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Original Article – Clinical Science

Real-world assessment of topical glaucoma medication persistence rates based on national pharmaceutical claim data in a defined population

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ABSTRACT

Importance: The rate and determinants of persistence to topical glaucoma medications are important for identifying patients at high-risk of discontinuing medications and designing targeted approaches to improve persistence.

Background: To evaluate the rate and determinants of persistence to topical glaucoma medication among middle-aged and older Australian adults.

Design: Population-based cohort study.

Participants: Participants in need of persistent topical glaucoma medications in the 45 and Up Study.

Methods: The 45 and Up Study is a large-scale population-based cohort study. Participants were classified as needing persistent topical glaucoma medications if at least 3 claims with related prescriptions were recorded. Persistence was defined as topical glaucoma medications were filled within 90 days.

Main Outcome Measures: The rates and determinants of medication persistence at 2-year.

Results: A total of 12,899 patients requiring persistent topical glaucoma medications were identified. Among them, 9,019(69.9%) had persisted with their glaucoma

medications for at least 2 years. Multiple logistic regression analysis documented significant effects of patient-related factors (gender, socioeconomic status, language spoken at home, lifestyle and comorbidities) and drug related factors (total number and drug class) on the persistence rate. Those most at risk groups of non-persistence were those patients living in remote areas (odds ratio(OR): 0.59,95% confidence interval(CI):0.37-0.92), having family income over 70000 AUD/year (OR:0.53,95%CI:0.45-0.62), speaking other languages at home (OR:0.61,95%CI:0.53-0.68), and using cholinergic classes of medications (OR:0.55,95%CI:0.38-0.79).

Conclusions and Relevance: Our data has shown a medium level of persistence to topical glaucoma medication among middle-aged and older Australian adults. However, efforts are still needed to improve the rate of persistence.

Keywords: glaucoma topical medication, persistence rate.

1. INTRODUCTION

Glaucoma is the term used for a group of progressive optic neuropathies characterized by loss of retinal ganglion cells and loss of visual field.[1] It is one of the leading causes of irreversible visual impairment and blindness worldwide[2] and affects approximately 1.6-3.4% of the Australian population aged over 50.[3] As the population continues to age, the number of glaucoma patients worldwide is expected to reach 76.0 million in 2020 and 111.8 million in 2040.[4] In addition, the global disease burden of blindness and visual impairment due to glaucoma has shown to be significantly associated with a decline in quality of life,[5] physical functioning,[6] and mental health.[7]

Despite the fact that the underlying pathophysiology of glaucoma remains unknown, elevated intraocular pressure (IOP) is a well-established risk factor and the only factor that can be modified.[1] Intra-ocular pressure lowering therapy remains the first line treatment in most glaucoma cases.[1] Consistent evidence from epidemiological studies and clinical trials has clearly documented the benefits of IOP control in reducing the risk of visual field loss and minimizing the progression of glaucoma.[8-15] However, similar to other chronic and asymptomatic conditions, many glaucoma patients have struggled to maintain high rates of persistence, with studies showing rates as low as 10% at 1-year follow-up.[16-27] Non-persistence can affect patient glaucoma management, leading to great costs and rapid disease progression.

However, previous studies exploring persistence rates of topical glaucoma drugs have been calculated using only hospital-based pharmaceutical claim data, which has the potential to cause selection bias.[16-18,24] Even though several studies have utilized

insurance-based claims databases, limited demographic information, lifestyle and comorbidities were collected other than age and sex.[19-23] To date, only one cohort study in Taiwan and the Glaucoma Adherence and Persistency Study (GAPS) have reported the patient-related determinants of persistence rates for topical glaucoma medications using insurance-based pharmaceutical claims data.[25,27]

Little is known about the rate and determinants for topical glaucoma medication persistence in an Australian population. Only one conference' abstract by Healey et al has documented glaucoma medication persistence, which was 23.7% at 2 years using a 3 month cessation cut off.[28] However, like previous studies utilizing claims databases, Healey's analysis could not evaluate the determinants of persistence rates with respect to patient-related factors. A better understanding of patients at high-risk of discontinuing topical glaucoma medication will allow stakeholders design targeted approaches to improve persistence. As such, the aim of this study was to evaluate the rate and determinants of topical glaucoma medication persistence at 2-year follow-up in a large population-based cohort study using national pharmaceutical claim data in Australia.

