Ocular lubricants: Utilisation analysis using MedicineInsight data

Drug utilisation sub-committee (DUSC)

February 2021

Abstract

Purpose

PBAC requested a review of the utilisation of ocular lubricants at its July 2020 meeting. The analyses in this report are based on general practice data from MedicineInsight.

Data Source / methodology

This study is a descriptive analysis of MedicineInsight data exploring the prescribing of ocular lubricants in general practice. It uses de-identified patient data from the clinical information systems (CIS) of between 423–441 participating general practices and 1.67 million to 1.96 million patients (depending upon study year). The study covered the period between 1 January 2015 to 31 December 2019, with a one year look back period for analyses of initiation.

Key Findings

- Consistent with the patterns seen in the PBS dispensing analysis, the percentage of MedicineInsight patients prescribed:
 - \circ $\,$ an ocular lubricant decreased from 1.31% in 2015 to 1.06% in 2019;
 - a preservative containing (PC) ocular lubricant decreased from 0.97% (16,310 patients) in 2015 to 0.64% (12,309 patients) in 2019; and
 - a preservative free (PF) ocular lubricant increased from 0.40% (6,718 patients) in 2015 to 0.47% (8,965 patients) in 2019.
- The largest groups of MedicineInsight patients dispensed an ocular lubricant per year are females (55%) and males (27%) aged 65+ years.
- There was very little private prescribing of ocular lubricants among MedicineInsight
 patients, less than < 0.1% of all eligible MedicineInsight patients and less than 8.0% of
 all patients prescribed an ocular lubricant. Given many of these formulations can be
 purchased cheaply over the counter, this suggests that patients who are not concession
 card holders are unlikely to visit their GP for a prescription for these medicines.
- The prevalence of dry eye among all regularly attending MedicineInsight patients was estimated to be 2.2%. When extrapolated to MBS data, this suggests that between 416,907 and 526,620 Australians who visit their GP during the year will have dry eye.
- Dry eye was recorded in approximately half of patients prescribed any ocular lubricant, a PC ocular lubricant, a PF ocular lubricant or sodium hyaluronate. Please note that

information about the reason for prescribing ocular lubricants may be included in GP progress notes which are not collected by MedicineInsight for privacy reasons.

- A significantly larger proportion of patients prescribed a PF ocular lubricant had a record of an autoimmune diseases or blepharitis/Meibomian gland dysfunction than among patients prescribed a PC ocular lubricant.
- Over the study period, the number of patients started on a PF ocular lubricant without any record of a prior PC ocular lubricant prescription increased. Among regularly attending patients in 2015–16, 3,340 were started on a PF ocular lubricant and 71.0% of these had no previous record of having been prescribed a PC ocular lubricant. Among, regularly attending patients in 2018–19, 5,460 patients were started on a PF ocular lubricant and 74.9% had no record of previous PC ocular lubricant prescriptions.
- Among patients newly started on a PF ocular lubricant, more than 70% of patients who had previously used a PC ocular lubricant, and more than half of patients without a prior PC ocular lubricant prescription had a record of at least one condition associated with the development of dry eye syndrome. This may be because patients with a prior prescription of PC ocular lubricants have been managed by their GP for a longer period and may have a more complete record of their condition.
- Very few MedicineInsight patients (0.05%) were prescribed both a PC ocular lubricant and a PF ocular lubricant at least once during 2019.

Purpose of analysis

In its consideration of cationic ophthalmic emulsion at its July 2020 meeting, the PBAC noted the substantial growth in the utilisation of preservative-free ocular lubricants (eye drops). In response, the PBAC requested a review of these listings, noting the last review was completed in June 2014.

Of the 54 ocular lubricants listed on the PBS, 24 are preservative-free formulations available as authority required listings for patients sensitive to preservatives. Twelve of the 24 preservative-free authority required listings are multidose products. Figure 1 shows the rapid growth in the number of patients treated with the preservative-free formulations in the 10-year period to December 2019.

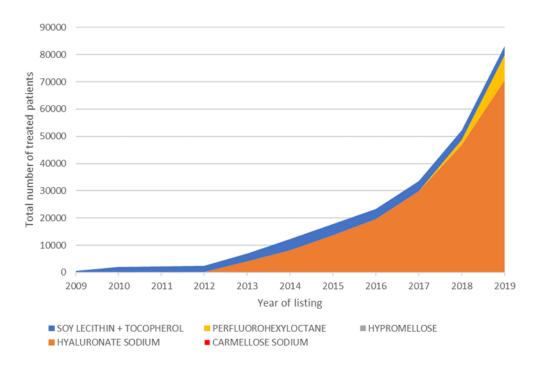


Figure 1: Number of patients treated with preservative-free ocular lubricants by PBS listing

Note: The data were extracted based on the date of supply and include the following PBS item codes: 9448G, 5545W,'02181T', 2184Y, 2253N, 2171G, 11446K, 11439C, 11852T, 11853W, 11842G and 11849P.

Source: compiled by the DUSC Secretariat based on the PBS service data

It was noted that the rising costs were driven mainly by increased uptake of hyaluronate sodium despite the authority required listing requiring a patient to be sensitive to the preservatives in multi-dose eye drops. Possible explanations suggested by the PBAC for this increase could be:

 potential use of preservative-free products without demonstrating sensitivity to products with preservatives (possibly in response to increasing patient concern about use of eye drops containing preservatives) • reports in the literature that treatment with hyaluronate sodium results in more favourable outcomes over other preparations, including faster symptom relief and reduction in keratitis (inflammation of cornea).¹

At its June meeting, DUSC requested that the utilisation of ocular lubricants, including use of preservative free ocular lubricants, be reviewed using both PBS dispensing data and MedicineInsight data.

This paper reports on the MedicineInsight prescribing data analysis.

Background

Clinical situation

Eye health relies upon a constant flow of tears. Insufficient tear production, or problems with the mucus or oily layers of the tears, may lead to dry eye syndrome (also known as dry eye disease).

Estimates of the prevalence of dry eye symptoms and dry eye syndrome are highly variable. Population based studies that report on symptomatic disease range from 6.5% to 52.4%, with an average prevalence of $22.8 \pm 13.3\%$.² Prevalence increases with age although recent studies suggest that there is also a relatively high prevalence among younger adults and school age children – possibly due to use of digital devices.² Dry eye syndrome appears to be up to 4 times more prevalent in contact lens wearers.

There have been two Australian studies which have investigated the prevalence of dry eye symptoms and dry eye syndrome but neither are recent. In a 1998 study, the prevalence of dry eye syndrome among randomly selected Melbourne residents aged 40 years or older ranged from 1.5% to 16.3% depending on the test or symptoms used to define the condition.³ In a 1999–2001 study, the prevalence of dry eye syndrome among residents of the NSW Blue Mountains region aged 49 years or older, more than half (57.5%) reported having at least one of the dry eye symptoms and 16.6% reported at least one moderate to severe symptom. Three or more symptoms were reported by 15.3% of participants.⁴

Dry eye syndrome is a multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and

¹ Gross D, Childs M, Piaton JM. Comparative study of 0.1% hyaluronic acid versus 0.5% carboxymethylcellulose in patients with dry eye associated with moderate keratitis or keratoconjunctivitis. Clin Ophthalmol. 2018;12:1081-8.

² Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS II Epidemiology Report. Ocul Surf. 2017;15(3):334-65.

³ McCarty CA, Bansal AK, Livingston PM, Stanislavsky YL, Taylor HR. The epidemiology of dry eye in Melbourne, Australia. Ophthalmology. 1998;105(6):1114-9.

⁴ Chia EM, Mitchell P, Rochtchina E, Lee AJ, Maroun R, Wang JJ. Prevalence and associations of dry eye syndrome in an older population: the Blue Mountains Eye Study. Clin Exp Ophthalmol. 2003;31(3):229-32.

neurosensory abnormalities play aetiological roles.⁵ Symptoms of dry eye syndrome include dryness, stinging, burning, foreign-body sensation, gritty feeling, itching, and the eyes feeling heavy and tired. It may also cause paradoxical excessive tearing.

The prevalence of Sjögren syndrome is estimated to be in the order of 0.6% (0.19–1.39%).²

Women are more likely to develop dry eye syndrome than men.(2) Dry eye syndrome can be caused, or exacerbated by:^{6,7,8,9}

- some medicines such as antihistamines or antidepressants
- certain medical conditions such as Bell's Palsy or blepharitis/meibomian gland dysfunction
- autoimmune diseases such as lupus, Sjögren's syndrome or rheumatoid arthritis
- older age
- smoking or environmental conditions (ie, air conditioning, pollution, a dry or windy climate)
- vision correction surgery
- wearing of contact lenses.

The most common pathological causes of dry eye syndrome are meibomian gland dysfunction, Sjögren's syndrome (a systemic autoimmune disease in which immune cells attack and destroy the exocrine glands that produce tears and saliva) and non-Sjögren's lacrimal disease.⁶

There is no 'gold standard' diagnostic test for dry eye syndrome, and so a combination of signs and symptoms is commonly used as diagnostic criteria. The Tear Film & Ocular Surface Society International Dry Eye Workshop (TFOS DEWS) II report identified 17 different questionnaires that had been used to identify disease or determine disease severity of varying utility.² This uncertainty may make it difficult for clinicians to determine disease severity.

Treatment of dry eye syndrome may involve:⁶

- use of ocular lubricants drop, gel or ointment depending on severity of symptoms.
- treatment of concurrent inflammatory skin conditions or infections
- use of warm compresses or eye masks to optimise meibomian gland function
- increasing air humidity, reducing computer use or increasing the frequency of breaks for eye rest, 'conscious blinking'.

⁵ Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, et al. TFOS DEWS II Definition and Classification Report. Ocul Surf. 2017;15(3):276-83.

⁶ Findlay Q, Reid K. Dry eye disease: when to treat and when to refer. Aust Prescr. 2018;41(5):160-3.

⁷ AMH. Australian Medicines Handbook. Adelaide: Australian Medicines Handbook Pty Ltd; 2020 [accessed 15 October 2020].

⁸ Drug utilisation sub-committee (DUSC). Ocular lubricants: analysis of utilisation (June 2014). Canberra; 2014. <u>www.pbs.gov.au/info/industry/listing/participants/public-release-docs/ocular-lubricants/ocular-lubricants</u>

⁹ Nelson JD, Craig JP, Akpek EK, Azar DT, Belmonte C, Bron AJ, et al. TFOS DEWS II Introduction. Ocul Surf. 2017;15(3):269-75.

- review of medicines that may exacerbate eye symptoms (e.g. antihistamines, beta blockers, tricyclic antidepressants, selective serotonin reuptake inhibitors, isotretinoin, eye drops with preservatives).
- treatment of underlying systemic disease
- topical anti-inflammatories, ciclosporin, autologous eye drops or surgery in more severe disease.

