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Factors influencing adherence in long-term use of statins

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Keywords:	Epidemiologic determinants, Medication adherence, Statins
Abstract:	<p>Purpose: To assess the factors influencing adherence in long-term medication use as exemplified by statins.</p> <p>Methods: Data from an in-depth survey of Australians aged 45 years and over were linked to national prescription reimbursement data to assess medication possession ratio (MPR) for statins for the middle two years of a four-year period of statin possession. Poisson regression was used to calculate the relative risk (RR) for adherence (MPR\geq80%) for patient characteristics and factors related to access to and need for health care services. Separate models were fit for patients receiving healthcare concession subsidies and those who do not ('general beneficiaries').</p> <p>Results: 42,492 concessional and 16,110 general beneficiary patients were included in the analysis with 80.1% and 56.7% showing MPR\geq 80%, respectively. In both models, RR for adherence was significantly elevated for older (age 65+) and less healthy (worse self-rated health, pre-existing heart condition or obese) individuals, and for those who had private health insurance. Significantly lower RR (i.e. more non-adherence) was found for individuals reporting speaking a language other than English at home, who were smokers, employed, had higher levels of education, and for those who reported psychological distress. Income had no significant relationship with adherence, and the pattern of adherence by remoteness of area of residence was inconsistent.</p> <p>Conclusions: Poor adherence in long-term use of statins is commonplace, but a number of key predictors – including age, language other than English spoken at home, smoking status and psychological distress – are readily assessable by the prescribing practice.</p>

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For Review Only

Factors influencing adherence in long-term use of statins

Running head: Factors influencing adherence in long-term use of statins

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Keywords: Epidemiologic determinants; Medication adherence; Statins

Key Points:

- Poor adherence in long-term use of statins is commonplace, but a number of key predictors are readily assessable by the prescribing practice
- Patients who are older, obese, have less than excellent self-rated health or prior history of heart disease are more likely to adhere in long-term use of statins
- Speaking a language other than English at home (in an English-speaking country) is a major risk factor for non-adherence in long-term use of statins
- Other significant risk factors for non-adherence include being a smoker, employed and reporting substantial psychological distress

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Abstract

Purpose: To assess the factors influencing adherence in long-term medication use as exemplified by statins.

Methods: Data from an in-depth survey of Australians aged 45 years and over were linked to national prescription reimbursement data to assess medication possession ratio (MPR) for statins for the middle two years of a four-year period of statin possession. Poisson regression was used to calculate the relative risk (RR) for adherence (MPR \geq 80%) for patient characteristics and factors related to access to and need for health care services. Separate models were fit for patients receiving healthcare concession subsidies and those who do not ('general beneficiaries').

Results: 42,492 concessional and 16,110 general beneficiary patients were included in the analysis with 80.1% and 56.7% showing MPR \geq 80%, respectively. In both models, RR for adherence was significantly elevated for older (age 65+) and less healthy (worse self-rated health, pre-existing heart condition or obese) individuals, and for those who had private health insurance. Significantly lower RR (i.e. more non-adherence) was found for individuals reporting speaking a language other than English at home, who were smokers, employed, had higher levels of education, and for those who reported psychological distress. Income had no significant relationship with adherence, and the pattern of adherence by remoteness of area of residence was inconsistent.

Conclusions: Poor adherence in long-term use of statins is commonplace, but a number of key predictors – including age, language other than English spoken at home, smoking status and psychological distress – are readily assessable by the prescribing practice.

Introduction

Poor adherence (also known as *compliance*) to long-term medication is a major issue undermining the effective delivery of healthcare.¹ It is frequently overlooked by prescribing physicians when intensifying treatment.^{2,3} Statins, as a case in point, are a central element in cardiovascular disease (CVD) risk management as per guidelines in Australia⁴ and internationally.⁵ It is known that the rate of failure to maintain statin therapy for 12 months after initiation is high⁶ even when initiated after acute coronary events.⁷ Poorer levels of statin adherence are associated with higher rates of long-term mortality after acute myocardial infarction⁸ and in coronary artery disease generally.⁹

Better understanding of the circumstances where good adherence is less likely could help to focus adherence-promoting interventions. In the present study, we investigated the factors associated with poor adherence, in terms of poor maintenance of medication supply, for patients engaged in long-term (multi-year) use of statins. We used baseline questionnaire data from Australia's largest cohort study – the 45 and Up Study – linked with administrative data of medication reimbursement to identify risk factors for poor adherence in long-term use of statins.

Methods

The 45 and Up Study is a cohort study of more than 250,000 men and women aged 45 years and over resident in New South Wales (NSW), Australia; its methods have been described previously.¹⁰ Participants were randomly sampled from the Medicare Australia database and joined the study by completing a mailed self-administered questionnaire and providing consent for long term follow-up, including linkage to health records. The response rate was 18%.¹⁰ Recruitment to the 45 and Up Study commenced in 2005 and was completed in 2009; 21% of participants completed the survey in 2006-2007 and 78% completed the survey in 2008.