2. METHODS

2.1 Data source and study design

The Sax Institute's 45 and Up Study is the largest population-based prospective cohort study in Australia and recruited participants from the general population aged 45 years and above living in New South Wales (NSW). The study methodology has been described in detail elsewhere.[29] All participants were randomly sampled from the

Department of Human Services (DHS), formerly Medicare Australia, enrolment database and received a mailed invitation including a study questionnaire, information leaflet and a consent form. The overall response rate was 18% and nearly 10% of the entire New South Wales population aged 45 years or older were included in the final sample. A total of 266,896 participants completed a postal questionnaire at baseline (distributed from January 2006 to December 2009) and gave informed consent for follow-up and extraction of their health information from Government databases. The baseline questionnaire data from study participants was linked to the Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) by the Sax Institute using a unique identifier provided by the DHS. Through the MBS, the Australian Government subsidises a list of Medicare services, including professional consultations, pathology and other diagnostic tests. The PBS is Australia's universal pharmaceutical insurance scheme which subsidises essential medications to all residents.[30] Residents contribute a co-payment for the cost of each subsidized medication and the remaining cost is covered by the PBS.[31] A Concession Card is available for social security beneficiaries who are aged 65 years and older, severely disabled, unemployed or low-income earners. Concession Card holders have a relatively lower subsidy co-payment threshold than general beneficiaries.[32] Transaction for each subsidized medication dispensed from a community pharmacy is recorded in the PBS. We conducted this analysis by extracting pharmaceutical claims data for participants during the period of 1st January 2006 to 31st December 2016.

Ethical approval for the 45 and Up Study was granted by the University of New South Wales Human Research Ethics Committee (HREC 05035/HREC 10186) and the SEEF

Study by the University of Sydney Human Research Ethics Committee (reference number: 10-2009/12187).

2.2 Inclusion and exclusion criteria

The inclusion and exclusion criteria of the study sample can be found in Figure 1. A participant was identified as requiring persistent topical glaucoma medication if at least 3 claims with related prescriptions were recorded within 1st January 2006 to 31st December 2016. The first glaucoma medication claim data during this period was defined as the index date. Exclusion criteria of the current analysis were as follows: (1) In the absence of detailed medical records, we could not verify whether patients who received laser therapy or glaucoma surgery during the observation period required persistent topical glaucoma medication. Therefore, participants who underwent glaucoma surgery or laser treatment during the study period were excluded; (2) Participants could not be followed up at 2 years after the first glaucoma medication claim date were also excluded.

2.3 Definition of persistence and non-persistence

Persistence with topical glaucoma medications was defined as the time intervals of drug refills equal to or less than 90 days based on PBS data. Non-persistence was defined as a gap in two prescription claims exceeding 90 days. A sensitivity analysis was also conducted using treatment gaps based on 60 days or 120 days to explore whether differences existed at different intervals. To verify the robustness of our results, we also assessed persistence as a continuous outcome variable (medication possession ratio, MPR and proportion of days covered, PDC). The MPR was defined as the sum of glaucoma prescription supply days divided by the total days during the

observation period (two years: 730.5 days). The PDC was calculated by the ratio of days the glaucoma patient was covered by the topical glaucoma medication to the number of days during the observation period (two years: 730.5 days). We assumed that each glaucoma medication prescription may cover 90 days. Sensitivity analysis were also performed for 60 days and 120 days.

2.4 Covariates

2.4.1 Patient-related covariates

Patient-related covariates were derived from the self-administered questionnaire at baseline. Demographic covariates included age, gender, household income, education level, social economic status (SES), remoteness index, spoken language at home and health insurance cover. Health-related factors included body mass index (BMI), history of diabetes, history of hypertension, drinking and smoking status, and physical activity. Age at index date was calculated as the age at which glaucoma medication was first claimed during the study period. Household income was divided into four groups (Australian dollars): <$20,000 per year, $20,000 to $40,000, $40,000 to $70,000 and more than $70,000. Education level was categorized into three groups: less than 10 years of education, high school/Trade or apprenticeship and University degree or higher. Participants' SES was determined by Index of Relative Social-Economic Advantage and categorized into quintile, with quintile 1 standing for highest SES and quintile 5 standing for lowest SES. Remoteness index is a standard index of remoteness and can be classified into major cities, inner regional, outer regional, and remote areas. Spoken language at home was categorized into English and other. Health insurance type included private with extras, private with no extras, veteran's card (white or gold), health care concession card and others. Body mass index was

