

The future is old – Patients with topical ocular hypotensive treatment in the Nordic region between 2008 and 2017 with projections for 2040

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ABSTRACT.

Purpose: The primary objective was to evaluate prescribing trends for topical ocular hypotensive treatment in the Nordic region during the last decade and, by population projections, estimate the glaucoma burden in 2040. A secondary objective was to analyse national variations in prescription patterns across the Nordic region.

Methods: A retrospective analysis of national pharmacy data between 2008 and 2017 on the dispensation of topical ocular hypotensive treatment in the Nordic region was performed. Predictions of the glaucoma burden in 2040 were calculated from official population projections.

Results: The total number of patients with ocular hypotensive treatment in the Nordic region increased from 346 000 to 418 000 (21%) between 2008 and 2017. The number of patients with ocular hypotensive treatment in the age group of 50 years and older increased from 3.6% to 3.9%. The daily defined dose (DDD) per patient and day during the study period increased from 1.22 to 1.26. Adjusted for beta-blocker combinations, the same value increased from 1.49 to 1.67. Across the Nordic countries, Finland had almost twice as many DDD per patient and day in 2017 (2.1) compared with Iceland (1.1). Between 2008 and 2017, the annual treatment cost for ocular hypotensive treatment in the Nordic region decreased from 96 million to 87 million Euro (−9%). In 2040, the number of patients with ocular hypotensive treatment in the Nordic region is estimated to 633 000 individuals (+51% compared with 2017).

Conclusions: The study revealed an increased use of glaucoma medications in the Nordic region the last decade. This was mainly caused by an increased number of patients with ocular hypotensive treatment, but also because of a more intensive treatment. Marked national differences were detected. Due to the introduction of generic medications, the total cost for ocular hypotensive treatment did however decrease during the last decade. In 2040, the current number of individuals with ocular hypotensive treatment is estimated to have increased with an additional 50% due to a growing number of ageing individuals. This will lead to higher costs, not only for medications but also for diagnosing, monitoring and other aspects of glaucoma care.

Key words: clinical practice patterns – costs and cost analysis – drug consumption – drug prescriptions – forecasting – glaucoma – ocular hypertension – prevalence

Introduction

Glaucoma is the global leading cause of irreversible blindness (World Health Organization 2017). In 2013, the estimated worldwide prevalence of the most common form, primary open-angle glaucoma (POAG), was over 3% of the population aged 40 to 80 years. As ageing is one of the major risk factors for the disease, the prevalence will increase in an ageing society and is estimated to affect 112 million people in 2040 compared with 76 million in 2020 (Tham et al. 2014). Lowering of intraocular pressure (IOP) is the only treatment proven to slow down glaucoma deterioration (Heijl et al. 2002; Garway-Heath et al. 2015). The most common treatment is ocular hypotensive medications.

Several studies have shown a steady growth in the usage of glaucoma medications during the last decades with a corresponding increase in total cost (Knox et al. 2006; Macleod et al. 2008; Connor & Fraser 2014; Heng et al. 2016). The increase in prescriptions might have several causes. It may be explained by an increase in the detection of glaucoma, for example by optician screening, and a change in clinical practice to more frequent treatment of ocular hypertension. In the face of expanding treatment options, it may also be explained by a tendency to strive for even better control of IOP. The main reason in many countries is however an increase in the number of

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glaucoma patients due to a rising life expectancy (Tuck & Crick 2003).

Besides an increase in dispensed IOP-lowering medications, the choice of ophthalmic solutions has also grown in the last decade with a simultaneous increase of the proportion of combination drugs (Kolko et al. 2015). However, even if the number of prescribed items has increased the last 10 years, the total costs has decreased due to generic latanoprost that was introduced in 2011–2012 (Hogg & Connor 2020).

In order to make policies and plans for future eye care services, information is needed on the current as well as estimates for tomorrow's prevalence of glaucoma. The purpose of this study was to explore prescribing trends for topical ocular hypotensive treatment in the Nordic region during the last decade to evaluate the number of treated patients, prescribed ophthalmic solutions and costs. From population projections, these data were used to estimate the glaucoma burden in 2040. A secondary objective was to analyse national variations in the prescription across the Nordic countries.

