been prescribed a course (or courses) of the selected corticosteroids (prednisone, dexamethasone or methylprednisolone) in that year. Those figures, as in the previous trial, were forwarded to the biostatistician for advice on the sample size of the study. In consultation, it was decided that all inpatient notes should be reviewed to discover whether corticosteroids had been prescribed. Then, taking those who had been prescribed corticosteroids, entering every third patient on the database would give sufficient numbers for validity.

2.3.4: Sample size calculations

Six hospices were chosen from the 32 hospices in New Zealand to give an estimated sample size of 1250 inpatients from which to calculate the proportion on corticosteroids. From those patients identified as being prescribed corticosteroids (estimated 625), the records of a sample of one-third of patients (estimated 210) were studied in detail.

Table 17 below demonstrates the precision of estimates of the percentage of hospice in-patients prescribed corticosteroids and those prescribed corticosteroids with reviews based on these sample sizes:

<table>
<thead>
<tr>
<th>Table 17: Precision estimates based on sample sizes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of inpatients in sampled hospices</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>1250</td>
</tr>
<tr>
<td>Number of inpatients prescribed corticosteroids whose records were reviewed. (33%)</td>
</tr>
<tr>
<td>210</td>
</tr>
</tbody>
</table>
Thus, a sample size of 1250 in-patients enabled estimation of the true proportion of 50% of patients prescribed corticosteroids throughout New Zealand, with a confidence interval of ± 2.8%. For the patients prescribed corticosteroids whose records were examined, a sample size of 210 enables an estimation of a true proportion of 30% of patients with a drug review, with a 95% confidence interval of 6.1%.

2.4: Data recording considerations

In tandem with the sample size being determined, a draft Excel database was trialled, initially at the home hospice using seven sets of patient notes, when it was found to require considerable refining. There was far too much detail for the researcher to capture. Further discussions with the biostatistician and supervisor led to a simplification of the database and to a second trial, this time at Hospice 1, on three sets of patient notes. The database contained two sections, the first to collect patient information, and the second to record corticosteroid prescribing by a patient review. Data was collected only on patients prescribed corticosteroids who were selected as part of the study sample. Further refinements were needed to produce an effective database with a balance between ‘comprehensiveness’ and ease of recording/analysis.

2.4.1: The patient information sheet

The first section of the database Table 18 overleaf collected hospice and patient demographics to include a code for each hospice and patient, patient age, gender and diagnosis, an indication for corticosteroid use, along with the corticosteroid start dose and stop date. It also recorded information on whether the prescriber was from hospital or hospice, or a general practitioner. In addition, the sheet recorded whether four medicines, omeprazole, phenytoin, NSAIDs (e.g. diclofenac) and zopiclone were prescribed concurrently with corticosteroids.
Table 18: An example of the patient information database sheet for one of the sample hospices

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
<th>19</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospice code</td>
<td>Patient code</td>
<td>Indication number</td>
<td>Cancer</td>
<td>Patient age</td>
<td>Gender</td>
<td>Date started</td>
<td>Initial dose</td>
<td>Initial dose prednisone</td>
<td>Methyprednisolone</td>
<td>Dexamethasone</td>
<td>Type of indication</td>
<td>Morphine</td>
<td>Omeprazole</td>
<td>NSAIDS</td>
<td>Phenol</td>
<td>Zolpidem</td>
<td>Drug stopped</td>
</tr>
<tr>
<td>6</td>
<td>601</td>
<td></td>
<td>1</td>
<td>57</td>
<td>2</td>
<td>Unknown</td>
<td>Nil</td>
<td>16mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>602</td>
<td>1</td>
<td>1</td>
<td>43</td>
<td>1</td>
<td>26.07.07</td>
<td>Nil</td>
<td>12mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>603</td>
<td>1</td>
<td>1</td>
<td>59</td>
<td>2</td>
<td>30.03.07</td>
<td>Nil</td>
<td>4mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>604</td>
<td>1</td>
<td>1</td>
<td>76</td>
<td>2</td>
<td>22.06.07</td>
<td>Unknown</td>
<td>Nil</td>
<td>Nil</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>605</td>
<td>1</td>
<td>1</td>
<td>57</td>
<td>1</td>
<td>06.10.07</td>
<td>Nil</td>
<td>4mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>606</td>
<td>1</td>
<td>1</td>
<td>70</td>
<td>1</td>
<td>12.01.07</td>
<td>Nil</td>
<td>16mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>607</td>
<td>1</td>
<td>1</td>
<td>54</td>
<td>2</td>
<td>11.04.07</td>
<td>Nil</td>
<td>8mg</td>
<td>Nil</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>608</td>
<td>1</td>
<td>1</td>
<td>64</td>
<td>2</td>
<td>20.01.07</td>
<td>Nil</td>
<td>8mg</td>
<td>Nil</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>609</td>
<td>1</td>
<td>1</td>
<td>42</td>
<td>2</td>
<td>03.04.07</td>
<td>Nil</td>
<td>8mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>609</td>
<td>1</td>
<td>1</td>
<td>42</td>
<td>2</td>
<td>24.04.07</td>
<td>Nil</td>
<td>4mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>609</td>
<td>2</td>
<td>1</td>
<td>42</td>
<td>2</td>
<td>14.06.07</td>
<td>Nil</td>
<td>8mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>610</td>
<td>1</td>
<td>1</td>
<td>86</td>
<td>1</td>
<td>22.09.07</td>
<td>10mg</td>
<td>Nil</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>611</td>
<td>1</td>
<td>1</td>
<td>49</td>
<td>1</td>
<td>11.01.07</td>
<td>Nil</td>
<td>12mg</td>
<td>Nil</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>612</td>
<td>1</td>
<td>1</td>
<td>65</td>
<td>1</td>
<td>27.10.07</td>
<td>5mg</td>
<td>Nil</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>613</td>
<td>1</td>
<td>1</td>
<td>71</td>
<td>1</td>
<td>31.07.07</td>
<td>Nil</td>
<td>8mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>614</td>
<td>1</td>
<td>1</td>
<td>62</td>
<td>2</td>
<td>25.01.07</td>
<td>Nil</td>
<td>6mg</td>
<td>Nil</td>
<td>1</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>614</td>
<td>2</td>
<td>1</td>
<td>62</td>
<td>2</td>
<td>27.02.07</td>
<td>Nil</td>
<td>2mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>615</td>
<td>1</td>
<td>1</td>
<td>72</td>
<td>2</td>
<td>02.02.08</td>
<td>Nil</td>
<td>4mg</td>
<td>Nil</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>615</td>
<td>1</td>
<td>1</td>
<td>72</td>
<td>2</td>
<td>20.03.08</td>
<td>Nil</td>
<td>2mg</td>
<td>Nil</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>616</td>
<td>1</td>
<td>1</td>
<td>73</td>
<td>2</td>
<td>27.02.07</td>
<td>Nil</td>
<td>1mg</td>
<td>Nil</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Table 19 overleaf illustrates the breakdown of the columns within the patient information database. These columns have been numbered 1 to 19, some columns being more complex than others.
**Table 19:** An explanation of the patient information database sheet by column

<table>
<thead>
<tr>
<th>Column</th>
<th>Database information sheet</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hospice code 1 to 6 identifying the hospice being researched</td>
</tr>
<tr>
<td>2</td>
<td>Patient code numbered to identify individual patients</td>
</tr>
<tr>
<td>3</td>
<td>Indication number 1, 2 or more, depending on number of separate incidents requiring the use of corticosteroids per patient</td>
</tr>
<tr>
<td>4</td>
<td>A code: 1: a diagnosis of cancer; 2: non cancer patients</td>
</tr>
<tr>
<td>5</td>
<td>Patient age</td>
</tr>
<tr>
<td>6</td>
<td>Patient gender: 1: male; 2: female</td>
</tr>
<tr>
<td>7</td>
<td>Date, where possible, when the corticosteroid was commenced</td>
</tr>
<tr>
<td>8</td>
<td>Initial dose of prednisone prescribed</td>
</tr>
<tr>
<td>9</td>
<td>Initial dose of dexamethasone prescribed</td>
</tr>
<tr>
<td>10</td>
<td>Initial dose of methylprednisolone prescribed</td>
</tr>
<tr>
<td>11</td>
<td>Route: 1: oral; 2: subcutaneous; 3: intramuscular; 4: intravenous</td>
</tr>
<tr>
<td>12</td>
<td>Prescribed by: 1: by a hospital doctor; 2: GP; 3: hospice doctor</td>
</tr>
<tr>
<td>13</td>
<td>Indication (reason) for corticosteroid prescribing: 1: non-specific/generic wellbeing; 2: neurological symptoms; 3: capsular stretching; 4: soft tissue infiltration; 5: tenesmus; 6: syringe driver sites; 7: not clear/other; 8: chemotherapy</td>
</tr>
<tr>
<td>14</td>
<td>Omeprazole prescribed concurrently with a corticosteroid: 1: yes; 2: no</td>
</tr>
<tr>
<td>15</td>
<td>NSAIDs prescribed concurrently with a corticosteroid: 1: yes; 2: no</td>
</tr>
<tr>
<td>16</td>
<td>Phenytoin prescribed concurrently with a corticosteroid: 1: yes; 2: no</td>
</tr>
<tr>
<td>17</td>
<td>Zopiclone prescribed concurrently with a corticosteroid 1: yes; 2: no</td>
</tr>
<tr>
<td>18</td>
<td>How was the corticosteroid stopped? 1: gradually; 2: abruptly stopped; 3: patient died while still on their corticosteroid</td>
</tr>
</tbody>
</table>

**2.4.2: The patient review sheet**

The second section of the database Table 20 overleaf included the same hospice and patient code as the information database sheet. It had columns collecting information on whether a corticosteroid was reviewed, the date of review, an indication change, the resulting changes of the review, a new corticosteroid introduced and the dose for that new corticosteroid, a change of route and adverse effects. The final column was for pertinent comments.
Table 20: An example of the patient review sheet database for one of the sample hospices

<table>
<thead>
<tr>
<th>Hospice code</th>
<th>Patient code</th>
<th>Indication number</th>
<th>Reviewed Date</th>
<th>Indication change</th>
<th>Decision</th>
<th>Reason</th>
<th>New dose</th>
<th>Route</th>
<th>New drug</th>
<th>New drug route</th>
<th>Adverse effects</th>
<th>Prescribed by</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 601</td>
<td>1 1</td>
<td>08.06.07</td>
<td>2 1 3</td>
<td>12mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td>Patient moved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 602</td>
<td>1 1</td>
<td>30.07.07</td>
<td>2 1 3</td>
<td>17mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td>10mg =4mg plus 3mg x 2 17mg = 2mg plus 3mg x 3</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 602</td>
<td>1 1</td>
<td>31.07.07</td>
<td>2 1 4</td>
<td>12mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td>plus 6mg stat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 602</td>
<td>1 1</td>
<td>15.08.07</td>
<td>2 2 1</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>3</td>
<td>Died 17.08.07</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 1</td>
<td>17.04.07</td>
<td>2 4 5</td>
<td>12mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td>Tapering dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 2</td>
<td>22.04.07</td>
<td>2 1 5</td>
<td>8mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 2</td>
<td>27.04.07</td>
<td>2 1 5</td>
<td>6mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 2</td>
<td>02.05.07</td>
<td>2 1 5</td>
<td>4mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 2</td>
<td>04.05.07</td>
<td>2 3 5</td>
<td>Nil</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 1</td>
<td>14.05.07</td>
<td>2 4 1</td>
<td>12mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 1</td>
<td>3</td>
<td>Pain SCC?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 1</td>
<td>16.05.07</td>
<td>2 1 3</td>
<td>8mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 1</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 1</td>
<td>17.05.07</td>
<td>2 1 3</td>
<td>4mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 1</td>
<td>3</td>
<td>Adverse effects +++</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 603</td>
<td>1 1</td>
<td>21.05.07</td>
<td>2 2 3</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>2 1</td>
<td>3</td>
<td>No further steroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 604</td>
<td>1 1</td>
<td>27.06.07</td>
<td>2 2 2</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>2</td>
<td>Short course</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 605</td>
<td>1 1</td>
<td>13.10.07</td>
<td>2 2 1</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td>Short course</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 606</td>
<td>1 2</td>
<td>17.01.07</td>
<td>2 1 5</td>
<td>12mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td>Prev course 06 pain and leg swelling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 606</td>
<td>1 2</td>
<td>19.01.07</td>
<td>2 1 5</td>
<td>6mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 606</td>
<td>1 2</td>
<td>21.01.07</td>
<td>2 1 5</td>
<td>6mg</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>2 3</td>
<td>1</td>
<td>Reducing dose</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 21 overleaf illustrates the breakdown of the columns within the patient review database. These columns have been numbered 1 to 16, some columns being more complex than others.
Table 21: An explanation of the patient review database sheet by column

<table>
<thead>
<tr>
<th>Column</th>
<th>Database patient review sheet</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hospice code identifying the hospice being researched</td>
</tr>
<tr>
<td>2</td>
<td>Patient code numbered to identify individual patients</td>
</tr>
<tr>
<td>3</td>
<td>Indication number 1, 2 or more depending on number of separate incidents requiring the use of corticosteroids per patient</td>
</tr>
<tr>
<td>4</td>
<td>Was the drug reviewed? 1: reviewed; 2: not reviewed</td>
</tr>
<tr>
<td>5</td>
<td>Date of review</td>
</tr>
<tr>
<td>6</td>
<td>Indication change for giving corticosteroid: 1: for yes if so return to the information sheet and start over; 2: for no so continue with review sheet</td>
</tr>
<tr>
<td>7</td>
<td>Dose change decision: 1: decrease dose of corticosteroid; 2: stop corticosteroid; 3: no change to dose of corticosteroid; 4: increase dose of corticosteroid; and 5: change corticosteroid</td>
</tr>
<tr>
<td>8</td>
<td>Reason for dose change: 1: patient deterioration; 2: no change in patient; 3: improvement in patient; 4: not recorded</td>
</tr>
<tr>
<td>9</td>
<td>New dose</td>
</tr>
<tr>
<td>10</td>
<td>Route: 1: oral; 2: subcutaneous; 3: intramuscular; 4: intravenous</td>
</tr>
<tr>
<td>12</td>
<td>New drug dose</td>
</tr>
<tr>
<td>13</td>
<td>Route changed: 1: yes; 2: no</td>
</tr>
<tr>
<td>14</td>
<td>Adverse effects to corticosteroids: 1: yes; 2: no; and 3: not recorded</td>
</tr>
<tr>
<td>15</td>
<td>Corticosteroids prescribed by: 1: hospital doctors; 2: GPs; and 3: hospice doctors</td>
</tr>
<tr>
<td>16</td>
<td>Comment: any points of interest</td>
</tr>
</tbody>
</table>

2.5: Data collection

In Phase One, all six hospices were visited between February 2009 and December 2009. Although the hospices were numbered one to six, they were not necessarily visited in that order. The dates of the visits were organised to fit around mutually convenient times to the hospice and the researcher.

Hospice 1 was visited for data on three separate occasions, Hospice 2 and Hospice 6 required two visits, while the other three hospices needed only one trip. By Hospice 3, the researcher realised that if the hospice had computerised their patient admissions it was possible to do some preliminary work before a planned visit. Patients were entered alphabetically on an electronic database, those with multiple admissions were identified and entered only once, so that at the time of the visit the number and identity of the inpatients had been clarified.
Each hospice had a unique method of presenting patient notes and there was no consistency. This meant that systems knowledge gained at one hospice was not necessarily useful for the next. Across the six hospices, information around patient admissions and patient notes were collected very differently, with some hospices using hardcopy and others using a mixture of hardcopy and electronic recording. Depending on how a patient was listed, he/she may have been re-entered into a system numerous times and in different ways. A nickname or second name was common. Their National Health Index (NHI) numbers, if available, were used for data recording, since this was the only way of identifying a patient accurately.

Once the patients admitted in 2007 were identified, the next step was to find their notes. Some hospices kept these in filing cabinets in remote locations in the hospice (e.g. basements), others had their notes off-site, which required retrieval. Another set was lodged in filing rooms in the basement of a public hospital. Within the filing cabinets and off-site boxes, the notes were filed or packed differently: some alphabetically, others by date, or year of death, or by NHI number.

Once the notes for the inpatients for 2007 had been found, a search was made for missing individuals’ notes. Some were easy to track as they were identified as patients who were still alive and they were withdrawn from the review. Other patient notes were being used in research elsewhere, while others proved untraceable or had been discharged from the service. These groups were also withdrawn from the study. Of those remaining, those who had been prescribed corticosteroids were identified for the purposes of this analysis. Every third patient was selected for recording on the database. This was initially entered by hand on hardcopy, and later transferred to an electronic database.

Patient data was complex and had been entered on a simplified database, which was unable to capture all the intricacies. A decision was made to collect case study scenarios from each of the hospices in recognition of this complexity, to illustrate key issues in prescribing.

2.5.1: Hospice 1

Hospice 1 was an 18-bed specialist palliative care service, which served a population of 295,400 people spread over a large urban area. There were 312
hospice inpatients for the year of 2007. Of these, 15 sets of notes were unable to be found, leaving 297 patients to be reviewed, of whom 204 were prescribed corticosteroids (69%). Of these, 70 were entered in the researcher’s database.

*The first visit February, 2009*

These two days were spent trying to identify the number of inpatients and to locate their notes. The hospice in-patient admissions of 2007 were not computerised, instead they were handwritten in a register of patients spread over 22 pages, with readmissions being common. Not all readmissions were identified as such and these patients’ surnames were sometimes spelt incorrectly, or listed by a second name or nickname. An address or NHI number could at times track patients if these were recorded.

The actual patient notes were held in a filing room under the hospice and were filed alphabetically (first three letters of surname) according to the year of the patient’s death, which was not necessarily in 2007.

Of the ‘unfound’ 15 sets of notes, two patients were identified as being discharged from the service, one patient was still alive and therefore was removed from the study, the other 12 sets of notes were not found and were removed from the study.

*The second visit June, 2009*

By this occasion the visits to, and the data collection from, Hospice 2 had been completed. The decision had been made with the biostatistician and the supervisor to search all inpatients notes for a “yes” or “no” to corticosteroids and then to take every third set of notes for entry in the database. This had been trialled successfully.

This second visit to Hospice 1 identified the patients who had been prescribed corticosteroids. 50 sets of relevant details from the required 70 sets of notes were initially entered into a hardcopy of the database, and subsequently entered into the electronic database. Some possible case studies to support the entries were indentified.
The third visit July, 2009

The final 20 sets of patient details were entered on the hardcopy database sheets. This visit allowed a review of notes from the previous visit, which were not clear when transferred to the electronic database. Five case studies supporting the data were selected, recorded and checked for accuracy with the entry on the database.

2.5.2: Hospice 2

Hospice 2 was a 12-bed specialist palliative care service, which served a population of 180,000 spread over a wide geographical area both urban and rural. There were 251 hospice inpatients for the year of 2007. For these patients, 16 sets of notes were unable to be found, leaving 235 patients to be reviewed of whom 144 were prescribed corticosteroids (61%). Fifty of these patients were entered in the database.

The first visit March, 2009

The 2007 patient notes for this hospice were not stored on-site and they were retrieved from storage before the retrospective study commenced. Day one was spent identifying the patients taking corticosteroids, and in which box those patient notes were stored. They were filed according to the patient’s date of death, not alphabetically. The researcher numbered the boxes and that number was transferred to the alphabetical list of patient names for ease of location when the relevant details required entering on the database. As with Hospice 1, it was common for these patients’ surnames to be spelt incorrectly or to be listed by a second name or nickname. An address or NHI number could sometimes track patients if these were recorded.

Of the ‘unfound’ 16 sets of notes, seven patients were identified as being discharged from the service and three patients were still alive and were removed from the study. The other six sets of notes were not in the retrieved boxes and again were removed from the study. By the end of this visit, the 27 sets of patient notes were recorded on the hardcopy database sheets.

The plan had been for the researcher to return to this hospice and complete the data collection the following month. After discussion with the supervisor and biostatistician to discuss progress so far, it was agreed that having separated...
those prescribed corticosteroids, the method of randomly collecting data from one-third of those patients was successful and of sufficient number for the analysis. The data sheets were reviewed once more and it was found although some columns could be simplified, on the whole the database worked well. This process and database became the template for the remainder of the quantitative study.

The second visit May, 2009

On this visit, 23 sets of patient notes were entered on the hardcopy database sheets while also looking for notes to act as representative case studies. Before the completion of this visit, notes were written on five case studies.

2.5.3: Hospice 3

Hospice 3 was a ten-bed specialist palliative care service, which served a population of 102,000 spread over a wide urban area. There were 186 hospice inpatients for the year of 2007. Of these, 11 sets of notes were unable to be found leaving 175 patients to be reviewed of whom 120 were prescribed corticosteroids (69%). Of these, 40 were entered on the database.

Visit August, 2009

As with Hospice 2, these patient notes were stored off-site and needed to be retrieved before the start of the study. Three boxes of notes listed for the 2007 year appeared to be missing, however these were found within the hospice environment having been returned previously for another study.

Of the “unfound’ 11 sets of notes, six patients were identified as being discharged from the service, three patients were still alive and were removed from the study, the other two sets of notes were missing so again were removed from the study.

This was the first hospice in which the researcher was able to take advantage of a computerised admissions list and some preliminary work was achieved before the planned visit. Patient details were entered on the researcher’s laptop alphabetically. Those with multiple admissions were identified and entered only once and by the time of the visit, the number and identity of the inpatients had been confirmed. This enabled all 40 patient reviews and data entries on to hardcopy data sheets to be completed within this visit. Five case studies were also written.
This hospice differed from the others in that patients who had been prescribed corticosteroids had a separate individualised corticosteroid protocol sheet in their notes. Doses of the prescribed corticosteroid were not written on the medication chart but instead: ‘as per protocol’ was written on the medication chart. These protocols listed reducing doses.

2.5.4: Hospice 4

Hospice 4 was a five-bed palliative care service that served a population of 60,000 spread over a wide geographical area, both urban and rural. There were 115 hospice inpatients for the year of 2007. Of these, four sets of notes were unable to be found. One hundred and eleven were patients to be reviewed, of whom 71 were prescribed corticosteroids (64%). Of those, 24 were entered in the database. Four case studies were also written.

Visit November, 2009

As with Hospice 3, it was possible to do some preliminary work using the inpatient computerised admissions list. The inpatients were identified and listed in preparation for the review. The plan had been to visit this hospice in December but the months were swapped to fit more easily with a request from Hospice 5.

The inpatient notes were stored on-site. These notes were partially hardcopy, partially Medtech32, an electronic medical practice management system. Of the ‘unfound’ four sets of notes, two patients were identified as being discharged from the service, one patient was still alive so was removed from the study. The last set of notes was not found in the boxes and again was removed from the study.

This was the smallest hospice to review so during the days spent there, it was possible to complete the whole data extraction process. The selected sample of 24 was reviewed and details entered on the hardcopy database sheets. From these patients, four case studies were identified and recorded. It was possible to enter the 24 patients on the electronic database during this visit, a feat achieved only at this hospice.

2.5.5: Hospice 5

Hospice 5 was a six bed palliative care service that served a population of 104,000 spread over a wide geographical area both urban and rural. There were 163 hospice inpatients for the year of 2007. Of these, 21 sets of notes were
unable to be found leaving 142 patients to be reviewed, of whom 94 were prescribed corticosteroids (64%). Of these, 31 were entered on the database. Four case studies were also written.

*Visit December, 2009*

This was the final hospice to be visited. The planned November visit was moved to December at the request of the hospice staff.

Very little time during this visit was spent at the hospice, since the notes for these patients were integrated with the local hospital notes and were stored there rather than on the hospice premises. On this visit, a filing clerk located the notes for the researcher and these were delivered to review within the hospital precincts.

Of the ‘unfound’, 21 sets of notes, one patient was identified as being discharged from the service, five patients were still alive so were removed from the study, the other fifteen sets of notes were either out on loan or not found and again were removed from the study.

This was the first time the researcher had encountered integrated notes. They held the patient’s complete District Health Board history so separating out hospice admissions was challenging. Thirty one sets of notes were selected to be entered on the hardcopy database sheets. Four case studies followed to support the data taken.