calculated as self-reported weight in kilograms divided by self-reported height in meters squared ($kg/m^{2)}$ and divided as four groups: underweight (<18.5), normal (18.5-24.9), overweight (25.0-29.9) and obesity ($\geq$30). History of diabetes and hypertension were based on self-report to the question. The approximate number of alcoholic drinks consumed per week was calculated from the baseline questionnaire and categorized as: <14 drinks and $\geq$14 drinks per week. Participants' smoking status was classified into three groups: never, former and current smoker. Physical activity (weekly number of sessions and total time of moderate to vigorous physical activity) was evaluated using the Active Australia Survey which has been found to be a reliable[33] and valid[34] measure. Total minutes of moderate to vigorous physical activity (MVPA) per week was calculated by adding minutes of walking, minutes of moderate physical activity, and double the minutes of vigorous physical activity.[35] Based on current exercise guidelines of moderate intensity physical activity per week, the MVPA was categorized into three groups: $\geq$ 300, 150-300 and $\leq$ 150 minutes per week.

2.5 Drug-related factors

During initial analysis, drug-related covariates were based on the last prescription claims of topical glaucoma medications, including the total number and the class of topical glaucoma medication. Sensitivity analysis was repeated using initial prescription claims.

2.6 Statistical analysis

Statistical analysis was performed using SAS 9.4. Descriptive statistics were conducted for baseline characteristics of the study participants using the total number of events and persistent status. Categorical variables were expressed as proportions. Univariate

and multivariate logistic models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) of baseline characteristics for persistence. Statistical significance was defined as a P value of <0.05.

3. RESULTS

A total of 19,303 patients were identified as requiring persistent glaucoma medications. Of these patients, 4,882 (25.3%) had glaucoma-related surgery or laser therapy during the study period and 1,522 (7.88%) did not reach 2 years after the index day, therefore were excluded from analysis. In total, 12,899 (66.8%) patients were included in the current analysis (Figure 1). Among the patients who met the inclusion criteria, 9,019 (69.9%) had persisted with their topical glaucoma medications for at least 2 years, whilst 3,880 (30.1%) patients discontinued their topical glaucoma medications for an interval of more than 90 days during the 2-year follow-up. Patient-related and drug-related characteristics of included participants by persistent status are presented in Table 1.

The univariate analysis for each patient-related and drug-related variable indicated that patient-related covariates, including age, gender, household income, education level, index of social-economic status and remoteness, language spoken at home, insurance type, diabetes and hypertension status, and drug-related covariates, including total number of medications, beta-blocker, carbonic anhydrase inhibitor, prostaglandin analogues and FDC classes of medications were significantly associated with persistence rates. These findings are shown in Table 2.

Multivariate adjusted results are summarised in Table 2. After controlling for all covariates, females had a significantly higher rate of persistence than males (OR=1.19, 95% CI: 1.09-1.29). Patients with lower household income and those from a disadvantaged socioeconomic background (5^{th} quintile of SES) were less likely to discontinue their topical glaucoma medication treatments than those who had a household income more than 40000 AUD/y and patients with higher SES (all $P < 0.05$). Relative to patients living in urban areas, those from remote areas were more likely to discontinue their glaucoma treatments (OR=0.59, 95% CI: 0.37-0.92), while those living in the inner regional areas tended to have better persistence with their topical glaucoma medications at 2-year follow-up (OR=1.10, 95% CI: 1.00-1.21). Patients who spoke English at home had a higher rate of persistence than those who spoke other languages at home (OR=1.65, 95% CI: 1.46-1.87). Health insurance type, diabetes and hypertension status, physical activity, and smoking habit were also associated with the patient's persistence (all $P < 0.05$).

In terms of drug-related variables, those prescribed a greater number of glaucoma medications had an increased chance of being more persistent than those who were prescribed one topical glaucoma medication (two medications: OR: 2.08, 95% CI: 1.71-2.53; more than two medications: OR: 3.23, 95% CI: 1.71-6.09). Those who used adrenergic, beta-blocker, or cholinergic classes of medication at the last prescription tended to discontinue treatment compared to those not using the corresponding class of medication (all $P < 0.05$).

The persistence rate was 44.3% and 80.6% at the 2-year follow-up with the criteria for non-persistence as a gap of more than 60 days and more than 120 days,

respectively. Multivariate analysis based on these definitions led to similar findings. Repeated analysis based on the first prescription claims data also resulted in similar findings (Supplement table 1). We also observed results comparable to those of the main analysis when persistence was assessed as a continuous variable (MPR or PDC) in the models (Supplement table 2).

4. DISCUSSION

In the current study, we found a medium level of persistence (69.9% at 2-year) for topical glaucoma medication in a large Australian population-based cohort study. This study further documented significant effects of patient-related factors (gender, socioeconomic status, language spoken at home, lifestyles and comorbidities) and drug related factors (total number and classes of drugs) on the persistence rates. The most at risk groups for non-persistence were patients living in remote areas, having family income more than 70,000 AUD/y, speaking language other than English at home, and using the cholinergic class of medications.