Ocular lubricants lubricate the surface of the eye and are often referred to as artificial tears and are used to relieve the symptoms associated with dry eye syndrome.⁷

Preservatives¹⁰ are often found in eye drops, including ocular lubricants. Multidose ocular lubricants may contain a preservative or be preservative free. Single dose units are preservative free. Preservatives may irritate the corneal and conjunctival epithelium, particularly if it is already inflamed. Normally tears quickly dilute and remove preservatives; however, in dry eye syndrome (particularly when severe) reduced tear secretion may result in increased sensitivity to preservatives.⁷

The TFOS DEWS II report reviewed management options and identified that many treatments did not have a strong evidence base. There were very few randomised trials that directly compared the effectiveness of different types of ocular lubricants. As a result, and because of considerable variability in the severity and character of disease from patient to patient, the committee made management suggestions, rather than recommendations. It suggested treatment begins with commonly available therapies such as over-the-counter lubricants for mild disease (as well as education and modification diet, medicines and the local environment). However, if this is insufficient to manage disease, it recommends preservative-free (PF) ocular lubricants in order to minimise preservative induced toxicity.¹¹

This advice is echoed in Australian guidance with the Australian Medicines Handbook noting that reduced tear secretion (particularly in severe dry eye syndrome) increases risk for preservative toxicity. Preservative-free (PF) products are preferred for patients with severe dry eye syndrome; this is more important than choice of lubricant for these patients.⁷ Similarly, a recent article in Australian Prescriber noted that while preservative containing (PC) eye drops remain suitable for mild dry eye syndrome because the preservatives are diluted in the tear film, non-preserved ocular lubricants are preferred. In more severe disease, preservative-free eye drops are recommended.⁶

The recent Australian Prescriber article noted that assessment of severity is confounded by variability in clinical presentation and questionnaires are not in common use.⁶ In a 2012 survey of Australia optometrists, half reported that they assessed dry eye severity via 'clinical judgement' and the overwhelming majority never or only rarely used a standardised questionnaire to determine severity. Regardless of whether the dry eye

¹⁰ Benzalkonium chloride, polyquaternium, sodium chlorite, stabilised oxychloro complex and sodium perborate

¹¹ Jones L, Downie LE, Korb D, Benitez-Del-Castillo JM, Dana R, Deng SX, et al. TFOS DEWS II Management and Therapy Report. Ocul Surf. 2017;15(3):575-628.

syndrome was considered to be mild, moderate or severe, preservative free ocular lubricants were preferred over preservative containing ocular lubricants for treatment.^{12,13}

The PBS criteria (see below) do not provide a definition of what is considered to be severe dry eye syndrome.

Many ocular lubricants are available at low cost over the counter at pharmacies. These supplies are not captured on the PBS.

Pharmacology

Ocular lubricants lubricate the surface of the eye and are often referred to as artificial tears.

Therapeutic Goods Administration (TGA) approved indications

Ocular lubricants are registered with the TGA as class III medical devices.

Dosage and administration

Ocular lubricant eye drops are used every 1 to 12 hours on an as required basis.

The current Product Informations (PI) and Consumer Medicine Informations (CMI) are available through <u>the TGA website product information access page</u> and <u>the TGA website</u> <u>consumer medicines information access page</u>.

PBS listing details (as at December 2020)

Streamlined

There are numerous ocular lubricant products listed on the PBS. For details of the current PBS listings refer to the PBS website.

All of the preservative-free ocular lubricants (single or multidose) are listed on the PBS as Authority required (Streamlined). To be eligible patients must have severe dry eye syndrome AND be sensitive to preservatives in multi-dose eye drops. They may be prescribed by a medical practitioner (GPs or specialists), nurse practitioners or optometrists.

Table 1 provides an overview of the PBS restrictions for preservative-free (PF) ocular lubricants.

¹² Downie LE, Keller PR, Vingrys AJ. An evidence-based analysis of Australian optometrists' dry eye practices. Optom Vis Sci. 2013;90(12):1385-95.

¹³ Downie LE, Rumney N, Gad A, Keller PR, Purslow C, Vingrys AJ. Comparing self-reported optometric dry eye clinical practices in Australia and the United Kingdom: is there scope for practice improvement? Ophthalmic Physiol Opt. 2016;36(2):140-51.

Table 1: Summarised PBS restrictions for preservative-free (PF) ocular lubricants as atDecember 2020

Active ingredient(s)	e ingredient(s) Brand		Optometrist authority required (streamlined) PBS code*	
Single dose				
carmellose sodium	Optifresh Plus	2324H	5505R	
	Optifresh Tears	2338C	5506T	
	Celluvisc	8823J	5509Y	
	Theratears (until Oct 2018)	8824K	05510B	
carmellose sodium + glycerol (until Mar 2016)	Optive	9307W	5561Q	
carbomer 974P	Poly Gel	8514D	5502N	
carbomer 980	Viscotears SDU	8578L	5504Q	
carbomer + triglycerides (until Apr 2015)	Artelac	2058H	2090B	
hypromellose + dextran- 70	Bion Tears	8299T	5521N	
polyethylene glycol (until Sept 2014)	Blink Intensive Tears	9493P	5560P	
polyethylene glycol-400+ propylene glycol	Systane	9170P	5532E	
Multidose	I	I	I	
carmellose sodium (listed Dec 2019)	Evolve Carmellose	11852T	11853W	
hypromellose (listed Dec 2019)	Evolve Hydromellose	11842G	11849P	
sodium hyaluronate	Hylo-Forte	2181T	2171G	
	Hylo-Fresh	2253N	2184Y	
perfluorohexyloctane (listed Sept 2018)	Novatears	11446K	11439C	
soy lecithin + tocopherol + vitamin A	tearsagain	9448G	5545W	

*Severe dry eye syndrome and the patient must be sensitive to preservatives in multi-dose eye drops

All of the ocular lubricants containing preservatives listed on the PBS are multidose and can be prescribed under one of two Restricted benefit listings:

- Patients must have severe dry eye syndrome, including Sjögren's syndrome. They may be prescribed by a medical practitioner (GPs or specialists), nurse practitioners or optometrists
- Patients must have severe dry eye syndrome, including Sjögren's syndrome AND be under a GP Management Plan or Team Care Arrangements. These PBS items may only be prescribed by medical practitioners.

Table 2 provides an overview of the PBS restrictions for preservative containing (PC) ocular lubricants.

Table 2: Summarised PBS restrictions for multidose preservative containing (PC) ocular
lubricants as at December 2020

Active ingredient(s)	Brand	Restricted benefit PBS code†	Restricted benefit PBS code (requires GPMP)‡	Optometrist restricted benefit PBS code†
carmellose sodium	Refresh Tears Plus Refresh Liquigel	8548X 8593G	9211T 9212W	5507W 5508X
carmellose sodium + glycerol	Optive	9355J	9356K	5556K
hypromellose	Methopt Genteal (listed Mar 2019) In a Wink Moisturising (listed Mar 2019)	2956N 8287E (until July 2019) 11625W	9214Y 9213X (until July 2019) 11643T	5517J 5518K (until July 2019) 11634H
hypromellose + dextran-70	Poly-Tears Tears Naturale	1509K	9216C	5520M
carbomer 980	Optifresh PAA Viscotears Geltears (until Sept 2013)	8384G	9210R	5503P
carbomer + triglycerides (until Apr 2014)	Artelac	2041K	2044N	2082N
hypromellose + carbomer-980	Genteal HPMC PAA	8564R	9215B	5519L
polyethylene glycol (until Sept 2014)	Blink Intensive Tears	9491M	9492N	5559N
polyethylene glycol-400+ propylene glycol	Systane	8676P	9219F	5524R

polyvinyl alcohol	PVA tears	2682E	9220G	5526W
	Liquifilm Tears	2681D (until March	9222J (until March	5525T (until March
	Vistil (until Apr	2015)	2015)	2015)
	2019)	8831T (until Apr	9221H (until Apr	5527X (until Apr
	Vistil Forte	2019)	2019)	2019)
	(until Apr 2019)	8832W (until Apr 2019)	9223K (until Apr 2019)	5528Y (until Apr 2019)

⁺ Severe dry eye syndrome, including Sjögren's syndrome

‡ Severe dry eye syndrome, including Sjögren's syndrome and patient must be receiving treatment under a GP Management Plan or Team Care Arrangements where Medicare benefits were or are payable for the preparation of the Plan or coordination of the Arrangements

Date of listing on PBS and changes to listing

A summary of the listing dates and relevant changes to the listings of ocular lubricants from 2012 onwards can be found in Appendix A.

Current PBS listing details are available from <u>www.pbs.gov.au</u>

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

Ocular lubricant products have been considered by the PBAC as minor submissions and recommended on a cost minimisation basis.

Previous reviews by the DUSC

In June 2014, DUSC reviewed the utilisation of ocular lubricants. Of note, it found:

- The total number of prescriptions for ocular lubricants had been fairly steady in the ten years to 2013, increasing gradually to a peak of 2.53 million in 2009, and then slowly decreasing to 2.46 million in 2012.
- Expenditure across the whole group of ocular lubricants had been fairly stable in the last ten years to 2013. Expenditure in 2012 was \$26.2 million.
- Almost all prescriptions for ocular lubricants were over the patient co-payment (97%).
- Concessional prescriptions compile the bulk of prescriptions for ocular lubricants, with 85% of prescriptions in 2012.
- Multi-dose products account for the majority of PBS prescriptions for ocular lubricants supplied. In 2013 (until end September), 85% of prescriptions were for multi-dose products.
- Prescribing of single dose unit products was gradually increasing. Single dose unit products comprised 6.7% of prescriptions supplied 2003, 14% in 2012 and 15% in 2013 (to end September). This was considered to be the likely explanation for the gradual increase in expenditure on ocular lubricants despite stable prescription numbers.
- The most common prescribers of ocular lubricants were GPs, followed by ophthalmologists. In 2013 (to end September), approximately 72% of prescriptions supplied were prescribed by GPs and 19% by ophthalmologists. Optometrists accounted for approximately 1% of prescriptions supplied.

For details of the DUSC consideration of ocular lubricant medicines, refer to the <u>Public</u> <u>Release Document</u> from the June 2014 DUSC meeting.

Methods

MedicineInsight

MedicineInsight is a large-scale primary care data set of longitudinal de-identified electronic health records (EHR) in Australia. MedicineInsight was initially established by NPS MedicineWise in 2011, with core funding from the Australian Government Department of Health, to collect general practice data to support quality improvement in Australian primary care and post-market surveillance of medicines. The monthly collation of collected data can be analysed for the purposes of improving patient care, quality improvement and evaluation, performing population health analysis, research and developing health policy.

MedicineInsight utilises third-party data extraction tools which extract, de-identify, encrypt and securely transmit whole-of-practice data from the clinical information systems (CIS) of over 700 general practices. Patient level data are de-identified 'at source' meaning patients' personal identifiers such as name, date of birth and address are not extracted by the tool, although year of birth and postcode are extracted, enabling the calculation of age and Socio-Economic Indexes for Areas [SEIFA]. Each patient is assigned a unique number within the dataset which allows all the records (clinical, prescription, referral etc) held in the database to be linked to the associated patient identifying number. Further information is available online: <u>https://www.nps.org.au/medicine-insight</u>

This is a descriptive analysis of 5 years of data extracted from 441 practices that participate in the national MedicineInsight program and meet data quality criteria (1 January 2015 to 31 December 2019, with a one year look back period for analyses of initiation).

Study ethics and approval

In December 2017, NPS MedicineWise was granted ethics approval for the standard operations and uses of the MedicineInsight database by NPS MedicineWise. This program approval was given by the RACGP NREEC (NREEC 17-017).

The use of MedicineInsight data for the purposes of this report was approved by the independent Data Governance Committee (2020–036) in December 2020.

Eligible practices

Analyses were conducted using de-identified patient data from 423–441 individual general practices (depending upon study year) which met the standard data quality criteria.¹⁴ See

¹⁴ Eligible criteria were that the site had been established for at least 2 years as of October 2020; and had no significant interruptions (of longer than 2 months in the 2 years prior) to their practice data and met the minimum threshold of clinical activity (i.e., at least 50 patients in the last 2 years).

Appendix B for information on the number of participating practices that have contributed data in each calendar year.

Eligible patients

The study time period is for 5 calendar years from 1 January 2015 to 31 December 2019, inclusive, unless otherwise specified. Historical records outside of this study period were consulted when exploring patient demographics, diagnoses and prior use of ocular lubricants.

Patients were eligible for inclusion in the general study population if:

- they had valid information for age (0–112) and sex (male or female)
- had at least three clinical encounters¹⁵ on different days recorded between 1 January 2015 to 31 December 2019.

For the analyses that report data by individual calendar years (trend analyses), patients had to have had at least one clinical encounter in the calendar year in question.

The analyses on condition prevalence, prior use of medicines that may be implicated in the development of dry eye and co-administration were based on 'regularly attending patients' with at least three visits at a MedicineInsight practice between 1 January 2018 and 31 December 2019.

A final analysis, which looked at changes in demographics and conditions recorded among patients starting preservative free ocular lubricants, used data from regularly attending patients from two study periods: between 1 January 2015 and 31 December 2016 and between 1 January 2018 and 31 December 2019 (study period 2).

