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Medicine treatment of glaucoma in Australia 2012–2019: prevalence, incidence and persistence

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ABSTRACT

Objective Medical therapy can halt or significantly slow the progression of glaucoma if medicines are used in accordance with the guidelines. We used dispensing claims for a 10% sample of all Australians dispensed publicly subsidised glaucoma medicines to determine the prevalence and incidence of glaucoma medicine treatment and to examine treatment persistence between July 2012 and June 2019.

Methods We estimated incidence and prevalence per 10 000 population for Australian financial years (1 July to 30 June). We defined prevalence as at least one dispensing of any glaucoma medicine and incidence as a dispensing of any glaucoma medicine with no previous dispensing during the preceding 12 months. We estimated duration of treatment for a cohort initiating glaucoma medicines and used Kaplan-Meier methods to estimate the proportion of people persisting on treatment at 6, 12, 18 and 36 months after initiation. We stratified analyses by the number of repeats prescribed at initiation, age, sex and medicine class.

Results Prevalence remained stable over the study period at around 180/10 000 people/year; incidence was also stable around 36/10 000/year. Among 34 900 people initiating glaucoma medicines, 37.0% remained on treatment at 6 months from initiation, 29.8% at 12 months and 19.2% at 36 months. Median duration of treatment was 13.2 months (IQR: 2.5—not reached) for people initiating prostaglandin analogues and less than 3 months for those initiating other medicine classes.

Conclusion Prevalence and incidence of glaucoma treatment have not changed in Australia over the past decade. Persistence to treatment increased with age but remained poor throughout the study period.

Key messages

What is already known about this subject?

► Glaucoma is a chronic condition that requires persistent treatment for optimum management.

What are the new findings?

► Persistence to glaucoma medicine in Australia is poor, with just 37% of those initiating glaucoma medicines still adherent to treatment 6 months later, dropping to 30% after 12 months. Fixed-dose combination formulations have not improved the situation.

How might these results change the focus of research or clinical practice?

► Population-based linkage studies may elucidate that the key characteristics responsible for prolonged persistence to medical therapy and may help in designing intervention to improve adherence to treatment.

INTRODUCTION

Glaucoma is a chronic, blinding, neurodegenerative disease of the optic nerve, the incidence and progression rate of which increases with increasing intraocular pressure (IOP). It affects approximately 3% of Australians 50 years and older and increases exponentially with age.[1] It is the leading cause of irreversible, preventable blindness in Australia and the world.[2–4] There is no cure for glaucoma, but early detection and treatment with medicines to reduce IOP can halt or significantly slow the progression of vison loss and preclude more invasive surgical interventions. Clinical practice guidelines recommend topical eye drops as a first treatment option to prevent damage to the optic nerve by reducing pressure in the eye(s); followed by laser treatment in conjunction with or as an alternative to drops.[2 5]

As a chronic condition, glaucoma requires persistent treatment for optimum management. Most medical treatments are topical and administered once or two times per day, for as long as they are effective. However, research using electronic bottle monitoring found that people do not consistently take their prescribed antiglaucoma eye drops in 45% of cases.[6] Other factors, such as difficulty instilling eye drops, mental and physical health conditions and forgetfulness present challenges to optimal adherence[7]

In Australia, population-based estimates of persistence to incident treatments have been reported at less than 40% at 12 months, dropping further to 24% at 24 months.[8] However, this research is over a decade old and the contemporary patterns of glaucoma medicine use and persistence in the country are unclear. Therefore, we aimed to describe the use of glaucoma medicines in Australia using contemporary, population-based data.

We detailed the incidence and prevalence of glaucoma therapy between 2012 and 2019 and estimated the persistence to glaucoma treatment in a cohort of people initiating glaucoma medicines.

DATA SOURCES AND METHODS

Study setting and data

Australia maintains a publicly funded, universal healthcare system entitling all citizens and eligible residents to subsidised prescription medicines through the Pharmaceutical Benefits Scheme (PBS). PBS dispensing claims are processed and recorded by Services Australia, which also maintains a data set of these claims for a randomly selected 10% sample of PBS-eligible Australians used for research and planning purposes.[9 10] These deidentified, population-based individual-level data include demographic information (sex, year of birth and PBS beneficiary status) and records of dispensed prescription medicines, including the name of medicine, date of dispensing, the number of repeats originally prescribed (prescribers may write out how many prescriptions a patient may fill before the patient needs to return to the doctor for another prescription; zero to six repeats are permitted) and prescriber specialty.