**2.5.6: Hospice 6**

Hospice 6 was a nine bed specialist palliative care service, which served a population of 426,000 spread over a wide metropolitan area. Although this hospice was classified as Hospice 6, it was not the final hospice to be visited. There were 243 hospice inpatients for the year of 2007. Of these patients, 24 sets of notes were unable to be found, leaving 219 patients to be reviewed of whom 135 had been prescribed corticosteroids (62%), 45 of these patients were entered on the database.

*The first visit September, 2009*

Like Hospice 4, this hospice used a combination of Medtech32 and hardcopy patient notes. The hardcopy proved easier to read than the Medtech32 screen. The 2007 clinical patient notes were filed in two separate areas depending on the
year the patient died. Three different systems of filing existed amongst these notes: Patients of 2007 who had died in 2007 were filed alphabetically; the 2008 deaths were filed by the last three numbers of their NHI numbers, while those who died in 2009 were a mixture of both the previous systems.

Of the ‘unfound’ 24 sets of notes, two patients were identified as being discharged from the service, one patient appeared not to exist, six patients were still alive and were removed from the study. The other 15 sets of notes were not found and again were removed from the study.

The selected sample for this hospice to be reviewed in-depth contained 45 sets of patient notes. All data extraction except selecting and writing up the case studies was completed that week.

The second visit October, 2009

A further day was spent at Hospice 6 in October 2009 to tidy up a few inconsistencies from the September trip and to select and write up five case studies.

2.6: Data analysis

Once the data entry was completed, in discussion with the statistician and supervisor, specific data was selected to be reviewed between the six hospices.

The validity of the data was verified in two ways. Initially as the data was transferred from hardcopy to the electronic database abnormalities identified were rechecked for accuracy against the patient notes at a later visit.

The case studies became the second validity tool. There were 260 patients entered on the database. Twenty-eight case studies/cameos were taken, which represented approximately one in ten patients recorded in greater detail than in the database entries. They were compared to the data entered to check the database for accuracy.

2.6.1: Statistical analyses

Frequencies with 95% confidence intervals, medians and ranges were used to describe the characteristics of the patients and their treatments. Chi-square tests were used to test for differences in the proportions of patients receiving particular treatments between hospices. The clustering of data where patients had more
than one record was allowed for in the analyses and calculation of confidence intervals. SAS v 9.12 was used in the analyses of the data. As the hospices were not randomly selected, but for ease of access, they were included as fixed factors where appropriate.
Chapter 3 Results: Phase One

This chapter reports results from Phase One of the study, a retrospective review of corticosteroid prescribing in a sample of six hospices.

### 3.1: Patient characteristics

At the time of this retrospective review of corticosteroid prescribing in the year 2007 across the six hospices, 1179 inpatient notes were reviewed. Corticosteroids were prescribed for 768 patients (65%). Of these, a sample of 260 patients were recorded in the database. Twenty-eight case studies/cameos were recorded to illustrate some of the main issues of the data entered on the database. Table 22 shows demographic data collected from the six sample hospices.

**Table 22: Patient characteristics**

<table>
<thead>
<tr>
<th>Facility</th>
<th>Cancer</th>
<th>Gender</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes %</td>
<td>No %</td>
<td>Male %</td>
</tr>
<tr>
<td>Hospice 1 n=70</td>
<td>94%</td>
<td>6%</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>n=66</td>
<td>n=4</td>
<td>n=28</td>
</tr>
<tr>
<td>Hospice 2 n=50</td>
<td>100%</td>
<td>–</td>
<td>56%</td>
</tr>
<tr>
<td></td>
<td>n=50</td>
<td></td>
<td>n=28</td>
</tr>
<tr>
<td>Hospice 3 n=40</td>
<td>90%</td>
<td>10%</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td>n=36</td>
<td>n=4</td>
<td>n=18</td>
</tr>
<tr>
<td>Hospice 4 n=24</td>
<td>87%</td>
<td>13%</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>n=21</td>
<td>n=3</td>
<td>n=12</td>
</tr>
<tr>
<td>Hospice 5 n=31</td>
<td>100%</td>
<td>–</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>n=31</td>
<td></td>
<td>n=11</td>
</tr>
<tr>
<td>Hospice 6 n=45</td>
<td>98%</td>
<td>2%</td>
<td>49%</td>
</tr>
<tr>
<td></td>
<td>n=44</td>
<td>n=1</td>
<td>n=22</td>
</tr>
<tr>
<td>Total</td>
<td>248</td>
<td>12</td>
<td>119</td>
</tr>
</tbody>
</table>

The number of patients recorded in each facility, ranged from Hospice 1, the largest hospice, with 70 patients to Hospice 4 the smallest hospice with 24. There was little variation between the cancer and non-cancer, gender and age data across the hospices. The four most common cancer types recorded were gastrointestinal tract cancers, urogenital cancers, and cancers of the lung and breast.
3.2: Corticosteroid prescribing

The proportion of patients prescribed corticosteroids across each hospice varied from 61% to 69% with the average being 65%. Figure 10 illustrates the consistency across the hospices.

**Figure 10: Proportion of patients prescribed corticosteroids**

![Graph showing proportion of patients prescribed corticosteroids across hospices.

\[ n=\text{number of patients recorded per hospice} \]

No significant differences were detected in corticosteroid prescribing rates across the sample hospices \((p = 0.3675)\). This consistency was remarkable and is discussed further in Chapters 5 and 6.

3.3: Common indications for corticosteroid prescribing

In palliative care, corticosteroids are prescribed for many indications. Eight indications were selected and entered in the database for this 2007 study.

**Table 23: Description of indications**

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Non-specific/‘general wellbeing’: to include lack of appetite, wellbeing, fatigue, nausea, vomiting, pain and shortness of breath</td>
</tr>
<tr>
<td>2</td>
<td>Neurological to include: raised intracranial pressure, cerebral tumours, spinal cord compression and nerve compression or infiltration</td>
</tr>
<tr>
<td>3</td>
<td>Capsular stretching: to include liver metastases and other visceral organ metastases</td>
</tr>
<tr>
<td>4</td>
<td>Soft tissue infiltration: to include head and neck tumours and abdominal and pelvic tumours</td>
</tr>
<tr>
<td>5</td>
<td>Tenesmus: rectal pain due to invasive tumours</td>
</tr>
<tr>
<td>6</td>
<td>Inflammation with syringe driver sites (subcutaneous route)</td>
</tr>
<tr>
<td>7</td>
<td>Not clear/other: to include any indication, which was either not clear or did not fit in the other categories</td>
</tr>
<tr>
<td>8</td>
<td>Chemotherapy</td>
</tr>
</tbody>
</table>

56
Using the descriptors in Table 23 above, the three most common indications for which corticosteroids were prescribed were non-specific/‘general wellbeing’, neurological symptoms and soft tissue infiltration. These three accounted for the great majority of all prescribing events.

Non-specific/‘general wellbeing’, was the most commonly prescribed indication. The percentages prescribed across the hospices ranged from 33% to 61% with an average figure of 40%. Figure 11 illustrates the differences between the hospices.

**Figure 11**: Proportion of patients prescribed corticosteroids for non-specific indications

The different prescribing percentages among the New Zealand sample hospices was considered of significance ($p = 0.0261$). There was a significant difference between Hospice 4 and the others. This is discussed further in Chapter 6.

Neurological symptoms were the second most commonly prescribed indication for these medicines. The proportion of patients prescribed corticosteroids for these symptoms ranged from 16 to 32% with an average over the hospices of 25%. No significant differences were identified (Figure 12).
Figure 12: Proportion of patients prescribed corticosteroids for neurological symptoms

There was no evidence that the proportion of corticosteroids prescribed for neurological indications differed across the hospices but numbers involved were relatively small ($p = 0.37$).

Soft tissue infiltration symptoms were the third most common indication. The proportion of patients prescribed corticosteroids for soft tissue infiltration symptoms ranged from zero to 20% with an average of 13%. Hospice 4 had no patients listed for this indication. Figure 13 identifies this group:

Figure 13: Proportion of patients prescribed corticosteroids for soft tissue infiltration symptoms

There was weak evidence that the proportion of corticosteroid prescribed for soft tissue infiltration indications differed across the hospices but numbers involved were relatively small ($p = 0.068$).
Figure 14 illustrates the balance of the indications where corticosteroids were prescribed across the sample hospices.

**Figure 14:** Proportion of patients prescribed corticosteroids for the balance of the recorded indications

![Graph showing the proportion of patients prescribed corticosteroids by hospice](image)

These indications include capsular stretching, tenesmus, syringe driver sites, chemotherapy and a group labelled not clear/other. These percentages range from 7% for hospice 4 to 33% for hospice 5. Capsular stretching equates to 15% of corticosteroid prescribing for hospice 5. None of the other hospices exceed 5% for this indication.

### 3.4: Corticosteroids agents prescribed

Three corticosteroids were prescribed in the six sample hospices these were prednisone, dexamethasone and methylprednisolone. The following Table 24, 25 and 26 show the proportion of patients (%) by indication, on these medicines.
### 3.4.1: Prednisone

#### Table 24: Proportion of patients prescribed prednisone by indication

<table>
<thead>
<tr>
<th></th>
<th>Non-specific</th>
<th>Neurological</th>
<th>Capsular Stretching</th>
<th>Soft tissue infiltration</th>
<th>Not clear/other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospice 1</strong></td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hospice 2</strong></td>
<td>86%</td>
<td>9%</td>
<td></td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>(n=22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hospice 3</strong></td>
<td>92%</td>
<td>2%</td>
<td>2%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>(n=52)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hospice 4</strong></td>
<td>95%</td>
<td></td>
<td></td>
<td></td>
<td>5%</td>
</tr>
<tr>
<td>(n=40)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hospice 5</strong></td>
<td>90%</td>
<td></td>
<td></td>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>(n=21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hospice 6</strong></td>
<td>70%</td>
<td>5%</td>
<td></td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>(n=20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(n=\) number of prednisone prescribing events

In all sample hospices prednisone was prescribed predominantly for non-specific symptoms with proportions for that indication ranging from 70% to 100%. Hospice 1 did not prescribe prednisone for any other indication. No hospices prescribed prednisone for tenesmus, syringe driver sites (this indication is not treated with an oral preparation) or chemotherapy during this study. Prednisone was prescribed on 183 occasions for these indications. One hundred and sixty-six of these were for non-specific symptoms.
3.4.2: Methylprednisolone

Table 25: Proportion of patients prescribed methylprednisolone by indication

<table>
<thead>
<tr>
<th>Indications</th>
<th>Non-specific</th>
<th>Neurological</th>
<th>Soft tissue infiltration</th>
<th>Not clear/other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospice 2, n=29</td>
<td>10%</td>
<td>42%</td>
<td>48%</td>
<td></td>
</tr>
<tr>
<td>Hospice 3, n=27</td>
<td>7%</td>
<td>26%</td>
<td>67%</td>
<td></td>
</tr>
<tr>
<td>Hospice 5, n=1</td>
<td></td>
<td></td>
<td></td>
<td>100%</td>
</tr>
</tbody>
</table>

n=number of methylprednisolone prescribing events

Methylprednisolone was not prescribed by hospice 1, 4 or 6 and prescribed only once during the study by hospice 5. On that occasion, it was given as a single dose the reason for which was unclear. Neurological symptoms and soft tissue infiltration were the main indications for the use of methylprednisolone. The methylprednisolone used by these hospices was a parenteral formulation, with all prescribing for short courses. Methylprednisolone was prescribed on 57 occasions for these indications.

3.4.3 Dexamethasone

Table 26: Proportion of patients prescribed dexamethasone by indication

<table>
<thead>
<tr>
<th>Indications</th>
<th>Non-specific</th>
<th>Neurological</th>
<th>Capsular Stretching</th>
<th>Soft tissue infiltration</th>
<th>Tenesmus</th>
<th>Syringe driver sites</th>
<th>Not clear/other</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospice 1, n=234</td>
<td>15%</td>
<td>50%</td>
<td>21%</td>
<td>3%</td>
<td>2%</td>
<td>8%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Hospice 2, n=102</td>
<td>31%</td>
<td>34%</td>
<td>3%</td>
<td>11%</td>
<td>2%</td>
<td>3%</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>Hospice 3, n=92</td>
<td>26%</td>
<td>40%</td>
<td>7%</td>
<td>9%</td>
<td></td>
<td></td>
<td>16%</td>
<td>2%</td>
</tr>
<tr>
<td>Hospice 4, n=77</td>
<td>51%</td>
<td>47%</td>
<td>3%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospice 5, n=136</td>
<td>18%</td>
<td>38%</td>
<td>18%</td>
<td>14%</td>
<td>1%</td>
<td>11%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Hospice 6, n=135</td>
<td>23%</td>
<td>44%</td>
<td>7%</td>
<td>18%</td>
<td>2%</td>
<td>4%</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>

n=number of dexamethasone prescribing events
Dexamethasone was the most commonly prescribed corticosteroid throughout this study. Both the oral and parenteral route were used. The two indications with the highest proportion of dexamethasone prescribing events were non-specific (186) and neurological symptoms (335). Dexamethasone was the only medicine to be prescribed for all eight indications and was prescribed on 776 occasions for these indications.

3.5: Corticosteroids by indication, dose range and average dose

3.5.1: Prednisone

Table 27 illustrates the prescribing of prednisone by indication, dose range and average dose for the six sample hospices.

<table>
<thead>
<tr>
<th></th>
<th>Non-specific</th>
<th>Neurological</th>
<th>Capsular Stretching</th>
<th>Soft tissue infiltration</th>
<th>Not clear / other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospice 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>5–40mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>24mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hospice 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>5–40mg</td>
<td></td>
<td>20mg</td>
<td></td>
<td>10mg</td>
</tr>
<tr>
<td>Average Dose</td>
<td>19mg</td>
<td></td>
<td>20mg</td>
<td></td>
<td>10mg</td>
</tr>
<tr>
<td><strong>Hospice 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>20–40mg</td>
<td>10–40mg</td>
<td>40–80mg</td>
<td>10–20mg</td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>38mg</td>
<td>23mg</td>
<td>60mg</td>
<td>15mg</td>
<td></td>
</tr>
<tr>
<td><strong>Hospice 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>5–60mg</td>
<td></td>
<td></td>
<td></td>
<td>6mg</td>
</tr>
<tr>
<td>Average Dose</td>
<td>23mg</td>
<td></td>
<td></td>
<td></td>
<td>6mg</td>
</tr>
<tr>
<td><strong>Hospice 5</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>20–40mg</td>
<td></td>
<td></td>
<td></td>
<td>80mg</td>
</tr>
<tr>
<td>Average Dose</td>
<td>30mg</td>
<td></td>
<td></td>
<td></td>
<td>80mg</td>
</tr>
<tr>
<td><strong>Hospice 6</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>5–20mg</td>
<td>50mg</td>
<td>20–35mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>16mg</td>
<td>50mg</td>
<td>27mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Non-specific was the only indication for which prednisone was prescribed in all six hospices. The dose range was 5mg to 60mg with the range of average doses among the hospices being 16mg to 38mg. No significant difference was found for this indication across the hospices ($p = 0.49$).
3.5.2: Methylprednisolone

Table 28 illustrates the prescribing of methylprednisolone by indication, dose range and average dose.

Table 28: Methylprednisolone by dose range by indication by hospice

<table>
<thead>
<tr>
<th>Hospice 2</th>
<th>Non-specific</th>
<th>Neurological</th>
<th>Soft tissue infiltration</th>
<th>Not clear/other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose range</td>
<td>125mg</td>
<td>80–125mg</td>
<td>125mg</td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>125mg</td>
<td>116mg</td>
<td>125mg</td>
<td></td>
</tr>
<tr>
<td>Hospice 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>125mg</td>
<td>125mg</td>
<td>125mg</td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>125mg</td>
<td>125mg</td>
<td>125mg</td>
<td></td>
</tr>
<tr>
<td>Hospice 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td></td>
<td></td>
<td></td>
<td>1000mg</td>
</tr>
<tr>
<td>Average Dose</td>
<td></td>
<td></td>
<td></td>
<td>1000mg</td>
</tr>
</tbody>
</table>

Methylprednisolone was prescribed in three hospices only. Hospice 2 and Hospice 3 prescribed this corticosteroid similarly and for the same indications. The single dose of 1000mg prescribed for a Hospice 5 patient, during a hospital stay, was for an indication that was not clear to the researcher.

3.5.3: Dexamethasone

The prescribed dose range of dexamethasone for the three main indications was:

Non-specific: 1mg to 8mg with the range of averages among the hospices being 3mg to 6mg. The difference shown in the range prescribed for this indication was not significant ($p = 0.35$).

Neurological symptoms: 2mg to 48mg with the range of averages among the hospices being 9mg to 14mg. The difference shown in the range prescribed for this indication was not significant ($p = 0.63$).

Soft tissue infiltration: 4mg to 35mg with the range of averages among the hospices being 6mg to 12mg. The difference shown in the range prescribed for this indication was not significant ($p = 0.24$).

Table 29 overleaf illustrates the prescribing of dexamethasone by indication, dose range and average dose.
Table 29: Dexamethasone by dose range by indication by hospice

<table>
<thead>
<tr>
<th>Hospice 1</th>
<th>Non-specific</th>
<th>Neurological</th>
<th>Capsular Stretching</th>
<th>Soft tissue infiltration</th>
<th>Tenesmus</th>
<th>Syringe driver sites</th>
<th>Not clear /other</th>
<th>Chemo-therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose range</td>
<td>1–8mg</td>
<td>2–16mg</td>
<td>4–16mg</td>
<td>8mg</td>
<td>0.5–1mg</td>
<td>4–8mg</td>
<td>16mg</td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>4mg</td>
<td>9mg</td>
<td>8mg</td>
<td>8mg</td>
<td>0.625mg</td>
<td>5mg</td>
<td>16mg</td>
<td></td>
</tr>
<tr>
<td>Hospice 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>2–8mg</td>
<td>2–16mg</td>
<td>4–8mg</td>
<td>8mg</td>
<td>0.5–1mg</td>
<td>4–40mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>4mg</td>
<td>9mg</td>
<td>8mg</td>
<td>6mg</td>
<td>8mg</td>
<td>0.67mg</td>
<td>17mg</td>
<td></td>
</tr>
<tr>
<td>Hospice 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>2–8mg</td>
<td>4–40mg</td>
<td>8mg</td>
<td>8–12mg</td>
<td>4–16mg</td>
<td>12mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>5mg</td>
<td>10mg</td>
<td>8mg</td>
<td>9mg</td>
<td>9mg</td>
<td>12mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospice 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>4–8mg</td>
<td>4–16mg</td>
<td>4mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>6mg</td>
<td>9g</td>
<td>4mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospice 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>2–4mg</td>
<td>4–16mg</td>
<td>2–8mg</td>
<td>4–8mg</td>
<td>4–8mg</td>
<td>12mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>3mg</td>
<td>10mg</td>
<td>5mg</td>
<td>6mg</td>
<td>5mg</td>
<td>12mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospice 6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose range</td>
<td>2–8mg</td>
<td>2–48mg</td>
<td>8–12mg</td>
<td>8–35mg</td>
<td>1mg</td>
<td>4–8mg</td>
<td>4–8mg</td>
<td></td>
</tr>
<tr>
<td>Average Dose</td>
<td>5mg</td>
<td>14mg</td>
<td>9mg</td>
<td>12mg</td>
<td>1mg</td>
<td>5mg</td>
<td>6mg</td>
<td></td>
</tr>
</tbody>
</table>

3.6 Adverse effects to corticosteroids

3.6.1 Recording of adverse effects

Figure 15 overleaf demonstrates the level of recording of adverse effects from corticosteroid prescribing and the differences between the six hospices in the recording of adverse effects in patient notes.
Figure 15: Proportion of patients who had adverse effects recorded

Non-recording of adverse effects ranged from 53% to 85% of cases. Hospices 1, 2, 3 and 6 recorded actual adverse effects and to a lesser degree recorded when there were no adverse effects. Hospices 4 and 5 recorded adverse effects only.

There was a significant difference between the hospices in the recording or non-recording of adverse effects ($p = 0.0004$).

In most cases, the researcher could not know if adverse effects had occurred or been recognised because there appeared to be a lack of recording in patient notes.

3.6.2 Proportion of patients with recorded adverse effects

Figure 16 demonstrates the proportion of patients who had adverse effects to corticosteroids, which were recorded in their notes. This graph relates to the blue section only of the previous graph (Figure 15).

$n$ = number of patients recorded per hospice
Chapter 3 Results: Phase One

Figure 16: Proportion of patients with adverse effects to corticosteroid prescribing

The proportion of patients with adverse effects recorded to corticosteroid prescribing varied across the six hospices with a range of 15% to 45%. A significant difference between the hospices was found ($p = 0.0001$). However, because of the high level of non-recording it is not possible to draw useful conclusions from this data. This is discussed further in Chapter 6.

3.7 Stopping of corticosteroids

Data was collected on the manner corticosteroids were stopped, that is whether they were reduced gradually or stopped abruptly. Also considered was the length of time a patient was prescribed a corticosteroid.

Figure 17: Proportion of patients where corticosteroids were stopped abruptly

$n=$number of adverse effects events recorded

$n=$number of patients recorded per hospice
The percentage of corticosteroids being stopped abruptly varied from 14% to 34% of cases. Of those patients whose medicines were stopped suddenly, 49% had been prescribed a corticosteroid for longer than three weeks after which adrenal suppression may be anticipated. No differences were found by hospice \((p = 0.52)\), but numbers involved were relatively small.

### 3.8 Medicines co-prescribed with corticosteroids

Within this study four medicines prescribed concurrently with corticosteroids were reviewed. They were: omeprazole, non steroidal anti-inflammatory drugs, NSAIDs (e.g. diclofenac), phenytoin and zopiclone.

#### 3.8.1 Omeprazole co-prescribed with a corticosteroid

Omeprazole, a proton pump inhibitor (PPI), is prescribed frequently in palliative care to protect the gastrointestinal tract from haemorrhage. Figure 18 shows the percentage of omeprazole co-prescribed with a corticosteroid.

![Figure 18: Proportion of patients co-prescribed corticosteroids and omeprazole](image)

The percentage prescribing of omeprazole concurrently with corticosteroids ranged from 70 to 82%, with a 77% average. Only a small group of patients were not prescribed omeprazole.

#### 3.8.2 NSAIDs co-prescribed with a corticosteroid

Non steroidal anti-inflammatory drugs (NSAIDs), as well as corticosteroids, are prescribed as adjuvant medicines for pain relief in palliative care. Figure 19 illustrates the percentage of NSAIDs prescribed concurrently with corticosteroids.
Figure 19: Proportion of patients co-prescribed corticosteroids and NSAIDs

Forty-seven percent of patients from Hospice 2 and 39% from Hospice 3 were co-prescribed NSAIDs and corticosteroids with an increased risk of gastrointestinal haemorrhage if they did not have a proton pump inhibitor (PPI) prescribed for gastrointestinal protection (see Figure 18). Significant statistical differences were found, by hospice, in the proportion of patients prescribed NSAIDs ($p = 0.002$).

3.8.3 Phenytoin co-prescribed with a corticosteroid

Phenytoin was the most commonly prescribed anticonvulsant for the treatment of seizures in patients with brain tumours or brain metastases. Figure 20 shows the proportion of phenytoin prescribed concurrently with a corticosteroid.

Figure 20: Proportion of patients co-prescribed corticosteroids with phenytoin

$n=$number of patients recorded per hospice
Phenytoin can affect the metabolism of the corticosteroid, reducing their efficacy. The percentages of the sample population prescribed this medicine ranged between 2% to 7% ($p = 0.68$). This was not considered of statistical significance but there were very small numbers of patients involved.

### 3.8.4 Zopiclone co-prescribed with a corticosteroid

Zopiclone is a common hypnotic prescribed in palliative care. Figure 21 demonstrates the prescribing of zopiclone.

**Figure 21:** Proportion of patients co-prescribed corticosteroid with zopiclone

Zopiclone, whose efficacy is affected by the co-prescribing of a corticosteroid was prescribed in two hospices 50% of the time and in a third hospice 49% of the time. The percentage range across the hospices was 24% to 50% with a range average of 41% of patients prescribed zopiclone. This difference in proportion of patients prescribed zopiclone by hospice was considered of statistically significance ($p = 0.018$).