Through the Pharmaceutical Benefits Scheme (PBS), the Australian Government substantially subsidises medications “necessary to maintain the health of the community”¹¹ including statins. The scheme has a differential per-prescription cost for Concession Card holders (A\$5.80) and General Beneficiaries (A\$34.40), up to an annual Safety Net threshold such that after annual family payments total A\$348.00 for Concession Card holders prescriptions are free, and after annual family payments total A\$1363.30 for General Beneficiaries they pay the regular Concession amount (2012 rates; these have been indexed for inflation and the Safety Net advanced in increments over the study period).¹² Concession status for PBS can be awarded for ‘pensioners’ (from aged 60 and up), as well as disability, low income or facing a large burden of dependants.¹³

Deterministic data linkage between 45 and Up Study questionnaire data and PBS claims data was performed by the Sax Institute (participant numbers for the initial survey and for subsequent PBS claims data are both based on Medicare number). The PBS data provides a transaction record for each subsidised dispensing from a community pharmacy to a 45 and

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3 Up Study participant and includes the subsidy status (Concession or General Beneficiary) and
4 whether they had reached the Safety Net threshold at the time of the transaction.
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Statin adherence was assessed in terms of a Medication Possession Ratio (MPR), computed as the proportion of days covered by dispensing to the patient as indicated from the PBS records. We took the common threshold of $MPR \geq 80\%$ as indicating adherence.¹⁴ To identify long-term statin users, persons with at least one statin dispensed in each of 2008 and 2011 were identified and their dispensing in 2009-2010 used to indicate a 24-month MPR. Computation for statins is relatively straightforward in the PBS data as statins at all common strengths are packaged for 30-day supply per dispensed (i.e. the dosage instructions, absent in PBS records, are not required). As such, we simply counted the number of distinct days with PBS records for statins in 2009-2010 (as per ATC¹⁵ codes, including combination products, see Appendix) and divided by 24, taking this as the MPR, excluding anomalous cases showing $MPR \geq 140\%$. Our MPR threshold would be forgiving of hospitalisations, or similar community care disruptions, of up to four months.

Relative risks (RRs) of statin adherence ($MPR \geq 80\%$) were calculated in a modified Poisson regression model,^{16,17} to take into account the common nature of the outcome. Candidate predictor variables for the model (Table 1) were identified from the 45 and Up Study questionnaire data with consideration of the Behavioural Model of Health Services Use, which divides factors into pre-disposing, enabling (or access) and need,¹⁸ and theoretical determinants of adherence in terms of factors leading to the intention to take medication as prescribed and subsequent barriers.¹⁹ Where applicable, data definitions align with previous use of 45 and Up Study baseline questionnaire data to assess service utilisation.²⁰

Study participants were classified as Concession Card holders, General Beneficiaries, or a mixture of General Beneficiary and Concession status using all claims for statin dispensation from 2008-2011. We computed separate models for Concession Card holders and General Beneficiaries as the two groups have quite different age, socioeconomic and need profiles, and face different cost regimens around patient co-payment – in particular, for General Beneficiary claims not meeting the Safety Net less expensive statins would be omitted from the claims dataset.²¹ Those participants with claims mixed between the categories were excluded from the analysis. To assess whether levels of statin adherence differed between claimant cohorts beyond the difference in age and socioeconomic profile, a combined model was run treating Concession Card holder or General Beneficiary status as an additional predictor variable. Patients who reported holding a Department of Veterans Affairs (DVA) card in the baseline survey were excluded from analysis due to the data being held separately from other PBS claims.

Missing values were modelled as a separate category; these RRs have not been reported. To assess the impact of missing data, a sensitivity analysis was performed excluding participants with at least one missing variable. Due to the strong correlation between age and a number of variables in the model, a further sensitivity analyses was run stratifying the model by age for Concession Card holders. All analyses were carried out in SAS 9.2.