To be included in the initiation cohorts, patients had to meet the general study criteria, have evidence of being prescribed a PF ocular lubricant for the first time during one of the two study time periods and have a clinical encounter at least a year, but not more than four years, before the start of the study period to ensure at least a year of attendance at the practice prior to the first prescription of PF ocular lubricant. The look back period was calculated using the exact date of the first ocular lubricant prescription between January 2018 and December 2019.

Ocular lubricants

Patients were defined as having had a prescription for an ocular lubricant if they had at least one record of a medicine in the tables Table 1, Table 2 or Table 3 in the Script item table. Because the ATC code for artificial tears (S01XA20) did not differentiate between the different active ingredients, we categorised the different ocular lubricants as being preservative containing (PC) or preservative free (PF) in the following step-wise manner:

¹⁵ A clinical encounter, or any professional exchange between a patient and a healthcare professional (GP or nurse), was defined as all those encounters at the practice site that were: a) not identified as administrator entries nor encounters that have been transferred/imported from another practice and b) were not identified by pre-defined 'administration-type' terms found in the 'reason for encounter' field such as "administrative reasons", "forms", and "recall".

- active ingredient if this allowed us to categorise the formulation as a PC ocular lubricant or PF ocular lubricant we stopped here (e.g. perfluorohexyloctane which only comes in a PF formulation);
- the brand name if this allowed us to categorise the formulation as a PC ocular lubricant or a PF ocular lubricant we stopped here (eg, Evolve Carmellose which only comes in a PF formulation);
- if there was an entry in the Authority Indication field which included terms associated with dry eye AND preservative sensitivity it was recorded as being a PF ocular lubricant;
- information about whether a formulation was provided as unit doses or multidose. If the formulation was provided in unit doses it was classified as being a PF ocular lubricant.

Eye ointments containing paraffin or lanolin, and which are typically used at night rather than during the day, were excluded.

A number of other ocular lubricants which are not listed on the PBS are also available and may be prescribed privately. Table 3 shows the non-PBS listed ocular lubricants as listed in the Australian Medicines Handbook.⁷

Active ingredient(s)	Brand		
Multidose preservative free (PF) ocular lubricants			
phospholipid enzymes	Murine Eye Mist		
Single dose preservative free (PF) ocular lubri	cants		
sodium hyaluronate	Luxyal Monodose		
0.4% macrogol 400 + 0.3% propylene glycol	Systane Ultra		
0.5% carmellose + 1% glycerol + polysorbate 80	Optive Advanced		
0.1% sodium hyaluronate + 0.5% carmellose +1.0 glycerol	Optive Fusion		
0.5% carmellose + 0.9% glycerol	Optive Sensitive		
0.25% macrogol 400	Blink Intensive Tears		
0.25% carmellose	Theratears		
0.5% carmellose	Refresh Plus		
1.4% polyvinyl alcohol + 0.6% povidone	Refresh		
hydroxypropyl guar + macrogol + propylene glycol + sodium hyaluronate	Systane Hydration		
Multidose preservative containing (PF) ocular lu	bricants		
0.15% sodium hyaluronate	Luxyal		
0.5% carmellose + 1% glycerol + polysorbate 80	Optive Advanced		
0.1% sodium hyaluronate + 0.5% carmellose + 0.9% glycerol	Optive Fusion		
0.6% propylene glycol	Systane Balance		

Table 3: Non-PBS listed ocular lubricants as listed in Australian Medicines Handbook⁷

0.4% macrogol + 0.3% propylene glycol	Systane Ultra
0.4% macrogol + 0.3% propylene glycol	Systane Gel Drops
0.5% polyvinyl alcohol + 0.6% povidone	Murine Revital Eyes, Murine Tears
0.25% macrogol 400	Blink Intensive Tears
0.5% carmellose	Refresh Contacts
phospholipid enzymes	Optrex Actimist

It should be noted that many of the ocular lubricants can be purchased cheaply over-thecounter (OTC) without a prescription. This report did not attempt to identify instances where a GP advised the use of an OTC medicine (outside of issuing a prescription) as it was considered unlikely that comprehensive information on OTC medicines would be captured in the dataset and any that is recorded may not be representative.

Definitions

Socio-demographics in the analysis included age, sex, SEIFA, remoteness and Aboriginal and Torres Strait Islander status (as reported in the CIS).

Patients were defined as having a condition (Table 4) if they had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields – diagnosis, reason for encounter or reason for prescription - recorded at any time from the patient's earliest record up to the end of the study period. Given the variety of recording practices among GPs, we did not attempt to distinguish 'dry eye' when recorded as a symptom from 'dry eye disease' or 'dry eye syndrome'.

Table 4: Terms used to identify patients with conditions that may be associated with ocular lubricant use

Condition	Included terms
dry eye syndrome or symptom*	dry eye, kerataconjunctivitis
rheumatoid arthritis	arthritis (juvenile rheumatoid or rheumatoid or seronegative), Caplan syndrome, JRA, juvenile rheumatoid arthritis, lipoid (dermatoarthritis or rheumatism), multicentric reticulohistiocytosis, RA, rheumatoid arthritis, rheumatoid arthritis (juvenile or pneumoconiosis), seronegative arthritis, seronegative rheumatoid arthritis or stills disease
lupus	DLE, SLE, lupus
Sjogren's syndrome	Sjogren
blepharitis	blepharitis
meibomian gland dysfunction	meibomian dysfunction
facial palsy (including Bells)	facial palsy, (facial or face or Bells) and (palsy or paralysis or weakness)
contact lens use	contact lens
laser eye surgery/lasik	Lasik, laser and (cornea or excimer or kerato or refract or vision)

* Given the variety of recording practices among GPs, we did not attempt to distinguish 'dry eye' when recorded as a symptom from 'dry eye disease' or 'dry eye syndrome'.

The TFOS DEWS II report on iatrogenic causes, adverse effects that are directly caused by medical treatment, of dry eye syndrome identified a large number of systemic medicines and classes of systemic medicines that are associated with an increased risk of developing dry eye syndrome.¹⁶ The use of some of these medicines in the year prior to the date of a patient starting a PF ocular lubricant was explored. Medicine classes were selected if the TWOS DEWS II report identified that they were associated with a doubling of risk (an odds ratio of 2.0 or more) of developing dry eye syndrome and had been reported in at least one large epidemiological study. The medicine classes meeting this criterion are shown in Table 5 and were identified using ATC codes.

 Table 5: ATC codes used to identify medicines that have been associated with an increased risk of developing dry eye syndrome

Medicine class	ATC codes
inhaled steroid	R03BA01, R03BA02, R03BA05, R03BA07, R03BA08, R03BA09, R03AK06, R03AK07, R03AK08, R03AK09, R03AK10, R03AK11, R03AK12, R03AK13, R03AK1'
benzodiazepine or anxiolytic	N05B, N03AE
antidepressant or antipsychotic	N05A, N06A

¹⁶ Gomes JAP, Azar DT, Baudouin C, Efron N, Hirayama M, Horwath-Winter J, et al. TFOS DEWS II iatrogenic report. Ocul Surf. 2017;15(3):511-38

We did not search for all conditions and causes of dry eye, only those that we considered would be most likely to be recorded in the CIS of a general practice. We did not attempt to look for factors such as environmental pollution, etc. that may explain their use. In addition, it is possible that information about the reason for prescribing ocular lubricants may be included in GP progress notes which are not collected by MedicineInsight for privacy reasons.

Statistical analysis

Analyses were conducted on the October 2020 download of MedicineInsight data using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), including the use of the SURVEYFREQ procedure. Measures included descriptive statistics, frequencies, proportions and odds ratios as appropriate. To indicate the reliability of the estimates of prevalence and proportions, 95% confidence intervals (adjusted for clustering by practice site) and p-values are reported as needed.

If a particular result was only reported in 1-4 patients, this result has been reported as < 5 (with the exception of missing variables).

Guide to interpreting MedicineInsight data

When interpreting the information presented in this report, readers should note some of the limitations or caveats related to the MedicineInsight data:

- Information in CIS is collected to provide clinical care to a patient, not for research purposes. All analyses are therefore dependent upon on the accuracy and completeness of data recorded in, and available for extraction from, the general practice CISs.
- Medicines use information from MedicineInsight relates to records of GP
 prescribing, and therefore differs in several important ways from national PBS
 dispensing data as not all prescriptions and repeats will be dispensed. Specialist and
 hospital prescriptions are not included. There may be a delay of up to 12 months
 between prescribing and dispensing.
- Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out.
- Due to confidentiality issues we do not have access to progress notes or access to correspondence, which may contain further information on reasons for prescriptions, reasons for encounters and diagnoses.
- Patients are free to visit multiple other practices. We do not have data on patients from non-MedicineInsight clinics. Currently we cannot identify patients who have attended multiple MedicineInsight practices.
- Information on OTC medicines is limited and may not be representative.

Results

Trend analyses

Baseline populations

MedicineInsight is an open cohort and so the number of patients eligible for inclusion in each calendar year will vary. The number of eligible patients seen during a particular calendar period varied from 1.67 million to 1.96 million (see Appendix Table C1).

Patients prescribed an ocular lubricant by PBS status

Figure 2 and Table 6 show the total number of patients who were prescribed any ocular lubricant (preservative containing or preservative free) according to whether they were prescribed lubricants only on the PBS, only privately or 'both' if they were prescribed both PBS and private prescriptions in the same calendar year.

Over the five-year study period, the total number of MedicineInsight patients prescribed an ocular lubricant has fallen from 1.31% of all eligible MedicineInsight patients in 2015 to 1.06% of all eligible MedicineInsight patients in 2019. This is consistent with the fall in the number of unique patients who were dispensed an ocular lubricant at least once in the PBS.

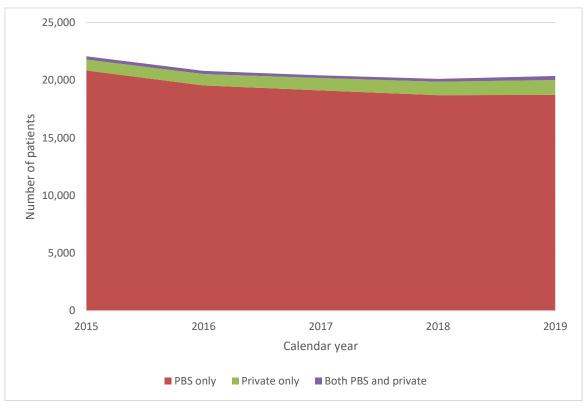


Figure 2: Number of patients prescribed any ocular lubricant at least once during the year in 2015 to 2019 by prescription PBS status

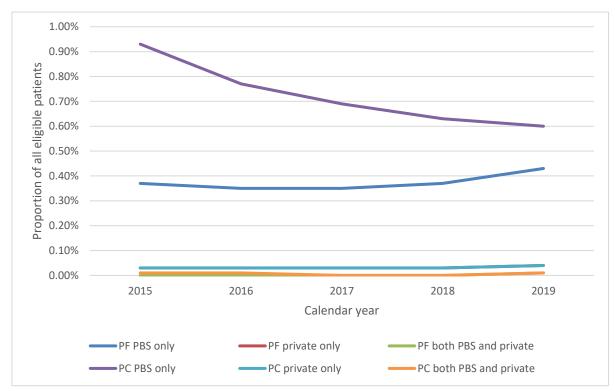
Most (> 90%) ocular lubricant prescriptions across all years were prescribed under the PBS (Table 6). However, there has been a small but significant fall in the proportion of patients who were only prescribed ocular lubricants through the PBS. When expressed as a proportion of all eligible patients (regardless of whether they have been prescribed an ocular lubricant tor not), 1.24% of all eligible patients in 2015 were only prescribed an ocular lubricant through the PBS compared with 0.98% of all eligible patients in 2019. When expressed as a proportion of all patients prescribed an ocular lubricant, 94.4% of patients in 2015 were only recorded as having received PBS prescriptions compared with 92.0% of patients in 2019.