### 3.9: Duration of corticosteroid courses

#### 3.9.1 Duration of corticosteroid courses overall

The length of time patients were prescribed corticosteroids across the sample hospices varied from a single dose prescribed for one day only, to a course continuing for 477 days. These were estimations, as not in all cases could a course duration be determined as it was not always possible to find a start date. Between the hospices the differences in treatment periods (days) was considered of significance ($p = 0.032$). Table 30 shows this difference between the hospices.
Table 30: Duration of corticosteroid courses (in days)

<table>
<thead>
<tr>
<th>Hospice</th>
<th>Observations</th>
<th>Minimum (days)</th>
<th>Median (days)</th>
<th>Maximum (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospice 1</td>
<td>51</td>
<td>2</td>
<td>25</td>
<td>423</td>
</tr>
<tr>
<td>Hospice 2</td>
<td>43</td>
<td>1</td>
<td>21</td>
<td>432</td>
</tr>
<tr>
<td>Hospice 3</td>
<td>45</td>
<td>2</td>
<td>21</td>
<td>122</td>
</tr>
<tr>
<td>Hospice 4</td>
<td>17</td>
<td>3</td>
<td>41</td>
<td>171</td>
</tr>
<tr>
<td>Hospice 5</td>
<td>24</td>
<td>4</td>
<td>53</td>
<td>477</td>
</tr>
<tr>
<td>Hospice 6</td>
<td>34</td>
<td>2</td>
<td>30</td>
<td>341</td>
</tr>
</tbody>
</table>

3.9.2 Duration of corticosteroid courses by indication

The length of time patients were prescribed corticosteroids varied considerably for each indication, as illustrated in Table 31. The maximum number of treatment days was for neurological symptoms and non-specific indications. These were estimations, as with 3.9.1 as not in all cases could a start date be determined.

Table 31: Duration of corticosteroid courses by indication - all hospices combined

<table>
<thead>
<tr>
<th>Type of Indication</th>
<th>Number of Observations</th>
<th>Minimum (days)</th>
<th>Median (days)</th>
<th>Maximum (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-specific</td>
<td>83</td>
<td>1</td>
<td>28</td>
<td>432</td>
</tr>
<tr>
<td>Neurological</td>
<td>64</td>
<td>2</td>
<td>34</td>
<td>477</td>
</tr>
<tr>
<td>Capsular stretching</td>
<td>9</td>
<td>2</td>
<td>18</td>
<td>312</td>
</tr>
<tr>
<td>Soft tissue infiltration</td>
<td>39</td>
<td>2</td>
<td>14</td>
<td>101</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Syringe driver sites</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Not clear/other</td>
<td>16</td>
<td>3</td>
<td>28</td>
<td>172</td>
</tr>
</tbody>
</table>

There was a significant difference in the average time on a corticosteroid for the different indications \( p = 0.022 \)
3.10 Corticosteroid reviews

The recorded reviews of corticosteroid prescribing varied between the hospices with percentages ranging from 29% to 68%. Figure 22 demonstrates that difference. For hospices 1, 2, and 6 (the first three visited) the researcher made the assumption that a change in dose meant a corticosteroid review had taken place. This was not necessarily the case but instead due to a reducing dose regime. For hospices 3, 4, and 5, unless a review was recorded in the patient notes it was not considered a review. Where the database allowed some identification of this with the first three hospices it was corrected. It is the researcher’s opinion that the recorded review percentages for hospice 1, 2, and 6 reflect a reasonable accuracy.

![Figure 22: Corticosteroid reviews recorded across the sample hospices](image)

*Figure 22: Corticosteroid reviews recorded across the sample hospices*

3.11 Corticosteroid guidelines

Guidelines were evident in only one of the six sample hospices (hospice 3). Each patient had a separate corticosteroid sheet on which the reducing corticosteroid regime was written. The medication chart when referring to the corticosteroid stated ‘as per protocol’.

3.12 Case studies

During site visits, Twenty-eight case studies were documented to illustrate various aspects of the prescribing of corticosteroids. Of these, four which were representative were chosen to demonstrate instances of both good and problematic prescribing.
3.12.1: Case study 1

This case study is an example of good management of corticosteroid and the emergence of adverse effects.

**Patient profile**

Patient number 15 was a New Zealand born 62 year-old female with a diagnosis of metastatic ovarian cancer with ascites. The metastases were in her lungs, abdomen and lymph nodes. She was also a non-insulin dependent diabetic.

**Medications on admission**

The patient was admitted with a sub-acute bowel obstruction. Her medications were many, including omeprazole and zopiclone, as well as several medications administered by two Graseby syringe drivers subcutaneously.

**Corticosteroid dosage and regime**

- 05.03.07 Methylprednisolone (Solu-medrol™) 125mg IM daily
- 06.03.07 Methylprednisolone (Solu-medrol™) 125mg IM daily
- 07.03.07 Methylprednisolone (Solu-medrol™) 125mg IM daily
- 08.03.07 Methylprednisolone (Solu-medrol™) 125mg IM daily
- 09.03.07 Methylprednisolone (Solu-medrol™) 125mg IM daily

Sub-acute bowel obstruction resolved. Solu-medrol™ 125mg IM swapped to dexamethasone 4mg orally

- 10.03.07 Dexamethasone 4mg in the morning
- 11.03.07 Dexamethasone 4mg in the morning
- 12.03.07 Dexamethasone 4mg in the morning
- 13.03.07 Dexamethasone 4mg in the morning
- 14.03.07 Dexamethasone 4mg in the morning
- 15.03.07 Dexamethasone 4mg in the morning
- 16.03.07 Dexamethasone reduced to 2mg in the morning

The patient was then discharged home with a prescription for a reducing dose of dexamethasone as follows:

- Dexamethasone 2mg in the morning for four days
- Dexamethasone 1mg in the morning for four days
- Dexamethasone 0.5mg in the morning for four days
- Dexamethasone 0.5mg alternate mornings for four days
- Dexamethasone dose stopped

The patient had no further prescriptions for a corticosteroid and died on the 17th April 2007.
Corticosteroid adverse effects recorded

1. Skin integrity compromised
2. Oedema
3. Fungal infection
4. Diabetes (previous to corticosteroid introduction)

Commentary
This case illustrates the prescribing of two different corticosteroids methylprednisolone and dexamethasone. The methylprednisolone was delivered intramuscularly as the patient at that time was unable to swallow oral medicines. The choice of methylprednisolone was because of its smaller injection volume. Once the bowel obstruction was resolved and the patient was able to swallow, the methylprednisolone was changed to oral dexamethasone. The gradual reduction of dexamethasone to alternate day dosing before stopping follows evidence-based guidelines and good practice. This case study also suggests that a course of corticosteroids of less than a month in duration can produce adverse effects.

3.12.2: Case study 2
This case study is an example of differences in divided daily dose prescribing between hospital/hospice. Dexamethasone was prescribed for more than one month then stopped abruptly. This case study also showed corticosteroid adverse effects were recorded.

Patient profile
Patient number 21 was a New Zealand born 69 year old male with a diagnosis of metastatic melanoma. The disease had metastasised to brain, bone and lung. He had no known drug allergies.

Corticosteroid dosage
An unspecified dose of dexamethasone (hospital prescribed) was written in the patient’s notes on the 11.05.07. The dexamethasone dose was confirmed on the 05.06.07 as 8mg in the morning and 4mg at night. The patient remained on this dose until 14.06.07 when it was reduced to 8mg in the morning. The patient was admitted to the Hospice on 16.06.07.

Medication on admission
- Slow release morphine (m-Eston™) 60mg twice daily
- Omeprazole 20mg twice daily
- Docusate Sodium 50mg with sennosides 8mg one to two twice daily
- Ibuprofen 400mg three times daily
- Dexamethasone 8mg in the morning
- Sodium valproate 200mg three times daily

The patient being unable to swallow, all oral medications were stopped on the 17.06.07 and a syringe driver commenced with pain relief. On the 18.06.07 the patient was restless and crying with a headache, he was given ketamine, levomepromazine and midazolam but the restlessness worsened. Clonazepam and phenobarbitone (100mg x2) was added to the mix. By then, the patient was heavily sedated.

The patient died 20.06.07, the last dose of dexamethasone 8mg given 17.06.07.

Corticosteroid adverse effects recorded
1. Candidiasis
2. Proximal myopathy

Commentary
This case illustrates three different issues:

While under hospital care, this patient was prescribed a twice daily divided dose of dexamethasone, one dose in the morning the second in the evening. This dose remained divided until a hospice admission when it was reduced to a single morning dose. Evidence suggests that because of the long biological half life of dexamethasone, a single daily dose in the morning is best practice. It has also been shown that an evening dose can ‘hype’ a patient up and prevent sleep.

This patient, who was diagnosed with brain secondaries, had been prescribed dexamethasone 8mg for over a month, yet when he could no longer swallow his dexamethasone was ceased abruptly. Evidence suggests if a patient has been on corticosteroids for more than three weeks, it should not be stopped abruptly as this may lead to an adrenal crisis and increased terminal restlessness.

The literature also suggests that a corticosteroid should be continued by a change to a parenteral route once the oral route is no longer possible.

As with case study one, this patient showed adverse effects from his corticosteroid prescribing.
3.12.3: Case study 3

This case study is an example of a patient on dexamethasone and phenytoin. Dexamethasone was administered as a divided dose and stopped suddenly when the patient could no longer swallow.

*Patient profile*

Patient 414 was a New Zealand Maori aged 72. He had no drug allergies. While on a trip to the USA in July 2007, he had two seizures and was admitted to hospital where he recovered and was able to return to NZ. Whilst in hospital in the USA, 11.07.07 to 18.07.07 he was commenced on phenytoin 300mg daily and dexamethasone 4mg three times daily. At this stage, he was alert and well orientated. Investigations continued in NZ. On 30.07.07, he was advised to continue the phenytoin at the same dose but to reduce the dexamethasone to 2mg three times daily. A biopsy was performed while in hospital between 14.08.07 and 17.08.07, resulting in the diagnosis of a high grade astrocytoma. It was suggested during this stay that the dexamethasone could be reduced further depending on an oncology opinion. On 17.08.07, the dose of dexamethasone was 2mg three times daily. Phenytoin remained at 100mg three times daily and he was on several other medicines. Six weeks of radiotherapy was completed on 15.11.07.

*Medications at time of general practitioner referral to hospice 27.08.07*

- Paracetamol and codeine Two tablets four times daily as needed
- Slow release morphine (m-Eslon™) 10mg twice daily
- Omeprazole 20mg daily
- Phenytoin 100mg three times daily
- Simvastatin 40mg at night
- Docusate and sennosides Two tablets twice daily
- Kiwi crush™
- Metoclopramide 10mg three times daily (max of 30mg in 24 hours) as needed.
- Dexamethasone: 2mg three times daily (the hospice initial assessment on 28.08.07 states dexamethasone was now reduced to 1mg twice daily. There appeared to be confusion over the dose).

*Outpatient medicines record (green sheet) states:*

- 28.08.07: Dexamethasone 1mg twice daily
- 30.08.07 Dexamethasone increased to 2mg twice daily
- 27.09.07 Dexamethasone 6mg in the morning
- ?.10.07 Dexamethasone 4mg in the morning and at lunchtime
Admission to hospice: 20.11.07

Patient unable to communicate well though is able to understand conversation, expressive dysphasia and constipated. Medication once admitted:

- Hospice enema
- Docusate and sennosides Two tablets twice daily
- Kiwi crush™
- Glycerine suppositories
- Oxycodone slow release 5mg twice daily
- Omeprazole 20mg daily
- Phenytoin 100mg three times daily
- Dexamethasone 4mg twice daily

From 10.12.07 to 28.12.07 the patient went on holiday, the medications included with the referral notes to the closest hospice were as above (minus the hospice enema). The dexamethasone dose remained at 4mg twice daily.

Admission to hospice 29.12.07

Patient had deteriorated, profound right hemiparesis, expressive dysphasia.

Medication once admitted

- Dexamethasone increased to 8mg in the morning and at midday
- Phenytoin 100mg three times daily
- Omeprazole 20mg daily
- Oxycodone SR 5mg twice daily
- Pilocarpine eye drops use 1 to 2 drops in each eye four times daily
- Docusate and sennosides Two tablets daily
- Lactulose: 10ml to 20ml twice daily

Corticosteroid dosage and regime

- 29.12.07 to 03.01.08 Dexamethasone 8mg morning and midday
- 4.01.08: Given 8mg dexamethasone that morning. Offered an additional dose of 4mg but unable to swallow it. (Plan was to have a total of 12mg in the morning and 8mg at midday). After not being able to swallow the 4mg dose, all oral medications including the dexamethasone were discontinued.

Notes comment: patient not swallowing and unable to take extra dexamethasone. He lapsed into a coma and was commenced onto the Liverpool care pathway (LCP) for dying patients.

- 04.01.08 Syringe driver s/c commenced with midazolam 45mg over 24 hours
- 05.01.08 Syringe driver s/c changed to morphine 30mg and midazolam 15mg over 24 hours
- 09.01.08 Syringe driver changed to morphine 50mg and midazolam 20mg over 24 hours
- Breakthrough doses of: morphine 10 to 15mg s/c and midazolam 5mg s/c given
The patient died on the 10\textsuperscript{th} of January 2008.

**Corticosteroid adverse effects**
Not recorded throughout.

**Commentary**
This case illustrates a dexamethasone course prescribed initially as a divided dose with a dose of three times daily in hospital. As in case study two, this regime is not recommended in the literature. Similarly in case study two, this was reviewed in the hospice environment and changed to a twice daily dose, the second dose being at lunchtime, not in the evening. The patient was first prescribed phenytoin and dexamethasone in hospital in the USA and this combination was continued throughout this man’s journey until he could no longer swallow. Nowhere recorded in his notes was there an allowance made for the interactions between them, and the effects on each drug’s metabolism of this combination.

This patient, diagnosed with a brain tumour, had been prescribed dexamethasone continuously for six months. His high dose dexamethasone was stopped abruptly when he could no longer swallow. No consideration appeared to have been given to the long-term effects of use of the dexamethasone treatment, the threat of adrenal crisis or of the option of a change from the oral to a parenteral route.

No corticosteroid adverse effects were recorded throughout.

**3.12.4: Case study 4**
This case study is a snapshot of four different regimes of prednisone prescribed by three different consultants for the same patient with the same symptoms.

**Patient profile**
Patient 527 was a 65 year old female with a diagnosis of cancer of the upper left lobe of her lung with metastases in her liver. She also had COPD. She had a history of short courses of prednisone for shortness of breath before 2006. Her concurrently prescribed medicines often included roxithromycin.

**20.11.06:** Admitted very short of breath, settled well on antibiotics, quality of life poor with not long to live. She had been prescribed multiple discharge
medications including roxithromycin 300mg for five days, prednisone 20mg in the morning for five days and zopiclone 7.5mg at night (Consultant 1).

15.01.07: The patient was admitted short of breath and given regular asthma treatment nebulisers for this, and zopiclone to promote sleep. Long acting morphine and paracetamol were given for pain relief. She was prescribed prednisone as a pulse of 20mg for four days then 10mg for four days on discharge. Her other discharge medications included nystatin 1ml four times daily for thrush and omeprazole 10mg at night to protect her gastrointestinal tract (Consultant 2).

26.02.07: The clinical management on admission included roxithromycin and IV amoxycillin clavulanate plus regular nebulisation for shortness of breath, zopiclone 7.5mg at night and omeprazole 20mg at night. Prednisone was prescribed 40mg for three days. On discharge three days later her medications included: zopiclone 7.5mg, roxithromycin 150mg twice daily for seven days, nystatin 1ml four times daily, omeprazole 10mg at night and prednisone 30mg daily for two days, 20mg daily for two days then 10mg daily for two days (Consultant 3).

12.06.07: Admitted to treat COPD and alleviate emotional distress. She became settled on antibiotics and lorazepam and was aware of the finality of her condition. She was prescribed multiple medications including zopiclone 7.5mg at night, omeprazole 20mg twice daily and prednisone 40mg for two days but no roxithromycin. Her discharge medications included zopiclone 7.5mg at night and prednisone 20mg for six days then 10mg for five days. No omeprazole was prescribed on this occasion (Consultant 1).

The patient requested that her final cares be in a hospice or hospital environment. She died during August 07 with no further corticosteroids being prescribed.

*Corticosteroid adverse effects recorded*

Candidiasis.

*Commentary*

This case illustrates the prescribing of corticosteroids on four separate occasions for a hospice programme patient with COPD who was admitted to the same hospital. Each admission was for shortness of breath and on each occasion the
dose of prednisone was prescribed differently. Of the four prescribers, one was a repeat prescriber. The doses varied from one course of 20mg for five days, (Consultant 1) to second course of 20mg for four days then 10mg for four days (Consultant 2). The third prescribed 40mg for three days, 30mg for two days, 20mg for two days then 10mg for two days (Consultant 3). The final prescriber (also the first prescriber) prescribed prednisone 40mg for two days, 20mg for six days and then 10mg for five days (Consultant 1). There appeared to be no consistency in the prednisone prescribing. This case study showed no peer review of prescribing or evidence of re-evaluation of the notes from previous admissions nor was a set of guidelines apparent.

Summary

This chapter identifies the main findings of the retrospective study of corticosteroid prescribing from Phase One and included four case studies supporting these results and differences in prescribing.

It was significant how close the hospices were in the proportion of patients prescribed corticosteroids. This amounted to approximately two thirds of all hospice inpatients. There was also a close similarity in the corticosteroid chosen and the dose ranges used.

Of the eight indications for the prescribing of corticosteroids reviewed, the results demonstrated that ‘general wellbeing’ was the most common indication but within the sample hospices this proportion varied considerably.

A large dissimilarity was evident in the recording of adverse effects and the recording of reviewing and monitoring of the corticosteroids. This disparity was also apparent in the duration of corticosteroid courses prescribed and the method of stopping these medicines.

The results showed that a high proportion of patients were co-prescribed omeprazole with their corticosteroid. This proportion appeared unaffected in the hospices whose medical practitioners prescribed the higher proportions of non-steroidal anti-inflammatory drugs concurrently. Zopiclone and phenytoin were also co-prescribed with a corticosteroid independent of interaction.

The four case studies were representative of the six sample hospices and demonstrated differences in prescribing practice. They endorsed the results
found in this phase. The first was an example of good prescribing practice while case studies 2, 3, and 4 demonstrated issues found.

The results from Phase One of the study were used in the development of the semi-structured interview questions for Phase Two.
Chapter 4 Methods: Phase Two

4.1: Purpose of Phase Two

Phase Two, the qualitative phase of this study, was developed to complement Phase One, which was a retrospective snapshot of corticosteroid prescribing in 2007. The purpose of Phase One was to document how corticosteroids were prescribed, monitored and reviewed in a sample of New Zealand hospices. The main findings of this part of the study demonstrated that the hospices, despite their mutual isolation, were remarkably similar in their proportion of patients prescribed corticosteroids, the choice of corticosteroid used, the dose ranges prescribed and the indications where corticosteroids were used. However, the hospices differed considerably in their recording of corticosteroid adverse effects, their recording of reviewing and monitoring their usage, and the process of stopping these medicines.

Phase Two of this study was developed to explore clinicians’ perceptions of these drugs, and to determine whether prescribing of corticosteroids was evidence-based, anecdotal or intuitive and if there were any other influences on their prescribing. This was approached by completing semi-structured interviews with a selected number of medical practitioners and nurses from the sample of hospices from Phase One. The questions for these interviews were formulated from Phase One data (see an example Appendix G).

4.2: Ethics approval

As this research was to be conducted over more than one region in New Zealand, Ethics approval was required to be given by the Multi-regions Ethics Committee. This was applied for and granted in July 2008 and reviewed and renewed on an annual basis.

4.3: Semi-structured interviews

The Phase Two semi-structured interview questions were developed and refined in the first half of 2010 as the data from Phase One was processed and the results became evident. The refinement and piloting of these questions was conducted over time, with supervisor input, and required a number of iterations.
The question framework is shown below in Table 32

**Table 32:** Phase Two: Semi-structured interview frame

1) General questions around:
   a) Background?
   b) Qualifications relating to palliative care?
   c) Role and involvement in palliative care?

2) The philosophy of palliative care, Linking to their overall philosophy of drug prescribing in palliative care
   a) Given context of palliative care should corticosteroid prescribing be of concern?
   b) Are they comfortable about their corticosteroid prescribing? (Nurses, who do not prescribe, were asked their opinion).

3) Knowledge and understanding of corticosteroids:
   a) Are they a ‘fix it all’ drug?
   b) A ‘comfort’ drug?
   c) Are corticosteroids prescribed for specific and non-specific indications?
   d) How are they stopped-abruptly or a tailored reduction

4) What influences prescribing of corticosteroids:
   a) Is it evidence-based?
   b) Is it intuition or anecdote?
   c) Are guidelines followed?
   d) Is there peer review of corticosteroid prescribing?

5) What influences choice of corticosteroid:
   a) Which corticosteroid?
   b) For what indications?
   c) In what doses?
   d) What are the choices of range?

6) Questions around Phase One: Specific data and graphs:
   a) Were there any surprises or observations?
   b) Have there been changes in corticosteroid prescribing since 2007?

7) Issues and concerns:
   a) Lack of monitoring and reviewing?
   b) Learn more about issues (whose responsibility is the reviewing and monitoring)?
   c) Issues raised by interviewees

The semi-structured interviews commenced with broad open-ended questions around the interviewees’ palliative care background, leading to more specific questions about reasons for the prescribing, monitoring and reviewing of corticosteroids. These questions were linked to the results of Phase One because Phase One had shown both similarities and differences in practice between each hospice. The questions were designed to elucidate the reasons for this. Although data from the Phase One 2007 review for each hospice was the specific data
discussed, the main focus of discussion was the practitioners’ perceptions of corticosteroid prescribing at the time of the semi-structured interviews in 2010.

The nurses interviewed did not have prescribing rights, so were asked their opinions on the questions around prescribing. The more general questions remained the same.

The interviews were designed to last between 30 to 60 minutes, Six months was considered a reasonable time frame in which to complete the interviews, which commenced in August 2010 and were completed in December 2010.

4.4: Sample frame

Eighteen clinicians were considered a sufficient number to interview (Guest, Bunce, & Johnson, 2006), three selected from each hospice, comprising two medical practitioners and one senior nurse. Ideally clinicians from 2007 would always have been interviewed but this was occasionally not possible due to staff changes in the lapsed period. This sample was considered appropriate to address the objectives of Phase Two.

4.4.1: Medical practitioners

Of the twelve medical practitioners interviewed, seven were palliative care specialists, and five were general practitioners. The Medical Director from each hospice was interviewed along with a second medical practitioner. In the larger units, it was not unusual for two palliative care specialists to be interviewed. One hospice had a specialist and a general practitioner. In the smaller hospices, the Medical Directors did not have specialist palliative care qualifications but were very experienced in the field. They, and a second medical practitioner, were interviewed.

4.4.2: Nurses

All six nurses (one from each hospice) invited to be interviewed were generally senior registered nurses with varying palliative care experience.

4.4.3: Interviewee key

So the interviewees could remain anonymous a key (Table 33) was introduced to identify the participants by number (1 to 18) and by designation only.
Table 33: Interviewees by number and designation

<table>
<thead>
<tr>
<th>Number code</th>
<th>Designation of interviewee</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Medical Director-Palliative care specialist</td>
</tr>
<tr>
<td>2</td>
<td>Palliative care specialist</td>
</tr>
<tr>
<td>3</td>
<td>Registered nurse</td>
</tr>
<tr>
<td>4</td>
<td>Medical Director-Palliative care specialist</td>
</tr>
<tr>
<td>5</td>
<td>Palliative care specialist</td>
</tr>
<tr>
<td>6</td>
<td>Registered nurse</td>
</tr>
<tr>
<td>7</td>
<td>Medical Director-Palliative care specialist</td>
</tr>
<tr>
<td>8</td>
<td>Palliative care specialist</td>
</tr>
<tr>
<td>9</td>
<td>Registered nurse</td>
</tr>
<tr>
<td>10</td>
<td>Medical Director</td>
</tr>
<tr>
<td>11</td>
<td>General practitioner</td>
</tr>
<tr>
<td>12</td>
<td>Registered nurse</td>
</tr>
<tr>
<td>13</td>
<td>Medical Director</td>
</tr>
<tr>
<td>14</td>
<td>General practitioner</td>
</tr>
<tr>
<td>15</td>
<td>Registered nurse</td>
</tr>
<tr>
<td>16</td>
<td>Medical Director-Palliative care specialist</td>
</tr>
<tr>
<td>17</td>
<td>General practitioner</td>
</tr>
<tr>
<td>18</td>
<td>Registered nurse</td>
</tr>
</tbody>
</table>

4.5: Organisation of site visits

As with Phase One of the study, the interviews were not conducted in the numerical order of the sample hospices (one through to six). Instead the hospices were asked which of the allotted months were most convenient for them. The visits also needed to fit around the Montreal Palliative Care Conference 2010 and the Hospice New Zealand Conference 2010 as some of the interviewees were presenting at or attending these conferences. There were days, weeks or months that suited some interviewees more than others. Hospice 6 was visited in August, Hospice 1 and Hospice 3 in September, Hospice 4 and 5 in October and Hospice 2 in November.