Method

Between 2008 and 2017, the total number of ocular hypotensive eye drops dispensed from pharmacies was obtained for all the Nordic countries, that is Denmark, Finland, Iceland, Norway and Sweden. For inclusion in the study, subjects have to have at least one dispensation of ocular hypotensive eye drops per given year. Data records were available at the governmental web pages, and additional information was requested from the authorities when needed (Danish Health Data Authority; Icelandic Medicines Agency; National Board of Health and Welfare; Norwegian Institute of Public Health; The Social Insurance Institution of Finland).

In national prescription databases, drugs are classified according to WHO's Anatomical Therapeutic Chemical (ATC) system. The term daily defined dose (DDD) is used, which is defined as the commonly everyday prescribed dose of the drug in question. A fixed dose regardless of strength has been established for all different types of ocular IOP-lowering medications. This also applies for combination drugs. For

eye drops administered once daily, the DDD is 0.1 ml; for eye drops administered twice daily, the DDD is 0.2 ml. For single-use packages, one dose is the volume of one package (WHO Collaborating Centre for Drug Statistics Methodology 2018).

The following information was extracted and analysed from the Nordic prescription databases: DDD for ocular hypotensive treatment (ATC code: S01E), drug cost and number of unique patients categorized in five-year age groups, and the highest being subjects of 85 years or older. The data were also separated in subgroups of glaucoma drugs: S01ED = β -blockers, S01EE = prostaglandin analogues (PGA), S01EC = carbonic anhydrase inhibitors, S01EA = α 2-adrenergic agonists, S01EB = parasympathomimetics and S01ED51 = fixed combination drugs with β -blockers. For comparison of costs, all prices were converted to Euro according to the annual average exchange rates for each year (Sveriges Riksbank 2019). All prices were analysed without value added tax (VAT). As the DDD does not consider combination medications, adjustments were made where one DDD of beta-blocker combinations was counted as two DDDs.

All Nordic countries publish population projections to estimate future demands. These are based on assumptions regarding childbearing, mortality rates, immigration and emigration. Migration is the most difficult factor to forecast, both in a short and a long perspective (Statistics Sweden 2018). Population data and future population projections were obtained from the national statistics offices (Statistics Denmark; Statistics Finland; Statistics Iceland; Statistics Norway; Statistics Sweden). The projections were organized in the same way as in the prescription databases. In the projection of glaucoma burden in 2040, the number of DDD per patient, cost per DDD, exchange rates and the proportion of patients in each age group were assumed to remain on the same levels as in 2017.

As our study looked at the whole population of interest, it was not meaningful to perform tests of significance. These methods are instead used to draw conclusions about the generalizability of a sample. All detected changes were therefore real population

changes, and no statistical analysis was required to test their significance.

The current study used anonymized information freely available in the public domain, and no ethical approval was therefore required.

Results

Dispensations in the population

Between 2008 and 2017, the frequency of dispensed topical ocular hypotensive treatment in the Nordic region increased from 17 to 19 DDD/1000 inhabitants per day (Table 1). Adjusted for beta-blocker combinations, the figure increased further, from 21 to 35. Considerable differences were seen between the countries as Finland had an increase from 21 to 25 DDD/1000 inhabitants per day (adjusted for beta-blocker combinations) while the other countries showed only minor changes (Fig. 1).

Prevalence

Between 2008 and 2017, the total number of patients with topical ocular hypotensive treatment in the Nordic region increased from 346 000 to 418 000 (21%). The share of patients with topical ocular hypotensive treatment of among the population over 50 years increased from 3.6% to 3.9% during this time period (Table 1). Differences were detected between the countries with around 14% of individuals 80 years or older in Sweden and Iceland being treated with ocular hypotensive drops compared with 8% in Denmark. Patients with topical ocular hypotensive treatment below an age of 65 years were uncommon in all countries (Fig. 2).