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3 The research was approved by the NSW Population & Health Services Research Ethics
4 Committee (reference 2011/12/362) and the University of Western Sydney Ethics Committee
5 (reference H9517).
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8 9 **Results**

10 Of the 267,091 45 & Up Study participants, 67,307 had PBS records indicating long-term
11 statin use through 2008-2011. This included 42,857 Concession card holders, 16,130 General
12 Beneficiaries, and 8,315 participants with a mixture of Concession and General Beneficiary
13 statin dispensations.
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16 Among Concession Card holders, n=303 participants were excluded for reporting having a
17 DVA card, and n=62 for having an anomalous MPR $\geq 140\%$, leaving a total of n=42,492
18 participants for analysis. Among General Beneficiaries, n=16 participants were excluded for
19 reporting having a DVA card and n=4 for having an anomalous MPR $\geq 140\%$, leaving a total
20 of n=16,110 participants for analysis.
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23 Concession Card holders had higher levels of adherence, with 80.1% (n=34,033) having an
24 MPR $\geq 80\%$ compared to 56.7% (n=9,141) among General Beneficiaries (Figure 1).
25 Concession holders were on average older than General Beneficiaries, were less likely to
26 work, had lower levels of education, were more likely to smoke, and had worse physical and
27 mental health status (Figures 2 and 3). Adherence levels were significantly lower among
28 General Beneficiaries than Concession Card holders (RR: 0.76, 95% CIs: 0.75-0.77), even
29 when adjusting for the full set of predictor variables (RR:0.78, 95% CIs: 0.76-0.79). The
30 frequency of claims for the less expensive statins were lower among General Beneficiaries
31 than Concession Card holders (see Appendix), consistent with the hypothesis that claims
32 below the reimbursement threshold are not being captured in the data. All further analyses
33 were stratified by claimant cohort accordingly.
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38 Despite having different demographic, health and socioeconomic profiles, and different
39 reimbursement criteria, the pattern of adherence risk was generally similar between
40 Concession Card holders (Figure 2) and General Beneficiaries (Figure 3), although RR values
41 for General Beneficiaries tended to lie slightly further from the null value than the
42 corresponding RRs for Concession Card holders. Patients aged 65+ tended to be more
43 adherent, with a trend to greater adherence with increasing age. Furthermore, participants
44 who had a partner (Concession Card holders only) or private health insurance were more
45 likely to be adherent, as were people who were obese, had less-than-excellent self-rated
46 health (or fair to poor health for General Beneficiaries) or who reported prior heart disease.
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50 Adherence tended to be lower for people who were employed or had higher levels of
51 education, as well as for people who were current smokers or reported moderate to very high
52 levels of psychological distress. People who lived in 'regional' areas (see definition with
53 Table 1) had somewhat higher adherence than those who lived in either urban or remote areas
54 (more strongly and consistently for General Beneficiaries). The strongest predictor of poor
55 adherence was speaking a language other than English (LOTE) at home. A breakdown of
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3 statin adherence by reported country of origin for LOTE individuals (Table 3) indicate
4 adherence was highest among Australian and European born individuals, and lowest among
5 participants born in other Oceanic countries, Asia and the Americas.
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8 The sensitivity analysis excluding participants with any missing data resulted in a similar
9 pattern of adherence for all variables (data not shown), despite up to 44% of participants
10 being removed from the analysis (n=18,681 Concession Card holders, n=4,853 General
11 Beneficiaries). Relative risk patterns were very largely consistent for the analysis stratified by
12 age (data not shown). Although few factors were significantly associated with adherence in
13 the 85+ years age group, employed people in that age group (n=37) had higher adherence
14 than those who were not employed.
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17 18 19 Discussion