The medium rate of persistence (69.9% at 2-year) among glaucoma patients in our study was comparable to findings reported from European data (69%-84% follow-up at 2 to 3 years).[16-18] Whilst it was higher than those from United States Medicare and Asian which showed consistently lower persistence rates across different classes of agents (11.5-64%) with a mean interval of therapy up to 3 years.[21,23-25,36-38] In comparison to a previous report by Healey et al that found relatively low persistence rates (23.7% at 2-year using the 3 month cessation ruling)[28] we reported that more than two thirds of patients in need of persistent topical medications had continued to

use their drugs at 2-year follow-up. Interestingly, Healey's report was based on claims data before the 2010 Australian National Health and Medical Research Council Guidelines for the Screening, Prognosis, Diagnosis, Management and Prevention of Glaucoma recommendations were released. These guidelines recommended once-daily topical prostaglandin analogues as first line treatment. The higher persistence rates in our study may potentially be explained by the fact that a high proportion of patients in our study were first prescribed medication following the release of these guidelines and the greater tolerability and efficiency associated with the use of prostaglandin analogues.[39] Despite of the difference in study period, this disparity of persistence rate between our study and Healey's report may also be related to the differences in population characteristics (e.g., age distribution, socioeconomic status, severity of glaucoma), study methodology (logistic regression model versus Cox proportional regression model), definition of patients in need of persistent glaucoma medications (at least three versus one glaucoma-related medication claims).

Speaking English at home was found to have a significant impact on persistence to topical glaucoma medication in comparison to those who spoke other languages at home. This finding might be due to the difficulty in communicating with doctors and cultural barriers.[40,41] Interestingly, we found that patients from more disadvantaged socioeconomic backgrounds and those living in inner regional areas were associated with higher glaucoma medication persistence, which was inconsistent with previous studies.[25,42-44] Previous studies have reported that glaucoma patients who are from a low socioeconomic background were less likely to be screened and treated for glaucoma[45] and therefore, were more likely to present with advanced disease when

they were prescribed with topical glaucoma medications.[46] The fear of blindness might improve those patients' persistence. We found that female glaucoma patients were more persistent with their treatment than males, which is supported by previous studies.[47,48] A large number of studies have confirmed gender differences in health care behaviors,[49] which may be one of the reasons why female patients tended to have better topical glaucoma medication persistence. In the present analysis, patients with hypertension were more persistent with their treatment while diabetic patients were less likely to continue their topical glaucoma medication treatment. Evidence suggests that both untreated hypertension and over-treated hypertension with resultant low blood pressure (BP), particularly with low night time BP, are closely associated with glaucoma progression.[50] This may explain the greater persistence among patients with hypertension. However, the relationship between diabetes and glaucoma is still conflicting.[51] Nevertheless, growing evidence indicates that metformin, a first-line anti-diabetic agent, is associated with a reduction in the risk of developing glaucoma.[51] Furthermore, a recent cohort study found that primary open angle glaucoma (POAG) patients with type 2 diabetes mellitus (DM), particularly with treated type 2 DM, had significantly slower rates of retinal nerve fiber layer thinning compared to those without DM.[52] Over-expression of vascular endothelial growth factor in the retina of diabetics[53] or protective effects of metformin on mitochondrial function and retinal ganglion cells[54,55] may be the underlying mechanism for the protective effect against glaucomatous damage. All these findings may imply that the relatively slower progression of glaucoma may be a potential explanation for the poorer persistence among diabetic patients. The better persistence among non-smoking and physically active patients may be the result of a healthier lifestyle or a better awareness and knowledge of glaucoma. The type of health insurance also

correlated with persistence rate. The relatively lower subsidy co-payment threshold than general beneficiaries may explain the better persistence with topical glaucoma medication among concession card holders. One potential reason why patients who hold a veteran's card were more likely to discontinue their glaucoma treatment may be due to their potential access to pharmaceuticals under a separate funding scheme.