In Australia, once a medicine is PBS subsidised, the government bears the cost, less a copayment.[9] The copayment for a PBS medicine depends on an individual's PBS beneficiary status: general beneficiaries, comprising the majority of all PBS beneficiaries, are required to pay up to AUD$41 for each dispensed medicine (for medicines costing less than this amount, general beneficiaries pay the full cost); concessional beneficiaries (people 65 years and older, low-income earners and others receiving government entitlements) pay AUD$6.60/medicine. Private insurance does not provide reimbursement for medicines already subsidised through public programmes, and our data likely capture the vast majority of glaucoma medicines dispensed in Australia.

Medicines of interest

We included all antiglaucoma preparations as defined by the WHO Anatomical Therapeutic Chemical classification S01E, publicly subsidised in Australia through the PBS and dispensed between 1 July 2012 and 30 June 2019 (online supplemental table A). We considered fixed-dose combinations (FDCs) as distinct medicines as opposed to their component medicines.

Study design and outcomes of interest

We used a drug utilisation design to examine annual trends in treatment prevalence and incidence for all glaucoma medicines dispensed to adults (≥18 years of age) in Australia through the PBS between 1 July 2012 and 30 June 2019 (the study period). We grouped dispensings by Australian financial years (1 July to 30 June) and refer to each year by the calendar year ending the financial year (ie, 1 July 2013 to 30 June 2014 as 2014).

Prevalence of glaucoma medicine treatment

We calculated the annual prevalence of treatment (per 10 000 population) as the number of people dispensed a PBS-listed glaucoma medicine at least once in each year. We used the 1 December population estimates from the Australian Bureau of Statistics (ABS) for each year as the denominator.[11] As our data are based on a 10% sample of the Australian population, we divided the ABS population estimates by 10.

Incidence of glaucoma medicine treatment

We calculated the annual incidence of treatment (per 10 000 population) as the number of people dispensed a glaucoma medicine after a period of at least 12 months during which no such medicines were dispensed, divided by the estimated 1 December Australian population for each year (adjusted for the 10% sample as for prevalence). As this analysis requires a 12-month lookback period to determine new medicine use, we calculated incidence estimates for years 2014–2019. We calculated both prevalence and incidence overall and stratified by sex, age group (broken into unequal age groupings to provide more detail for older aged patients: 18–34, 35–49, 50–64, 65–74, 75–84, 85+ years) and medicine class.

Treatment persistence

We used a cohort design to examine persistence to glaucoma treatment among people who initiated treatment between 2014 and 2019 (incident medicine users). We identified our incident cohort as those dispensed a glaucoma medicine with no dispensings of glaucoma medicines during the preceding 12 months. We defined persistence as time on glaucoma medicine treatment and estimated time on treatment based on dispensings—grouping sequential dispensings into periods of time from the first dispensing date until the last dispensing date, plus 30 days or the number of days to death or the end of the study period, whichever was sooner. We considered a period of >90 days between dispensings as a break in treatment, with a subsequent dispensing >90 days later beginning a new treatment episode. The PBS 10% data set only includes the year of death and we estimated the time of death by applying a previously validated proxy for PBS data.[12] We censored people who died during follow-up or who were still on treatment at the end of the study period (30 June 2019). We examined the duration of the initiated treatment (until a 90-day gap/treatment break between dispensings, death or censor), allowing people to switch medicine classes as long as the switch was within 90 days of the previous dispensing. As a sensitivity analyses, we varied the period of time used to define the end of a treatment episode, substituting >30 and >180 days to define a treatment break.