20 This study found a number of predictors of poor adherence in long-term medication use. In
21 general, younger and healthier patients were less adherent, with age being a dominant factor.
22 Furthermore, a number of predictors were identified that would be readily detectable by
23 prescribing practices, such as speaking a language other than English at home, being single,
24 being a current smoker, and reporting moderate to high levels of psychological distress (the
25 latter could be assessed in the practice waiting room by the same K-10 instrument that we
26 used in the baseline survey²²). Better understanding of these at-risk subgroups may provide
27 greater means in the promotion of effective adherence.
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31 For this study we had the opportunity to combine comprehensive national reimbursement
32 data with an in-depth survey on a large patient cohort to establish factors associated with
33 adherence in the context of long-term use of statins. We examined patients who had been
34 prescribed, and gone to the effort and expense to have dispensed, statins in both 2008 and
35 2011 to look at adherence factors among patients who have been started on statin therapy and
36 appear to concur to some degree with the choice of therapy. They are patients that have
37 already been identified to start a statin, who were not stopped due to side-effects (at least not
38 permanently) and who did not drop out of therapy in the short term (or, who at least gave it
39 another try after a few years).
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43 Many of the identified adherence risk factors have precedent in previous related studies.
44 Older patients with CVD are more likely to be on indicated medications²³ and younger
45 patients report more unintentional non-adherence to medications for their long-term
46 conditions.²⁴ Adherence rates are known to be higher in secondary than primary CVD
47 prevention.^{25,26} Heart failure patients who are smokers have lower medication refill
48 adherence.²⁷ With respect to psychological distress, depressive symptoms are associated with
49 lower statin adherence in older people⁶ and with lower adherence to cardiovascular
50 medications in general among people with coronary heart disease.^{28,29} Married patients report
51 better adherence to blood pressure lowering medications.³⁰
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55 The significantly lower level of adherence for people who speak a language other than
56 English at home may be due to a combination of difficulty in understanding provider
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3 instructions and cultural barriers (e.g. preference for traditional medicine). In looking at
4 cardiac medication use after acute myocardial infarction, Lai et al.³¹ found some (although
5 inconsistent) adherence risk for Chinese and South Asian groups compared to non-Asian
6 Canadians. More consistent with our findings, Wisnivesky et al.³² found limited English
7 proficiency was associated with poorer self-management and worse outcomes among older
8 people with asthma with respect to Hispanic American populations. While the findings of our
9 study could result from an under-estimation of medication supply due to medications
10 obtained overseas (e.g. if active links are maintained with their country of origin), it is
11 difficult to justify the observed disparity on that basis alone. It is important to note that the 45
12 and Up Study includes only people who could complete the survey questionnaire in English.
13 Higher levels of acculturation have been shown to be associated with higher levels of
14 medication adherence among US Latinos with hypertension³³, suggesting that our MPR
15 estimates for LOTE groups might be higher than those for the relevant community
16 populations. Among people with low levels of English language proficiency, it is not known
17 how using a provider who speaks the community language, rather than English, might
18 influence adherence.
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24 The general pattern of relative risk for adherence was similar across the range of factors
25 investigated between Concession Card holders and General Beneficiaries – two cohorts with
26 different levels of employment, income, and pharmaceutical subsidy. Internationally, lower
27 income and requirement to make a co-payment are associated with lower statin adherence²⁶,
28 and in the US setting, where patients bear significant direct cost of medication, amount of co-
29 payment has been shown to decrease adherence;^{34,35} however, we found no significant
30 association of adherence with income within either cohort. Unfortunately, since some statins
31 appeared to be under the subsidy threshold for General Beneficiaries, we are unable to
32 comment on whether the different subsidy regimes between the cohorts accounts for an
33 adherence difference. People with private health cover were more likely to be adherent,
34 especially those with ‘extras’ cover (e.g. optical, dental), even though this does not cover
35 statin co-payments in the Australian system; this could indicate better adherence at higher
36 levels of discretionary income, or simply where health is given higher priority. The level of
37 subsidy for pharmaceuticals in Australia during the study period was such that many
38 individuals reported that they were close to facing difficulties with prescription costs³⁶ and
39 reductions in statin use have followed increases in patient co-payments since 2005.³⁷
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45 The associations we found with respect to education and remoteness worked in a surprising
46 direction, since lack-of-education can work against adherence³⁸ and there is little question
47 that health access outside of metropolitan areas in Australia can be challenging.³⁹ In the case
48 of education, for the Concession Card group in particular, it may be that having obtained
49 education in times when it was historically rarer is associated with a variety of latent health
50 advantages that bias these individuals in the direction of younger counterparts. The
51 remoteness effects, while small, are less easily interpreted, although they could be explained
52 in terms of rural Australians having a higher effective age than their urban counterparts
53 and/or that the access challenges for statins are not significant impediments to adherence.
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3 It is possible that statin users in the 45 and Up Study are not entirely representative of the
4 broader population. In keeping with other similar large-scale population-based cohort studies,
5 its response rate was 18%.¹⁰ A comparative analysis found that the prevalence of many
6 factors in the 45 and Up Study, including country of birth, educational attainment, fruit
7 consumption, body-mass index and falls, was similar to the NSW Population Health Survey
8 (PHS), a population-based survey which has a response rate of around 60%. However, 45 and
9 Up participants tended to have higher incomes, and had lower prevalence of smoking,
10 psychological distress, hypertension, diabetes and asthma.⁴⁰ This suggests that 45 and Up
11 Study participants are in general “healthier” than the overall population.
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15 Overall, absolute rates of adherence from this study should be interpreted with caution.
16 Supply-based MPR is, of course, an indirect measure of adherence, although widely accepted
17 due to its practical applicability at the population level as compared to direct monitoring, and
18 with less vulnerability to over-estimating adherence as compared to pill counts or self-
19 report.^{14,41,42} The observed difference in adherence rates between Concession Card holders
20 and General Beneficiaries (80% versus 57%) is likely due to the different co-payment
21 thresholds and subsequent capture of non-subsidised claims for less-expensive statins,
22 although Concession Card holders should have reasonably complete representation of
23 community-based supply. Despite this limitation, the pattern of adherence among General
24 Beneficiaries was very similar to Concession Card holders, indicating the transferability of
25 the model of adherence risk to a generally younger and more able cohort. With respect to the
26 relationship of the 45 and Up Study participants to the general population, it seems likely that
27 the adherence rates in the general population are somewhat poorer than the 80% observed for
28 our Concession Card holders. In New Zealand, which has a similar healthcare system to
29 Australia, but a more universal regimen of strong medication subsidy, 50% adherence to
30 overall long-term medications was observed, and 60% (across all adult patients) for
31 simvastatin in particular.⁴³ Benner et al. specifically examined statin adherence drop-off over
32 the long term from initiation of therapy for subsidized older Americans, finding low
33 adherence (MPR<80%) rates at 61% after 1 year and 68% after 10 years.⁶ However, we have
34 importantly reported relative measures of effect (RRs) calculated from internal comparisons
35 within the 45 and Up Study, which will be valid provided there is sufficient heterogeneity
36 within the predictor variables.⁴⁴ Moreover, empirical data demonstrate that RRs for a wide
37 range of exposure-outcome relationships in the 45 and Up Study are very similar to those
38 calculated using ‘representative’ PHS data.⁴⁰
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46 A further limitation of our study was its reliance on self-reported data for some predictors
47 including demographic variables, health-related behaviours and prior health conditions.
48 Validation studies involving participants in the 45 and Up Study, however, have found
49 excellent agreement between self-reported country of birth and that recorded in hospital
50 data⁴⁵ and between body mass index categories from self-reported and measured data⁴⁶.
51 Nonetheless, the survey response captures only a single point in time (modally in 2008) and
52 some patient factors (e.g. psychological distress) may have changed substantially between the
53 response time and the period for which we assessed adherence (2009-2010).
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We did not have access to prescriptions in the present study, thus we are unclear as to whether prescribers would have been able to detect poor adherence directly from their practices' electronic medical record systems, which do not presently link automatically to national dispensing data. In New Zealand, prescriptions for long-term medications were found to be followed by a dispense within one week 93% of the time⁴³, indicating that prescribers would usually have an indication of low MPR based on their own prescription records alone.