PBS status	2015 N=1,679,478	2016 N=1,834,712	2017 N=1,927,310	2018 N=1,960,694	2019 N=1,917,114
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Total (any ocular lubricant)	22,072 (1.31)	20,802 (1.13)	20,426 (1.06)	20,108 (1.03)	20,357 (1.06)
		Any ocula	r lubricant		
PBS only	20,838 (1.24)	19,540 (1.07)	19,108 (0.99)	18,698 (0.95)	18,727 (0.98)
Private only	961 (0.06)	990 (0.05)	1076 (0.06)	1167 (0.06)	1288 (0.07)
Both	273 (0.02)	272 (0.01)	242 (0.01)	243 (0.01)	342 (0.02)
	Preserva	tive-free single dos	se or multidose for	mulation	
PBS only	6196 (0.37)	6388 (0.35)	6784 (0.35)	7233 (0.37)	8187 (0.43)
Private only	469 (0.03)	592 (0.03)	637 (0.03)	610 (0.03)	671 (0.04)
Both	53 (0.00)	71 (0.00)	60 (0.00)	64 (0.00)	107 (0.01)
Any PF ocular lubricant	6718 (0.40)	7051 (0.38)	7481 (0.39)	7907 (0.40)	8965 (0.47)
	Preservative containing multidose formulation				
PBS only	15,589 (0.93)	14,052 (0.77)	13,214 (0.69)	12,262 (0.63)	11,441 (0.60)
Private only	587 (0.03)	505 (0.03)	546 (0.03)	649 (0.03)	744 (0.04)
Both	134 (0.01)	102 (0.01)	91 (0.00)	96 (0.00)	124 (0.01)
Any PC ocular lubricant	16,310 (0.97)	14,659 (0.80)	13,851 (0.72)	13,007 (0.66)	12,309 (0.64)

Table 6: Number* and proportion of patients with a record of at least one prescription for
an ocular lubricant (total and by PBS status) by calendar year

*Some patients had a record of both PC and PF ocular lubricants in the same year. These patients are included under the 'Both' category.

The number and proportion of patients who have a record of being prescribed a PC ocular lubricant has fallen from 16,310 patients (0.97% of eligible patients) in 2015 to 12,309 patients (0.64% of all eligible patients) in 2019 (Table 6 and Figure 3). In contrast, the number of patients prescribed a PF ocular lubricant has increased from 6,718 patients



(0.40%) in 2015 to 8,965 (0.47%) in 2019. This pattern is consistent with that seen in the PBS analysis.

Figure 2: Proportion of all eligible patients prescribed a PF ocular lubricant or a PC ocular lubricant at least once during the year in 2015 to 2019 by prescription PBS status

Demographics of patients prescribed at least one ocular lubricant by calendar year

Consistent with the PBS analyses, the majority of patients with a record of a prescription for an ocular lubricant are aged 65+ years and are female (Figure 3 and Appendix Table C2). The largest group of patients prescribed an ocular lubricant are females aged 65+ years who accounted for 54.2–58.5% of all patients prescribed an ocular lubricant each year while males aged 65+ years accounted for another 26.7–27.5% of patients. These figures are almost identical to those reported in the PBS dispensed analysis, 55% for women and 26–27% for men aged 65+ years.

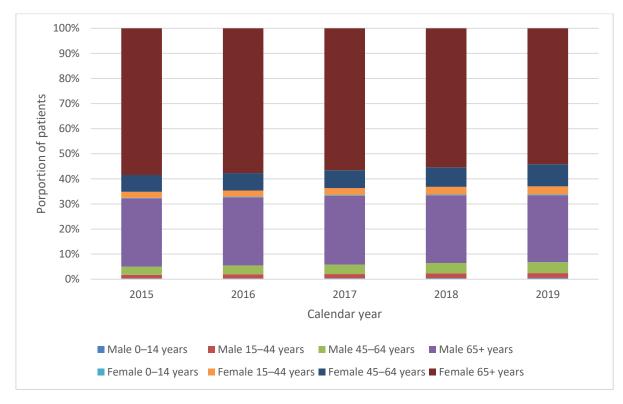


Figure 3: Proportion of unique patients with at least one record of a prescription for an ocular lubricant between January 2015 and December 2019, by age-sex groups

Table 7 shows the prevalence of ocular lubricant use within each patient demographic. As can be seen, the proportion of male patients who were prescribed an ocular lubricant was 0.8–1.0% across all years while the proportion of female patients prescribed an ocular lubricant was 1.2–1.6%. Women aged 65+ years were the most likely to be prescribed an ocular lubricant with 5.2% of women in this group having a record of being prescribed an ocular lubricant compared with 3.1% of men aged 65+ years.

		, ,	each jean jean		
Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% CI)				
Total eligible patients in each calendar year	1,679,478	1,834,712	1,927,310	1,960,694	1,917,114
Patients with at least one					
ocular	22,072	20,802	20,426	20,108	20,357
lubricant script	1.3 (1.1, 1.5)	1.1 (1.0, 1.3)	1.1 (0.9, 1.2)	1.0 (0.9, 1.1)	1.1 (0.9, 1.2)
		Se	ex		
Male	7106 1.0 (0.8, 1.1)	6803 0.8 (0.7, 0.9)	6796 0.8 (0.7, 0.9)	6728 0.8 (0.7, 0.9)	6825 0.8 (0.7, 0.9)

Table 7: Patient-demographic-specific prevalence of at least one record of prescription of
any ocular lubricant in each calendar year, in each yearly patient cohort

Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Female	14,966	13,999	13,630	13,380	13,532
	1.6 (1.4, 1.8)	1.4 (1.2, 1.5)	1.3 (1.1, 1.4)	1.2 (1.1, 1.4)	1.3 (1.1, 1.4)
		A		Γ	
0–14 years	120	117	136	147	169
	0.1 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)
15–44 years	850	847	907	998	1039
	0.1 (0.1, 0.2)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)
45–64 years	2192	2168	2224	2393	2677
	0.5 (0.4, 0.5)	0.5 (0.4, 0.5)	0.4 (0.4, 0.5)	0.5 (0.4, 0.5)	0.5 (0.5 <i>,</i> 0.6)
65+ years	18,910	17,670	17,159	16,570	16,472
	4.7 (4.4, 5.1)	4.3 (4.0, 4.6)	4.2 (3.9, 4.5)	4.1 (3.8, 4.4)	4.2 (3.9, 4.5)
		Age	-sex		
Male 0–14	77	69	78	93	105
years	0.1 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)	0.1 (0.0, 0.1)
Male 15–44	304	342	339	373	391
years	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)
Male 45–64	718	727	768	831	888
years	0.4 (0.3, 0.4)	0.3 (0.3, 0.4)	0.4 (0.3 <i>,</i> 0.4)	0.4 (0.3, 0.4)	0.4 (0.4, 0.5)
Male 65+ years	6007	5665	5611	5431	5441
	3.3 (3.1, 3.6)	3.0 (2.8, 3.2)	3.0 (2.7, 3.2)	3.0 (2.7, 3.2)	3.1 (2.8, 3.3)
Female 0–14	43	48	58	54	64
years	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)
Female 15–44	546	505	568	625	648
years	0.2 (0.1, 0.2)	0.1 (0.1, 0.1)	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)	0.2 (0.1, 0.2)
Female 45–64	1474	1441	1456	1562	1789
years	0.6 (0.5 <i>,</i> 0.7)	0.5 (0.5 <i>,</i> 0.6)	0.5 (0.5, 0.6)	0.6 (0.5, 0.6)	0.7 (0.6, 0.7)
Female 65+	12,903	12,005	11,548	11,139	11,031
years	5.9 (5.5, 6.3)	5.4 (5.0, 5.7)	5.2 (4.8, 5.5)	5.1 (4.8, 5.4)	5.2 (4.9, 5.6)
		Aboriginal or Tor	res Strait Islander		
Yes	271	261	284	275	358
	0.6 (0.5, 0.7)	0.5 (0.4, 0.6)	0.5 (0.4 <i>,</i> 0.6)	0.5 (0.4, 0.5)	0.6 (0.5, 0.7)
No	18,155	17,412	17,191	16,976	17,320
	1.4 (1.2, 1.6)	1.2 (1.0, 1.4)	1.1 (1.0, 1.3)	1.1 (1.0, 1.2)	1.1 (1.0, 1.3)
Not recorded	3,646	3,129	2,951	2,857	2,679
	1.1 (1.0, 1.2)	0.9 (0.8, 1.0)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)
		Remo	teness		
Major city	13,709	13,079	12,869	12,741	13,032
	1.4 (1.2, 1.5)	1.2 (1.0, 1.3)	1.1 (1.0, 1.2)	1.0 (0.9, 1.1)	1.1 (1.0, 1.2)
Inner regional	5,891	5,460	5,420	5,206	5,109
	1.4 (0.9, 1.8)	1.2 (0.8, 1.6)	1.1 (0.8, 1.5)	1.1 (0.8, 1.4)	1.1 (0.8, 1.4)

Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Outer regional	2,305	2,101	1,977	1,982	2,035
	1.1 (0.9, 1.3)	0.9 (0.8, 1.1)	0.9 (0.7, 1.0)	0.8 (0.7, 1.0)	0.9 (0.8, 1.0)
Remote/very	167	162	160	179	180
remote	0.7 (0.3, 1.1)	0.5 (0.3, 0.8)	0.5 (0.3, 0.7)	0.6 (0.3, 0.9)	0.6 (0.4, 0.9)
	Soci	oeconomic status	(SEIFA IRSAD quin	tile)	
1 (most	4,400	4,200	4,074	3,873	3,918
advantage)	1.5 (1.2, 1.8)	1.3 (1.1, 1.6)	1.3 (1.0, 1.5)	1.2 (1.0, 1.4)	1.2 (1.0, 1.5)
2	4,738	4,357	4,385	4,087	4,186
	1.4 (1.1, 1.6)	1.2 (1.0, 1.4)	1.1 (0.9, 1.4)	1.1 (0.9, 1.3)	1.1 (0.9, 1.3)
3	4,892	4,657	4,549	4,649	4,758
	1.4 (1.1, 1.6)	1.2 (1.0, 1.4)	1.1 (0.9, 1.3)	1.1 (0.9, 1.3)	1.1 (0.9, 1.3)
4	3,499	3,405	3,330	3,497	3,472
	1.1 (0.9, 1.3)	1.0 (0.8, 1.1)	0.9 (0.8, 1.0)	0.9 (0.8, 1.1)	0.9 (0.8, 1.1)
5 (least	4,543	4,183	4,088	4,002	4,022
advantage)	1.2 (1.1, 1.4)	1.0 (0.9, 1.2)	1.0 (0.8, 1.1)	0.9 (0.8, 1.0)	0.9 (0.8, 1.1)

Missing patient postcode has led to equal numbers of missing patients in Remoteness and SEIFA for each year as follows: **2015**: 119. **2016**: 132. **2017**: 132. **2018**: 123. **2019**: 135.

Patients living within major cities are more likely to have received been prescribed an ocular lubricant each year (in 2019 1.1%; 95% CI 1.0% to 1.2%) than patients living within a remote or very remote area (0.6%; 95% CI 0.4% to 0.9%). This may be a true difference or may be a chance finding.

There have been no substantial changes with regards to the proportion of Aboriginal and Torres Strait Islander patients prescribed ocular lubricants over time. Similarly, there have been no changes in the proportion of patients prescribed an ocular lubricant within socioeconomic groups or by remoteness (Table 7).

Similar results can be seen when the analysis is stratified according to whether a patient was prescribed a PF ocular lubricant or a PC ocular lubricant Over the study period the likelihood that a patient aged 65+ years would be prescribed a PF ocular lubricant increased from 1.4% in 2015 to 1.9% in 2019 (Appendix Table C3). In contrast, use of a PC ocular lubricant in this group decreased from 3.5% in 2015 to 2.6% in 2019 (Appendix Table C4).

Sodium hyaluronate alone

Table 8 shows the prescribing of sodium hyaluronate to MedicineInsight patients over the 5 year study period. As can be seen the overwhelming majority of prescriptions were for PF sodium hyaluronate (with negligible prescribing of PC sodium hyaluronate) and were prescribed on the PBS rather than privately.