Dispensations per patient

The DDD of ocular hypotensive eye drops per patient and day during the study period increased from 1.22 to 1.26. Adjusted for beta-blocker combinations, the same value climbed from 1.49 to 1.67 (Table 1). During this time period, the proportion of beta-blocker combinations increased from 21% to 30%. PGA was the most common monotherapy in all countries 2017. National variations were seen, as beta-blocker combinations consisted of nearly half of all the dispensations in

Table 1. Topical ocular hypotensive treatment in the Nordic region from 2008 to 2017 with estimations for 2040 based on population projections.

Region	Denmark			Finland Finland			Iceland			Norway			Sweden			Nordic Region		
Year	2008	2017	2040	2008	2017	2040	2008	2017	2040	2008	2017	2040	2008	2017	2040	2008	2017	2040
Total population (millions)	5.5	5.8	6.2	5.3	5.5	5.5	0.3	0.3	0.3	4.8	5.3	6.1	9.2	10.1	11.5	25.1	27.0	29.8
Patients with ocular hypotensive therapy (thousands)	55	72	118	74	93	135	5	5	10	68	76	121	144	172	249	346	418	633
Proportion of population with ocular hypotensive treatment (%)	1.0	1.3	1.9	1.4	1.7	2.4	1.5	1.5	2.5	1.4	1.4	2.0	1.6	1.7	2.2	1.4	1.6	2.1
>=50 years of age (%)	2.6	3.0	4.4	3.4	3.9	5.1	5.1	4.8	6.0	4.0	3.8	4.7	4.1	4.3	5.2	3.6	3.9	4.9
50–64 years of age (%)	1.1	1.1	1.2	1.1	1.2	1.2	1.7	1.7	1.7	1.3	1.2	1.2	1.5	1.7	1.1	1.3	1.3	1.4
65–79 years of age (%)	3.5	4.1	3.7	4.9	4.7	5.2	8.4	7	7.5	5.5	4.9	5.2	4.9	5.1	5.4	6.7	4.8	4.9
>= 80 years of age (%)	7.8	8.1	11.1	10.3	11.5	11.8	14.5	14.3	14.3	11.6	11.5	11.4	13.5	13.9	14.1	11.4	11.8	12.4
DDD/1000 inhabitants/day	11	13	17	16	25	36	14	13	22	19	18	25	20	21	27	17	19	26
Adjusted for beta-blocker combinations	13	17	22	21	35	51	15	17	29	23	23	32	24	28	35	21	26	35
DDD/patients with ocular hypotensive therapy/day	1.1	1.0	1.0	1.2	1.5	1.5	0.9	0.9	0.9	1.3	1.2	1.2	1.2	1.2	1.3	1.2	1.3	1.3
Adjusted for beta-blocker combinations	1.3	1.4	1.4	1.5	2.1	2.1	1.0	1.1	1.1	1.6	1.6	1.6	1.5	1.6	1.6	1.5	1.7	1.7
Cost (million Euro)	14	10	17	24	23	33	1	1	2	21	16	26	36	36	52	96	87	131
Per million inhabitants	2.5	1.8	2.8	4.5	4.1	6.0	4.7	3.7	7.0	4.3	3.0	4.2	4.0	3.6	4.5	3.8	3.2	4.4

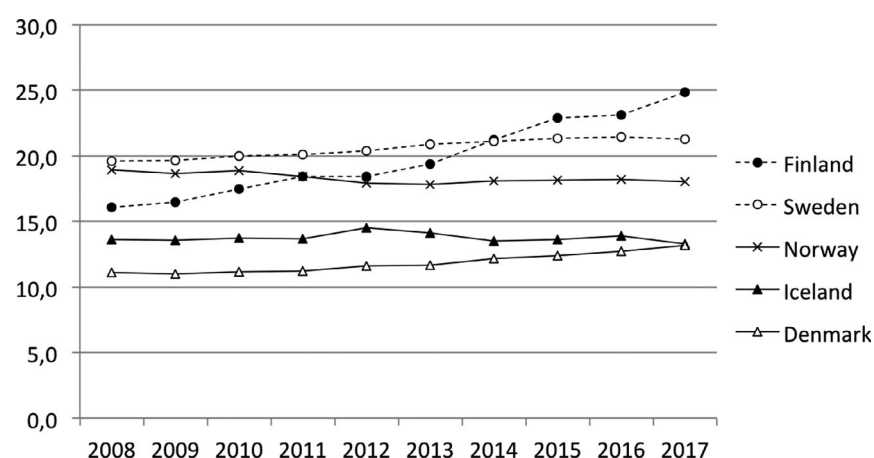


Fig. 1. Sales of topical ocular hypotensive drugs in the different Nordic countries from 2008 to 2017 as number of daily defined doses (DDD)/1000 inhabitants/day adjusted for beta-blocker combinations.