With respect to drug-related factors, the greater number of prescribed glaucoma medications was a significant predictor for better persistence rates. The effects of multiple medications on the persistence were still conflicting.[25,43,44] The inconvenience and tolerability of increased number of agents have been reported to negatively affect adherence.[56] However, the greater number of topical glaucoma medications may indicate the disease severity and more difficulty of controlling IOP, thus increasing the fear of blindness and improving persistence rates. In terms of the class of medication, we found a significant association between the use of prostaglandin analogues and better persistence rates in the unadjusted model, which was supported by findings from previous studies.[22,25,36,38] However, a significant association between the use of prostaglandin analogues and persistence was not seen after multiple adjustments, which may be due to the large proportion of patients using prostaglandin in the current analysis (59%). In contrast, the use of adrenergic, beta-blocker, and cholinergic classes of medications were significant barriers to persistence. Possible reasons for these patients discontinuing therapy might include side effects, inconvenience (more than once-a-day administration) and low efficiency of these classes of drugs.

Given the persistence to topical IOP-lowering medication is critical for delaying progression, subsequent vision loss and improving quality of life, our findings may have several practical implications. First, our findings provide evidence on the determinants of poor persistence with respect to patient-related and drug-related factors. This may identify patients at high-risk of discontinuing topical glaucoma medication. Second, health promotion-based efforts tailored to individual patient's specific barriers and health lifestyles will be effective toward promoting long-term adherence and resulting in better health outcomes among glaucoma patients. Such as, provision of well-trained translator services may eliminate language barriers for non-English speaking patients.

This study had a number of strengths. First, the large number of patients in need of topical glaucoma medication provides strong statistical power. Second, the claims data better reflects real-world situation than those from controlled clinical trials. Third, our study provides a broad array of covariates to explore determinants of persistence rates of topical glaucoma medication. However, several potential limitations should also be considered. First, the overall response rate of the baseline questionnaire was only 18%, therefore, persistence rates with topical glaucoma medication in the present analysis can not be extrapolated to the entire population in NSW or in Australia. Nevertheless, the relationship between covariates and persistence of topical glaucoma medication is still reasonable and unaffected. Second, participants in the 45 and Up study tend to be healthier than the overall population,[57] which might overestimate the persistence rate. Third, as our study was only based on the PBS claims data, we were unable to access data on prescriptions filled in the public hospitals and exclude patients who died or left PBS system during the study period,

which might underestimate persistence rates. Fourth, patient characteristics were collected on a single occasion using self-report. During the follow-up period, participants behavior may change, which can have a direct impact on outcomes. Last but not least, patient medical records were not able to be reviewed. This means that accurate data on disease diagnosis and severity is absent. The definition of need for persistent topical glaucoma medication used may be seen as a potential limitation. The minimum of at least 3 claims related to topical glaucoma medication may have included patients requiring only short-term therapy (e.g., IOP spikes after cataract surgery, trauma), leading an underestimation of persistence.

In summary, this large-scale population-based cohort study showed medium rates of persistence to glaucoma medical therapy. Patient-related factors, including socioeconomic status, languages spoken at home and number and class of medications were predictors of better persistence at 2-years. Efforts are still needed for improving adherence, particularly among patients living in remote areas and speaking other languages other than English at home.

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FIGURE LEGEND

Figure 1: Schematic showing study participants included for the present analysis from the 45 and Up Study. A total of 19,303 patients were identified in need of persistent glaucoma medical treatment. Of these patients, 4,882 cases (25.3%) had glaucoma-related surgery during the study period and 1,522 cases (7.88%) reach the

study end date (Dec 31th 2016) within 2 years after the index day, thus leading to 12,899 (66.8%) patients in the current analysis.

* Index day is defined as the date when patient's condition was first treated with glaucoma medication during the study period.

TABLES

Table 1: Total patient-related and drug-related covariates of participants and persistence status

Characteristics	Overall	Subjects with Persistence	Subjects with Non-Persistence
Overall	12,899	9,019	3,880
Demographic			
Age at index date, yrs			
45-49	181 (1.4)	112 (1.2)	69 (1.8)
50-54	422 (3.3)	250 (2.8)	172 (4.4)
55-59	803 (6.2)	512 (5.7)	291 (7.5)
60-65	1,407 (10.9)	938 (10.4)	469 (12.1)
> 65	10,086 (78.2)	7,207 (79.9)	2,879 (74.2)
Female gender	6,390 (49.5)	4,627 (51.3)	1,763 (45.4)
Household income (AUD/y)			
< 20000	3,799 (29.5)	2,823 (31.3)	976 (25.2)
20000-40000	2,647 (20.5)	1,935 (21.5)	712 (18.4)
40000-70000	1,599 (12.4)	1,048 (11.6)	551 (14.2)
>70000	1,369 (10.6)	755 (8.4)	614 (15.8)
Highest education			
No qualification	2,108 (16.3)	1,527 (16.9)	581 (15.0)
Certificate/diploma/trade	8,220 (63.7)	5,866 (65.0)	2,354 (60.7)
University	2,231 (17.3)	1,397 (15.5)	834 (21.5)
Quintile of SES			
1st Quintile	3,095 (24.0)	2,236 (24.8)	859 (22.1)
2nd Quintile	2,631 (20.4)	1,926 (21.4)	705 (18.2)
3rd Quintile	2,286 (17.7)	1,613 (17.9)	673 (17.3)
4th Quintile	1,969 (15.3)	1,341 (14.9)	628 (16.2)
5th Quintile	2,635 (20.4)	1,705 (18.9)	930 (24.0)
Remoteness			
Major Cities	7,292 (56.5)	4,966 (55.1)	2,326 (59.9)
Inner Regional	4,192 (32.5)	3,053 (33.9)	1,139 (29.4)
Outer Regional	1,155 (9.0)	837 (9.3)	318 (8.2)