Table 8: Number of patients* with a record of at least one prescription for an ocularlubricant (total and by PBS status) by calendar year

Prescription type	2015	2016	2017	2018	2019
Number of patients prescribed sodium hyaluronate	466	909	1380	2166	3109
Preservative-free si	Preservative-free single dose or multidose formulation				
PBS only	439	778	1149	1917	2898
Private only or both private and PBS ⁺	24	121	212	229	198
Preservative containing multidose formulation					
PBS or private or both‡	<5	11	20	20	13

*Some patients had a record of both PC and PF sodium hyaluronate

⁺ Due to small numbers patients with only private PF sodium hyaluronate or a mixture of both private and PBS PF sodium hyaluronate have been combined into a single category

‡Due to small numbers patients prescribed any type of PC sodium hyaluronate, regardless of whether it was on the PBS or privately, have been combined into a single category

Regularly attending patient analyses

The above analyses looked at trend information. Analyses from this point forward are based on 'regularly attending patients' with at least three visits at a MedicineInsight practice between January 2015 and December 2016 (2015–16) or between January 2018 and December 2019 (2018–19).

Among all regularly attending patients (n = 1,947,094) in the 2018–19 study period, 31,353 (1.61%) were prescribed some kind of ocular lubricant at least once. There were 20,101 patients (1.03%) who were prescribed a PC ocular lubricant and 13,158 patients (0.68%) who were prescribed a PF ocular lubricant.

Prevalence of conditions among all regularly attending patients

Table 9 shows the patient prevalence of the various conditions that may contribute to dry eye among all regularly attending patients who visited their general practice at least 3 times between January 2018 and December 2019. As can be seen, 2.2% (95% CI 1.9% to 2.4%) of regular patients had a record of 'dry eye' at any time in their patient history. Due to the variety of recording practices among GPs it was not possible to distinguish dry eye syndrome from dry eyes as a symptom.

In the 2018–19 financial year, 21.9 million patients had at least one GP visit (non-referred MBS attendance).¹⁷ Applying the prevalence of dry eye among MedicineInsight patients to this figure suggests that between 416,907 and 526,620 Australians who visit their GP at least once over the year are likely to have dry eye. In the associated PBS analysis report,

¹⁷ Annual Medicare Statistics (Table 1.6).

https://www1.health.gov.au/internet/main/publishing.nsf/Content/Medicare%20Statistics-1

approximately 400,000 unique patients were prescribed an ocular lubricant on the PBS per calendar year.

The prevalence of any of the conditions associated with increased risk of dry eye was 4.4% (95% CI 4.1% to 4.8%). If this figure is applied to the MBS attendance statistics this suggests that between 899,642 and 1.05 million Australian who visit their GP at least once are likely to have one of these conditions.

Table 9: Conditions recorded among regularly attending MedicineInsight patients (at least
3 clinical encounters between January 2018 and December 2019)

	Regular MedicineInsight patients		
Condition	No. % (95% CI)		
Dry eye	42,058	2.2 (1.9,2.4)	
Autoimmune disease (Sjogren's syndrome, rheumatoid arthritis, lupus)	24,948	1.3 (1.2, 1.4)	
Blepharitis or Meibomian gland dysfunction	18,906	1.0 (0.9, 1.1)	
Facial palsy (including Bell's palsy)	6,374	0.3 (0.3, 0.4)	
Laser eye surgery or contact lens use	972	0.0 (0.0, 0.1)	
At least one of the above conditions	86,382	4.4 (4.1, 4.8)	
None of the above	1,860,712	95.6 (95.2 <i>,</i> 95.9)	

Among the 42,058 regularly attending patients with a record of dry eye, 37.3% (95% Cl 36.1% to 38.5%) had a record of at least one prescription of an ocular lubricant. The proportion of patients with a record of dry eye who had a PC ocular lubricant prescription was 23.4% (95% Cl 22.4% to 24.3%) and the proportion who had a PF ocular lubricant was 16.8% (95% Cl 15.8% to 17.9%).

Prevalence of conditions among regularly attending patients prescribed an ocular lubricant

Among the 31,353 regularly attending patients during 2018–19 who had been prescribed at least one ocular lubricant, 50% had a record of dry eye in their medical history (Table 10). The proportion of patients with dry eye recorded was similar among patients prescribed a PC ocular lubricant, a PF ocular lubricant or sodium hyaluronate.

A statistically significantly larger proportion of patients prescribed a PF ocular lubricant (8.1%) had a record of one of the autoimmune diseases than patients prescribed a PC ocular lubricant (5.3%). Blepharitis or Meibomian gland dysfunction was also more commonly recorded among patients prescribed a PF ocular lubricant.

Table 10: Conditions recorded* among regularly attending MedicineInsight patients (at least 3 clinical encounters between January 2018 and December 2019) by type of ocular lubricant prescribed

Condition*	lubri	ocular icant† 1,353)	lubr	ocular icant† 0,101)	PF ocular Sodiur lubricant† hyalurona (n=13,158) (n=427		uronate†	
	No.	% (95% Cl)	No.	% (95% Cl)	No.	% (95% CI)	No.	% (95% Cl)
Dry eye	15,684	50.0 (47.4, 52.6)	9825	48.9 (46.2, 51.6)	7080	53.8 (50.8, 56.8)	2359	55.2 (51.4, 58.9)
Autoimmune disease (Sjogren's disease, rheumatoid arthritis, lupus)	1943	6.2 (5.8, 6.6)	1072	5.3 (5.0, 5.7)	1066	8.1 (7.5, 8.7)	349	8.2 (7.3, 9.0)
Blepharitis or Meibomian gland dysfunction	2071	6.6 (6.1, 7.1)	1251	6.2 (5.7 <i>,</i> 6.8)	1017	7.7 (7.0, 8.4)	326	7.6 (6.6, 8.6)
Facial palsy (including Bell's palsy)	532	1.7 (1.5, 1.9)	357	1.8 (1.6, 2.0)	208	1.6 (1.3, 1.8)	72	1.7 (1.2, 2.2)
Laser eye surgery or contact lens use	41	0.1 (0.1, 0.2)	13	0.1 (0.0, 0.1)	29	0.2 (0.1, 0.3)	14	0.3 (0.2, 0.5)
At least one of the above	17,636	56.2 (53.9, 58.6)	11,025	54.8 (52.4, 57.3)	7958	60.5 (57.8, 63.1)	4275	61.3 (58.1, 64.5)

*Patients may have had a record of more than one condition

Includes both prevalent and new (incident) users

We did not search for all conditions and causes of dry eye, only those that we considered would be most likely to be recorded in the CIS of a general practice. We did not attempt to look for factors such as environmental pollution, etc. that may explain their use. In addition, it is possible that information about the reason for prescribing ocular lubricants may be included in GP progress notes which are not collected by MedicineInsight for privacy reasons.

Initiation

Between 2015–16 and 2018–19 there was an increase in the direct initiation of PF ocular lubricants over time. The proportion of patients who were started on a PF ocular lubricant without any record of a prior PC ocular lubricant prescription was significantly higher among regularly attending patients in 2018–19 than among regularly attending patients in 2015–16 (Table 11). Among regularly attending patients in 2015–16, 3,340 were started on a PF ocular lubricant and 71.0% of these had no record of having been prescribed a PC

ocular lubricant prior. Among, regularly attending patients in 2018–19, 5,460 patients were started on a PF ocular lubricant and 74.9% had no record of prior PC ocular lubricant use.

Table 11: Number and proportion of regularly attending patients started on a preservative free ocular lubricant in 2015–16 and 2018–19, by prior prescription of preservative containing ocular lubricant (i.e. indirect and direct initiation)

Study period	Patients started on PF ocular lubricant	Prior PC use No. (%; 95% Cl)	No prior PC use No. (%; 95% Cl)
2015–16	3340	968 (29.0; 27.0, 309.9)	2,372 (71.0; 69.1, 73.0)
2018–19	5460	1368 (25.1; 23.5, 26.6)	4092 (74.9; 73.4, 76.5)

As expected, women made up the majority of patients who were started on a PF ocular lubricant in both study periods regardless of whether they had a record of a prior PC ocular lubricant prescription or not (Table 12). However, there were a significantly higher proportion of patients aged 45–64 years (and a correspondingly smaller proportion of patients aged 65+ years) who were started directly on a PF ocular lubricant in both study periods. Among patients who were started directly on a PF ocular lubricant the proportion of patients aged 45–64 year was 20%, compared with 10% among patients who had a record of a PC ocular lubricant prescription beforehand.

Patients living within major cities made up the greatest proportion of patients started on an ocular lubricant, regardless of whether they had a record of being prescribed a PC ocular lubricant beforehand or not. However, this merely reflects the larger number of eligible MedicineInsight patients who live within these areas (Appendix Table B1). There were no significant differences between prior use of PC ocular lubricants and SES status in either study period, nor were there any significant changes between study periods (Table 12).

	2015–16 (I	N = 3340)	2018–19 (N = 5460)		
Characteristic	Prior PC use	No prior PC use	Prior PC use No prior P			
	No. (%; 95% Cl)	No. (%; 95% Cl)	No. (%; 95% Cl)	No. (%; 95% Cl)		
		Sex				
Male	294	775	423	1,334		
	(30.4; 27.5, 33.3)	(32.7; 30.6, 34.7)	(30.9; 28.2, 33.6)	(32.6; 31.0, 34.2)		
Female	674	1597	945	2,758		
	(69.6; 66.7, 72.5)	(67.3; 65.3, 69.4)	(69.1; 66.4, 71.8)	(67.4; 65.8, 69.0)		
Age						
0–14 years	0	17 (0.7; 0.4, 1.1)	<5*	71 (1.7; 1.2, 2.2)		
15–44 years	14 (1.4; 0.6, 2.3)	147 (6.2; 5.0, 7.4)	<25*	334 (8.2; 6.9, 9.5)		

Table 12: Demographic distribution of regularly attending patients started on a preservative free ocular lubricant in 2015–16 and 2018–19, by prior prescription of preservative containing ocular lubricant (i.e. indirect and direct initiation)

	2015–16 (N = 3340)	2018–19	N = 5460)
Characteristic	Prior PC use	No prior PC use	Prior PC use	No prior PC use
	No. (%; 95% Cl)	No. (%; 95% Cl)	No. (%; 95% CI)	No. (%; 95% Cl)
45–64 years	93	468	138	810
	(9.6; 7.5, 11.7)	(19.7; 17.7, 21.7)	(10.1; 8.3, 11.9)	(19.8; 18.2, 21.4)
65+ years	861	1,740	1,209	2,877
	(88.9; 86.6, 91.3)	(73.4; 70.8, 75.9)	(88.4; 86.3, 90.5)	(70.3; 67.8, 72.8)
		Remoteness		
Major city	641	1461	867	2636
	(66.2; 56.5, 75.9)	(61.6; 53.3, 69.9)	(63.4; 54.8, 72.0)	(64.4; 57.2, 71.7)
Inner regional	245	671	360	981
	(25.3; 15.5, 35.1)	(28.3; 20.1, 36.5)	(26.3; 17.6, 35.0)	(24.0; 17.3, 30.7)
Outer regional	73	214	127	431
	(7.5; 4.5, 10.6)	(9.0; 5.8, 12.2)	(9.3; 5.6, 13.0)	(10.5; 6.8, 14.2)
Remote/very remote	9	26	14	44
	(0.9; 0.0, 1.8)	(1.1; 0.0, 2.2)	(1.0; 0.0, 2.2)	(1.1; 0.3, 1.8)
	Socioeconomic	status (SEIFA IRSAD	quintile)	
1 (most advantage)	169	441	237	716
	(17.5; 11.7, 23.2)	(18.6; 13.8, 23.4)	(17.3; 12.6, 22.1)	(17.5; 13.2, 21.8)
2	217	478	316	796
	(22.4; 16.9, 27.9)	(20.2; 15.5, 24.8)	(23.1; 17.6, 28.6)	(19.5; 14.9, 24.0)
3	239	527	331	946
	(24.7; 18.7, 30.6)	(22.2; 17.0, 27.4)	(24.2; 18.6, 29.8)	(23.1; 18.4, 27.9)
4	164	359	217	697
	(16.9; 12.7, 21.2)	(15.1; 11.9, 18.4)	(15.9; 11.9, 19.8)	(17.0; 13.4, 20.7)
5 (least advantage)	179	567	267	937
	(18.5; 13.5, 23.5)	(23.9; 18.4, 29.4)	(19.5; 14.7, 24.3)	(22.9; 18.0, 27.8)

*Exact cell numbers have been supressed (with complementary suppression of the adjoining cell) due to low counts

A number of medicine classes were identified in the TFOS DEWS II as being associated with a doubling of the risk of the development of dry eye syndrome and we assessed use of these medicine classes among regularly attending patients in the year prior to initiation of a PF ocular lubricant. A third of patients who were prescribed a PF ocular lubricant for the first time (regardless of prior PC ocular lubricant use) between January 2018 and December 2019, had been prescribed an antidepressant or antipsychotic in the previous year while approximately 10% had been prescribed an inhaled steroid or a benzodiazepine/anxiolytic (Table 12). While the nature of this study means we are unable to comment on causality, the proportion of patients prescribed these medicine classes was higher in the cohort of patients prescribed a PF ocular lubricant than among all regularly attending MedicineInsight patients.