It has been observed that adherence is largely unrelated to drug class (and by inference, to side-effects) for CVD medications,²⁵ and thus the results of this study should generalise well to antihypertensive medications and aspirin. On the other hand, long-term adherence to other classes of medication where the effect is more overt, such as antipsychotics,⁴⁷ is likely to operate somewhat differently.

We have defined 'long-term' adherence with respect to the middle two years of four where there is some degree of statin possession in the first and last years. This stands at variance to other uses of 'long-term' in the literature – which, for example, may be taken as still reporting use 12 months after a hospital discharge.²⁹ The results highlight the substantial levels of adherence issues, and available predictors thereof, even among patients that persist with their medication in the long-term (in the sense of having at least one dispensed prescription in the fourth year). We believe our results are particularly relevant to quality improvement for family practice as they relate to suboptimal health delivery in cases where patients are maintaining a degree of long-term relationship to their health providers.

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Factors influencing adherence in long-term use of statins

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Table 1. Predictors of adherence from 45 and Up Study baseline questionnaire

Variable	Description
Age	At time of survey completion (2005-2009)
Gender	As per Australian Medicare profile (which can be updated by the individual)
Highest Education Qualification	Self-reported
Language other than English (LOTE)	Language spoken at home – regional breakdown of country of origin in Table 3
Partnership Status	Marriage or partner versus never married, separated, divorced or widowed
ARIA+ remoteness	Accessibility and Remoteness Index for Australia Plus (ARIA+) score for the postcode of residential address*
Private Health Insurance	Self-report of private insurance (at levels of basic private hospital cover or 'with extras,' indicating additional cover for ancillary non-hospital services), or Health Care Card ¹³
Employment status	Including self-employed
Annual income	Self-reported
Body Mass Index	From self-reported height and weight [†]
Current Smoking Status	Self-reported
Alcohol Drinks / week	Self-reported
Sufficient Physical Activity	At least 150 MET (Metabolic Equivalent Task) adjusted minutes over 5 sessions per week
Self Rated Health	Self-reported "Overall health"
Ever Told Heart Disease	Response to "Has a doctor ever told you that you have any of the following..." with tick-box for Heart Disease
Functional Limitations	Medical Outcomes Study Physical Functioning (MOSPF) scale ⁴⁸
Psychological Distress	Kessler-10 (K10) score ²²

* ARIA+ is based on sum of ratios of road distances to population centers of five distinct sizes as compared to Australian national averages⁴⁹. We label ARIA+ bands: 0 – 1.84 = Metro; >1.84 – 3.51 = Inner Regional; >3.51 – 5.80 = Outer Regional; >5.80 – 9.08 = Remote; and >9.08 = Very Remote.

† We label BMI categories conventionally as Underweight (BMI < 20), Normal weight (BMI 20 – < 25), Overweight (BMI 25 – < 30) and Obese (BMI 30 and higher).