The sample hospices were approached, to obtain suitable interviewees. Once these clinicians had been identified, they were provided with a Participant Information Sheet (Appendix E) and a Participant Consent Form (Appendix F). All
agreed to be interviewed. The majority did not return their consent forms but instead gave them to the interviewer at the time of the interview.

A week before each hospice was visited, the interviewees were provided with the specific data results from Phase One of the retrospective study consisting of written results and graphs. The results were specific to each hospice but the graphs compared their hospice against the average of all the hospices in the sample. An example of this specific data and graphs is attached (Appendix G).

**4.6: Structure of the Interviews**

What follows is a brief description of the structure of the interviews conducted at the different hospices.

**4.6.1: Hospice 1**

Hospice 1, the second hospice visited, was visited on the 9th of September 2010 and all three interviews were conducted on that day and over a 3 hour period. The first interview was with the Medical Director, a palliative care specialist, who had also practiced at another sample Hospice. The second interviewee was another palliative specialist who had a special interest in corticosteroids. The final interview was with a senior palliative care registered nurse with experience both in the United Kingdom and New Zealand. The duration of two of the interviews was longer than 60 minutes.

**4.6.2: Hospice 2**

This hospice was visited on the 15th of November 2010; it was the final hospice to be seen. The first appointment was with the registered palliative care nurse, and ran to time and went smoothly. The second interviewee was to be with the hospice medical officer (not a palliative care specialist) and was cancelled at the time of the appointment. This was the only interview booked that did not eventuate and a disappointment as this medical practitioner had audited Hospice 2’s corticosteroid prescribing.

A palliative care specialist, working between the hospital and the hospice, volunteered to be interviewed in her place. This interview was conducted at the hospital not the hospice. The final interview was with the Medical Director, another palliative care specialist. This interview had a change in time and day
due to work commitments. The interviews with the two palliative care specialists were of shorter duration than that of the registered nurse.

4.6.3: Hospice 3

Hospice 3 was visited on the 7th and 8th of September 2010. The first interview was on the afternoon of the 7th with a palliative care specialist who had been in this hospice only since 2008 however he had spent some of 2007 in one of the other sample hospices. This specialist, unlike all the other palliative care specialists was the only specialist interviewed who had not been ‘grand-parented’ into the specialty when palliative care was granted speciality status.

On the afternoon of the 8th the interview was with the Medical Director, an experienced palliative care specialist who has practised palliative care in this hospice for 23 years. The final interview was with an experienced palliative care nurse who had worked in palliative care for 30 years.

4.6.4: Hospice 4

Hospice 4 was visited on the 5th of October. This hospice was the smallest hospice and did not employ a palliative care specialist. The first interview was with a newly employed part-time medical practitioner. The interview was brief as this medical practitioner was not at Hospice 4 in 2007 so was unable to answer some of the questions.

The second interview was with the Medical Director, an experienced palliative care practitioner with a diploma in palliative care from Flinders University in South Australia.

The final interview was with a palliative care registered nurse. She had previously been employed by one of the other sample hospices so was able to describe the similarities and differences between the two environments. As with the previous three nurses, she had considerable experience and was very considered in her opinions and thoughtful in her replies.

4.6.5: Hospice 5

Hospice 5 was visited on the 7th of October 2010. Concerns around timeframes for interviews had been voiced from this hospice and apprehension was expressed about the availability of medical practitioners for those interviews due
to lack of medical resources. Before the researcher’s arrival, there had been uncertainty around the timing of the interviews and the interviews eventuating. This uncertainty was unfounded and all three interviews occurred in the expected timeframe.

Like Hospice 4, this hospice did not employ a palliative care specialist. The researcher was very aware of the limited hours the part-time general practitioner worked and was conscious of taking that time. This was not a long interview, although this general practitioner had been at the hospice in 2007. Interview two was with one of the hospice’s registered nurses. She answered the interview questions very cautiously and briefly and required drawing out. She did not show the confidence and knowledge base of some of the previous nurses.

The final interview was with the Medical Director who, although not a specialist, had many years of palliative care experience and a diploma in palliative care through the University of Auckland, New Zealand.

4.6.6: Hospice 6

Hospice 6 was visited on the 12th and 13th of August 2010. This was the first hospice visited and was the first time the questions were attempted, apart from a trial with the researcher’s supervisor. The first interview was with the Director of Nursing who was in a management role rather than working in the field. Her knowledge when answering the questions referred back to her previous nursing practice.

The second interview was with the Medical Director, an experienced palliative care specialist, who responded confidently and in depth to all questions asked. This was a longer interview. Interview three was with a general practitioner who had worked many years part-time at the hospice. Unfortunately, he had not received his data so his responses tended to be brief.

4.7: Interview recording and transcribing

The 18 interviews were taped on an Olympus DS-55 digital voice recorder. Once recorded, the information was saved onto a USB data stick then couriered to the University for transcribing to hardcopy. After transcription, the written data was checked by the researcher’s husband (a pharmacist) against the digital recordings then rechecked by the researcher to address inaccuracies. The
relevant information from these 18 transcripts was then entered on an NVivo 8 qualitative data analysis programme.

4.8: Data analysis

NVivo 8, a tool designed to assist qualitative data analysis, was the software programme used in Phase Two of this study. This programme provided tools for data management, organisation, responses to questions, and reporting.

Once the 18 interviews had been transcribed into Word documents, the data was imported into NVivo 8 to be stored. Broad themes (nodes) were identified from the initial readings of the transcripts and a basic coding structure was developed. This structure was chosen to fit with the research questions but was later revised to fit instead with the questions asked in the semi-structured interviews.

The themes (nodes) recognised were reviewed during the coding process, and new themes were added and the content of these nodes printed out and reviewed by the researchers supervisor and qualitative methods advisor then refined further on NVivo 8. Once these themes (nodes) were finalised, they became the content of the qualitative research.

Figure 23 overleaf illustrates the tree nodes classified by research question then refined down to the semi-structured interview questions.
The themes identified in this chapter are discussed in depth in Chapter 5 supported by quotes from the interviewees.
Chapter 5 Results: Phase Two

Chapter 5 provides the results based on the Phase Two semi-structured interviews described in Chapter 4. These interviews were conducted across the six hospices from August to November 2010. The questions for these interviews, around the prescribing of corticosteroid drugs in palliative care, had been identified and developed from the original objectives of this study. A sample of 18 interviewees was considered sufficient to interview for data saturation. Of the eighteen participants, twelve were medical practitioners (seven with specialist palliative care qualifications), and six were senior registered nurses.

Once the interviews had been completed and common themes recognised, these were entered as tree nodes on an NVivo 8 database. The themes identified showed the interviewees' perceptions of evidence versus actual prescribing practice, the culture of the medical practitioners' prescribing, whether guidelines and protocols were of value and the participants opinions around the recording of reviewing and monitoring. The themes identified with quotes from the interviewees about their prescribing practice were the basis of the results presented in this section. Each quote is identified by a number and that number relates to Table 33 of Chapter 4, which describes the interviewees by designation.

5.1: Palliative care prescribing

Interviewees were asked their opinions on whether palliative care prescribing was different to prescribing in other medical specialities. From the earlier quantitative results it appeared that this was case, therefore this stage of the study aimed to identify the possible reasons for this.

The general response from interviewees was that the goal of prescribing in palliative care should be, as in all areas of medicine, to use the smallest number of drugs for the best gain and the fewest adverse effects. However, all interviewees agreed that prescribing in palliative care was specific to the discipline and did differ from mainstream prescribing.

Most of respondents thought that the biggest difference was the use of drugs ‘off-registration’, where the medicine is prescribed for a helpful side-effect, rather than its registered indication. In New Zealand, Medsafe registers medicines for specific uses,
but a medical practitioner may legally choose to prescribe them off-registration under provision of section 25 of the Medicines Act. Section 29 of this Act also allows for medicines as yet unlicensed to be prescribed provided certain processes are followed.

As one of the palliative care specialists suggested:

“Different in the sense we prescribe a number of things off registration. That would be far more so than any other discipline I have worked in and I would hate to think what percentage of our prescriptions are not registered.” *(4)*

An example of this was the prescribing of sodium valproate, which is licensed as an anticonvulsant drug yet was being prescribed for nerve pain because of its membrane stabilising properties.

Another subtlety in palliative care prescribing is the ‘layering’ of medicines. Although palliative care physicians are wary of drug combinations because of the problems of combination, there is a tendency in this environment to prescribe multiple medications (‘layering’) to treat different aspects of the same symptom:

“We are more wary of drugs because a lot of our problems are caused by drugs. Whether that is a delirium, or constipation or steroids... but on the other hand we are great poly pharmacy people and we do layer on a whole bunch of drugs, just on one problem – nausea being one of them.” *(1)*

In the palliative care field, it is common for medical practitioners to prescribe opioids on a frequent basis for patients requiring pain relief. As a result, clinicians become very familiar with their use:

“We prescribe lots of Controlled Drugs of course for pain. I think the knowledge is greater when we are more experienced, more comfortable with using controlled drugs.” *(13)*

A further difference in the prescribing of opioids, mentioned by several of the interviewees, was the higher doses prescribed in palliative care:

“When I first came to work here I could not get my head round the high doses used for opioids.” *(18)*

The doses prescribed are often higher than doses seen in other medical specialties because as the disease process escalates there can be a need for increased levels of pain relief. Patients may also develop tolerance to opioids, reducing their effectiveness at a given dose level.
The level of confidence with opioid prescribing appeared in the interviews to relate to practitioner experience and frequency of use. Those who were experienced or familiar with opioid prescribing were more comfortable with the doses used in palliative care. Some suggested that, even with experience, general practitioners (who are typically less familiar with this group of drugs and the doses used) were reluctant to prescribe an adequate dose of a Controlled Drug:

“It depends how much experience the general practitioner has had. Quite often there is a lot of reluctance even among some of those you would expect to be experienced.” (13)

One of the possible reasons for this apparent lack of unease regarding opioid prescribing in palliative care could be that those working in this field are less concerned about addiction:

“Probably we are less worried about addiction so I would be more likely to prescribe.” (11)

It appears that some general practitioners may be apprehensive about their patient’s opioid dose or perhaps an addiction issue, while for most palliative care practitioners this is a lesser consideration. Their concern is adequate pain relief and quality of life for a patient who has only a short time to live.

Respondents indicated that, within palliative care, there was an opportunity to reduce non-essential drugs. For instance, medicines no longer relevant given the patients’ expected short life-span and those with potential for side effects (e.g. statins: cholesterol lowering drugs):

“We try and reduce non-essential drugs quite early on if we feel the risk benefit is not worth it for patients or the side-effects are too much.” (13)

They also suggested that part of their prescribing was non-pharmaceutical, in that “prescribing” was often for psychosocial intervention for instance art therapy or chaplaincy services:

“We also have this other phase that actually we are all about communication, co-ordination and that sort of holistic thing.” (1)

Within the hospice context more time is available to give and spend with each patient because the staff/patient ratio is higher than is usual in the hospital setting. This provides time and an opportunity to explore the subtleties of symptom management from both the physical and emotional perspectives. It also allows staff the time to be
unhurried in their care and communication with patient and their families so the whole person is treated, not just physical symptoms.

Palliative care prescribing was clearly different to prescribing in other medical specialties. There is a range of possible reasons as to why this may be the case. Palliative care is a relatively new specialty and consequently prescribing is not always evidence-based or guideline led. The type of evidence-based practice designed for the curative approach in general medicine may not be appropriate for palliative care patients with a short life expectancy.

There are medical practitioners who have difficulty in accepting that death is part of life, rather than a failure of practice. Hospice services developed as a result of patients dying badly in the acute setting. For medical practitioners who have trained in a model where the expected outcome is cure, the curative approach may lead to feeling of unacceptable failure when this is no longer possible.

In response to palliative care practice, medical practitioners’ perceptions have changed to keeping the dying patient comfortable and with the focus on end-of-life care. There is a shift in practice: quality of life, no matter how short, becomes the priority.

Drugs and doses (both high and low) may be prescribed off-licence, but the palliative care prescriber may be questioned about the evidence-base of their prescribing by those in other fields who may be disturbed by this practice.

Although palliative care practitioners attempt to reduce non-essential medications to prevent adverse effects, this is not always achieved, as with disease progression, more medicines may be added. To maintain patient comfort, more than one medicine may be needed to treat the same symptom. This practice is frequent in palliative care although it may be questioned by other medical specialities requiring the prescriber to justify his/her decision.

The responses in this section illustrate the differences in palliative care prescribing and some of the inherent tensions in trying to incorporate traditional evidence-based approaches in this area.
5.2: Corticosteroid prescribing and associated issues

In addition to the general differences in palliative care prescribing, the researcher was interested to examine any specific differences within corticosteroid prescribing. When asked if the prescribing of corticosteroids in palliative care was atypical of general medicine, all interviewees responded that corticosteroids were prescribed more frequently in palliative care. They suggested that corticosteroids were prescribed for many different indications, which was dissimilar to general medicine where the range of prescribing indications was narrower e.g. asthma, arthritis treatments and allergic reactions.

Typical responses from the participants were:

“I think they are prescribed a lot more often for a start. There are a number of conditions that we see commonly, frequently that we would use them for. I think we are probably using them more often as an analgesic perhaps than many specialties would.” (2)

“Significantly more widely in palliative medicine than in general medicine and the range of steroids in particular. I think we have a lower threshold for prescribing steroids than general medicine.” (16)

When asked if the respondents had concerns around the prescribing of corticosteroids, there was a wide range of views:

“Personally, I am confident and comfortable. Absolutely.” (2)

“Not really to be honest. I like rules; it seems to be a bit wishy-washy.” (14)

This range of views did not appear to be determined by role (medical practitioner or nurse) but was influenced by the experience of the interviewees. Medical practitioners who worked part-time in palliative care, or who were less experienced, voiced a lesser confidence in their prescribing. This is possibly due to a perceived lack of clear guidelines.

Some specific opinions on corticosteroids were expressed. For example, some participants who had reservations with their use, saw the point of prescribing them short-term, but suggested they were only a stop-gap:

“Steroids are not the answer. They are the stop-gap until you figure out the answer for a lot of our patients.” (1)
One participant voiced concern around the ethics of corticosteroid prescribing for a dying patient and suggested they gave false hope:

“I am not entirely comfortable. Because I’m aware that sometimes they have a very miraculous effect, and people who were apparently dying sometimes make quite a comeback for a little while. It is very time specific I think. Sometimes I really question the ethics with that. Not entirely comfortable with it. Still have questions in my mind about that.” (10)

Alternatively, it was said by some that all palliative care patients should have a course of corticosteroids at some stage of their palliative care journey:

“It’s almost said that you don’t get a good death without somebody having had a honeymoon of steroids at some stage. It’s amazing how often that actually does happen.” (17)

The researcher also explored the interviewees’ perspectives on whether they saw corticosteroids as ‘comfort’ or ‘fix it all’ drugs. When asked if a corticosteroid was ever prescribed in palliative care as a ‘comfort drug’ for the patient, the responses were divided between those who supported or rejected this proposition.

Those interviewees who saw a corticosteroid as a ‘comfort drug’ did, however, place stipulations appearing to justify their use:

“Sometimes I do use them for that – You are often killing two birds with one stone – if you see what I mean. I would see that as a beneficial side-effect if you like.” (2)

There appeared to be some dissension amongst the interviewees over the researcher’s choice of the word ‘comfort’. For some, the term appeared not specific or scientific enough. A number of respondents did not see a corticosteroid being prescribed as a ‘comfort drug’ at all and were unhappy with this terminology. They felt that ‘comfort’ came from specific symptom management:

“They are a symptom management drug I think and I think that is what we are in the business of. If that provides comfort then that is a bonus. Usually I would not call them really a ‘comfort drug’. I would call them a specific drug for specific symptoms.” (10)

“Loss of energy, loss of appetite and wellbeing to me is an indication that I could prescribe steroids for. I would not use the term ‘comfort drug’ I would not know what that would mean. It is for loss of energy, loss of appetite.” (8)

Some participants went so far as to suggest the corticosteroid was prescribed for the ‘comfort’ of the clinician rather than the patient.
A nurse suggested:

“Perhaps we did see it as a ‘comfort drug’, not for the patients but for us, so that we are actively doing something.” (6)

While a palliative care specialist physician responded:

“Certainly for the prescriber yes.” (4)

When the researcher expanded this question to ask if a corticosteroid could possibly be described as a ‘fix it all’ drug, most interviewees replied in the negative. Their response was that a corticosteroid should be prescribed for a specific reason:

“No. I would never just prescribe them as oh well I can’t think of anything better let’s try … No – I don’t see them as a ‘fix-it-all’. They are too dangerous to do that with. They have too many side-effects.” (2)

Two respondents, neither palliative care specialists, did see the value of a corticosteroid as a ‘fix at all’ drug, but showed some reservation in their response:

“That’s when we might see it as a ‘fix-it-all’. When we have got a number of things and you think what could we fix with all of this and it seemed to me that dexamethasone was the ideal thing that would do most. Kept our fingers crossed and it did it.” (12)

“I do. I think there is some merit in why that’s true.” (17)

Although all interviewees agreed corticosteroids were used more frequently in palliative care, there was a divergence of opinion over their usefulness. This could relate to the experience and confidence of the palliative care clinician. Palliative care prescribers face extra challenges in the use of these medicines, there is a demand for them to be more creative, with little evidence-base (see Chapter One) in the palliative care situation. A tension may be created between palliative care prescribers and other prescribers whose corticosteroid prescribing is more specific and protocol based.

The use of the word ‘comfort’ when referring to the prescribing of corticosteroids, tests the prescriber’s confidence in their knowledge of the value of these medications. In this era of expected evidence-based practice, some clinicians appear to struggle with words like ‘comfort’ and ‘fix it all’ as they are not specific enough for them. There was no discernible difference, amongst the medical practitioners and nurses, between those who agreed with corticosteroids being called ‘comfort drugs’ or ‘fix it all drugs’ and those who did not. These responses highlight the dilemma of
the practitioner between the art and the science of medicine where there is tension between strictly evidence-based practice, difficult to find in palliative care, and practice informed by experience, anecdote and intuition. It appears that the same dilemmas expressed in the previous section on prescribing in palliative care, are amplified in the context of corticosteroid prescribing.

5.3: Views, knowledge and understanding of corticosteroids

This section discusses the perceptions of the interviewees around the use of corticosteroids for specific and non-specific indications, the consequences of that use, and the choice of corticosteroid.

Several of the interviewees commented about familiarity and casualness in long-term corticosteroid usage and claimed that it was easy once they had been added to a patient’s regime for them to be forgotten:

“I think drugs like steroids can slip under the radar a bit.” (18)

In contrast, others thought in recent years they had become more aware of the potency of corticosteroids and were now becoming more considered and less liberal in their use:

“I think in recent years, we probably are a little bit more aware of how often we are using them and what we are actually using them for. I think there was a time where we used to think it was a bit of a wonder drug and we just throw it in there but we actually think a little bit more about what we are trying to achieve nowadays and probably use it for the right reasons, for better reasons.” (6)

Many suggested they tried to be very clear why the corticosteroid was being used and that it would be for a specific indication:

“I try to know the indication I am using when I am prescribing steroids. Try to be clear to myself. But also to the team, what I am trying to achieve. What the indication is.” (8)

All prescribers were confident with prescribing corticosteroids for specific indications for instance, neurological symptoms or a bowel obstruction. In contrast, there were some who dissented from the non-specific label when prescribing for non-specific indications were suggested, especially when they realised most corticosteroids were being prescribed for these reasons. Most respondents were quick to propose that
within the non-specific label of ‘general wellbeing’ there were some very specific reasons for their prescribing:

“We do use them a lot for a sense of well being but looking at appetite as well. That is the reason we prescribe them. To try and improve the appetite, and with that comes a sense of well being.” (7)

“Loss of energy, loss of appetite and wellbeing to me is an indication that I could prescribe steroids for.” (8)

Some interviewees felt that because of the potency of corticosteroids, adverse effects were inevitable. They suggested it was very difficult to recognise such effects as corticosteroid in origin and could easily be mistaken for effects due to the general malaise of the dying patient. As a result, the corticosteroid effects were frequently not identified until they were very obvious, for example being manifest as Cushing’s syndrome:

“Out of all, it is the long term side effects that are actually important and they are subtle and sneak up on you and I think that is important.” (1)

Other respondents suggested that when no other medications seemed to be helping difficult symptoms, a trial of corticosteroids was merited:

“I think they are sometimes used as a last measure.” (14)

“They are a panacea when all else fails or the “drug of last resort.” (10)

It became apparent that when some prescribers feel a helplessness with not being able to manage a patient’s symptoms with any other medicine, that a corticosteroid may be given.

There appeared to be movement amongst the clinicians towards recognising that corticosteroids were potent medicines, and that their prescribing around these drugs needed to be more considered. In contrast, when asked in the interviews “Has your prescribing of corticosteroids changed since 2007?” the majority responded “no.”

Despite prescribers becoming more aware of the potency of these agents, there appeared to be little urgency to review corticosteroid use in practice.

The interviewees were asked during the interviews for their preference of corticosteroid. Dexamethasone was the corticosteroid of choice in the six hospices. Some of the reasons given for that choice follow.
Medical practitioners who had worked internationally responded that dexamethasone was the corticosteroid they had used in other countries, they were familiar with its use, and there was no evidence to suggest a change in practice:

“I can comfortably say that in my palliative career looking at steroid prescribing ... every environment I have been in they were using dexamethasone ... I stick to the devil I know rather than trying to find out about the devil I don't know unless there is hard, compelling evidence and most probably in common with most older prescribers.” (16)

Sometimes a medical practitioner would admit a lack of knowledge: A part-time medical practitioner, new to palliative care and unfamiliar with prescribing corticosteroids suggested that she relied on the advice of an oncologist for her dexamethasone prescribing:

“Dexamethasone I have not used anything else and that is what is usually advised by the oncologist, that we prescribe dexamethasone.” (11)

The reasons for the choice of corticosteroid could be obscure or guideline driven. Another medical practitioner when asked the reason for dexamethasone being the drug of choice at her hospice replied:

“I have no idea. I don’t know. That is where my knowledge is lacking. I just do it because it says here.” (14)

Several nurses, who don’t have prescribing rights, responded when asked about corticosteroid choice:

“I think it is the medical practitioner’s preference.” (9)

When asked about prednisone prescribing, the participants suggested that prednisone was prescribed within the palliative care unit for non-specific (symptoms:

“For well being, loss of appetite, loss of energy we use medium dose of prednisone.” (7)

Or occasionally when it was felt a patient would benefit from a steroid but not one as strong as dexamethasone and perhaps for a longer course:

“I have used that for somebody that I felt would benefit from a steroid but not as powerful a steroid and perhaps somebody who might be on it for longer.” (13)

But mostly the interviewees felt the prescribing of prednisone came from hospital medical practitioners and general practitioners usually for long-term conditions:
“Generally it is the patients that have been started on it from someone else like the team over in the hospital or their general practitioners.” (15)

It is not surprising that general practitioners tend not to prescribe dexamethasone. The drug regulations in New Zealand require that dexamethasone is funded only on a prescription by a specialist or on specialist recommendation. It is not always easy for a general practitioner to access that specialist recommendation.