Table 12: Selected medicine prescriptions recorded among regularly attendingMedicineInsight patients (at least 3 clinical encounters between January 2018 andDecember 2019) in the year prior to the date of initiation of a PF ocular lubricant

	Med prescribe	egularly attending icineInsight patients ed an PF ocular lubricant g 2018–19 (N = 5,460)	Regularly attending MedicineInsight patients during 2018–19 with at least one encounter prior to 2017* (N= 1,237,222)
Prescription recorded in the year prior to the date of PF ocular lubricant initiation (or in 2018 for the regular attenders (right-hand column))	No. % (95% CI)		% (95% CI)
Inhaled steroid	728	13.3 (12.2, 14.4)	7.5 (7.3, 7.7)
Benzodiazepine or anxiolytic	598	10.9 (10.0, 11.9)	5.0 (4.8, 5.2)
Antidepressant or antipsychotic	1,695	31.0 (29.5, 32.6)	18.2 (17.7, 18.8)

*To ensure to ensure at least a year of attendance at the practice

While 50.1% of all regularly attending patients prescribed an PF ocular lubricant for the first time in 2018–19 had a record of dry eyes, this proportion was higher among patients prescribed a PC ocular lubricant before starting a PF ocular lubricant (64.8%) than those directly initiated on PF ocular lubricant (45.1%; Table 13). This may be a true finding or it may be because patients with prior use of a PC ocular lubricant are more likely to have had their condition managed for a longer period than those who are directly started on PF lubricant. As such, this difference may be a reflection of this longer management and more complete record of their condition. Similar patterns were seen in 2015–16 and for all other numbers were too small to analyse.

Among patients newly started on a PF ocular lubricant, more than 70% of patients who had previously used a PC ocular lubricant, and more than half of the patients without prior PC ocular lubricant, had a record of at least one condition associated with development of dry eye syndrome (Table 13).

Table 13: Conditions recorded among regularly attending MedicineInsight patientsstarted on a preservative free ocular lubricant (with or without prior preservativecontaining ocular lubricant) in 2015–16 and 2018–19

	2015–16	N = 3340)	2018–19	N = 5460)
Characteristic	Prior PC use No. (%; 95% Cl)	No prior PC use No. (%; 95% Cl)	Prior PC use No. (%; 95% Cl)	No prior PC use No. (%; 95% Cl)
Dry eye	630 (65.1; 60.0, 70.1)	1,203 (50.7; 46.0, 55.4)	887 (64.8; 60.6, 69.0)	1,847 (45.1; 41.5, 48.8)
Autoimmune disease (Sjogren's disease, rheumatoid arthritis, lupus)	77 (8.0; 6.0, 9.9)	151 (6.4; 5.3, 7.4)	106 (7.7; 6.3, 9.2)	211 (5.2; 4.5, 5.9)
Blepharitis or Meibomian gland dysfunction	112 (11.6; 9.1, 14.0)	185 (7.8; 6.5, 9.1)	128 (9.4; 7.6, 11.1)	241 (5.9; 5.2, 6.6)
Facial palsy (including Bell's palsy)	21 (2.2; 1.3, 3.1)	52 (2.2; 1.5, 2.8)	31 (2.3; 1.5, 3.0)	59 (1.4; 1.1, 1.8)
Laser eye surgery or contact lens use	nr	nr	nr	nr
Any of the above conditions	690 (71.3; 66.8, 75.8)	1,375 (58.0; 53.8, 62.1)	964 (70.5; 66.9, 74.0)	2,099 (51.3; 48.0, 54.6)

nr: not reported due to small numbers

Coadministration

Very few of the 1.95 million regularly attending MedicineInsight patients between January 2018 and December 2019 were prescribed both a PC ocular lubricant and a PF ocular lubricant during 2019 (Table 12). Only 917 patients (0.05%) were prescribed both at least once during 2019. Even fewer patients (366 or 0.02%) were prescribed both on the same day at least once. Among those who were prescribed both a PC ocular lubricant and a PF ocular lubricant in the same year or on the same day, most were prescribed both types of ocular lubricants on the PBS.

Table 12: Regularly attending MedicineInsight patients (at least 3 clinical encounters
between January 2018 and December 2019) who have been prescribed both a PC ocular
lubricant and a PF ocular lubricant during calendar year 2019

		2019	2019 Same day		
Condition		% (95% CI)	N	% (95% CI)	
All PBS scripts	755	0.04 (0.03, 0.05)	296	0.02 (0.01, 0.02)	
All private scripts	9	0.00 (0.00, 0.00)	7	0.00 (0.00, 0.00)	
A mix of both PBS and private scripts	153	0.01 (0.01, 0.01)	63	0.00 (0.00, 0.00)	
Total	917	0.05 (0.04, 0.05)	366	0.02 (0.02, 0.02)	

Discussion

In 2019, there were 20,357 MedicineInsight patients (1.06% of all eligible patients) who were prescribed an ocular lubricant at least once during the year. This is a decrease from 2015 when 22,072 patients (1.31% of all eligible patients) were prescribed an ocular lubricant. Consistent with the patterns seen in the accompanying PBS analysis, the percentage of MedicineInsight patients prescribed a PC ocular lubricant has decreased (0.97% to 0.64% of all eligible patients) while the percentage of patients prescribed a PF ocular lubricant increased (0.40% to 0.47%).

Most MedicineInsight patients prescribed an ocular lubricant were females (55%) and males (27%) aged 65+ years.

There was little private prescribing of ocular lubricants among MedicineInsight patients, with over 92% prescribed under the PBS across all years. More than 90% of prescriptions for sodium hyaluronate were prescribed on the PBS rather than privately. As noted in the accompanying PBS analysis, many of these formulations can be purchased cheaply over the counter and so there would be no real benefit for non-concession card holding patients to get a prescription because the price of each formulation (\$14–37) is under the general patient co-payment.

This study did not find any evidence that prescribing of ocular lubricants varied by socioeconomic status. The majority of prescriptions were provided to patients from metropolitan areas, but this reflects the larger number of eligible MedicineInsight patients who live in these areas.

The prevalence of dry eye among all regularly attending MedicineInsight patients was estimated to be 2.2%. This suggests that between 416,907 and 526,620 Australians who visit their GP during a year will have dry eye. In the accompanying PBS report, approximately 400,000 unique patients were supplied an ocular lubricant on the PBS per calendar year.

Over the study period, the number of patients started on a PF ocular lubricant without any record of a prior PC ocular lubricant prescription has increased. Among regularly attending patients in 2015–16, 71.0% had no record of having been prescribed a PC ocular lubricant prior, and among regularly attending patients in 2018–19, 74.9% had no record of prior PC ocular lubricant use.

Dry eye was recorded in approximately half of the patients prescribed any ocular lubricant, a PC ocular lubricant, a PF ocular lubricant or sodium hyaluronate. A significantly larger proportion of patients prescribed a PF ocular lubricant had a record of an autoimmune diseases or blepharitis/Meibomian gland dysfunction than among patients prescribed a PC ocular lubricant.

Among patients newly started on a PF ocular lubricant, more than 70% of patients who had previously used a PC ocular lubricant, and more than half of the patients without prior PC ocular lubricant, had a record of at least one condition associated with development of dry eye syndrome. This may be because patients with a prior prescription of PC ocular

lubricants have been managed by their GP for a longer period and may have a more complete record of their condition.

Very few MedicineInsight patients (0.05%) were prescribed both a PC ocular lubricant and a PF ocular lubricant at least once during 2019.

Finally, as we did not search for all possible causes of dry eye syndrome, and do not search GP progress notes for privacy reasons, we may not have fully captured potential diagnoses and reasons that explain the prescribing of ocular lubricants in some patients.

DUSC consideration

DUSC considered the utilisation reports prepared by NPS MedicineWise using its MedicineInsight data and a 10% PBS sample. DUSC considered that the addition of MedicineInsight data to the reporting gave a useful perspective about patient management through primary care. DUSC noted the MedicineInsight sample did not identify patients in aged care facilities.

DUSC commented that both reports were comprehensive and noted that there was a large ocular lubricant market with a total of 54 listings on the PBS, and of those listings, 12 are preservative-free, multi-dose products.

DUSC noted:

- Its previous consideration of ocular lubricants in June 2014, where the total number of
 prescriptions had been steady for 10 years (to 2013) and expenditure across the whole group of
 ocular lubricants had been stable. In 2013, 85% of prescriptions were for multi-dose products,
 and that the prescription of single dose units had gradually increased from 6.7% in 2003, to 15%
 in 2013.
- That there is a large variance in the prevalence of dry eyes and there has been substantial growth in the use of PF ocular lubricants, with rising costs driven mainly by increased uptake of hyaluronate sodium.
- The multi-dose PF products were listed on the PBS at a higher price compared to PC products.
- There is a lack of clinical criteria for the diagnosis of severe dry eye disease and guidance for its treatment.
 - There is substantial ongoing growth in the market which may indicate that stricter restriction criteria is required.
- PBS criteria to access PF products is not being adhered to in a large proportion of patients.
 - Most patients who were initiated on a PF ocular lubricant were started directly on it without first using a PC ocular lubricant. This is despite the PBS authority listing requirement that a patient must be sensitive to preservatives in multi-dose eye drops to be eligible. This was observed in the MedicineInsight general practice data which also accounted for the use of over-the-counter products.
- There appears to be low levels of co-administration and switching between products.
 - While the number of patients started on a PC ocular lubricant has decreased year on year, the majority of patients who are started on this type of formulation are not switched to a PF listing in subsequent years. Fewer than 10% of patients started on a PC listing were switched to a PF listing in subsequent years.

 Once patients have been switched from a PC to a PF ocular lubricant, few are dispensed another PC listing as co-administration. DUSC noted that in the two years after a patient had been switched from a PC to a PF product, 1.9% or fewer patients had been prescribed another PC product.

DUSC Actions

DUSC requested that the report be provided to the PBAC for consideration.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

The sponsors' have no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date

when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

To the extent provided by law, DoH makes no warranties or representations as to accuracy or completeness of information contained in this report.