Remote or very Remote	83 (0.6)	49 (0.5)	34 (0.9)
English language speaking at home	11,624 (90.1)	8,263 (91.6)	3,361 (86.6)
Health insurance type			
Private with extras	4,141 (32.1)	2,701 (29.9)	1,440 (37.1)
Private no extras	1,356 (10.5)	943 (10.5)	413 (10.6)
Veterans card	187 (1.4)	120 (1.3)	67 (1.7)
Concession card	5,528 (42.9)	4,081 (45.2)	1,447 (37.3)
None of above	1,356 (10.5)	935 (10.4)	421 (10.9)
Clinical			
BMI, kg/m^2			
Underweight	218 (1.7)	149 (1.7)	69 (1.8)
Normal	4,488 (34.8)	3,250 (36.0)	1,238 (31.9)
Overweight	4,686 (36.3)	3,223 (35.7)	1,463 (37.7)
Obesity	2,523 (19.6)	1,704 (18.9)	819 (21.1)
Diabetes	1,949 (15.1)	1,303 (14.4)	646 (16.6)
High blood pressure	6,020 (46.7)	4,323 (47.9)	1,697 (43.7)
Lifestyle			
Smoker			
No	7,573 (58.7)	5,321 (59.0)	2,252 (58.0)
Past smoker	4,799 (37.2)	3,358 (37.2)	1,441 (37.1)
Current smoker	521 (4.0)	337 (3.7)	184 (4.7)
Alcohol consumption per week ($\geq$14 drinks)	2,284 (17.7)	1,577 (17.5)	707 (18.2)
PA (session/week)			
<5	2,812 (21.8)	1,953 (21.7)	859 (22.1)
$\geq$5-9	3,270 (25.4)	2,326 (25.8)	944 (24.3)
$\geq$9	2,787 (21.6)	1,949 (21.6)	838 (21.6)
MVAP			
$\geq$300 min	5,442 (42.2)	3,803 (42.2)	1,639 (42.2)
150-300 min	1,565 (12.1)	1,061 (11.8)	504 (13.0)
$\leq$150 min	5,050 (39.2)	3,572 (39.6)	1,478 (38.1)
Medication-related factors (Last visit)			
No. of medications			
1	12,059 (93.5)	8,334 (92.4)	3,725 (96.0)
2	759 (5.9)	616 (6.8)	143 (3.7)

≥3	81 (0.6)	69 (0.8)	12 (0.3)
Use of FDC	2,490 (19.3)	1,789 (19.8)	701 (18.1)
Use of beta-blocker	2,109 (16.4)	1,427 (15.8)	682 (17.6)
Use of adrenergic	905 (7.0)	634 (7.0)	271 (7.0)
Use of cholinergic	138 (1.1)	87 (1.0)	51 (1.3)
Use of CAI	575 (4.5)	441 (4.9)	134 (3.5)
Use of prostaglandin analogues	7,606 (59.0)	5,398 (59.9)	2,208 (56.9)

Values are all listed as n(%). Abbreviation: SES = social economic status; PA = physical activity; MVPA = moderate to vigorous physical activity; FDC = fixed combination; CAI = carbonic anhydrase inhibitor

Table 2: Unadjusted and multiple-adjusted logistic regression analysis of determinants for persistence