We estimated the duration of the first initiated treatment course using Kaplan-Meier methods, presented as the median number of months and IQR. We determined the proportion (%) of people who remained on the initiated treatment episode at 6 months, 12 months,

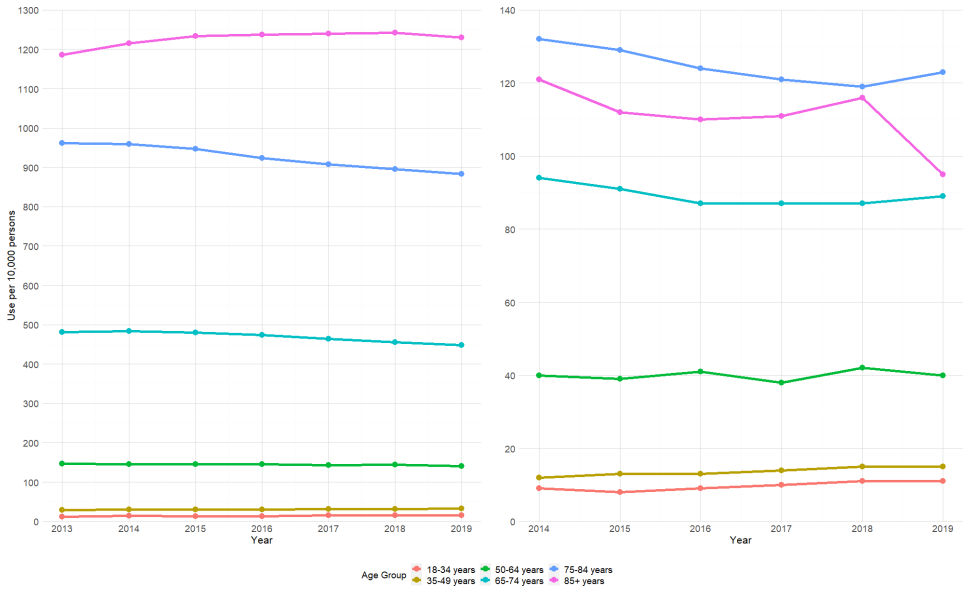

Figure 1 Prevalence (left) and incidence (right) of glaucoma medicine treatment by age group.

24 months and 36 months from initiation. We calculated persistence with glaucoma medicines overall and stratified by the initiation medicine class (allowing for switches to different medicine classes so long as they did not take place >90 days from the previous dispensing), the number of repeats prescribed at initiation, sex and age group (18–34, 35–49, 50–64, 65–74, 75–84, 85+ years). We determined median follow-up time as the time from first antiglaucoma medicine dispensing until death or the end of the study period using according to the reverse Kaplan-Meier method.[13] Analyses were performed using SAS V.9.4 (SAS Institute, Cary, North Carolina) and R V.3.3.3.

RESULTS

Between 2013 and 2019, a total of 2 865 309 PBS-listed glaucoma medicines were dispensed to 67 785 people 18 years and older. Prostaglandin analogues (PA) accounted for 43% of all glaucoma medicine dispensings across the period, followed by FDCs (32%) and carbonic anhydrase inhibitors (CAIs) (9.4%).

Prevalence of glaucoma medicine treatment

The annual prevalence of treatment remained consistent across the study period; 180 per 10 000 population in 2013 and 184 per 10 000 population in 2019 (online supplemental table B). Prevalence of treatment increased with each age group and peaked among people aged 85 years and older (figure 1/ online supplemental table B). PAs were the most prevalent glaucoma medicine, followed by FDCs and CAIs (online supplemental table B). Women had slightly higher treatment prevalence than men throughout the study period.

Incidence of glaucoma medicine treatment

Incidence also remained stable across the study period; with 36 new users per 10 000 population in 2013 and 37 new users per 10 000 population in 2019 (online

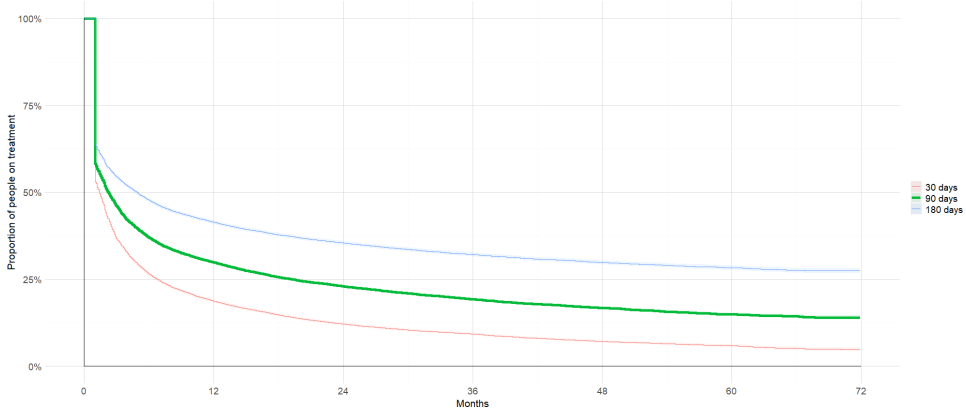

Figure 2 Persistence with glaucoma medicine treatment. Main analysis (90-day period with no dispensings used to define a treatment break) shown in green; sensitivity analyses (30-day and 180-day periods used to define treatment break) shown in red and blue. NR, not reached.