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Appendix A: Ocular lubricant history from 2012 onwards

Date	Drug	Detail
1 December 2012	Hyaluronic acid (Hylo-Forte)	PBS listing: 02171G, 02181T, 02184Y, 02253N
30 September 2013	Carbomer Eye gel 2 mg per g, 10 g NB: Geltears brand only	Delisting: GelTears brand only 08384G, 09210R
30 April 2014	Carbomer with triglyceride lipids: Eye gel 2 mg-10 mg per g, 10 g (Artelac)	Delisting: 02041K, 02044N, 02082N
30 September 2014	 Polyethylene glycol 400 (Blink Intensive Tears) Eye drops 2.5 mg per mL, 15 mL Eye drops 2.5 mg per mL, single dose units 0.4 mL, 20 Eye drops 2.5 mg per mL, 15 mL Eye drops 2.5 mg per mL, 15 mL Eye drops 2.5 mg per mL, single dose units 0.4 mL, 20 	Delisting: 05559N, 05560P, 09491M, 09492N, 09493P
31 March 2015	Polyvinyl alcohol Eye drops 30 mg per mL, 15 mL (Liquifilm Forte, PVA Forte)	Delisting: 05525T, 02681D, 09222J
30 April 2015	Carbomer with triglyceride lipids: Eye gel 2 mg-10 mg per g, single dose units 0.6 g, 30 (Artelac)	Delisting: 02058H, 02090B
31 March 2016	Carmellose with glycerin (Eye drops containing carmellose sodium 5 mg with glycerin 9 mg per mL, single dose units 0.4 mL, 30 (Optive)	Delisting: 05561Q, 09307W
1 September 2018	Perfluorohexyloctane (Novatears)	PBS listing: 11439C, 11446K
31 October 2018	 Carmellose (Theratears) Eye drops containing carmellose sodium 2.5 mg per mL, single dose units 0.6 mL, 24 Ocular lubricating gel containing carmellose sodium 10 mg per mL, single dose units 0.6 mL, 28 	Delisting: 05509Y, 05510B, 8823J, 8824K
1 March 2019	Hypromellose (Genteal, In a Wink Moisturising)	PBS listing: 1625W, 11634H, 11634H, 11643T
30 April 2019	 Polyvinyl alcohol Eye drops 14 mg per mL, 15 mL contains sodium chlorite/hydrogen peroxide as preservative (Vistil) 	Delisting: 05527X, 05528Y, 08831T, 08832W, 09221H, 09223K

Table A1: History of ocular lubricants on the PBS

	 Eye drops 30 mg per mL, 15 mL contains sodium chlorite/hydrogen peroxide as preservative (Vistil Forte) 	
31 July 2019	Hypromellose Eye drops 3 mg per mL, 15 mL (Genteal, In a Wink Moisturising)	Delisting: 05518K, 08287E, 09213X
1 December 2019	Evolve Hypromellose	PBS listing: 11842G, 11849P
1 December 2019	Evolve Carmellose (Evolve Carmellose)	PBS listing: 11852T ,11853W

Appendix B: Number of practice sites and practices in each calendar year

MedicineInsight extracts data from two general practice CISs – Best Practice (BP) and Medical Director (MD). Where multiple general practices share a CIS, this is a general practice site. A site may consist of several geographically and administratively distinct practices with discrete patient lists, or it may consist of a collection of practices with shared staff and patients. Patient electronic files from each general practice are amalgamated within the site's CIS, and it is not possible for MedicineInsight to distinguish within a site which general practice a specific patient's record comes from.

	2015	2016	2017	2018	2019
Number of practice sites	351	361	365	367	368
Number of individual practices	423	433	438	440	441

The number of practice sites and individual general practices is shown below.

Appendix C: Sociodemographics of eligible MedicineInsight patients

Characteristic	2015	2016	2017	2018	2019	Regular
	No.(%)	No. (%)	No. (%)	No. (%)	No. (%)	patients 2018–19* No. (%)
Total	1,679,478	1,834,712	1,927,310	1,960,694	1,917,114	1,947,094
			Sex			
Male	741,213	811,571	853,282	868,044	848,181	852,945
	(44.1)	(44.2)	(44.3)	(44.3)	(44.2)	(43.8)
Female	938,265	1,023,141	1,074,028	1,092,650	1,068,933	1,094,149
	(55.9)	(55.8)	(55.7)	(55.7)	(55.8)	(56.2)
			Age			
0–14 years	237,399	277,587	310,954	334,163	338,958	328,964
	(14.1)	(15.1)	(16.1)	(17.0)	(17.7)	(16.9)
15–44 years	598,036	667,994	708,936	723,662	699,267	713,547
	(35.6)	(36.4)	(36.8)	(36.9)	(36.5)	(36.6)
45–64 years	444,373	477,908	496,056	500,015	490,222	496,039
	(26.5)	(26.0)	(25.7)	(25.5)	(25.6)	(25.5)
65+ years	399,670	411,223	411,364	402,854	388,667	408,544
	(23.8)	(22.4)	(21.3)	(20.5)	(20.3)	(21.0)
			Age-sex			
Male 0–14	123,022	143,970	161,568	173,201	175,488	170,477
years	(16.6)	(17.7)	(18.9)	(20.0)	(20.7)	(20.0)
Male 15–44	242,669	270,614	285,634	289,313	278,249	276,792
years	(32.7)	(33.3)	(33.5)	(33.3)	(32.8)	(32.5)
Male 45–64	193,828	209,901	218,561	221,470	217,221	218,955
years	(26.2)	(25.9)	(25.6)	(25.5)	(25.6)	(25.7)
Male 65+	181,694	187,086	187,519	184,060	177,223	186,721
years	(24.5)	(23.1)	(22.0)	(21.2)	(20.9)	(21.9)
Female 0–14	114,377	133,617	149,386	160,962	163,470	158,487
years	(12.2)	(13.1)	(13.9)	(14.7)	(15.3)	(14.5)
Female 15–44	355,367	397,380	423,302	434,349	421,018	436,755
years	(37.9)	(38.8)	(39.4)	(39.8)	(39.4)	(39.9)
Female 45–64	250,545	268,007	277,495	278,545	273,001	277,084
years	(26.7)	(26.2)	(25.8)	(25.5)	(25.5)	(25.3)
Female 65+	217,976	224,137	223,845	218,794	211,444	221,823
years	(23.2)	(21.9)	(20.8)	(20.0)	(19.8)	(20.3)
		Aborigina	or Torres Strait	Islander		
Yes	45,135	51,908	56,089	58,965	57,844	59,579
	(2.7)	(2.8)	(2.9)	(3.0)	(3.0)	(3.1)

Table C1: Demographics of all eligible patients included in different study periods

Characteristic	2015	2016	2017	2018	2019	Regular
characteristic	No.(%)	No. (%)	No. (%)	No. (%)	No. (%)	patients
						2018–19*
						No. (%)
No	1,303,880	1,436,065	1,516,960	1,549,387	1,522,093	1,546,204
	(77.6)	(78.3)	(78.7)	(79.0)	(79.4)	(79.4)
Not recorded	330,463	346,739	354,261	352,342	337,177	341,311
	(19.7)	(18.9)	(18.4)	(18.0)	(17.6)	(17.5)
			Remoteness	1		
Major city	1,011,635	1,121,370	1,191,002	1,222,787	1,209,312	1,224,399
	(60.2)	(61.1)	(61.8)	(62.4)	(63.1)	(62.9)
Inner regional	433,714	460,685	474,974	474,382	457,301	466,146
	(25.8)	(25.1)	(24.6)	(24.2)	(23.9)	(23.9)
Outer regional	209,527	222,378	230,000	233,240	222,526	227,808
	(12.5)	(12.1)	(11.9)	(11.9)	(11.6)	(11.7)
Remote/very	24,483	30,147	31,219	30,162	27,840	28,597 (1.5)
remote	(1.5)	(1.6)	(1.6)	(1.5)	(1.5)	
Missing	119	132	115	123	135	144
	S	Socioeconomic	status (SEIFA IR	SAD quintile)		
1 (most	290,411	311,339	325,070	324,718	314,653	322,463
advantage)	(17.3)	(17.0)	(16.9)	(16.6)	(16.4)	(16.6)
2	345,419	368,949	382,282	383,649	374,593	378,209
	(20.6)	(20.1)	(19.8)	(19.6)	(19.5)	(19.4)
3	356,705	399,773	422,720	433,271	426,601	433,356
	(21.2)	(21.8)	(21.9)	(22.1)	(22.3)	(22.3)
4	315,334	351,224	371,287	383,501	375,225	382,149
	(18.8)	(19.1)	(19.3)	(19.6)	(19.6)	(19.6)
5 (least	371,490	403,295	425,836	435,432	425,907	430,773
advantage)	(22.1)	(22.0)	(22.1)	(22.2)	(22.2)	(22.1)
Missing	119	132	115	123	135	144
			l Almainht musatian l	-		1

* Patients with at least three visits at a MedicineInsight practice between 1 January 2018 and 31 December 2019 (regularly attending patients).

Table C2: Demographics of patients with a record of at least one prescription of any ocular lubricants by calendar year

Characteristic	2015 No.	2016 No.	2017 No.	2018 No.	2019 No.			
	% (95% CI)							
Total	22,072	20,802	20,426	20,108	20,357			
	Sex							
Male	7106 32.2 (31.3, 33.1)	6803 32.7 (31.8, 33.6)	6796 33.3 (32.4, 34.2)	6728 33.5 (32.5, 34.4)	6825 33.5 (32.6, 34.4)			

Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% CI)				
Female	14,966	13,999	13,630	13,380	13,532
	67.8	67.3	66.7	66.5	66.5
	(66.9 <i>,</i> 68.7)	(66.4, 68.2)	(65.8, 67.6)	(65.6, 67.5)	(65.6, 67.4)
		A	ge		
0–14 years	120 0.5 (0.4, 0.7)	117 0.6 (0.4, 0.7)	136 0.7 (0.5, 0.8)	147 0.7 (0.6, 0.9)	169 0.8 (0.6, 1.0)
15–44 years	850 3.9 (3.3, 4.4)	847 4.1 (3.4, 4.7)	907 4.4 (3.8, 5.1)	998 5.0 (4.3, 5.6)	1,039 5.1 (4.5, 5.7)
45–64 years	2192 9.9 (9.1, 10.8)	2168 10.4 (9.6, 11.3)	2224 10.9 (10.0, 11.8)	2393 11.9 (10.9, 12.9)	2677 13.2 (12.1, 14.2)
65+ years	18,910 85.7 (84.3, 87.0)	17,670 84.9 (83.5, 86.4)	17,159 84.0 (82.5, 85.5)	16,570 82.4 (80.8, 84.0)	16,472 80.9 (79.3, 82.6)
	(0.10) 0.10)	(colo) coll.) Age	· · ·	(0010) 0 110)	(1010) 0210)
Male 0–14	77	69	78	93	105
years	0.3 (0.2, 0.5)	0.3 (0.3, 0.4)	0.4 (0.3, 0.5)	0.5 (0.3, 0.6)	0.5 (0.4, 0.6)
Male 15–44 years	304 1.4 (1.1, 1.6)	342 1.6 (1.6, 1.9)	339 1.7 (1.4, 2.0)	373 1.9 (1.5, 2.2)	391 1.9 (1.6, 2.2)
Male 45–64 years	718 3.3 (2.9, 3.6)	727 3.5 (3.5, 3.9)	768 3.8 (3.3, 4.2)	831 4.1 (3.7, 4.5)	888 4.4 (3.9, 4.8)
Male 65+ years	6007 27.2	5665 27.2	5611 27.5	5431 27.0	5441 26.7 (25.8, 27.7)
	(26.4, 28.0)	(27.2, 28.1)	(26.5, 28.4)	(26.0, 28.0)	
Female 0–14 years	43 0.2 (0.1, 0.3)	48 0.2 (0.2, 0.3)	58 0.3 (0.2, 0.4)	54 0.3 (0.2, 0.4)	64 0.3 (0.2, 0.4)
Female 15–44 years	546 2.5 (2.1, 2.8)	505 2.4 (2.4, 2.8)	568 2.8 (2.4, 3.2)	625 3.1 (2.7, 3.5)	648 3.2 (2.8, 3.6)
Female 45–64 years	1,474 6.7 (6.1, 7.3)	1441 6.9 (6.9, 7.5)	1,456 7.1 (6.5, 7.7)	1,562 7.8 (7.1, 8.5)	1,789 8.8 (8.0, 9.6)
Female 65+ years	12,903 58.5	12,005 57.7	11,548 56.5	11,139 55.4	11,031 54.2
	(57.1, 59.8)	(57.7, 59.1)	(55.2, 57.9)	(54.0, 56.8)	(52.8, 55.6)
		Aboriginal or Tor	res Strait Islander		
Yes	271 1.2 (1.0, 1.5)	261 1.3 (0.9, 1.6)	284 1.4 (1.0, 1.7)	275 1.4 (1.0, 1.7)	358 1.8 (1.3, 2.2)
No	18,155 82.3	17,412 83.7 (81.0, 86.4)	17,191 84.2	16,976 84.4	17,320 85.1
	(79.4, 85.1)	(81.0, 86.4)	(81.5, 86.8)	(81.8, 87.1)	(82.6, 87.6)

Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Not recorded	3,646	3,129	2,951	2,857	2,679
	16.5	15.0	14.4	14.2	13.2
	(13.6, 19.4)	(12.3, 17.8)	(11.8, 17.1)	(11.6, 16.8)	(10.7, 15.6)
		Remo	teness		
Major city	13,709	13,079	12,869	12,741	13,032
	62.1	62.9	63.0	63.4	64.0
	(54.7, 69.5)	(55.7, 70.0)	(55.9, 70.1)	(56.2, 70.5)	(57.2, 70.9)
Inner regional	5,891	5,460	5,420	5,206	5,109
	26.7	26.2	26.5	25.9	25.1
	(19.6, 33.8)	(19.4, 33.1)	(19.6, 33.4)	(18.9, 32.9)	(18.5, 31.7)
Outer regional	2,305	2,101	1,977	1,982	2,035
	10.4 (7.1, 13.8)	10.1 (6.9, 13.3)	9.7 (6.6, 12.7)	9.9 (6.8, 12.9)	10.0 (6.9, 13.1)
Remote/very	167	162	160	179	180
remote	0.8 (0.2, 1.3)	0.8 (0.3, 1.3)	0.8 (0.3, 1.3)	0.9 (0.3 <i>,</i> 1.5)	0.9 (0.3, 1.5)
	Soci	oeconomic status	(SEIFA IRSAD quin	tile)	
1 (most	4,400	4,200	4,074	3,873	3,918
advantage)	19.9	20.2	19.9	19.3	19.2
	(15.0, 24.9)	(15.4, 25.0)	(15.3, 24.6)	(14.7, 23.8)	(14.9, 23.6)
2	4,738	4,357	4,385	4,087	4,186
	21.5	20.9	21.5	20.3	20.6
	(17.4, 25.5)	(17.0, 24.8)	(17.5, 25.5)	(16.3, 24.3)	(16.5, 24.6)
3	4,892	4,657	4,549	4,649	4,758
	22.2	22.4	22.3	23.1	23.4
	(17.6, 26.8)	(17.9, 26.9)	(17.8, 26.7)	(18.7, 27.6)	(19.0, 27.7)
4	3,499	3,405	3,330	3,497	3,472
	15.9	16.4	16.3	17.4	17.1
	(12.9, 18.8)	(13.4, 19.4)	(13.3, 19.3)	(14.2, 20.6)	(13.9, 20.3)
5 (least	4,543	4,183	4,088	4,002	4,022
advantage)	20.6	20.1	20.0	19.9	19.8
	(16.2, 25.0)	(15.9, 24.3)	(15.8, 24.2)	(15.9, 23.9)	(15.5, 23.7)

Table C3: Patient-demographic-specific prevalence of at least one record of prescription of any preservative free (PF) ocular lubricant in each calendar year, in each yearly patient cohort

Characteristic	2015 No. % (95% CI)	2016 No. % (95% CI)	2017 No. % (95% Cl)	2018 No. % (95% CI)	2019 No. % (95% Cl)
Total	6718	7051	7481	7907	8965
		Se	x		
Female	4880;	5082;	5355;	5644;	6448;
	0.5 (0.4, 0.6)	0.5 (0.4, 0.6)	0.5 (0.4, 0.6)	0.5 (0.4, 0.6)	0.6 (0.5, 0.7)
Male	1838;	1969;	2126;	2263;	2517;
	0.2 (0.2, 0.3)	0.2 (0.2, 0.3)	0.2 (0.2, 0.3)	0.3 (0.2, 0.3)	0.3 (0.3, 0.3)
		Ag	ge		
0–14 years	27; 0.0 (0.0, 0.0)	30; 0.0 (0.0, 0.0)	35; 0.0 (0.0, 0.0)	54 0.0 (0.0, 0.0)	65; 0.0 (0.0, 0.0)
15–44 years	234;	278;	322;	354;	402;
	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)
45–64 years	701;	778;	860;	955;	1174;
	0.2 (0.1, 0.2)	0.2 (0.1, 0.2)	0.2 (0.2, 0.2)	0.2 (0.2, 0.2)	0.2 (0.2, 0.3)
65+ years	5756; 1.4 (1.3 <i>,</i> 1.6)	5965; 1.5 (1.3, 1.6)	6264; 1.5 (1.4, 1.7)	6544; 1.6 (1.5, 1.8)	7324; 1.9 (1.7 <i>,</i> 2.0)
		Aboriginal or Torr	es Strait Islander		
Yes	69;	72;	89;	79;	130;
	0.2 (0.1, 0.2)	0.1 (0.1, 0.2)	0.2 (0.1, 0.2)	0.1 (0.1, 0.2)	0.2 (0.2, 0.3)
No	5653;	6043;	6445;	6855;	7776;
	0.4 (0.4, 0.5)	0.4 (0.4, 0.5)	0.4 (0.4, 0.5)	0.4 (0.4, 0.5)	0.5 (0.4, 0.6)
Not recorded	996;	936;	947;	973;	1059;
	0.3 (0.3, 0.3)	0.3 (0.2, 0.3)	0.3 (0.2, 0.3)	0.3 (0.2, 0.3)	0.3 (0.3, 0.4)
	1	Remot	eness		
Major city	4051; 0.4 (0.4, 0.4)	4354; 0.4 (0.3, 0.4)	4588; 0.4 (0.3, 0.4)	4947; 0.4 (0.4, 0.5)	5755; 0.5 (0.4, 0.5)
Inner regional	2012; 0.5 (0.3, 0.6)	2053; 0.4 (0.3, 0.6)	2160; 0.5 (0.3, 0.6)	2203; 0.5 (0.3, 0.6)	2335; 0.5 (0.3, 0.7)
Outer regional	618;	602;	688;	700;	805;
	0.3 (0.2, 0.4)	0.3 (0.2, 0.3)	0.3 (0.3, 0.3)	0.3 (0.3, 0.3)	0.4 (0.3, 0.4)
Remote/very	37;	42;	45;	57;	69;
remote	0.2 (0.0, 0.3)	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)	0.2 (0.1, 0.3)	0.2 (0.1, 0.4)
	So	cioeconomic status ((SEIFA IRSAD quintil	e)	
1 (most	1307;	1336;	1528;	1417;	1552;
advantage)	0.5 (0.3, 0.6)	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	0.5 (0.4, 0.6)
2	1412;	1394;	1738;	1558;	1791;
	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	0.5 (0.4, 0.6)

Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% Cl)	% (95% Cl)	% (95% Cl)	% (95% Cl)	% (95% CI)
3	1515;	1637;	1227;	1825;	2100;
	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	0.3 (0.3, 0.4)	0.4 (0.3, 0.5)	0.5 (0.4, 0.6)
4	1047;	1164;	1594;	1377;	1541;
	0.3 (0.3, 0.4)	0.3 (0.3, 0.4)	0.4 (0.3, 0.4)	0.4 (0.3, 0.4)	0.4 (0.3, 0.5)
5 (least	1437;	1520;	1528;	1730;	1980;
advantage)	0.4 (0.3, 0.4)	0.4 (0.3, 0.4)	0.4 (0.3, 0.5)	0.4 (0.3, 0.4)	0.5 (0.4, 0.5)

Table C4: Patient-demographic-specific prevalence of at least one record of prescription of any preservative containing (PC) ocular lubricant in each calendar year, in each yearly patient cohort

Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Total	16,310	14,659	13,851	13,007	12,309
		Se	ex		
Female	10,767;	9581;	8925;	8309;	7769;
	1.1 (1.0, 1.3)	0.9 (0.8, 1.1)	0.8 (0.7, 0.9)	0.8 (0.7, 0.8)	0.7 (0.6, 0.8)
Male	5543;	5078;	4926;	4698;	4540;
	0.7 (0.7, 0.8)	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)	0.5 (0.5, 0.6)	0.5 (0.5, 0.6)
		A	ge		
0–14 years	94;	89;	101;	95;	105;
	0.0 (0.0, 0.1)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
15–44 years	631;	586;	600;	661;	653;
	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)
45–64 years	1577;	1462;	1438;	1495;	1594;
	0.4 (0.3, 0.4)	0.3 (0.3, 0.3)	0.3 (0.3, 0.3)	0.3 (0.3, 0.3)	0.3 (0.3, 0.4)
65+ years	14,008;	12,522;	11,712;	10,756;	9957;
	3.5 (3.3, 3.7)	3.0 (2.8, 3.2)	2.8 (2.6, 3.0)	2.7 (2.5, 2.9)	2.6 (2.4, 2.7)
		Aboriginal or Tor	res Strait Islander		
Yes	208;	201;	209;	211;	241;
	0.5 (0.4, 0.6)	0.4 (0.3, 0.5)	0.4 (0.3, 0.4)	0.4 (0.3, 0.4)	0.4 (0.3, 0.5)
No	13,301;	12,141;	11,509;	10,812;	10,333;
	1.0 (0.9, 1.2)	0.8 (0.7, 1.0)	0.8 (0.7, 0.9)	0.7 (0.6, 0.8)	0.7 (0.6, 0.8)
Not recorded	2801;	2317;	2133;	1984;	1735;
	0.8 (0.7, 1.0)	0.7 (0.6, 0.8)	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)	0.5 (0.4, 0.6)
		Remo	teness		
Major city	10,236;	9304;	8826;	8305;	7819;
	1.0 (0.9, 1.1)	0.8 (0.7, 0.9)	0.7 (0.7, 0.8)	0.7 (0.6, 0.8)	0.6 (0.6, 0.7)

Characteristic	2015	2016	2017	2018	2019
	No.	No.	No.	No.	No.
	% (95% CI)				
Inner regional	4165;	3660;	3,537;	3233;	3060;
	1.0 (0.7, 1.3)	0.8 (0.6, 1.0)	0.7 (0.5, 1.0)	0.7 (0.5, 0.9)	0.7 (0.5, 0.8)
Outer regional	1777;	1568;	1368;	1342;	1313;
	0.8 (0.7, 1.0)	0.7 (0.6, 0.8)	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)
Remote/very	132;	127;	120;	127;	117;
remote	0.5 (0.2, 0.8)	0.4 (0.2, 0.6)	0.4 (0.2, 0.5)	0.4 (0.2, 0.6)	0.4 (0.3, 0.6)
Socioeconomic status (SEIFA IRSAD quintile)					
1 (most	3287;	3037;	2844;	2600;	2512;
advantage)	1.1 (0.9, 1.4)	1.0 (0.8, 1.2)	0.9 (0.7, 1.1)	0.8 (0.6, 1.0)	0.8 (0.6, 1.0)
2	3541;	3141;	3059;	2703;	2606;
	1.0 (0.8, 1.2)	0.9 (0.7, 1.0)	0.8 (0.6, 1.0)	0.7 (0.6, 0.8)	0.7 (0.6, 0.8)
3	3601;	3235;	3031;	3005;	2878;
	1.0 (0.8, 1.2)	0.8 (0.7, 0.9)	0.7 (0.6, 0.8)	0.7 (0.6, 0.8)	0.7 (0.6, 0.8)
4	2587;	2389;	2247;	2266;	2087;
	0.8 (0.7, 1.0)	0.7 (0.6, 0.8)	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)
5 (least	3294;	2857;	2670;	2433;	2226;
advantage)	0.9 (0.8, 1.0)	0.7 (0.6, 0.8)	0.6 (0.5, 0.7)	0.6 (0.5, 0.6)	0.5 (0.5, 0.6)