A small number of palliative care specialists prescribed methylprednisolone (Solu-Medrol™) when a patient was unable to swallow and there was a need for a parenteral route:

“I am prescribing Solu-Medrol because the person cannot swallow.” (7)

Two specialists suggested that it was kinder and gentler to give Solu-Medrol™ parenterally than dexamethasone, as the volume of the injection was considerably smaller:

“I know other hospices where I worked would give dexamethasone parenterally but that is four mg in a ml and if you give 16 mg of dexamethasone because somebody has intracranial pressure that is 4 ml either sub-cut or IM. Solu-Medrol comes 125mg in 1.5ml. It is kinder, gentler.” (7)

Interviewees were not asked specifically about the pharmacology of the corticosteroid drugs directly but some comments were made. One medical practitioner suggested that dexamethasone had less of a mineralocorticoid effect than prednisone:

“Yes. It has got less of mineralocorticoid effect.” (13)

Whilst a nurse incorrectly suggested that dexamethasone was chosen above prednisone as it had fewer adverse effects:

“We tend to use dexamethasone more because I believe there are fewer side effects with moon face, etc. so we are using dexamethasone more than prednisone now.” (9)

In contrast, a general practitioner working part time in palliative care was aware there were differences between dexamethasone and prednisone and said:

“Certainly you don’t see this wakefulness thing the same with prednisone. Dexamethasone certainly has people wired very quickly.” (17)

The same general practitioner thought:
“It appears to me that dexamethasone seems to have more initial effect. You give one dose and you know. And prednisone does not seem to have that.”

Prescribing choices appear to depend on the confidence and level of palliative prescribing experience of the medical practitioners involved rather than strict pharmacological considerations. Even amongst some experienced prescribers there seemed to be a certain lack of understanding of the pharmacology of these agents. The interview quotes show an element of institutional habit when saying this is what we always do here. In particular, the use of dexamethasone appears to be based on experience and intuition rather than scientific logic.

In the researcher’s opinion, the reasons for decisions behind the prescribing of corticosteroids may be variable with some prescribers taking limited ownership for the decision. The nurses, who do not prescribe, follow the medical practitioners’ preference in the choice of which corticosteroid. Given that nurses deal directly with the consequences of the adverse effects of these medicines in the long-term, it is surprising they do not show more interest in the prescribers’ choice of agent.

There seemed to be an acceptance from the participants that adverse effects for patients on corticosteroids are inevitable, even if not identified initially and not recorded in the patient notes. Adverse effects and lack of recording are discussed more fully in section 5.7.2

Unquestionably, the interviewees agreed that corticosteroids should be given for specific reasons. There is confusion and sometimes dissension over the terms non-specific and ‘general wellbeing’ with most clinicians feeling they prescribe corticosteroids for a specific reason such as appetite and that ‘general wellbeing’ comes because of that prescribing. Others considered ‘general wellbeing’ was a specific reason in itself.

It appeared that prescribers struggle with the more subjective and less scientific terminologies such as ‘general wellbeing’ as they do with the terms ‘comfort drug’ or ‘fix it all drug’ mentioned in section 5.2. Yet the indications for which corticosteroids are recorded most is non-specific/‘general wellbeing’ (see Chapter 3 section 3.3). In hindsight, the researcher wishes she had pursued this tension further and also asked the interviewees more on their pharmacological understanding of these medicines.
5.4: Factors influencing corticosteroid prescribing

After questioning the interviewees about their knowledge and understanding of corticosteroids in palliative care, the researcher was interested to elucidate the factors influencing the prescribing of corticosteroids. The participants were asked for their views on evidence-based practice and the place of intuitive and anecdotal practice.

When asked if the prescribing in palliative care was evidence-based, a few interviewees suggested that there was a body of literature around some specific indications for the use of corticosteroids:

“The evidence around cerebral oedema and the effects of corticosteroids are definitely evidence based. It is a bit of evidence based also around bowel obstruction and around appetite it is definitely evidence based, around widespread bone disease.” (4)

Other respondents felt that there were many articles of significance on the use of corticosteroids as an adjuvant therapy for cancer patients:

“There are quite a number of articles and quite a lot of literature around now. There are quite a few solid articles about the use of corticosteroids for cancer patients, for symptom management, adjuvant therapy.” (3)

But participants were equivocal about the quality of the evidence base. Opinions varied, with the majority interviewed unsure of the rigour of the evidence:

“In the monthly peer reviews we have speakers and a couple of times we have had steroids as a subject and they inevitably come back as the evidence base is so slack.” (1)

Others mentioned that they have looked at the literature and found it varied or confusing or that they tried to be evidence-based but felt the evidence was unclear:

“I find the literature on that slightly confusing.” (16)

“I don’t know if it is really – We try to be evidence-based but it is not very clear cut.” (13)

Some went so far as to say that there wasn’t evidence for corticosteroid prescribing at all resulting in corticosteroids being prescribed differently according to the prescriber’s understanding:

“I don’t think the evidence is out there actually.” (2)
One of the interviewees suggested that there was a lack of randomised controlled trials in palliative care and implied that the medicines used were those most referenced in the literature and the most commonly used at the time, but were not necessarily perfect:

“Not that palliative medicine has that much level 1 evidence still and I suppose the prescriptions are reflective of that we go for pain medicine – morphine is our gold standard not because it’s perfect but because it’s best written up and most readily available.” (16)

When discussing intuitive and anecdotal prescribing, all except one agreed that anecdote and intuition were major factors of prescribing, with some equating that with experience:

“I suspect so. I wonder sometimes can you always have a scientific reason for everything, I don’t know the world is a mystery to me.” (18)

“Probably I think so. I think it is certainly intuitive and probably anecdotal too because we go by past experience of what worked and what didn’t.” (12)

The single dissenting specialist stated that her prescribing was based on clinical findings:

“No. I think that the prescribing here would first of all be based on clinical findings. The patient is reviewed, examined, and an assessment made. And on the basis of that assessment, there will be one of the three pathways to follow. It is not really a gut feeling.” (7)

This prescriber claimed her decisions were clinically based and that her prescribing was not intuitive but guideline-based.

With the exception of the single dissenter, the theme that emerged through this section was that prescribing of corticosteroids is based on experience, anecdote and intuition, with little reliance on evidence-based practice. Practitioners are very aware of the lack of robust evidence. While there is literature available for some specific indications, which is useful, much of that literature is found to be confusing. Corticosteroids were being prescribed differently between medical practitioners and prescribers were sometimes unsure of doses or the length of time patients should be taking these medicines.

There also appeared to be tension between modern day evidence-based medicine demands and traditional hospice practice:
“I often say that we are witnessing the death of hospices. It is more specialist palliative medicine. I think there are quite a lot of losses. But it is our modern era and the patients do not know any differently so for them it is not a crisis. But for those of us who have known the more peaceful, tranquil journey to death that once patients had in hospices - do not see it all that often nowadays.”

“Palliative medicine has changed. No longer is it just hospice medicine. Now being a speciality. It’s more scientifically driven than the art of medicine driven. I think it has created a lot of the busyness as well instead of just being able to go with the flow with the patient. (The patient symptoms, talking through the fact that they were dying). A lot more interventive medicine in palliative medicine today.”

Hospice care, in the early days before being recognised as a medical speciality, was considered by some to have been akin to a ‘cottage industry’. Hospice care has, as a speciality, become more medicalised yet some traditional practice remains, which the more evidence-based practitioner can find difficult. Available literature however may not helpful. There are few clinical trials in palliative care on corticosteroid prescribing and prescribers may be commended for their successful prescribing considering the fundamental lack of supporting evidence.

5.5: Patterns in prescribing

5.5.1: Differences in prescribing corticosteroids within hospice, hospital and general practice

In this section, the interviewees were asked their views on the differences in prescribing in these three areas.

5.5.1.1: Hospice and hospital prescribing of corticosteroids

During the interviews, two issues emerged when discussing hospital and hospice practice with corticosteroid prescribing. These were sudden reduction of dosage and the divided dosage timing of these medicines across the various hospital specialities.

Most hospice patients have a diagnosis of cancer. As part of their treatment, they will have been seen by a hospital medical oncologist who may have prescribed chemotherapy. Medical oncologists have prescribing patterns dictated by their specific protocols; a chemotherapy or radiology protocol may include a corticosteroid.
Almost all interviewees mentioned issues with the practices of medical oncologists around the prescribing of high doses of corticosteroids, and the fast rate at which these doses were reduced by these specialists. Because hospice practitioners had seen the effects of quick reduction, they went so far as to say that it was one of the reasons why they, within hospices, reduced corticosteroids more gradually:

“Oncology drives a lot harder towards cutting down the steroids and that may to some extent actually fuel our keeping people because we are running into trouble because they are cutting them too quickly but it is because they use such nasty other drugs so they try and minimise the noise factor and steroids is almost a noise factor to them versus their chemotherapeutic intervention, which is the main thing, whereas for us the steroid itself is the important therapeutic element in what we do.” (16)

The respondents also suggested that when high doses were prescribed, those high doses tended to be instigated by medical oncologists rather than in the hospice environment:

“And then the interplay. It is oncology who gives big doses and stops them. Sometimes it works and sometimes it does not. This makes us consider what we are doing. They are the main counter balance in steroid usage, because they do use them differently.” (1)

When discussing the prescribing of divided doses of corticosteroids, interviewees consistently referred to the fact that this usage was hospital driven. Treatment given in oncology in most cases aims to be curative in nature, whilst with palliative care treatment there is an understanding that a cure is no longer possible. The respondents claimed that on admission to a hospice unit, corticosteroid dosing was changed to once daily in the morning, or if the dose needed to be divided it was given at lunchtime rather than at bedtime as previously prescribed. They observed that hospital prescribers did not necessarily see the results of their prescribing and the insomnia caused by an evening dose:

“Occasionally when people come in on divided doses we continue them. I have seen somebody on QDS dose, which I find very unusual. If we do divided doses, it would be morning and lunch time to try and reduce the effect of the insomnia. But generally try and make it once a day dose.” (13)

Corticosteroid prescribing in oncology is often adjuvant to chemotherapy where the prescribing of the corticosteroid supports a chemotherapy course rather than a specific symptom indication. Oncologists may prescribe high-dose corticosteroids acutely for symptom relief before a patient has radiotherapy, with instructions once
this has been completed to reduce the corticosteroid quickly because of concern of side effects. Follow up of the patient may not be closely monitored and the adverse effects of a very quick reduction may not be observed.

Because of confusion among the practitioners between plasma half-lives and biological half-lives (Chapter One, section 1.5), corticosteroids have been prescribed in divided doses at a frequency depending on the individual prescriber, which can vary from twice daily, morning and night, to a four times daily dosage regime. Once there was evidence of the long effective half-life of these medicines, some prescribers have changed their practice to a once a day morning dose. This is the favoured hospice practice.

It was very evident to the researcher that in the hospice practitioners’ opinion, hospital prescribers did not consider the long effective half-life of corticosteroids, which allows the total dose to be given earlier in the day.

5.5.1.2: Hospice and general practitioner prescribing of corticosteroids

Interviewees reported that, as with opioid prescribing, general practitioners were more cautious in their prescribing of corticosteroids. They demonstrated unease with the doses being prescribed by palliative care specialists.

General practitioners were used to prescribing prednisone for chronic conditions rather than the more potent corticosteroids used in palliative care. When asked if they had become accustomed to this usage, two general practitioners working part time in palliative care responded:

“I think general practitioners are certainly not. They are much more hesitant.” (17)

“The only time I would use steroids really is for COPD patients and asthma patients and arthritis in general practice. Here there seem to be lots of reasons.” (14)

When it came to reviewing and monitoring the patient’s corticosteroid use in the community, most of the interviewees commented it was only as good as the system put in place and varied according to the general practitioner cover. Patients may see more than one general practitioner in some practices and lose continuity of monitoring:
“Some of the patients don’t have their own general practitioners because they go to clinics. So you don’t get that continuous care by one person and they can fall through the cracks quite easily. Be left on a higher dose and not be monitored.” (17)

General practitioners, like hospital medical practitioners, work in the acute setting where patients they prescribe for tend to have an indefinite life expectancy. Potent medicines, like opioids and corticosteroids, prescribed long-term bring with them a profusion of adverse effects. Therefore, both these classes of medicines are prescribed with caution by this group with anticipation of cure. Most general practitioners see one or two dying patients a year and their experience of opioid and corticosteroid use in the dying patient is minimal. This prescribing tends to be specialist driven.

Optimal general practitioner monitoring and reviewing of palliative care patients who have been prescribed corticosteroids depends on good communication between the health services, and the systems put in place in each of those services to ensure patient follow up.

In summary, it became very apparent that there were differences in the prescribing of corticosteroids between medical specialities, the reason being their very different practice environments. The philosophy around hospital prescribing, general practice prescribing and hospice prescribing is different in that the first two concentrate on cure while the third concentrates on end of life issues, with cure no longer being the aim.

5.5.2: Influences in professional roles within the hospice team

This section was limited to medical practitioners and nurses as they were the only disciplines interviewed by the researcher.

The majority of nurses interviewed suggested that within the hospice inpatient unit, nurses took their lead from the hospice medical practitioners and did not influence prescribing to any great degree:

“We take our lead obviously from our consultants and the knowledge that they share with us.” (3)

This difference between disciplines was particularly noticeable in the larger hospices where medical teams were bigger and had separate meetings within disciplines. As a consequence, discussions around prescribing tended to take place within
prescribers' meetings rather than at a multi-disciplinary team meeting. If more than one medical practitioner was on duty at a time, prescribing queries would be medical practitioner to medical practitioner rather than involving nursing staff:

“Prescribing would be discussed between the medical staff and I am not privy to that necessarily.” (18)

The respondents suggested that education sessions, peer review and journal clubs were often separate as well:

“The medical practitioners have monthly meetings and reviewing of journal articles.” (9)

However, all participants commented that multi-disciplinary meetings did occur and they attended these meetings where the whole team gathered to review the patients on their palliative care programme.

A part-time inpatient medical practitioner, new to palliative care, went on to say how knowledgeable the established nursing staff were, and that she was quite comfortable asking their advice around the prescribing of corticosteroids:

“The nurses are extremely knowledgeable. When I started and even now, when I do not know something, I feel quite comfortable to ask the nurse.” (11)

The palliative care coordinators (PCC’s), who are experienced registered nurses working in the hospice community teams visit patients in their own homes. They had the ability to influence prescribing more, but suggested their input depended very much on the knowledge and the needs of the general practitioner, and how receptive he or she was to their suggestions:

“A very wide bank of knowledge out there, it fluctuates. Some are really well read and well versed and some aren't. A lot of them are very well led by the Palliative Care Coordinators really and we do encourage them to ring our Medical Officers but most of the leading is done by the PCCs.” (6)

The PCC’s in the community appeared to be very aware of their professional boundaries, and did not hesitate to consult with their hospice medical practitioners or recommend that the general practitioner refer back to their hospice medical practitioners themselves if the situation warranted it:

“Yes a bit of both. General practitioners vary in their level of expertise and understanding and so our nurses could always be having a conversation with our medical staff here and be supporting the general practitioner in a way. But
Finally, a hospice specialist when talking about the medical team suggested that with the medical staff meeting regularly and peer reviewing each other’s prescribing, if there was a concern it would be raised:

“We have regular contact with one another so if someone prescribes oddly then someone will ask them ‘what made you do that’.” (16)

It was interesting to note, but not surprising, that nurses working in the community (PCC’s) had a more obvious influence in the prescribing of corticosteroids than their counterparts in the inpatient unit and they tend to have more influence overall. PCC’s visit patients in their homes, sometimes on a daily basis, and may be the health professional the patient sees and relies on most. The dying patient and his/her family, who is very vulnerable, may develop a very intense relationship with his/her visiting palliative care community nurse.

A PCC may often be the person responsible for co-ordinating a patient’s care. They relate one to one with patients and families and, on occasion, need to make recommendations in isolation. They develop a close working relationship with the general practitioners in their area of work. This relationship is different to that of the hospice inpatient unit nurse who works, supported by his/her peers, an eight-hour shift with a set number of patients.

In some situations, the palliative care coordinators (PCCs) in the community were more knowledgeable than the practitioners they were working with. These experienced nurses appeared very skilled at responding to general practitioner need whilst staying within their professional boundaries.

The separation between disciplines was more obvious in those larger units where clinicians had peers of the same discipline working alongside them, rather than in a smaller hospice where there was only one medical practitioner and where prescribing discussions were more general across the disciplines.

5.5.3: Differences in corticosteroid prescribing within the hospice team

Overall, the participants’ assumption was that the prescribing within each palliative care team was similar, but there were some variations. The views of the senior
medical members of the teams were that prescribing within each unit was reasonably consistent:

“My assumption is that we prescribe them reasonably similarly.” (1)

Others described this consistency of prescribing as an institutional habit. It was what they had always done and would continue to do. Because these corticosteroids had been in circulation for such a long time they were very familiar with them and frequently used them:

“I think if we are talking about the drug, I think it is just a habit. What people are used to and what they are familiar.” (5)

However, some interviewees did not support this view and commented that within the team prescribing was different and often individual, so that even though the plan was to have consistency of prescribing this was difficult to achieve as everyone had their own prescribing patterns. Some participants commented that when new medical staff joined the team their prescribing was different from established prescribing:

“We work in a team and we try and get consistency of prescribing. If you try and get medical practitioners to prescribe the same way that’s like herding cats.” (16)

“We have got some new medical staff in “play” that look at prescribing medications differently.” (6)

Several acknowledged that prescribing related to the precedent set by the practice of the senior consultant and, so long as that consultant remained in the unit, prescribing remained consistent but once the consultant moved on, prescribing changed:

“Where the Senior Consultant has established a way of doing things the whole team will tend to follow and it only changes when the Consultant goes.” (7)

Interviewees who were working across palliative care teams or who had worked in other palliative care units previously, commented that they found corticosteroid prescribing differed from place to place:

“My experience in previous palliative care service is quite different from the experience of the palliative care service here.” (5)

A few interviewees considered that prescribing of corticosteroids was individual within the team and that each prescriber had their own way of prescribing. Others said it had altered from previously established patterns because their medical teams
had recently changed and with the new medical practitioners came different ideas. This supported the view of the participants who had responded that prescribing between different hospice units was not the same.

The general consensus of the interviewees was that if the senior medical staff remained stable, the established prescribing patterns remained the same. Some respondents went as far as to say prescribing was an ‘institutional habit’ as no one thought to question what was already in place. Some units had older more traditional prescribers, some had medical practitioners who were new to the field and other units were a mixture. Each unit appeared to have its unique culture. Across the units, dexamethasone was the most prescribed corticosteroid with similar dose ranges for the same indications, but each unit and most prescribers had their own methods of reducing these medicines and stopping them.

5.6: Perceptions of Phase One data

After discussing influences and choice of prescribing of corticosteroids, the respondents were invited to view and comment on the data that were generated in Phase One of the study pertaining to their specific hospice.

5.6.1: Agreement with individual hospice data presented

The interviewees accepted the accuracy of the 2007 data and graphs from Phase One of the research presented to them. This data was specific to each of the sample hospices and included patient characteristics, proportion of patients prescribed corticosteroids, choice of corticosteroid, dose and dose ranges prescribed, the recording of adverse effects reviewing and monitoring, methods of stopping corticosteroids, medicines concurrently prescribed with corticosteroids and whether guidelines were followed. When asked if there were concerns over the data, one respondent replied she was concerned about the omissions in practice that the graphs and data had demonstrated:

“These are not at all, more issues about our omissions.”

Some participants suggested it was interesting to see what other hospice units were doing and felt being able to compare themselves against the average results of the six hospices was a good benchmarking exercise:
“It is just interesting to see what other people do. It is like a benchmark. Because you always think are we on the right track.” (12)

Others confirmed that a peak or trough in a graph fitted in with the impression of their patient base for that year. One of the interviewees, identifying a peak in the neurological graph, (this graph showed the proportion of patients prescribed corticosteroids for neurological symptoms) went on to explain the reason for this. The year studied was a year that, by chance, many young patients presented with brain tumours. Because of their age and circumstances they had required additional help and support, leaving the interviewee with very clear memories of that time:

“We had a very high number of patients with brain tumours that year.” (3)

The interviewees were very accepting of the data and graphs presented to them and commented with interest on the results. Some were very quick to identify peaks and troughs within the graphs and give explanations for them. Others could see the information gained being of value.

5.6.2: General perceptions of hospice data

When asked about their perceptions of the hospice data, some interviewees responded with surprise, a few reacted with delight and a small number were disappointed in their results. Table 34 below summarises overall reactions to each of the graphs of the 2007 data shown at the time of the interviews in 2010.
The percentage use of the corticosteroids over the six sample hospices was 61% to 69% of inpatients, suggesting that approximately two-thirds of all hospice inpatients were prescribed corticosteroids in the year 2007. Some interviewees were surprised at where their hospice sat within the range, and were agreeably surprised at the closeness of that range across all hospices reviewed as it showed consistency. Some thought they would be higher, some lower.

The high corticosteroid percentage for non-specific/‘general wellbeing’ indications was commented on with surprise and/or disappointment by the interviewees. One interviewee asked how ‘general wellbeing’ had been identified. It was reiterated that

<table>
<thead>
<tr>
<th>Data</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>The percentage use of the corticosteroids over the six hospices for all admissions (61 to 69%)</td>
<td>The interviewees were mostly surprised where their relative corticosteroid usage lay: “Interesting. I would not have put us as great steroid users we are leading the ranks on this study.” (1) “I thought probably the use in [hospice name] was quite high and it is lower than the other hospices so that surprises me” (5) “I think that is very representative.” (7) “I was a little surprised it was so narrow.” (9)</td>
</tr>
<tr>
<td>The percentage use of the corticosteroids prescribed for non-specific/‘general wellbeing’ indications (33% to 61%)</td>
<td>All were surprised at the percentage of patients being prescribed corticosteroids for non-specific/‘general wellbeing’ indications and some went as far to say they found it disappointing “I am surprised that general well being is so high.” (17) “45% for wellbeing. Well that is disappointing.” (4)</td>
</tr>
<tr>
<td>The percentage of corticosteroid side effects not recorded.</td>
<td>There was no surprise here but it was acknowledged that it was an issue some said they found upsetting “The ‘not recorded’ it is always an issue.” (1) “I was pretty upset with the not recorded.” (7)</td>
</tr>
<tr>
<td>The method of stopping corticosteroids</td>
<td>Disappointment was expressed over abrupt ceasing of the corticosteroids particularly when the patient had been on them for more than three weeks. The general feeling was surprise at the low numbers of patients who had had their corticosteroids reduced gradually. “I was rather taken aback about the abrupt ceasing. That surprised me because that certainly will not be a conscious thing.” (16) “I am surprised that gradually is so small.” (17)</td>
</tr>
<tr>
<td>The percentage of corticosteroids monitored and reviewed</td>
<td>Surprise and disappointment were expressed at the low percentage of reviewed and monitored patients “I was surprised to see that only 57% of the patients were reviewed. I would have thought that it would have been higher than that.” (5)</td>
</tr>
<tr>
<td>Concurrent drugs prescribed with corticosteroids: Omeprazole Phenytoin Zopiclone</td>
<td>No one was surprised at the high levels of omeprazole prescribed and only a small minority related that prescribing to the concurrent use of a steroid and NSAID, and concerns over an intestinal haemorrhage. A few commented about the phenytoin- steroid combination but there was confusion as to what exactly the concern was with the CYP 450 enzymes: “I cannot remember whether the dexamethasone goes up and the phenytoin goes down or the phenytoin level goes up and the dexamethasone goes down. I know there is an interaction”. (8) Zopiclone’s potency being reduced by a corticosteroid was a surprise to all.</td>
</tr>
</tbody>
</table>

The percentage use of the corticosteroids over the six sample hospices

Table 34: Interviewees perceptions of their hospice graph results

113
the terms non-specific and ‘general wellbeing’ were interchangeable. The author recognised she may have inadvertently introduced a potential for bias in the interviews with both terms being used. Others suggested that when the reason for prescribing a corticosteroid for non-specific reasons was too difficult to explain to a patient, the term ‘general wellbeing’ was often used. Some suggested that the percentage would be lower in 2010 as they had been working hard not to prescribe corticosteroids for non-specific reasons.

The proportion of patients reviewed and monitored was a disappointment to the interviewees who suggested that reviewing and monitoring was not done well. There was a consensus that adverse effects were not well recorded in patient notes, so the participants did not show surprise when presented with their hospice graphs. Some went further to suggest that recording overall in patient notes was unsatisfactory.

Interviewees voiced concern at the number of patients who had had their long-term corticosteroids stopped abruptly. Participants were disappointed with the small number of corticosteroid regimes that were reduced gradually, as most were aware that this was better practice and that patients prescribed corticosteroids for more than two to three weeks may have developed adrenal insufficiency, which should be considered when corticosteroids are reduced or stopped.