Table 2. Regional distribution of country of origin and adherence rates for LOTE speakers

Region	Concessional			General Beneficiaries		
		% of LOTE	% with		% of LOTE	% with
	N	speakers	MPR ≥80	N	speakers	MPR ≥80
Australia	480	10.7	74.6	362	22.2	50.8
Other Oceania*	86	1.9	58.1	65	4.0	24.6
North-West Europe	744	16.6	72.0	183	11.2	44.8
Southern and Eastern Europe	1,546	34.6	71.5	319	19.5	43.9
North Africa and the Middle East	452	10.1	62.2	97	5.9	42.3
South-East Asia	420	9.4	59.5	237	14.5	30.0
North-East Asia	252	5.6	56.3	129	7.9	27.1
Southern and Central Asia	153	3.4	53.6	111	6.8	27.9
Americas	145	3.2	54.5	63	3.9	39.7
Sub-Saharan Africa	66	1.5	69.7	42	2.6	40.5
Missing /undetermined	130	2.9	76.2	24	1.5	37.5

* i.e. New Zealand and Pacific Islands.

Factors influencing adherence in long-term use of statins

Figure 1: Cumulative frequency of MPR scores among Concession Card holder and General Beneficiary long-term statin users

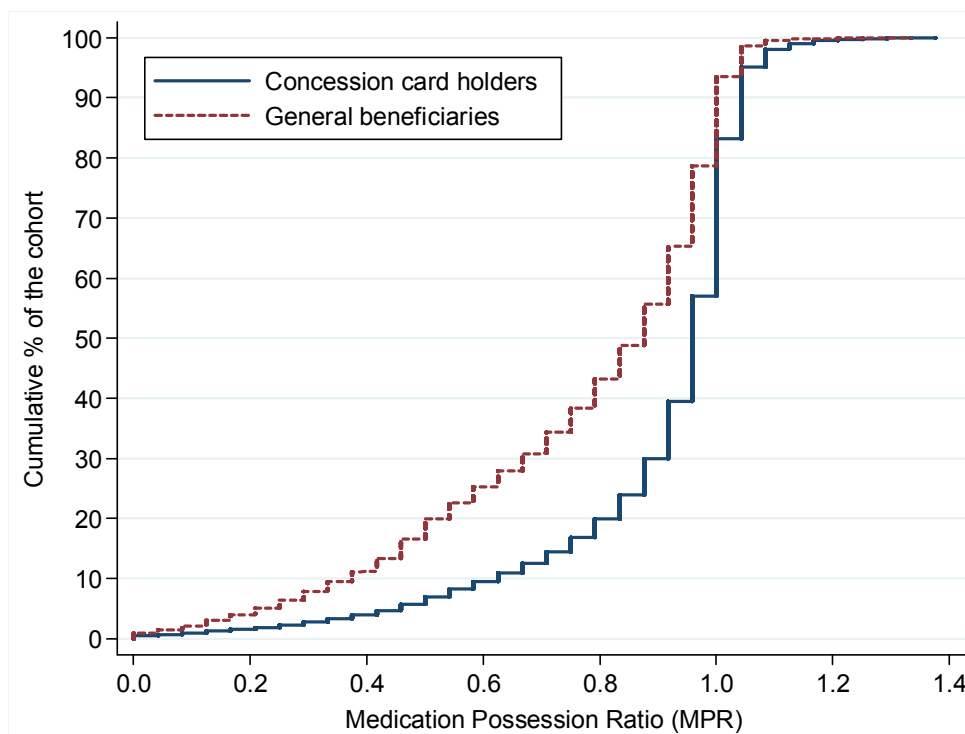
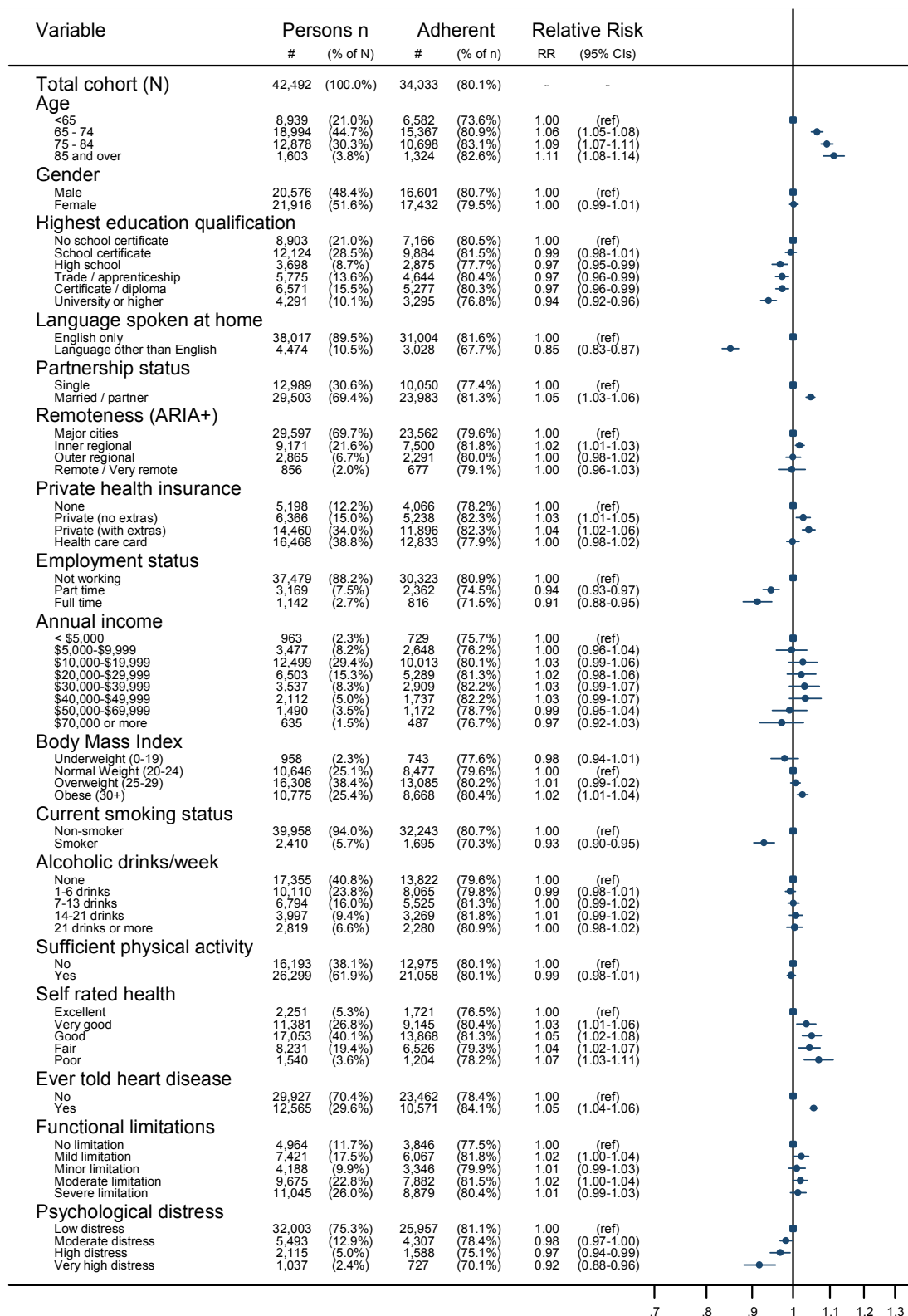
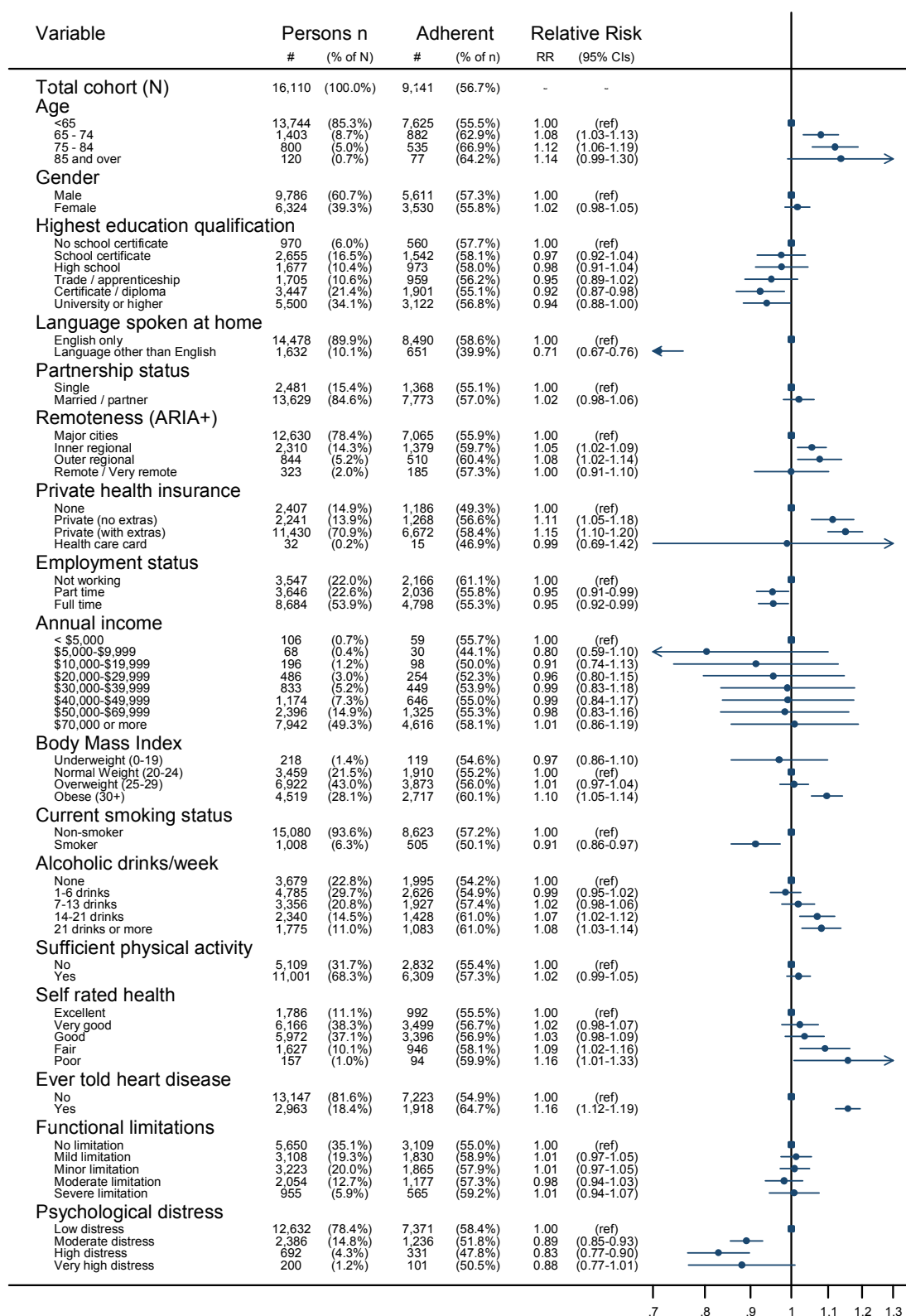