Characteristics	Persistence	Unadjusted		Multiple adjusted †	
	Event/N	OR (95% CI)	P value	OR (95% CI)	P value
Demographic					
Age at index date, yrs					
45-49 (Ref.)	112/181	Reference	<0.001	Reference	0.12
50-54	250/422	0.90 (0.63-1.28)		0.87 (0.60-1.25)	
55-59	512/803	1.08 (0.78-1.51)		0.98 (0.70-1.38)	
60-65	938/1,407	1.23 (0.89-1.70)		1.04 (0.75-1.45)	
> 65	7,207/10,086	1.54 (1.14-2.09)		1.11 (0.81-1.53)	
Female (Ref. male)	4,627/6,390	1.27 (1.17-1.36)	<0.001	1.19 (1.09-1.29)	<0.001
Household income (AUD/y)					
< 20000 (Ref.)	2,823/3,799	Reference	<0.001	Reference	<0.001
20000-40000	1,935/2,647	0.94 (0.84-1.05)		0.95 (0.84-1.06)	
40000-70000	1,048/1,599	0.66 (0.58-0.75)		0.72 (0.63-0.83)	
>70000	755/1,369	0.43 (0.37-0.48)		0.53 (0.45-0.62)	
Highest education					
No qualification (Ref.)	1,527/2,108	Reference	<0.001	Reference	0.07
Certificate/diploma/trade	5,866/8,220	0.95 (0.85-1.06)		1.04 (0.93-1.16)	
University	1,397/2,231	0.64 (0.56-0.72)		0.92 (0.80-1.06)	

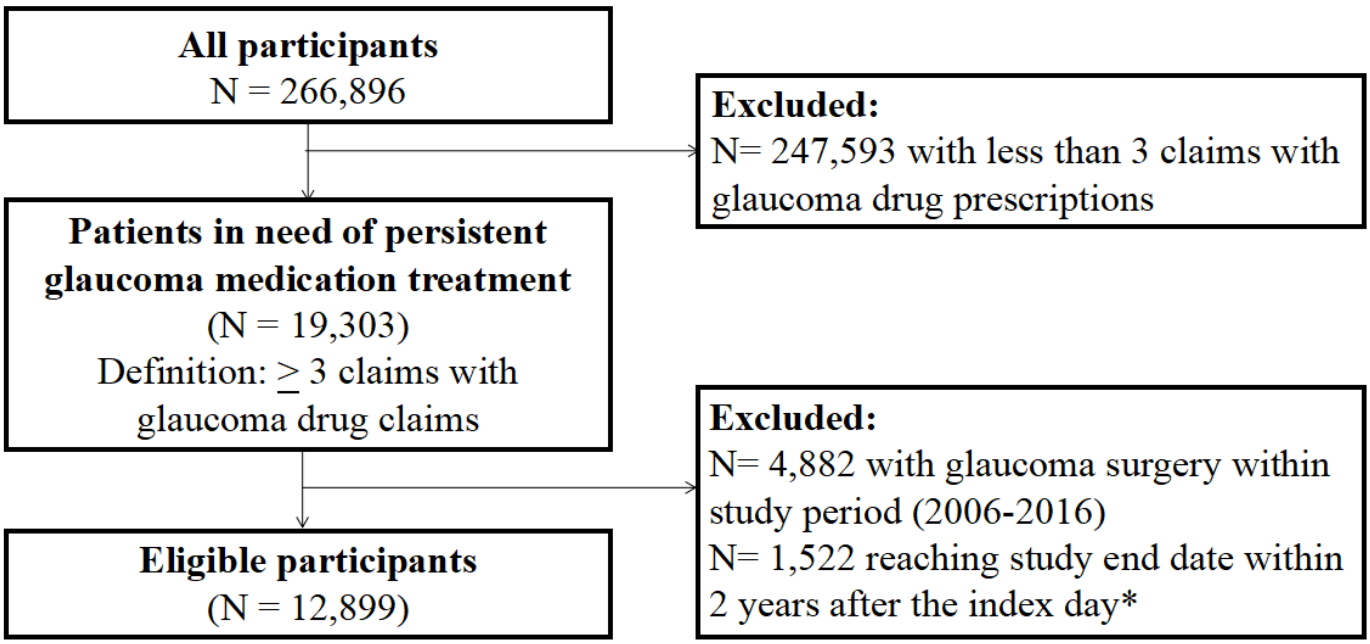
Quintile of SES					
1st Quintile (Ref.)	2,236/3,095	Reference	<0.001	Reference	0.005
2nd Quintile	1,926/2,631	1.05 (0.93-1.18)		1.09 (0.97-1.23)	
3rd Quintile	1,613/2,286	0.92 (0.82-1.04)		1.00 (0.88-1.13)	
4th Quintile	1,341/1,969	0.82 (0.73-0.93)		0.92 (0.81-1.05)	
5th Quintile	1,705/2,635	0.70 (0.63-0.79)		0.88 (0.77-1.00)	
Remoteness					
Major Cities (Ref.)	4,966/7,292	Reference	<0.001	Reference	0.002
Inner Regional	3,053/4,192	1.26 (1.15-1.37)		1.10 (1.00-1.21)	
Outer Regional	837/1,155	1.23 (1.07-1.42)		1.04 (0.90-1.21)	
Remote or very Remote	49/83	0.67 (0.43-1.05)		0.59 (0.37-0.92)	
English language speaking at home (Ref. other languages)	8,263/11,624	1.69(1.50-1.90)	<0.001	1.65 (1.46-1.87)	<0.001
Health insurance type					
Private with extras (Ref.)	2,701/4,141	Reference	<0.001	Reference	0.002
Private no extras	943/1,356	1.22 (1.07-1.39)		1.07 (0.93-1.22)	
Veterans card	120/187	0.95 (0.70-1.30)		0.70 (0.51-0.96)	
Concession card	4,081/5,528	1.50 (1.38-1.64)		1.17 (1.06-1.30)	
None of above	935/1,356	1.18 (1.04-1.35)		1.01 (0.88-1.16)	
Clinical					
BMI, kg/m^2					
Underweight (Ref.)	149/218	Reference	<0.001	Reference	<0.001