Of the medicines co-prescribed with corticosteroids, no one voiced surprise at the high proportion of patients prescribed omeprazole, this percentage did not appear to alter if an NSAID was added. Few were aware of the corticosteroid CYP 450 interaction with phenytoin and, if the participants were aware, some were unsure just what the interaction was. No interviewee was familiar with the zopiclone/corticosteroid CYP 450 interaction and the reduction in potency of zopiclone.

The researcher was surprised at the interviewees’ lack of concern at the high proportion of patients prescribed omeprazole. There appeared little knowledge of or consideration given to omeprazole being metabolised by the CYP 450 enzymes and the modifications this could cause. Overall there seemed to be limited awareness of the metabolising effect of CYP 450 enzymes and the change in the effective dose when medicines, affected by these enzymes, were co-prescribed.
5.6.3: Perceived need to achieve the average

It appeared that many interviewees thought that to be an outlier on a graph, was a negative factor, certainly not as comfortable as sitting safely with the majority. Most participants expressed delight with the findings from the Phase One graphs when the individual unit results were close to the average outcomes of all six hospices. There appeared to be no consideration of whether the average represented best practice, just simply relief and comfort to be seen the same:

“No that’s the thing it is very similar. It probably is a very pertinent result. May be it means that intuition or not, we are getting it right.” (5)

“Reassuring not to be outside the square.” (9)

“I am always quite pleased we are sort of in the middle.” (13)

The similar results over the six sample hospices were reassuring to the respondents in an environment where practice could be seen as anecdotal and intuitive in action and where there was a felt lack of solid evidence or what evidence there was considered confusing.

It is human nature not to want to standout and be noticed unless you are very sure of your facts. There was perhaps perceived safety in numbers. Achieving the average may have been seen to be congruent with best practice.

5.6.4: Changes in prescribing of corticosteroids since 2007

Around three-quarters of those interviewed said they did not think corticosteroid prescribing had changed since 2007. The main reason given was that medical staff had remained stable since that period and as a result prescribing had not altered:

“Our senior consultants have been consistent so we probably have not changed.” (3)

Additionally a participant suggested there had been no change in prescribing between the years 2007 and 2010 because guidelines that were in place in 2007 were still in place:

“Probably not really, we have still got our main medical practitioner and having guidelines in place now the medical practitioners follow.” (15)

The few interviewees who answered yes, or maybe, that prescribing had changed, thought the changes may have happened because they, since 2007, now had guidelines for corticosteroids in place and as a result were more focused on
reviewing and recording. It was also commented that more dexamethasone was being prescribed than prednisone now:

“I would say we are using more dexamethasone than prednisone by a long way and I would like to think you would find more recordings of why and that we have reviewed it. Because we have got guidelines and we were making more effort, I have become a bit more focused on that. We certainly raised the question more often round the table whether it is recorded or not, we will have to see.” (4)

There were those respondents whose ‘gut feeling’ was that corticosteroids were being prescribed less frequently for non-specific indications:

Again it is entirely anecdotal but my gut feeling would be that we use far less simply for well being and appetite issues than when did even three years ago.” (2)

It appeared to the researcher there were contradictory views from the interviewees when asked the question “Has your prescribing changed since 2007?” with the majority replying “no it had not,” others “yes it had,” and a few uncertain and commenting there may have been changes.

This section demonstrates uncertainty whether corticosteroid prescribing has changed since 2007. Some suggested that stable medical cover and guidelines in place meant prescribing had remained consistent. Others commented that now they had recent guidelines prescribing had changed because these were being followed.

Interview responses did, however, show there were changes since Phase One of the study in 2007. Five out of the six hospices now had some form of corticosteroid guidelines. One hospice had adopted these after a presentation from the researcher. There appeared to be a greater awareness of corticosteroids as a consequence of this study, with two of the medical directors commenting about changes in practice since the researcher’s visit. For some, any changes may have been subtle and imperceptible so not perceived.

5.7: Guidelines, reviewing and monitoring

5.7.1: Guidelines

The majority of those interviewed acknowledged there were some forms of guidelines for the use of corticosteroids in their palliative care unit. They stated that the guidelines used ranged from overall recommendations for the use of
corticosteroids (some very precise, others not), to very specific recommendations for individual indications for their use:

“Here at this hospice we have protocols, which are agreed upon by the medical team and then the team, when we initiate steroids, we prescribe them on a tapering protocol to zero. So that is how they get prescribed from the onset to completion.” (8)

“The guidelines are not particularly specific.” (16)

“Yes we do have guidelines for different situations. Certainly we have got one for spinal cord compression.” (10)

Some respondents said they used corticosteroid guidelines loosely for some indications but most of the time tended to prescribe empirically:

“For some things, but fairly loosely, mostly empirical.” (17)

A few respondents knew there were guidelines in their facility, but they had not seen them, or did not know what they said:

“We have clinical guidelines but I can’t tell you what the clinical guidelines say.” (18)

One participant suggested that guidelines must be there somewhere because the hospice was so well organised:

“Yes. I think there are guidelines here for everything. It is very well organised.” (11)

The interviewees from the hospices that did not have guidelines had varying opinions on the value of corticosteroid guidelines. One participant thought their hospice did not have corticosteroid guidelines but suggested it would be good to develop them:

“No. I don’t think we have got guidelines on the use of steroids. Might be something we should develop though, probably quite a good thing to develop - the use of guidelines.” (12)

Another interviewee commented that the prescribing of corticosteroids for palliative care patients should not be policy driven. The prescription needed to be individualised and varied to cover not only the physical symptoms of the patient but also to consider quality of life as well. This interviewee preferred not to follow guidelines:
A third interviewee suggested he was not a ‘guideline person’, nor did he think the hospice unit had guidelines:

“I am not a guidelines person, you see. I do not do guidelines particularly well. I am not saying that it is good thing or it’s a bad thing. I don’t think we have steroid guidelines.” (1)

There was no consistency of guideline use across the hospice units. The use of guidelines, if present, varied from very precise to quite loose in their interpretation. Some hospices had guidelines for a few specific indications only. Whilst some participants knew their hospice had guidelines, they were not familiar with them. A small number of interviewees chose not to have corticosteroid guidelines in their hospice at all as they preferred the freedom to prescribe individually for their patients.

In the early years of hospice, when little of the practice was evidence-based or guideline-driven, medical practitioners had a freedom to prescribe as they desired. To follow guidelines could suggest that prescribing was population based, therefore similar for all, rather than designed for the individual patient. There seems little point in having guidelines to meet an audit procedure if they are not being followed.

By not following guidelines suggests some medical practitioners prefer not to be restricted by conforming to a regime, but instead prefer the continued freedom to prescribe as he/she sees fit. It could be argued that a dying patient warrants that unique attention.

5.7.2: Lack of recording in patient notes

The background for the lack of recording in inpatient notes arose when, in Phase One of the study, the researcher attempted to collect data on the recording of corticosteroid adverse effects. It was found most patient notes did not detail the presence or absence of adverse effects although occasionally these were recorded. This issue was explored with the interviewees.

There are a lot of verbal interactions in hospices discussing points that do not reach paper. As far as Phase One of the research was concerned, if it was not recorded, it could not be assumed to have happened. The non-recording of adverse effects
extrapolated to non-recording around other issues in the notes. This is illustrated by the following:

“I have done a lot of audits over the years and it is the bug bear – isn’t it? Because that’s this huge number of people for whom you don’t know because no body has bothered to write it down and you have to include it in your figures in the hope that people might be competent in writing it down. Sort of the only result you get in an audit. People do not document.” *(2)*

The interviewees did not doubt that in long-term use (three weeks or more) of corticosteroids, patients would have some adverse effects. They were quite philosophical about the lack of recording of these and responded in a variety of ways. More were not surprised at the lack of recording and the majority suggested they weren’t very good at this:

“It does not surprise me that there is a large amount where it has not been recorded. I don’t think that we are very good at recording.” *(2)*

“It is surprising there are so many side effects. It would be interesting to know what they are. The fact that they are ‘not recorded’ does not mean that they did not have them. So I am quite interested to see that.” *(5)*

One of the participants who appeared not to be surprised at the lack of recording in 2007 suggested that they might still not be good at recording adverse effects in 2010, and that there were more important issues to be concerned about when a patient was dying than an adverse effect caused by a corticosteroid:

“Not recording corticosteroids side effects does not surprise me and probably still not very good at that. Probably we don’t care in a sense. You know what I mean?” *(4)*

Whilst another thought they should be more vigilant when recording adverse effects and suggested that seeing the 2007 results showing the lack of recording in patient notes was a salutary lesson:

“The thing we need to be a little more vigilant with is the side effects of the corticosteroids. It is quite a good learning thing this actually.” *(12)*

To conclude, there was a lack of surprise around the non-recording of commonly occurring corticosteroid adverse effects, with the majority of interviewees agreeing they were not good at recording. It was suggested this lack of recording was not corticosteroid-specific, it was accepted by the interviewees that overall recording in patient notes was not optimal.
Although the clinicians recognised its importance, little time seemed to be devoted to this task. The researcher questions, with so many aware of this omission, why more effort and time was not allotted to address this important issue? This raises a much more general issue around the use and accuracy of patient notes for research purposes and perhaps the need for a re-think as to how clinical data is reviewed and monitored.

5.7.3: Peer review of corticosteroid prescribing

All interviewees had peer review sessions of some description, with the medical practitioners’ peer reviewing appearing to be more formalised than that of the nursing staff. Depending on geographical area, some medical staff met monthly with other hospices to review journal articles and present case studies, while those who were more isolated were part of a teleconferencing peer group. Corticosteroids seldom come up as a separate topic, however they were discussed in some of the case studies reviewed.

Reviews and updating of corticosteroid guidelines were conducted as part of general policy reviews for quality assurance amongst some hospices:

“If I’m being quite honest, we have not reviewed the use of corticosteroids here for a while in terms of having if you like a full clinical session about them. They come up in the course of talking about some of our other symptom management as part of that symptom management.” (3)

“If we are doing a case review and steroids were part of the challenges and management of that person, we would be reviewing it. But apart from the general review of policies that we do as part of Quality Assurance and updating those every 2–3 years, nothing.” (9)

Occasionally, an audit was performed when one of the medical staff had a particular interest in corticosteroids. There did not appear to be much sharing of audit results as a peer review tool, either amongst the staff of the hospice the audit was conducted in, or in the wider palliative care community:

“An audit was done sometime back as far as I am aware but I’m not sure what the results of that are.” (5)

The review of corticosteroid prescribing was seldom on peer review agendas. Instead, it was more likely to be discussed generally in patient reviews in conjunction with other medicines.
It appears that corticosteroids are adjuvants in more ways than one. They are added into a drug regime when an extra medicine is required for pain relief, which may present as emotional as well as physical pain. They seldom warrant their own review as a stand-alone medicine. Corticosteroids, which have been relied on for sixty years and are so frequently prescribed in palliative care, tend to be treated with a casualness that is of concern for such a group of potent medicines. These medicines are seldom a subject of interest in clinical trials or expensive enough to be questioned by managers protecting their budget, and tend to be overlooked.

5.7.4: Review and monitoring

The interviewees asserted that if a patient was an inpatient of the hospice their corticosteroids, as well as their other medications, would be reviewed regularly because they were seen most days by a palliative care medical practitioner. It was also suggested that within all the units there were sufficient staff to monitor patient reactions to those medicines:

“We see them everyday and everyday all doses, all medication are reviewed.” (11)

“In the Inpatient unit you can do things more easily and comfortably because you have got staff there to monitor it all the time, whereas at home you don’t have that same luxury.” (3)

If patients were in hospital, not hospice, a regular review was dependent on the medical team they were under with reviews being more likely in some areas than others:

“In a hospital it tends very much, which team they are under. If they are under the Oncology/Radiation team then that would be generally reviewed regularly.” (5)

When the patient was back in the community, a regular review of corticosteroids was reliant on a variety of situations, which included clear instructions on discharge and someone being responsible for the reviewing. This could be a general practitioner or patient care coordinator relating back to the general practitioner and/or hospice:

“Yes I think we have lost patients to follow up because they are in general practice and perhaps it has not been picked up on the discharge summary or may be it has not even been written on the discharge summary to be fair. Sometimes it has been written.” (13)
“The monitoring is not what I liked it to be, where we had a list at our morning meeting. We would go through the file as we mention the patient, to make sure that we are on track. Now it is being left to the nurses who visit and when the patients come to Outpatient Clinics just to be sure they are on the right one, I think it is more open to error than the other way where we really kept a close watch.” [7]

Monitoring also related to the patient’s own understanding of taking and continuing to take their medications:

“I think it is about explanation about what the medication is for and understanding about the need to continue it until told to stop.” [5]

Most interviewees felt it was in the community that patients ran a risk of the monitoring of their corticosteroids being missed. This was affected by their socio-economic situation and geographic spread and in that general practitioners had different abilities in clinical skills, communication and compassion:

“We have got such a huge range of general practitioners from very good to abysmal. Not just in their clinical skills but in their communication and level of caring. So it can be very mixed. Some of the patients don’t have their own general practitioners because they go to clinics. So you don’t get that continuous care by one person and they can fall through the cracks quite easily. Be left on a higher dose and not be monitored.” [17]

It was also suggested that it was more difficult to monitor a patient’s corticosteroids on discharge from the hospital environment compared to the hospice environment:

“There is a potential obviously with steroids in stopping suddenly particularly stopping suddenly that is the danger. But I think if we try, certainly the hospice would make that very clear on their discharges but I think in the hospital it is a little bit different ball game we do not have the same control over what happens when people go home.” [5]

The theme coming through strongly was that discharging a patient on corticosteroids is not without its complications and relies on clear instructions at discharge and regular follow up. The reality is that this does not always happen and the patient may not be properly supervised for a variety of reasons:

“It’s really the ownership of the steroid that is the issue. We work together with Oncologists and everybody but the policing and the appropriation of the steroid that is where the system falters.” [16]

A palliative care patient may come under the care of several different medical disciplines for instance: palliative care, oncology, a general practitioner practice and sometimes a different hospital discipline depending on diagnosis. With the input of
so many teams it is very easy for no one team to take on the overseeing role or to make the assumption that another team has done so. Monitoring and reviewing may become intermittent or absent. The patient may also not realise the implications of not fully understanding or complying with the directions given once discharged from the hospice/hospital environment.

In conclusion: Chapter 5 reports the results of Phase Two of this study. Phase Two cannot be viewed in isolation as it was developed and built from the results of Phase One. This phase expresses the 18 interviewees’ opinions and perceptions on themes, which had been recognised and grouped. Various aspects of hospice prescribing were discussed but included specifically the prescribing of corticosteroids. The interviewees considered that prescribing in palliative care was different from other areas of medicine because of the goals inherent in the needs of the terminally ill patient. These differences included the use of ‘off-registration’ medicines and the ‘layering’ of different medicines to achieve good symptom management although they were aware of the dangers of poly-pharmacy.

Prescribing focused on quality of life rather than for cure.

Prescribing of opioids (like corticosteroids) tended to be more frequent and at higher doses than in other areas of medicine but in practice was very much dictated by the experience of the medical practitioner.

The interviewees agreed that corticosteroids were prescribed for many more indications than elsewhere. The doses, strengths, course duration, methods of stopping and choice of corticosteroid were also recognised as being different from general medicine and contained a greater ability to cause adverse effects. The level of comfort with the prescribing of these medicines varied with the experience of the practitioner as did the use of the terms ‘comfort’ drugs or drugs used for ‘general wellbeing.’ Non-specific indications were recorded as the chief indications for corticosteroid prescribing, which concerned many of the prescribers who preferred to view their prescribing as for more specific reasons.

There was frustration expressed over lack of rigorous evidence or pointers to best practice for corticosteroid prescribing. Literature was found to be confusing. This suggested that prescribing practice was mainly from experience, anecdote and intuition. As a result, it was not surprising that when the interviewees reviewed the
data from Phase One they found relief in their results being consistent with the other sample hospices.

A lack of recording of reviewing, of monitoring or of adverse effects, in patient notes had been indentified in Phase One, which appeared not to surprise the interviewees who confirmed there were omissions in these areas.
Chapter 6: Discussion

This research was initiated when the researcher, a clinical pharmacist working in palliative care, saw the adverse effects induced by the prescribing of corticosteroids. These adverse effects were not necessarily from long-term use or particularly high doses and ranged from oral candidiasis to Cushing’s syndrome. Although all these effects cause patient distress, the combination of adverse effects that is most devastating for patients and their families is Cushing’s syndrome. This is the result of long-term use of corticosteroids and is common in palliative care (refer to photographs in Chapter 1 p. 27).

These symptoms are so severe, both physically and emotionally that patients, their families, and hospice staff started to question the long-term prescribing of these medicines. This distress sparked in the researcher a desire to discover more about this group of medicines and this led to the initiation of a research study to investigate corticosteroid prescribing in palliative care.

The overall aim of this study was to explore how corticosteroids are prescribed in modern palliative care settings in New Zealand, and the influences and drivers of this prescribing. The broad questions that evolved were:

- Why are corticosteroids prescribed in palliative care?
- How are corticosteroids prescribed in palliative care?
- How are corticosteroids monitored and reviewed in palliative care?

Specific objectives included an evaluation of the usefulness of employing corticosteroids in palliative care and the perceptions of those prescribing or influencing the prescribing of corticosteroids in this area. It was intended that the results would inform the development of tools to optimise the use of corticosteroids for the benefit of palliative care patients and to challenge established practice.

Rather than use a single approach, this research used a ‘mixed methods’ format comprised of two phases, the first being a quantitative phase and the second a qualitative phase. The rationale behind this approach was to develop a comprehensive means of addressing the research questions, with the intention of the methods complementing each other to give a better understanding of the data.
A retrospective review of corticosteroid prescribing in a sample of New Zealand hospices was chosen as the most effective method of conducting Phase One as it gave the opportunity to review the data of corticosteroid prescribing and obtain a baseline on which to develop the qualitative second phase of the study designed to elicit prescribers’ perceptions of corticosteroid use. Semi-structured interviews were chosen as the most effective method of conducting Phase Two. The design of these interviews was flexible enough for the questions to be open ended to allow the interviewer or interviewee to digress if an idea or a point needed expansion.

**Phase One**

The year chosen for Phase One, the retrospective study, was 2007 and the collection of data commenced in 2008. The initial plan had been for an international study but this was recognised as too ambitious and not achievable in the timeframe available. On consideration, the study was reduced to a sample of six New Zealand hospices, a mixture of urban and rural, to give a cross section of the prescribing of corticosteroids in New Zealand hospices.

Because of the potential for over-familiarity and bias, the researcher’s home hospice was not chosen as one of the sample hospices. A base, however, was required to determine a credible sample size to investigate the proportion of patients being prescribed corticosteroids. In this hospice, 47% of inpatients in the year 2007 were prescribed corticosteroids and this figure was used to guide the design of the study.

For the purposes of this study, a suitable sample size depended on the proportion of patients being prescribed corticosteroids. International literature suggested that the proportion (%) of patients prescribed these medicines varied from 32% to 80% (Nauck et al., 2004; Shafford, 2006). These two percentages were at the extremes, most of the studies found showed the percentages of patients prescribed corticosteroids in the palliative care setting to be between 50% and 70% (Gannon & McNamara, 2002; Hanks et al., 1983; Hardy, 1998; Klepstad et al., 2005; S Mercadante et al., 2001a; Pilkey & Daeninck, 2008).

Within the selected hospices, reviews were conducted on 1179 inpatient notes. Corticosteroids were prescribed for 768 of these patients (65%). Of these, a sample of 260 patients (one in three of those prescribed corticosteroids) was selected for recording, using an electronic database. When this data was collected from the six
sample hospices, the proportion of inpatients prescribed corticosteroids in the year 2007 ranged from 61% to 69%, a higher proportion than in the pilot sample (47%) but this proportion sat within the range shown in some of the international papers reviewed (Hardy, 1998; S Mercadante et al., 2001a; Pilkey & Daeninck, 2008; Shafford, 2006), and was remarkably consistent across the six hospices.

If this proportion is truly representative of the majority of New Zealand hospices, it suggests that approximately two-thirds of hospice inpatients will be prescribed corticosteroids while in a palliative care programme. This is a high proportion of patients considering the potency of corticosteroids and the relative lack of published evidence for their use. This prompted the researcher to question whether corticosteroids were being prescribed casually, and if there were safer alternatives (refer p.25). Were prescribers considering other medicines with fewer adverse effects that might be more suitable for some aspects of symptom management? This aspect was not however pursued in this study.

While there were three corticosteroids prescribed within the sample hospices, the only corticosteroid prescribed across all indications was dexamethasone. There was limited prescribing of prednisone and methylprednisolone. When prednisone was prescribed, it was frequently for non-specific indications. The prescribers in one sample hospice chose prednisone in preference to dexamethasone for these indications.

Methylprednisolone was prescribed in three hospices. In one of those hospices it was prescribed once only as a single dose by a hospital prescriber, the reason for this dose was not clear. In the two other hospices, records were clear on its use. Methylprednisolone was prescribed for specific indications e.g. bowel obstruction, cerebral oedema and spinal cord compression, usually when patients were unable to swallow oral medicines. In these cases, methylprednisolone was injected intramuscularly instead of dexamethasone subcutaneously to take advantage of a smaller injection volume.

The methylprednisolone dose range for these two hospices was similar but the length of course differed. The justification for the use of methylprednisolone appeared to be historical experience because there was no recent published evidence found to support its prescribing in preference to dexamethasone. The
doses prescribed, however, provided symptom relief and, since the glucocorticoid effect was smaller, the potential for adverse effects was also less (Fernandez del Vallado et al., 1964; Fuenfer et al., 1975; Goodman & Gilman, 1975).

International literature suggests that, while all three medicines are prescribed, dexamethasone is currently the most commonly used (Bruera et al., 2004; Davis et al., 2006; Klepstad et al., 2005; Pilkey & Daeninck, 2008; Rajer & Kovac, 2008; Shafford, 2006; Shih & Jackson, 2007; Sturdza et al., 2008; Watanabe & Bruera, 1994). The reasons given for this are that dexamethasone has the greatest anti-inflammatory effect, and the longest biological half-life (Brunton, 2006).

In the palliative care field, corticosteroids are prescribed more widely than in other areas of medicine for both specific and non-specific reasons. Of the eight prescribed indications listed in this study, there were three principal reasons for prescribing corticosteroids: specifically for neurological symptoms and soft tissue infiltration symptoms, and non-specifically for ‘general wellbeing’ type symptoms.

‘General wellbeing’ includes symptoms such as lack of appetite, fatigue, nausea, vomiting, pain and shortness of breath. This indication was the most frequently cited indication of the study being a residual category for any symptom that did not have a specific diagnosis and related to those listed under the non-specific indication in earlier overseas studies. Of all those prescribed corticosteroids, 33% to 61% were for non-specific/‘general wellbeing’ but there were significant differences among the sample hospices in their prescribing for this indication. A paper written in 2006 in the United Kingdom confirmed the high proportion of patients being prescribed corticosteroids for non-specific reasons, in that country with a range of 48% to 54% (Shafford, 2006).

There is little published evidence to support this frequent use of corticosteroids for non-specific indications. Some literature suggests an improvement in non-specific symptoms short-term however there appears to be no substantial evidence to support this. A 2010 Cochrane review of the treatment of fatigue in palliative care patients, a common non-specific reason for corticosteroid prescribing, suggested that it was surprising that corticosteroids had not been a research focus for fatigue treatment (Peuckmann et al., 2010). A recent Australian study found that 71% of
inpatients who were prescribed dexamethasone received this agent for non-specific indications (Kiani et al., 2011).

Neurological symptoms, which included raised intracranial pressure, cerebral tumours, spinal cord compression, and nerve compression or infiltration, was the next most frequent indication for corticosteroids. The proportions were 18% to 32% of those prescribed corticosteroids amongst the sample hospices. Unlike non-specific reasons, the patient numbers were low and this difference was not of statistical significance.

Soft tissue infiltration, which included head and neck tumours, and abdominal and pelvic tumours, was the third most common indication for prescribing of corticosteroids. In the sample hospices, this percentage range was between zero percent and 20% of those prescribed corticosteroids. Again, because of low numbers this difference was not considered statistically significant. While no literature could be found to confirm the proportion of patients prescribed corticosteroids for these two indications, two United Kingdom studies, (one a prospective survey the other a retrospective study), acknowledged that some of the most common specific indications for corticosteroid prescribing were neurological symptoms and bowel obstruction (Gannon & McNamara, 2002; Hardy et al., 2001). This supports the New Zealand findings.