Table 1 Characteristics of people initiating glaucoma medicines (2014–2019), included in persistence analysis

	N	%
Total	34 900	100
Sex		
Female	18 366	52.6
Male	16 534	47.4
Age group, years		
18–34	3223	9.2
35–49	3495	10.0
50–64	8984	25.7
65–74	9659	27.7
75–84	7068	20.3
85+	2471	7.1
Medicine class		
Prostaglandin analogues	14 725	42.2
Carbonic anhydrase inhibitors	8062	23.1
Sympathomimetics	3554	10.2
Beta blocking agents	2699	7.7
Multiple medicine classes	1663	4.8
Para-sympathomimetics	606	1.7
Fixed dose combinations (all)*	3591	10.3
PA and BB	1560	4.5
SYM and BB	1207	3.5
CAI and BB	590	1.7
CAI and SYM	234	0.7
Prescriber type		
Ophthalmologist	18 085	51.8
General practitioner	6152	17.6
Other†	4979	14.3
Unknown‡	5684	16.3
Number of repeats prescribed at initiation		
0	10 511	30.1
1–3	4300	12.3
4–6	20 089	57.6
Number of dispensing in the first 12 months of initiation of treatment		
1	12 597	36.1
2–9	12 961	37.1
10+	9342	26.8
Died during study period		
Yes	2560	7.3
No	32 340	92.7

*The total number of fixed-dose combinations initiated, overall and stratified by combination are presented.
†All other specialities.
‡Prescriber type is missing for 16% of dispensing records.
BB, beta blocker; CAI, carbonic anhydrase inhibitor; PA, prostaglandin analogue; SYM, sympathomimetic.

supplemental table C). Incidence was similar between sexes and increased with each age group, peaking in ages 75–84 years (figure 1).

Persistence to treatment

Among the 34 900 people initiating glaucoma medicines during 2014–2019, 37.0% remained on treatment at 6 months from initiation, 29.8% at 12 months and 19.2% at 36 months (figure 2; online supplemental table D). The most frequently initiated treatments were PAs (42.2%), CAIs (23.1%) and sympathomimetics (10.2%; table 1). Most people were prescribed 4–6 repeats or zero repeats at initiation (table 1). With a median follow-up time of 31.3 months (IQR: 12.6–51.4), the median time on any glaucoma treatment was 2.3 months (IQR: 1.0–19.2). Treatment duration varied by the number of repeats prescribed at initiation, with those prescribed 4–6 repeats having the longest median treatment duration, 8.5 months (IQR: 1.7–51.5) and those prescribed zero repeats have the shortest treatment duration, 1.0 months (IQR: 1.0–1.0; online supplemental figure A). The median treatment duration was 13.2 months (IQR: 2.5—not reached) for those initiating PAs but less than 3 months for people initiating all other medicine classes (figure 3; online supplemental table D). Persistence increased with age—the proportion of people who remained on treatment at 12 months from initiation was 35.8%, 40.4% and 43.9%, respectively, among ages 65–74 years, 75–84 years and 85 years and older (figure 4; online supplemental table D).

DISCUSSION

Persistence with glaucoma medicines is crucial for treatment efficacy and our study suggests that most people in Australia have suboptimal persistence. Our national, population-based study highlights that only one-third of people initiating treatment remained on treatment 6–12 months following initiation. Such a low rate of persistence has implications for treatment efficacy—if these medicines are not being used in accordance with recommended guidelines, efficacy estimates from clinical trials may not be translating to the real world. Progression of glaucoma can often be managed with these treatments and our findings represent a potentially significant public health issue for Australia. While treatment persistence increased with age, and glaucoma is primarily a condition of old age,[2] our findings suggest the need for targeted interventions to improve treatment adherence in Australia.