Figure 2. Relative risk for adherence (MPR ≥ 80) for Concession card holders

Factors influencing adherence in long-term use of statins

Figure 3. Relative risk for adherence (MPR ≥ 80) for General Beneficiaries

Appendix

Table A1: Drug dispensations among concession card holders and general beneficiaries, 2009-2010

Statin dispensation				Concession card holders		General beneficiaries	
ATC code	Drug name	Strength	Mean \$	# claims	(% of claims)	# claims	(% of claims)
C10AA01	Simvastatin	10 MG	25.06	26775	(2.9%)	323	(0.1%)
		20 MG	33.24	79966	(8.7%)	2364	(0.8%)
		40 MG	44.55	99915	(10.8%)	23597	(7.8%)
		5 MG	19.82	1355	(0.1%)	13	(0.0%)
		80 MG	59.59	26563	(2.9%)	6588	(2.2%)
C10AA03	Pravastatin	10 MG	21.55	5219	(0.6%)	100	(0.0%)
		20 MG	30.71	19749	(2.1%)	324	(0.1%)
		40 MG	43.77	39097	(4.2%)	9010	(3.0%)
		80 MG	61.97	7477	(0.8%)	2009	(0.7%)
C10AA04	Fluvastatin	20 MG	26.50	1690	(0.2%)	26	(0.0%)
		40 MG	31.88	2630	(0.3%)	76	(0.0%)
		80 MG	47.78	834	(0.1%)	386	(0.1%)
C10AA05	Atorvastatin	10 MG	42.79	72070	(7.8%)	25454	(8.4%)
		20 MG	58.33	147082	(16.0%)	60354	(19.9%)
		40 MG	79.55	149139	(16.2%)	59900	(19.8%)
		80 MG	110.93	52149	(5.7%)	19519	(6.4%)
C10AA07	Rosuvastatin	10 MG	68.92	64096	(7.0%)	34018	(11.2%)
		20 MG	95.16	34636	(3.8%)	18788	(6.2%)
		40 MG	132.98	17198	(1.9%)	10098	(3.3%)
		5 MG	51.38	19466	(2.1%)	9324	(3.1%)
C10BA02	Simvastatin and ezetimibe	10 MG	115.54	26425	(2.9%)	10216	(3.4%)
C10BX03	Atorvastatin and amlodipine	10 MG	89.70	12967	(1.4%)	5702	(1.9%)
		5 MG	78.88	14614	(1.6%)	5095	(1.7%)

CONFLICT OF INTEREST DISCLOSURE

The Editors of *Pharmacoepidemiology and Drug Safety* recognize that most studies in pharmacoepidemiology cost money and thus pose a potential conflict of interest. As a conflict of interest may affect the assessment or judgment of an author, we ask that **all** authors (not just the Corresponding Author) complete the following form.

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