Some authors have suggested that, even in the presence of guidelines, there is a divergence of dose ranges (Shafford, 2006), however this was not found to be the case among the New Zealand sample hospices. The dose ranges of dexamethasone for specific and non-specific reasons did not differ significantly, regardless of the presence or lack of guidelines.

Corticosteroid guidelines were evident in only one of the sample hospices studied. It was reassuring to discover that without guidelines, dose ranges of dexamethasone amongst the hospices for the most common indications were similar. It became clear however, that within the sample hospices, individual prescribing was diverse. There were institutional differences from hospice to hospice. Prescribers seldom reduced doses in the same manner, used the same course duration or the same rate of reduction of dose. The observations of prescribing course durations varied considerably and were of statistical significance between the hospices. These
differences were also identified as occurring internationally and reported in the literature (Edwards & Elwyn, 2001).

A number of International researchers suggest that corticosteroids can be stopped abruptly if they have been prescribed for less than three weeks (some suggest two weeks) (Twycross & Wilcock, 2007), but should be titrated down after this period. Some prescribers in this study stopped administering corticosteroids at doses of 4mg and 8mg even when patients had been taking them for longer than three weeks.

In the current study, 49% of patients who had had their corticosteroid stopped suddenly, had been on that medicine longer than three weeks including those whose medicines were stopped when they could no longer swallow. There was little acknowledgement that these may be key medicines that once commenced should be continued through the final days of a patient’s life. Parenteral formulations of these medicines are available and a route change is possible. Some literature argues that stopping corticosteroids abruptly or stopping corticosteroid therapy when a patient can no longer swallow, is unethical and may lead to an adrenal crisis, restlessness, anxiety and hasten death (Anonymous, 1995; British Medical Association & Royal Pharmaceutical Association of Great Britain, 2006; Gannon, 2001; Hardy et al., 2001; Rousseau, 2004).

Monitoring and reviewing could not be assumed to have taken place if it had not been recorded in the patient notes. There was a wide variation in monitoring and reviewing of corticosteroid prescribing recorded amongst the hospices, with proportions of reviews varying from 29% to 68% of patients. The researcher is not clear whether this was a case of reviews and monitoring being conducted and not recorded in patient notes, or of reviews and monitoring not occurring at all.

Lack of recording in patient notes was also evident when entering adverse effects of corticosteroids on the database. It appeared these effects were under-reported in patient notes. Overall recording in patient notes appeared to be less than optimal and adverse effects reporting may only be an exemplar of this.

Two audits published in the United Kingdom reported on documentation of adverse effects. The first audit was incomplete, but the second showed that adverse effects were documented as having occurred in 75% of patients prescribed corticosteroids (Shafford, 2006). An Australian retrospective audit suggested that 63% of adverse
effects recorded in their study may have been attributable to dexamethasone (Kiani et al., 2011). The range of recorded adverse effects in the current study was 15% to 45%.

Since the current study commenced, a 2008 nationwide survey in Japan of palliative care specialists showed a large variation in specialists’ estimation of adverse effects. Overall, a low percentage of adverse effects were recorded, yet in 23% of these cases, severe adverse effects were noted e.g. severe myopathy, severe infection, or severe neuropsychiatric complications (Matsuo et al., 2011). Adverse effects may happen quickly, for instance the same Japanese study recorded 10% of patients had developed insomnia and hyperglycaemia within one week of taking corticosteroids (Matsuo et al., 2011). These findings support those of the current study.

Within this study, four medicines or groups of medicines prescribed concurrently with corticosteroids were reviewed: omeprazole a proton pump inhibitor, NSAIDs, phenytoin an anticonvulsant and zopiclone a hypnotic.

The proportion of patients on omeprazole was of interest in this study as this drug is commonly prescribed in palliative care to prevent gastrointestinal haemorrhage when corticosteroids are prescribed. Evidence suggests, however, that unless corticosteroids and NSAIDs are co-prescribed, when the risk jumps between 5 to 15 fold, there is little risk of gastrointestinal haemorrhage (Abbas, 2004; Twycross & Wilcock, 2007), yet 70% to 82% of all patients had been prescribed this medicine. This high proportion of patients’ was supported in a recent Australian audit with 79% prescribed gastrointestinal protection concurrently with a corticosteroid (Kiani et al., 2011).

The prescribing of omeprazole appeared to bear no relationship to the prescribing of NSAIDs in this sample group of hospices. As there seemed to be no obvious explanation in the patient notes and the omeprazole prescribing did not appear to relate to either corticosteroid or NSAID prescribing, it had to be assumed prescribing was for other reasons not evident to the researcher. Often when a patient is admitted to a hospice unit to find he/she has been prescribed omeprazole previously for reasons not listed, perhaps for indigestion. Unless there is a specific reason to remove it and because of patient vulnerability and concern around the fine balance of his/her medicines, a drug such as omeprazole tends not to be removed from a
regime. A hospice patient who may eat very little can have omeprazole added to their drug regimen if there is a suggestion of gastrointestinal irritation.

Phenytoin, zopiclone and corticosteroids are all metabolised by the cytochrome P (CYP) 450 group of enzymes. When either phenytoin or zopiclone is co-prescribed with a corticosteroid, there is an alteration of clinical effect in either or both of the drugs (Rossi, 2009). The phenytoin/corticosteroid interaction was first mentioned in the palliative care literature in 1994 (Twycross, 1994). This paper stated that phenytoin increased the clearance of corticosteroids, thus reducing the corticosteroid effective dose. Phenytoin was the most prescribed anticonvulsant in this current study for patients with brain tumours or brain metastases, with no suggestion in the notes of an increased corticosteroid dose, or that the anticonvulsant should be changed.

This interaction has been elucidated and it is now recognised that each medicine affects the other’s metabolism (Ruegg, 2002). Although the effective dose of phenytoin is reduced, the more important clinical interaction is that phenytoin reduces the clinical effect of the corticosteroid, some papers suggest, to a sub-optimal dose (Back, 2001; Rossi, 2009; Shafford, 2006; Twycross, 1994; Wilcock et al., 2005). The corticosteroid, by acting as an anti-inflammatory agent around brain tumours or brain metastases, has the effect being of itself, indirectly, an anticonvulsant. An increase of phenytoin, in response to seizures, demonstrates a lack of appreciation of this pharmacological interaction.

The zopiclone/corticosteroid co-prescription, while investigated in this study, was not considered of such clinical importance. A corticosteroid co-prescribed with zopiclone increases the zopiclone clearance, thus reducing the hypnotic effect. In three hospices, 49% to 50% of inpatients were prescribed zopiclone concurrently with corticosteroids.

The researcher would have preferred this study to include all New Zealand hospices but the practical reality was that the timeframe allotted for this research would not permit it. Discussion with supervisor and analyst led to six hospices as being considered sufficient to address the research questions. One New Zealand hospice in five was included in this study.
These hospices were selected in an attempt to obtain a cross section of prescribing of corticosteroids in New Zealand hospices. They were a mixture of city and urban hospices, some employing palliative care specialists, others not. The sample appeared to contain characteristics of all New Zealand hospices. The selection was considered to be appropriate, with the reservation that the study included only North Island hospices; there were no South Island hospices. The researcher had visited all New Zealand hospices in her career and felt this omission was unlikely to affect the results. South Island hospices were considered, but not included because of the extra travel and costs involved.

Ideally, every hospice inpatient who had been prescribed corticosteroids would have been reviewed but there was a need to balance the ideal and the achievable. The decision to review every third inpatient who was prescribed corticosteroids was made after a pilot study was performed at the researcher’s home hospice.

This ‘snapshot’ showed that the proportion of inpatients prescribed corticosteroids in that hospice was 47%. A one in three sample to be reviewed was considered sufficient for validity. When the six selected sample hospices’ inpatient corticosteroid prescribing was reviewed, it was discovered that the proportion of patients prescribed corticosteroids was considerably higher (61% to 69%) than the proportion in the home hospice. This led to more patients being reviewed than initially anticipated, and ultimately a larger overall sample.

It was difficult for the researcher to be completely confident that the sample population in this study was representative of all New Zealand hospice inpatients who were prescribed corticosteroids, because there are no published studies on this topic in New Zealand. Indeed, there was relatively little published on the subject internationally, but what there was suggested that the sample population was consistent with international findings.

The methodology chosen for this first phase was not free of challenges but these were usually resolvable with time. Repetition of this study would allow the opportunity to use the lessons from this study to refine the steps. The timeframe chosen for collecting the retrospective snapshot was sufficient.

Data entry and analysis was time-consuming and took longer than anticipated. The hospices were in the process of computerising their systems, which would be of
considerable benefit for a future researcher. The key contact person when visiting the units was the medical director or the chief executive officer. All had been previously known to the researcher who contacted them on a ‘needs be’ basis when requiring information or help.

Time would have been saved if the researcher had arranged formal sessions in each unit with an administrator to be shown the individual hospice systems, particularly the filing systems, and with a clinician to understand the formatting of the inpatient notes.

The database, although refined and reduced on several occasions with the assistance of the analyst and supervisor, was designed by the researcher who was a clinician with limited experience of database design. Despite this, on the whole it worked well. The work-sheets consisted of two sections, one to gather patient information and the other a review sheet. The problems for the advisory statistician in analysing the patient information sheet were minor and on explanation were quickly resolved.

The review sheet was more complicated. Greater explanation and documentation around the intended purpose of this data would have allowed the analyst to understand the process more fully and to tease out the information required. The researcher found that having captured a large and diverse quantity of data the dilemma was then to render it manageable for completion of this first research phase and then to take these results forward for Phase Two.

Data entry was time-consuming. Initially, the data was entered on hardcopy and transferred to an electronic form. While this process was laborious, it gave opportunity to review and query an entry at a subsequent visit. The case studies/cameos collected at each hospice identifying different prescribing trends allowed the researcher to critique the database entries for accuracy. The refined material omitted considerable data, which had been collected and not used in the final results of this study, but, which could be of benefit for future studies or papers.

Preparatory work prior to a visit was possible only where hospice patient admissions were computerised. This enabled the researcher to receive an inpatient list in advance and enter it electronically alphabetically to her database.
For those hospices not computerised or only partially computerised, gaining inpatient records required working through hard copy lists and there was no quick or simple way to do this. By 2010, several of the hospices had committed to a palliative care electronic programme ‘Pall care’. For future palliative care research, this programme has the ability to simplify many of the processes that were so time-consuming in 2008, when this study was instigated.

Once the inpatients for 2007 were identified, the next step was to find their notes. There was potential for patients to be missed due to re-admissions not being identified or lack of accurate recording of patient names or NHI numbers. Patient notes may have been stored either on the premises or off-site. Locating the desired patient notes within any one hospice was another challenge as the method of filing was different throughout the units. Typically 10% of patient notes could not be located. Those notes were sometimes held in another study portfolio, off-site and not recoverable, or more often simply missing. This percentage of un-retrieved case notes is similar to a United Kingdom study where 11% were found to be missing (Gannon & McNamara, 2002). Of those found, understanding the layout of the different hospice patient notes took time because the set up of notes and drug charts in each of the six hospices was not standardised. Therefore, knowledge of the chart layout at one hospice was not necessarily helpful at the next.

In the one hospice where guidelines were evident, the patient notes contained a separate corticosteroid protocol. This had its own challenges, because instead of the corticosteroid dose prescribed being written on the drug chart as with the other hospices, the dose and dose reductions were written on the protocol sheet. Drug charts stated: ‘dose as per protocol’. Some patients had several different protocols in succession updating each other but often overlapping in dates and with varying doses. These were not numbered or referenced so when a drug chart said ‘as per protocol’ it was difficult to know to which protocol it was referring. Some protocols were not updated, or a copy was updated but not the original. The back of the protocol had spaces for steroid adverse effects with some filled in, and others not. Despite this, because all prescribers in this hospice were using the same protocols, there was more consistency of prescribing within this unit.

The reasons for changes in prescribing of corticosteroids were not always apparent in a patient’s notes in any hospice, so such changes could not be assumed to have
been discussed or reviewed. The researcher realised, after recording reducing doses in the first three hospices, that a reducing dose, common in corticosteroid prescribing, did not necessarily imply that a review had taken place, but rather was part of a designated dosage regime. The database of these three hospices was corrected, from recordings written in the field notes.

**Phase Two**

Phase Two, the qualitative phase, complemented Phase One and included a range of research questions around corticosteroid prescribing, which could not have been addressed in Phase One. Phase Two involved 18 semi-structured interviews, three from each of the sample hospices. Of the interviewees, twelve were medical practitioners (seven palliative care specialists, five general practitioners, and six were registered nurses). The sample size was decided by a review of international qualitative literature to establish the number of interviews required for data saturation (Guest et al., 2006). Eighteen interviews were considered a sufficient sample size to find common themes in corticosteroid prescribing and meet the aims and objectives of this research. These interviews took place during the year 2010.

In discussions on whether corticosteroid prescribing was evidence-based, experiential, anecdotal or intuitive, there was never a consensus among the interviewees. If a common theme emerged in this part of the study, it was around lack of rigorous evidence and confusing international literature. Most interviewees suggested their prescribing of corticosteroids was based on experience and habit. Few commented on the potency of these medicines and the majority appeared to have relatively limited knowledge of their pharmacology.

When discussing the proportion of hospice inpatients prescribed corticosteroids, none of the interviewees seemed particularly surprised at the high percentage of patients taking this group of medicines because they were well aware that corticosteroids were some of the most commonly prescribed medicines in palliative care. Satisfaction was expressed at the closeness of the prescribing range of corticosteroids (61% to 69%) of all palliative care inpatients as they presumed this consistency gave more credibility to their prescribing.

In the current study three corticosteroids were prescribed: prednisone, methylprednisolone and dexamethasone. Prednisone and methylprednisolone were
prescribed to a limited degree while dexamethasone was prescribed across all indications for corticosteroid use. The interviewees suggested that prednisone was prescribed mostly for ‘general wellbeing,’ although some medical practitioners responded that even for this indication their choice would still be dexamethasone.

In the case of the two hospices where the medical practitioners prescribed methylprednisolone for some specific indications, interviewees acknowledged their prescribing of this drug was historical and experiential in origin. In the mid 1980s these practitioners had contributed to a successful methylprednisolone trial, were familiar in the use of this medicine, and chose to continue their practice (Della Cuna et al., 1989). These experienced prescribers of methylprednisolone saw the benefit to patient comfort of parenterally delivering a smaller volume of methylprednisolone than that required for a similar effect using dexamethasone.

Dexamethasone was the corticosteroid of choice and was prescribed for all indications investigated in this study. When the interviewees were asked the reason for this, the majority commented it was because of its international usage, it was what they were familiar with and, they guessed, habit.

Most interviewees’ knowledge around the pharmacology of these medicines seemed rather vague but the interview design did not explore this aspect in depth. It would be an interesting topic for a future study.

The interviewees acknowledged that prescribing in palliative care differed from other medical specialities and that corticosteroids were prescribed more frequently and more diversely. Most were comfortable with prescribing corticosteroids for specific reasons e.g. spinal cord compression or bowel obstruction since this prescribing could be justified using scans and X-rays. With evidence-based practice expected around a prescribing judgement, this confirmation was reassuring. The interviewees confirmed that neurological symptoms and soft tissue infiltration symptoms tended to be the specific reasons for which corticosteroids were most commonly prescribed.

Non-specific/ ‘general wellbeing’ was the main reason corticosteroids were prescribed (33% to 61% of all corticosteroids prescribed). Questions around prescribing of corticosteroids for non-specific reasons were responded to with reserve. It was suggested that under the guise of ‘general wellbeing’ there are specific reasons for corticosteroid prescribing. These indications (e.g. lack of
appetite or fatigue) can be nebulous, and sometimes difficult to define by scientific reasoning.

There was a wide variation of prescribing between the hospices for non-specific/‘general wellbeing’ reasons and those with the highest proportions expressed disappointment with these results. One medical practitioner (Hospice 4) commented that ‘general wellbeing’ might be recorded if the reasons for prescribing were felt to be too complicated for the patient to understand. Interestingly, this hospice had the highest proportion of prescribing (61%) for ‘general wellbeing’. Equally, corticosteroids being prescribed and described as ‘fix it all drugs’ or ‘comfort drugs’ left interviewees, who were trying to be evidenced-based in their practice, unhappy with the terminology.

By Phase Two of the study (2010), of the sample of six hospices, four had their own guidelines. One hospice had borrowed guidelines from elsewhere, while the last had chosen not to use guidelines for corticosteroid prescribing at all. In this hospice, the medical practitioners suggested that the prescribing of these medicines was individualistic and they did not wish to be limited but instead preferred the freedom of choice in practice. Prescribing dose ranges in this hospice fell within the ranges for all other hospices in the sample.

The guidelines used in the sample hospices were similar to those used internationally (on palliative drugs.com), which was not surprising as most had been based on and referenced to these. Guidelines do not only contain dose ranges, they can also make suggestions as to when to initiate corticosteroids, the length of time they should be prescribed, when to review and monitor these medicines, and methods of stopping. Although methylprednisolone and prednisone were mentioned in some guidelines to a limited degree, dexamethasone is the corticosteroid on, which most were based.

The prescribers’ perceptions of corticosteroid dose ranges as shown in the Phase One data were that they were similar among the hospices and showed little variation from the dose ranges quoted in the published guidelines, and this was indeed the case. In contrast, dose reductions, duration of corticosteroid course, method of stopping and the dose stopped at were often different between hospices and between prescribers with little apparent attention paid to guideline suggestions.
One of the greatest concerns identified in this study was the abrupt stopping of corticosteroid treatment after a long period of use rather than a gradual reduction from what was on some occasions a high dexamethasone (8mg) level. Within published guidelines there are suggestions on the winding down and the stopping of corticosteroids. Guidelines from the United Kingdom (Appendix 1) and New Zealand (Appendix 2) suggest that following high doses and periods of two to three weeks or more of continuous use, corticosteroids should be reduced gradually under supervision and they include suggestions for this reduction.

Some medical practitioners expressed surprise at the abrupt cessation of these medicines, having made the assumption they would be gradually wound down by another practitioner. Other practitioners were aware that these medicines had been discontinued at a relatively high dose, especially when a patient could no longer swallow but did not appear particularly concerned with this decision. A small number, who recognised the risks of adrenal crisis and an increase in terminal restlessness, insisted there be a route change and that the corticosteroids be continued until the patient’s death.

In Phase Two, the prescribers suggested that reviewing and monitoring of corticosteroids in the inpatient units was frequent although they admitted that this regular reviewing and monitoring may not have been recorded in the patient notes. Once a patient had left the unit, it was acknowledged that monitoring and reviewing may not be frequent or may not happen at all. One of the interviewees suggested this was an area not performed well because the responsibility of monitoring and reviewing became a shared responsibility and on many occasions not picked up at all. Hardy suggested that patients be reviewed and monitored closely to ensure that the beneficial effects of the corticosteroids outweigh the adverse effects caused by these medicines (Hardy, 1998).

Two related issues were identified in the current study: one of not recognising or appreciating corticosteroid adverse effects, and the other, the absence of the recording of adverse effects in patient notes. After reviewing the responses from the interviews, it became apparent that corticosteroid adverse effects were under-recorded and often not identified until a patient was Cushingoid. Additionally, some clinicians appeared not to recognise corticosteroid adverse effects at all, but rather thought of them as part of the dying process. Under those circumstances they would
not have considered recording them as adverse effects. This longstanding misconception was first reported in the literature in 1993 (Bruera, 1993). An interviewee also suggested that when trying to manage a dying patient’s distressing symptoms, adverse effects were not of prime consideration and therefore were unlikely to be recorded.

The interviewees agreed that lack of documentation was of concern but they appeared to have no immediate solution. This lack of documentation and the reasons for it requires further review. It would be an important study for future research.

During the interviews, some key points were identified when discussing the medicines co-prescribed with corticosteroids, which were of interest to the researcher in the first phase of this study. Few interviewees fully understood the pharmacology of these drug combinations and wondered why the selected medicines were included. CYP450 interactions are common but may be overlooked when prescribing corticosteroids.

There was no surprise demonstrated at the high proportion of inpatients prescribed omeprazole, a protein pump inhibitor with many CYP450 enzyme interactions. Most felt that it was common for palliative care patients to be prescribed this drug for any number of reasons unrelated to corticosteroid co-prescribing such as for acid reflux. This proportion did not appear to alter with the addition of an NSAID because those hospices with the higher proportion of NSAID prescribing did not necessarily have a higher proportion of omeprazole prescribing. The assumption could not be made that omeprazole prescribing could be related to NSAID prescribing.

Some interviewees were aware of the phenytoin/corticosteroid interaction although only a small number knew what that interaction was and which drug was affected. Most were vague about the interaction and a small number were not aware of it at all. The interaction of zopiclone with corticosteroids had not been identified by the interviewees, which was of concern considering how many patients were prescribed this combination.

The selection of the clinicians to be interviewed was determined in conjunction with the medical directors and chief executive officers of the hospices. As expected, in the larger hospices there were more practitioners available than in the smaller
hospices. The original plan had been to interview only those who had been employed in the same sample hospice in 2007, the year of the data collection for Phase One of the study. This was not possible for two interviews due to staff turnover. Of these two cases, one medical practitioner was new to the palliative care field and was therefore not able to respond to some of the questions. In the other, a palliative care specialist had been in a different sample hospice in 2007 to the one where he was interviewed in 2010. The interviewees were otherwise a fair representation of those medical practitioners and registered nurses working in the hospice environment.

Once the 18 interviewees had been selected and had accepted the invitation to be interviewed, dates and times were arranged to fit around busy schedules and practitioners who worked at the hospice only part-time. The interviews took place between August and November 2010 with one hospice’s clinicians being interviewed in August, four in September and October, and the final hospice staff were interviewed in November. The hospices visited in the same month were grouped for ease of travel by the researcher. This led to September and October being intense months. Interview times were determined by hospice rosters and availability on the day and generally worked well. While breaks between individual interviews would have been optimal, to allow the researcher time to collect her thoughts and write up notes, this was not always achievable.

All except one interviewee were interviewed as arranged. The exception, at the time of her interview, withdrew from the study for personal reasons, and was replaced by a hospital palliative care specialist who worked part-time at the same hospice unit. All interviews, except this one, were conducted within the interviewees’ home hospices. The one interview not conducted at a hospice was conducted at the hospital where the palliative care specialist was based. The environments (office or library) for conducting the interviews were suitable for the purposes.

These interviews were the first semi-structured interviews the researcher had conducted and process was new to her. Some interviews ran more easily than others depending on the experience of the interviewee and rapport with the interviewer. Some interviews were of longer duration than others, with some of the interviewees being very experienced practitioners but others less so. At the time of inviting the interviewees to be part of this second phase, concern had been
expressed by some medical practitioners about the length of the interview process and they questioned how it would fit in their busy schedules. They had been informed that the interviews would not exceed an hour, and in fact most were shorter with an average interview time of 44 minutes.

All interviewees had been supplied with their hospice’s results from Phase One of the study in advance of their interview times. These results included the individual hospice’s specific data with graphs identifying differences in prescribing from each other and the group average.

The basis of the questions for the semi-structured interviews was derived from the results of Phase One to meet the aims and objectives of the study. The choice of questions met the research needs well and the responses led to explanations and practitioner perceptions of corticosteroid prescribing and added considerable depth to the study.

Words such as ‘comfort drug’ or ‘fix it all’ proved a challenge, and on another occasion the researcher might choose other descriptors because such terms may have confused the issues. This was particularly true of questions on non-specific use of corticosteroids. While this did elicit varied responses, those obtained were valuable. Some questions revealed opportunities for further study. One example was the apparent lack of detailed pharmacological knowledge amongst many of interviewees.

Although the researcher had replayed and listened to the interview recordings, the deficiencies of the interviewing process became clearer once the interviews were transcribed onto hardcopy. The researcher did not receive the first group of transcripts until the last set of interviews were scheduled. By this point, modification of the presentation of the questionnaire was no longer practical. The transcripts identified questions the researcher would have phrased differently, particularly around the graphical results from Phase One, when a specific graph was not always identified in discussion. This was overcome because of the standardisation of the question order throughout the interview process.