Persistence and adherence to topical glaucoma therapy is a long standing challenge, with people self-reporting high levels of persistence that are not borne out by studies of pharmaceutical claims.[14–17] Our persistence findings were similar to those observed in a decade-old Australian study,[8] suggesting that little has changed in Australia to improve treatment persistence during the past decade. The previous study found that 39% of people remained on treatment at 12 months from initiation compared with 37% in the current analysis. Though the authors used a 6-month lookback period to define treatment initiation (compared with our use of 12 months to define initiation), the previous study used the same data source

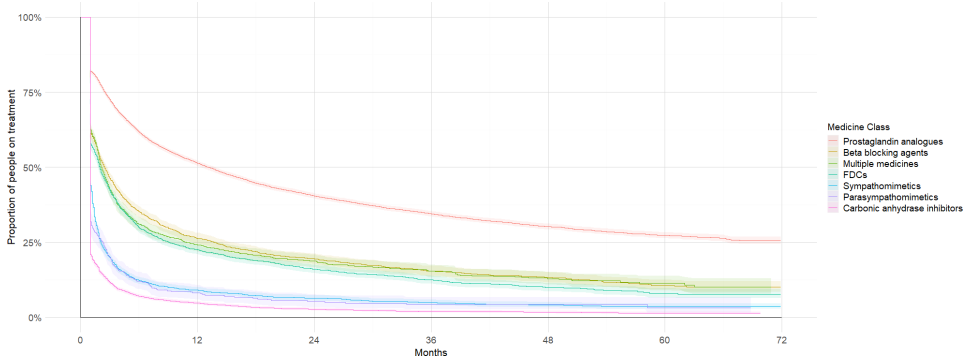

Figure 3 Persistence with glaucoma medicine treatment, by initiated medicine (90 days used to define treatment break). FDC, fixed-dose combinations; NR, not reached.

as our study and our results are a highly comparable. Our findings are also in line with those reported from a population-based study from Taiwan, where 24% of people persisted with treatment to 2 years, and the 2-year persistence rate increased with age and was higher for people receiving PAs.[16]

To account for the fact that some people may use IOP-lowering medicines short-term—such as those recovering from cataract surgery—we stratified our persistence analyses by the number of repeat prescriptions at initiation. A typical dispensing equates to a month's supply of medicine, and most people were dispensed medicines with either zero repeat prescriptions (one total prescription) or five repeats (six total prescriptions). Persistence was notably higher in those prescribed 4–6 repeats at initiation. While less than half of these people were on treatment at 1 year from initiation, 25% were still on treatment at 52 months or longer (per our 75th percentile estimate of treatment duration), highlighting that there is a subgroup of people who do persist with their initiated treatment.

The patient organisation, Glaucoma Australia, launched multiple educational campaigns aimed at improving treatment persistence during the study period.[18 19] Skalicky *et al* note that these programmes may have improved patients' knowledge about their treatment and reduced anxieties, but they did not impact medicine adherence.[20] FDC treatments are also seen as a strategy for improving medicine adherence as they reduce the number of medicines a person must remember to take.[2] We found that persistence with FDCs was low and similar to that with beta blockers or other, non-FDC medicine combinations. Interestingly, Hwang *et al* found that 2-year persistence was higher for people *not* taking FDCs and for those taking three or more medicines.[16] A recent, small-sample pilot study found that the biggest challenges to persistence with treatment were patient difficulty in administering medicines, patient memory and a diagnosis of depression.[7] The situation is further complicated by the 'white-coat adherence' phenomenon, whereby people begin using glaucoma medicines more regularly in the days leading up to a visit with their physician—causing their IOP to appear to be under control—only to reduce adherence again following the visit.[17] More research is needed to design effective interventions to improve treatment persistence and adherence.

Just as persistence has remained constant over the past decade in Australia, we observed steady annual prevalence and incidence for glaucoma medicine treatment of around 180/10 000 and 36/10 000 between 2013 and 2019. These figures are similar to those reported from international studies.[21 22] While prevalence and incidence have remained constant in Australia over the study period, the absolute size of the population entering the age groups at highest risk of developing glaucoma (65+ years) has grown dramatically and, as with many other conditions, treatment for glaucoma is likely to demand more resources in the coming decade. Non-medical