Normal	3,250/4,488	1.22 (0.91-1.63)		1.28 (0.95-1.73)	
Overweight	3,223/4,686	1.02 (0.76-1.37)		1.08 (0.80-1.45)	
Obesity	1,704/2,523	0.96 (0.72-1.30)		0.99 (0.73-1.34)	
Diabetes (Ref. No)	1,303/1,949	0.85 (0.76-0.94)	0.001	0.83 (0.74-0.93)	<0.001
High blood pressure (Ref. No)	4,323/6,020	1.18 (1.10-1.28)	<0.001	1.18 (1.09-1.27)	<0.001
Lifestyle					
Smoker					
No (Ref.)	5,321/7,573	Reference	0.03	Reference	0.03
Past smoker	3,358/4,799	0.99 (0.91-1.07)		1.01 (0.93-1.10)	
Current smoker	337/521	0.78 (0.64-0.93)		0.77 (0.63-0.93)	
Alcohol consumption per week	1,577/2,284	0.95 (0.86-1.05)	0.28	1.04 (0.93-1.15)	0.69
(≥14 drinks) (Ref. <14 drinks)					
PA (session/week)					
<5 (Ref.)	1,953/2,812	Reference	0.33	Reference	0.20
≥5-9	2,326/3,270	1.08 (0.97-1.21)		1.13 (1.00-1.26)	
≥9	1,949/2,787	1.02 (0.91-1.15)		1.05 (0.92-1.18)	
MVAP					
≥300 min (Ref.)	3,803/5,442	Reference	0.08	Reference	0.26
150-300 min	1,061/1,565	0.91 (0.80-1.02)		0.94 (0.83-1.07)	
≤150 min	3,572/5,050	1.04 (0.96-1.13)		1.02 (0.93-1.13)	
Medication-related factors (Last visit)					

No. of medications					
1 (Ref.)	8,334/12,059	Reference	<0.001	Reference	<0.001
2	616/759	1.93 (1.60-2.32)		2.08 (1.71-2.53)	
≥3	69/81	2.57 (1.39-4.75)		3.23 (1.71-6.09)	
Use of FDC (Ref. No)	1,789/2,490	1.12 (1.02-1.23)	0.02	1.02 (0.92-1.14)	0.69
Use of beta-blocker (Ref. No)	1,427/2,109	0.88 (0.80-0.97)	0.01	0.74 (0.66-0.81)	<0.001
Use of adrenergic (Ref. No)	634/905	1.01 (0.87-1.16)	0.93	0.80 (0.68-0.93)	0.005
Use of cholinergic (Ref. No)	87/138	0.73 (0.52-1.03)	0.08	0.55 (0.38-0.79)	0.001
Use of CAI (Ref. No)	441/575	1.43 (1.18-1.75)	<0.001	1.11 (0.91-1.37)	0.30
Use of prostaglandin analogues (Ref. No)	5,398/7,606	1.12 (1.04-1.22)	0.02	0.96 (0.87-1.05)	0.40

Abbreviation: OR = odds ratio; CI = confidence interval; SES = social economic status; PA = physical activity; MVPA = moderate to vigorous physical activity; FDC = fixed combination; CAI = carbonic anhydrase inhibitor;

† Adjusted for all factors in unadjusted models.



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