Once transcribed, the interview records were entered electronically into NVivo 8, an electronic qualitative data management system. This is a very effective programme, but was new to the researcher. Lack of familiarity with this programme led to the
process being time-consuming in entering data, grouping to headings, and then in recognition of the common themes. This process would be refined and used with more confidence and speed in a second study.

**Mixed methods**

This study utilised a mixed methods approach with both quantitative (Phase One) and qualitative (Phase Two) components. Phase One supplied the baseline data on how corticosteroids were prescribed in New Zealand palliative care, while Phase Two complemented and built on the results of Phase One. The questions in Phase Two were intended to reveal the reasons behind the prescribing decisions recorded in Phase One and what influenced those decisions.

New Zealand palliative care is a small community in which the researcher had worked many years. During her career, she had visited all New Zealand hospices. It was particularly important to minimise bias and ensure that data was recorded objectively. Bias in Phase One was unlikely because the researcher was dealing with quantitative data as expressed in patients’ notes and drug charts.

Many of the interviewees were personally known to the researcher and had heard her present on this subject. She was aware this had the potential to create bias in Phase Two and was careful to avoid this by using a set series of questions and by advising the interviewees of those questions before the commencement of the interview. On occasions the researcher was surprised by the openness of the responses which led her to believe in their reliability, but this cannot be guaranteed. It was not possible to know if the response differed from their usual interpretation and understanding of their practice. A formalised commencement and ending of the interview was used which may have resulted in potentially useful information, included in continuing conversation, being lost to the study.

A larger sample giving greater numbers with the lesser prescribed indications would have been of value, and a wider choice of hospices than the sample selected, may have given more validity to the findings. This had to be balanced against the practicality of the time available for data collection, and the researcher is confident that the data is robust.

If this study was replicated and guidelines developed the author would suggest that if symptoms with unclear aetiologies are to be grouped they are grouped under the
‘non-specific’ heading. The introduction of the term ‘general wellbeing’, while being understood within this study, has the potential to cause bias and confusion in a future study. While the two phases were separately very useful and gave a partial explanation of how and why corticosteroids are prescribed in palliative care, the real value of this study may be seen in the combination of these phases which provides a unique perspective and insight into that prescribing. Most International literature on corticosteroid prescribing is fairly dated and more generalised than the results of this New Zealand specific study, but by using a mixed methods approach in this research it was possible to confirm much of what had been previously described.

To place the results of both phases of this study in the context of existing literature, the author tabulated her research results against the published material (Table 35).
Table 35: A comparison of the literature findings, actual usage of corticosteroids, and practitioner perceptions as revealed by this research study

<table>
<thead>
<tr>
<th>International literature</th>
<th>Phase One: Recorded data of 2007</th>
<th>Phase Two: Practitioner perceptions in 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Palliative care a new speciality. Evidence-based literature scarce.</td>
<td>• Corticosteroid evidence-base often not evident</td>
<td>• Perception of corticosteroid evidence-based literature is limited and confused</td>
</tr>
<tr>
<td>• Rigour of evidence-based corticosteroid trials lacking</td>
<td>• Opioids not included in this phase</td>
<td>• Perception of more evidence-based practice around opioids</td>
</tr>
<tr>
<td>• Some International articles on corticosteroids were of value and very clear</td>
<td></td>
<td>• Opioids not treated as casually as corticosteroids</td>
</tr>
<tr>
<td>• Greater evidence-base for opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Information exists on corticosteroid pharmacology in literature.</td>
<td>• Not obvious in Phase One of study</td>
<td>• Interviews demonstrate knowledge of corticosteroid pharmacology sketchy, and sometimes inaccurate</td>
</tr>
<tr>
<td>• Dexamethasone was the most commonly prescribed corticosteroid</td>
<td>• Dexamethasone was the most commonly prescribed corticosteroid</td>
<td>• Dexamethasone was the most commonly prescribed corticosteroid</td>
</tr>
<tr>
<td>• Prescribing differed from prescriber to prescriber and palliative unit to palliative care unit</td>
<td>• Apart from the similarity of dose ranges the data showed prescribing variations</td>
<td>• Similar dose ranges for the same indications were prescribed, but each unit and most prescribers had their own methods of reducing these medicines and stopping them</td>
</tr>
<tr>
<td>• Published corticosteroid prescribing guidelines exist</td>
<td>• Guidelines obvious in only one unit in Phase One of study</td>
<td>• Corticosteroid prescribing mostly experience, intuition and anecdote despite guidelines being now present in five units</td>
</tr>
<tr>
<td>• Monitoring and reviewing essential to prevent toxicity of corticosteroids suggested</td>
<td>• Recording of reviewing and monitoring of corticosteroids sporadic</td>
<td>• Interviewees suggested reviewing and monitoring was frequent within the hospice unit but conceded it might not be recorded in patient notes.</td>
</tr>
<tr>
<td>• The proportion of palliative care patients prescribed corticosteroids is 32% to 80%</td>
<td>• The sample showed the proportion of inpatients prescribed corticosteroids was 61% to 69%</td>
<td>• On discharge it was accepted reviewing and monitoring might not be frequent and there was uncertainty as to whose responsibility it was</td>
</tr>
<tr>
<td>• Literature suggests that the most common indication for prescribing corticosteroids is for non-specific reasons yet the evidence to support this use is lacking</td>
<td>• The proportion of inpatients prescribed corticosteroids for non-specific reasons was 33% to 61% of those prescribed corticosteroids</td>
<td>• This proportion was not a surprise to the interviewees who took comfort in the closeness of this range</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The interviewees were disappointed with this high proportion and suggested within the term non-specific there were some very specific reasons for their prescribing</td>
</tr>
</tbody>
</table>

145
## International literature

<table>
<thead>
<tr>
<th>Phase One: Recorded data of 2007</th>
<th>Phase Two: Practitioner perceptions in 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literature suggests adverse effects are under-recorded and often not recognised</td>
<td>Results show adverse effects are under-recorded</td>
</tr>
<tr>
<td>Guidelines for dose ranges of corticosteroids for specific and non-specific indications suggested</td>
<td>Results show prescribers aware of dose ranges</td>
</tr>
<tr>
<td>Evidence suggests methods of reducing corticosteroids</td>
<td>Methods of corticosteroids reduction different between hospices and prescribers</td>
</tr>
<tr>
<td>Evidence for means of stopping corticosteroids when prescribed longer than two to three weeks. Concerns written re adrenal crisis</td>
<td>This evidence was not obvious in the results</td>
</tr>
<tr>
<td>Evidence suggests long-term corticosteroids are not to be stopped abruptly when a patient can no longer swallow. Concerns written re adrenal crisis and increased terminal restlessness</td>
<td>Results recorded to show change of route but not to the level of the dying patient</td>
</tr>
<tr>
<td>Evidence suggests omeprazole and corticosteroids do not need to be co-prescribed</td>
<td>Results show a high percentage co-prescribed. This does not appear to relate to either corticosteroid or NSAID prescribing</td>
</tr>
<tr>
<td>Corticosteroids and phenytoin affect each other’s metabolism Evidence suggests due to metabolism with CYP 450 enzymes. The main concern is phenytoin reducing the corticosteroid to a sub-optimal dose</td>
<td>No adjustment made when these medicines are combined</td>
</tr>
<tr>
<td>The hypnotic effect of zopiclone is reduced due to CYP 450 metabolism when co-prescribed with corticosteroids</td>
<td>Large proportions of patients are prescribed zopiclone and corticosteroids concurrently</td>
</tr>
</tbody>
</table>
As shown in Table 35, the great majority of findings in this New Zealand study supported those found in the literature, notably:

- Prescribing of corticosteroids was generally based on experience, anecdote and intuition, rather than published evidence
- Prescribing differed from prescriber to prescriber, and hospice to hospice
- The high proportion of patients prescribed corticosteroids was mirrored in the literature (but was more consistent in the New Zealand sample)
- Corticosteroids were prescribed more casually than some of the other groups of medicines used in palliative care e.g. opioids, anti-emetics
- Most commonly, corticosteroids are prescribed for non-specific reasons
- The reduction and stopping of corticosteroids was *ad hoc* even after long-term use
- Corticosteroid guidelines, if present, were not always followed
- There was a lack of recording of reviewing and monitoring of these drugs and their adverse effects
- Adverse effects tended to be undifferentiated from the dying process so not always recognised as corticosteroid induced
- The most commonly prescribed corticosteroid was dexamethasone

Where the study differed from the existing literature was:

- Clinicians showed relatively limited pharmacological understanding of the corticosteroid agents, including understanding of drug interactions
- There was little variation of corticosteroid dose ranges in the New Zealand study

**Improvements in clinical practice**

Overall, it has to be concluded that prescribing of corticosteroids in the New Zealand context is similar to that described in other published studies, with a few small variations in local practice. Based on this study, and with reference to the literature,
the researcher suggests a number of ways in which current practice in the prescribing of corticosteroids in palliative care could be improved.

There is a need to educate busy clinicians to understand the importance of recording corticosteroid prescribing decisions, not only to follow patient progress, but also to ensure that patients are not exposed to the often unacknowledged harmful effects of these agents. This requires systems to be developed for easy retrieval and sharing of recorded information, for instance standardised computer programmes across the hospices. These standardised electronic programmes could cover the reviewing and monitoring of patients’ medicine doses, course durations, and clinical outcomes.

This study has shown that evidence-based practice and guidelines for corticosteroid prescribing are not often used or available. An improved awareness of the pharmacology of corticosteroids would give a better understanding of these potent medicines and provide a rationale for why they should be treated conservatively.

The use of corticosteroid prescribing for non-specific reasons is questionable and other groups of medicines may be a better choice. A standardised method of defining the reasons for the prescribing of corticosteroids using a common terminology throughout palliative care would add clarity.

**Future research**

While the findings of the current study shed some light on the use of these agents, there is clearly a need for additional research to further understand and improve corticosteroid prescribing.

Some suggestions for future corticosteroid research studies are:

- The perceptions of palliative care patients, their family members, and clinicians concerning the effects of corticosteroid prescribing.

- Palliative care clinicians’ views on evidence-based practice in palliative care, using corticosteroids as the exemplar.

- Whether corticosteroids, as a group, are treated more casually in palliative care than other groups of medicines e.g. anti-emetics or opioids.

- Whether there are better alternatives to corticosteroids in the treatment of non-specific indications.
• Whether there is a dexamethasone dose-ceiling beyond which the adverse effects outweigh the benefits. Vecht et al. in an earlier study would suggest so (Vecht et al., 1994).

**Conclusion**

This study investigated the prescribing of corticosteroids in the New Zealand hospice setting. A mixed methods approach was employed to elucidate both how these agents are currently used (agent, dose, duration, etc.), and clinicians’ perceptions on the factors that influence their prescribing in palliative care.

The findings of the study generally confirmed those reported in the literature. A high proportion of palliative care patients received corticosteroids during their hospice treatment, often for non-specific indications. There was little use of guidelines and much prescribing was judged to be based on experience or intuition, rather than literature-based evidence. Recording and monitoring of prescribed corticosteroids was sporadic and adverse effects were not routinely recognised or recorded.

It is important that these potent adjuvant medicines, which have a legitimate role in palliative care, are prescribed with care and in accordance with available evidence, and that more attention is given to the recognition and prevention of the adverse effects associated with their use.
Appendices
Appendix A: Example of an International Corticosteroid Guideline, 2008

Guidelines for Corticosteroid Use in Palliative Care, 2008

- Review all "less toxic" alternatives before considering starting Corticosteroids
- Document each stage of the corticosteroid plan e.g. indication(s), expected outcome(s), predicted timescale of response, prior corticosteroid use and date of corticosteroid review
- Clarify the individual risk / benefit ratios for each patient:
  (a) Ensure specified indication(s) reflect current best practice
  (b) Discuss spectrum/incidence of adverse effects with the patient to obtain "consent" — highlighting common side effects (e.g. proximal myopathy) and potentially serious side effects even if rare, with discussions tailored to the individual
  (c) Highlight any need for additional caution
- Dexamethasone is the corticosteroid of choice in view of reduced fluid retention and higher potency / formulation offering a lesserened tablet burden compared to Prednisolone. Empirical doses are only a guide. Start at a sufficiently high dose to ensure any effect is not missed
- Arguably 4mg, 8mg and 16mg offer statistically equivalent neurological benefit in brain metastases, but with increasing toxicity, (Veitch, Hovesatيد & Verbiest, 1994) despite the seemingly different benefits observed in clinical practice
- Recommended doses are based on established palliative practice but are not supported by review data from oncological practice as even for steroids in brain secondaries there are no clear answers with inadequate reporting in trials (Miller et al. Clinical Oncology, 2004) while uncertain surrounds the role of steroids in SVCO (Rowell & Gleeson, 2002)

<table>
<thead>
<tr>
<th>Dexamethasone starting dose*</th>
<th>Indications</th>
</tr>
</thead>
</table>
| 2-4mg                       | - Anorexia
|                             | - To improve wellbeing / mood
|                             | - Weakness
|                             | - Non-specific pains
| 4-8mg                       | - Nerve compression pain
|                             | - Liver capsule pain
|                             | - As an anti-emetic
|                             | - Bowel obstruction
|                             | - To combat post radiation inflammation
| 12-16mg                     | - Raised ICP / brain metastases
|                             | - SVCO
|                             | - Carcinomatosis lymphangitis
|                             | - Malignant spinal cord compression

*Consider increasing / doubling the dose for patients on Phenoxytoin, Carbamazepine or Phenytoin

- Prescribe Dexamethasone as a single morning dose, or split morning doses if numerous tablets are required (do not give after 16:00h)
- Consider prophylactic prescribing of gastric protectants (e.g. Lansoprazole) if on a concurrent NSAID, and possibly if a relevant previous history of PUD, or a high cumulative corticosteroid dose of >140mg Dexamethasone (or equivalent), though as primarily symptomatic PPI / Misoprostol could be delayed until needed
- Consider prophylactic topical oral antifungal (e.g. Nystatin), if any current or recent oral symptoms that are suggestive of oral thrush
- Use a 3–7 day corticosteroid trial; if no clear clinical benefit is seen, discontinue corticosteroids abruptly for doses of 6mg daily or less (where no prior steroid exposure of note)
• If a corticosteroid response is uncertain (usually maximal between 3 and 7 days), consider a trial of up to 3 weeks, where abrupt withdrawal is still possible for doses of 6mg daily or less.
• When beneficial, corticosteroids should only be continued at a set dose for a maximum of 2-4 weeks, with a planned review date to consider corticosteroid withdrawal.
• Taper corticosteroids to the lowest dose required clinically, aim for Dexamethasone 4mg or less. Even when benefits are noted “maintenance therapy” should be avoided. Patients should always be on a reducing scale of corticosteroids, though this may incorporate dose increases or fixed periods of a stable dose (2-4 weeks) while continuing the overall weaning process.
• Involve the patient and other healthcare professionals in the corticosteroid management plan. All patients requiring ongoing corticosteroids need to be aware of the necessary basic precautions:
  • Mechanisms, indications and formulations of corticosteroids
  • Side effects of corticosteroids, and the need for short courses
  • Advice against stopping corticosteroids abruptly and indications for additional doses
  • Symptoms to watch for and action to take while corticosteroids are being tapered down
  • The need to seek medical help if more unwell while taking corticosteroids, or come into contact with infectious diseases, particularly chickenpox if not previously infected as this requires urgent medical attention
  • The need to carry a corticosteroid card (and possibly a Medic Alert bracelet) and to inform anyone treating them that they are on corticosteroids (and for one year after stopping them)
• Discontinue corticosteroids as soon as benefit is lost. However for corticosteroid doses greater than 6-8mg of Dexamethasone (or equivalent), or following periods longer than 3 weeks continuous use, corticosteroids should be discontinued gradually, under supervision, (time allowing). Reduce doses by 25-50% every 4-8 days (Raal & Vechi, 2004). If possible, reduce higher doses more rapidly then more slowly when nearing physiological doses i.e. Dexamethasone 1mg daily (or equivalent):

<table>
<thead>
<tr>
<th>Dexamethasone, daily doses</th>
<th>Empirical dose reductions</th>
</tr>
</thead>
<tbody>
<tr>
<td>above 4mg</td>
<td>reduce by 2 - 4mg every 4-8 days (and check for symptoms before the next dose drop), until reaching 4mg</td>
</tr>
<tr>
<td>4mg or less</td>
<td>reduce by 50% every 4-8 days, to 2mg, then 1mg, then 0.5mg, or on alternate days for a more conservative approach</td>
</tr>
</tbody>
</table>

• For Dexamethasone doses above 4mg daily, consider checking random blood glucose during first 2 – 4 weeks of treatment or whenever possible symptoms.
• If ongoing steroids appear likely consider osteoporosis prevention with Bisphosphonate therapy
• If corticosteroid induced myopathy occurs, reduce the dose and consider a switch to Prednisolone, and aim for <30 mg (or equivalent).
• As benefit is unlikely from withdrawal for patients in the terminal phase (<1-2 weeks prognosis), consider continuing corticosteroids to prevent rebound symptoms, withdrawal symptoms or clouding of cause of ongoing decline
• If the oral route is not available, ongoing corticosteroids should be given by subcutaneous infusion at equivalent doses (50%-100% of oral dose), or for small volumes via a SC stat line. Minimise the risks of precipitation by: adding last; and mixing slowly at body temperature (warmed in hand)
• For patients on corticosteroids or recently discontinued (1 week for a short course or 12 months for a course lasting months/years) consider additional doses for physiological stresses; pain; infection / fever; hypovolaemia; trauma e.g. fractured femur; and dying.
Appendix B: Example of a New Zealand Corticosteroid Guideline, 2008

Mercy Hospice Auckland
Use of Steroids in Palliative Care

- Steroids have both specific and general indications in the oncology and palliative care settings
- There is no specific dose response or other measurable indicator of efficacy and the clinical effects of steroid medication are often observed and subjective
- There are no specific dosage regimens for individual conditions and circumstances and a considered approach to prescription and monitoring of steroids is warranted
- Continuous use of steroids results in adrenal suppression and the risk of significant side effects increases with dose and length of use
- The aim of treatment should be to use an effective dose for a particular indication until the condition or symptoms are relieved, then stopping the steroids or reducing to the minimum effective maintenance dose
- There is a wide range of doses used. There is little evidence-based information about the best dose. Several principles guide prescription of steroids:
  - The indication for prescribing steroids should be clearly identified a priori to starting therapy
  - A single dose rarely if ever causes harm
  - Use is palliative not curative
  - The most appropriate dose is that which alleviates symptoms

- The duration of the course depends on response to treatment. If there is no response in 3 to 5 days, the course should be stopped
- In general pulse doses of 5 to 7 days duration should be used. Response to treatment should then be reviewed and steroids stopped or the indication, and dose reviewed
- Prolonged courses (greater than 3 weeks) are associated with more side effects. (hyperglycaemia; oral candida; fluid retention & weight gain; skin thinning; changed body image)
- It is generally safe to stop a course abruptly if it is of less than 2 weeks duration
- If Dexamethasone has been used for more than 2 weeks the dose should be reduced gradually with review at each dose change. Empirical dose reductions:
  - Dexamethasone above 2mg - reduce by 2 - 4mg every 5-7 days (and check symptoms before the next dose drop), until reaching
  - Dexamethasone 2mg or less - reduce by 0.5 - 1mg every 5-7 days
Relative doses of commonly used steroids

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose (mg)</th>
<th>Duration (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>25</td>
<td>12 - 36</td>
</tr>
<tr>
<td>Methylprednisolone (Medrol/SoluMedrol)</td>
<td>20</td>
<td>12 - 36</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>4</td>
<td>36 - 72</td>
</tr>
</tbody>
</table>

Indications and indicative doses

Note: These doses are for guidance and steroids are not the first or only pharmacological therapy for the following indications.

- **High dose (dexamethasone - 16mg/24 hours)**
  - Spinal cord compression
  - Raised intra-cranial pressure
  - Superior vena cava obstruction
  - Tracheal/bronchial compression
  - Pulmonary lymphangitis
  - Bowel obstruction

- **Moderate dose (dexamethasone - 8mg/24 hours)**
  - Nerve compression (at times may warrant higher dose)
  - Bone pain (at times may warrant higher dose)

- **Low dose (dexamethasone - 4mg equivalent to prednisone 25 mg/24 hrs)**
  - Improved general well being and appetite (say, two week course)
  - Maintenance of symptoms controlled initially on higher doses

Dexamethasone in syringe driver prescriptions

- Dexamethasone can be used cautiously in most syringe driver combinations
- In higher dose, it may cause crystallisation of the solution
- Dexamethasone should be added as the last constituent to a maximally diluted syringe solution
- Dexamethasone/cyclazine mixtures are best avoided
- In final illness setting consider the merits of reduction or cessation of steroids
- When there is reason to continue steroids, consider a single daily syringe dose of dexamethasone or methylprednisolone (16 mg Dexamethasone = 80 mg methylprednisolone [SoluMedrol])

References


Corticosteroid use in palliative care. Specialist Palliative Care Policies and Guidelines Group, Pan-Birmingham Palliative Care Network

www.birminghampalliativecare.com

www.palliativedrugs.co Document library/stereoids


Mercy Hospice Auckland clinical resource - provided for guidance only

Nov 200
Appendix G: Corticosteroids in Palliative Care Study: Specific Data for Hospice Two

Hospice 2 is a 12-bed specialist palliative care service which serves a population of 180,000 people spread over a wide geographical area both urban and rural. The hospice inpatients for the year of 2007 were 251. Of these patients, 16 sets of notes were missing leaving the patients reviewed at 235 of which 144 were on corticosteroids (61%) (Figure 1); 50 (a 1 in 3 sample) of these patients were entered on the database.

Results:
1) **Cancer:** Yes 100%
2) **The three most common cancers:** GI tract, Lung and Urogenital
3) **Gender:** 56% male; 44% female
4) **Age range:** 23 to 83 years
5) **Common indications for corticosteroids:** 45% for ‘general well being’; 23% for neurological; 10% for soft tissue infiltration and 11% not clear/other (figure 2)
6) **Corticosteroid use for each indication:**
   a) Methylprednisolone 10% for ‘general wellbeing’; 41% for neurological and 48% for soft tissue infiltration
   b) Dexamethasone 31% for ‘general wellbeing’; 34% for neurological; 3% for capsular stretching; 11% for soft tissue infiltration; 2% for tenesmus; 3% for syringe driver sites and 16% for not clear/other.
   c) Prednisone 86% for ‘general wellbeing’ and 9% for capsular stretching and 5% not clear/other.
7) **Daily dose range of methylprednisolone:** 125mg for ‘general wellbeing’;
   125mg for neurological and 80 to 125mg for soft tissue infiltration.
8) **Daily dose range of dexamethasone:** 1 to 8mg for ‘general wellbeing’; 1 to 16mg for neurological; 8mg for capsular stretching; 0.25 to 8mg for soft tissue infiltration; 2 to 8mg for tenesmus; 0.5 to 1mg for syringe driver sites and 0.5 to 40mg for not clear/other
9) **Daily dose range of prednisone:** 5 to 40mg for ‘general wellbeing’; 20mg for capsular stretching and 10mg for not clear/other
10) **Corticosteroid side effects:** Yes 44%; No, 2%; Not recorded 54% (Figure 3)
11) **Drug stopped stat:** 34% (Figure 4)
12) **Concurrent drugs while on corticosteroids:** (Figure 5)
   a) GI cover 77%
   b) NSAIDs 47%
   c) Phenytoin 5%
   d) Zopiclone 50%
13) **Reviewed:** 57%
14) **Guidelines:** Not evident though a previous study on corticosteroids had been done.

Figures:
1) Percentage of steroids for all six hospices
2) Side effects of corticosteroids
3) Mode of ceasing corticosteroids
4) Concurrent drugs while on corticosteroids

**Percentage of patients on corticosteroids over the six hospices studied**

![Graph showing percentage of patients on corticosteroids across six hospices.]

**Indications of corticosteroid use - Hospice 2**

![Bar chart showing indications of corticosteroid use for Hospice 2 and average of all hospices.]

- Neurological
- Capsular stretching
- Soft tissue infiltration
- Tenesmus
- Syringe driver sites
- Other
- Chemotherapy
Side effects of corticosteroids - Hospice 2

Mode of ceasing corticosteroids - Hospice 2

Patients on selected concurrent medications while on corticosteroids - Hospice 2
References


References