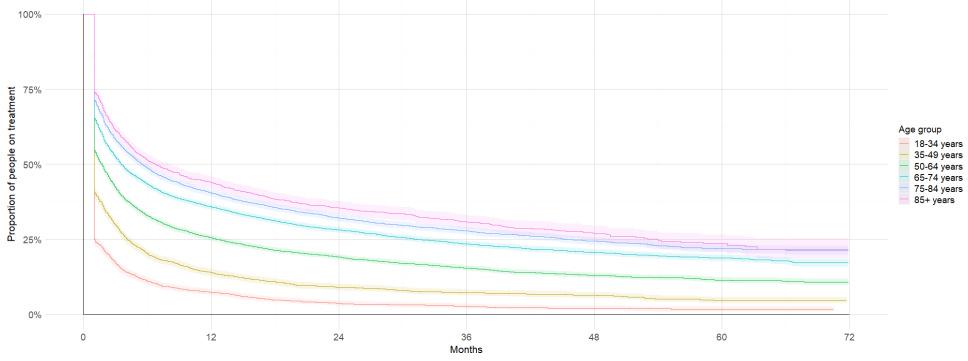

Figure 4 Persistence with glaucoma medicine treatment, by age group (90 days used to define treatment break).

therapies are being increasingly used to treat glaucoma, particularly laser trabeculoplasty.[2] Australian Medicare statistics show noticeable increases in several of these procedures from 2017 to 2018 (online supplemental figure B). These procedures have the potential to impact the use of glaucoma medicines.

Strengths and limitations

Our study has several strengths and limitations. We used a large, nationally representative data set comprising dispensing records for 10% of all Australian residents eligible for publicly subsidised medicines to examine the use of glaucoma medicines. Our findings are likely to generalise to populations of similar developed nations. These data do not include information on comorbidities, diagnoses or information related to individuals' glaucoma (ie, IOP measures). The study data do not include information on prescribed/intended duration of treatment, and we estimated this measure based on dispensing records. To account for this, we varied the period of time we used to define a treatment break, including analyses using 30 days and 180 days to define treatment discontinuation. We also stratified our persistence analyses by the number of repeats prescribed at initiation, reasoning that people prescribed no repeats were either initiating a therapeutic trial or for intended short-term pressure-lowering therapy in the absence of glaucoma, whereas those prescribed maximum repeats were more likely intended for chronic therapy. Our estimate of persistence to treatment for all people initiating glaucoma medicines is the result of a heterogenous patient group while those estimates were stratified by number of repeats—and particularly those based on 4–6 repeats—may more closely reflect the persistence of patients with a glaucoma diagnosis. This more conservative estimate still shows less than 50% persistence at 1 year and less than 25% persistence at 5 years.

PBS data include dispensing records for medicines publicly subsidised by the PBS, not medicines paid for privately, and our results may slightly underestimate the true outcomes where people self-funded their prescriptions. Most glaucoma medicines are below the PBS copayment threshold[9] for general PBS beneficiaries (most PBS beneficiaries <65 years of age; currently AUD$41.30), and some of these beneficiaries may have filled private prescriptions instead of PBS prescriptions. However, all glaucoma medicines cost above the threshold for concessional beneficiaries (all those 65 years and older; currently AUD$6.60), meaning that the overwhelming majority of Australians with glaucoma would have no motive to seek these medicines outside of the PBS. Finally, as in all studies based on dispensing data, we do not know whether individuals used the dispensed glaucoma medicines—meaning that the true figures of treatment persistence are no better than our estimates.

CONCLUSIONS

The prevalence and incidence of glaucoma treatment have not changed in Australia over the past decade, and real-world persistence with treatment remains poor. As a result, this form of treatment in real-world practice may be less effective than clinical trials have reported. The preventable disease progression implied by our findings represent a potentially important public health problem for Australia and similar countries. FDCs have not improved the situation to date and targeted interventions are required to improve treatment persistence. Population-based linkage studies may be helpful to elucidate the key characteristics responsible for prolonged persistence to medical therapy.

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Contributors BD, PH, IK, CB and HZ conceived of the initial concept and study design. CB and BD had access to the dataset and performed all data cleaning and analyses. BD wrote the original draft and all authors were involved in data interpretation, reviewing and editing the manuscript and the decision to submit for publication. BD acted as guarantor of the manuscript.

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Competing interests PH is a consultant to Allergan, an AbbVie company. IC was an employee of AbbVie when the study was conducted. BD, CB, and HZ have no competing interests to declare.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

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