Finland, while in Norway beta-blocker monotherapy was almost as common as combination therapy (Fig. 3). Finland

had almost twice as many DDD per patient and day in 2017 (2.1) compared with Iceland (1.1) (Table 1).

Costs

Between 2008 and 2017, in the Nordic region, the annual treatment cost for glaucoma medications decreased from 96 to 87 million Euro (–9%) (Table 1). From approximately 2012, a decrease of the annual cost per patient was seen in all countries (Fig. 4).

Future predictions

According to the national population projects, between 2017 and 2040, the population in the Nordic region will expand from 27.0 to 29.8 million inhabitants. The proportion of the elderly population between 65 and 79 years of age will increase from 15% to 17%, while the very elderly population over 80 years of age will increase from 5% to 8%. Assuming that the proportion of the population with glaucoma

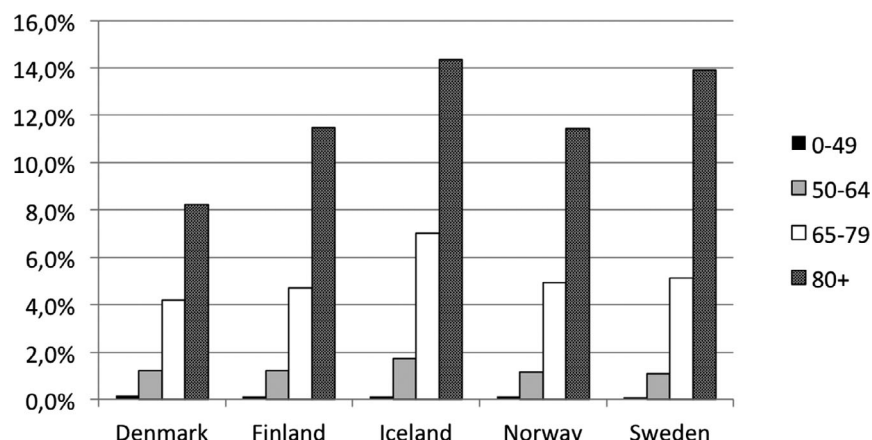


Fig. 2. Proportions of the population on topical ocular hypotensive treatment in the Nordic countries in 2017 by specified age groups.

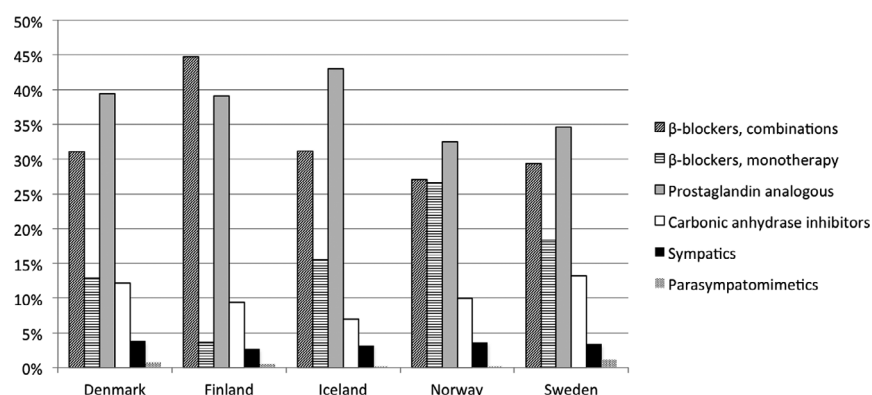


Fig. 3. Daily defined doses per day and patient for dispensed topical ocular hypotensive medications in the Nordic countries in 2017 by class of ocular hypotensive treatment.

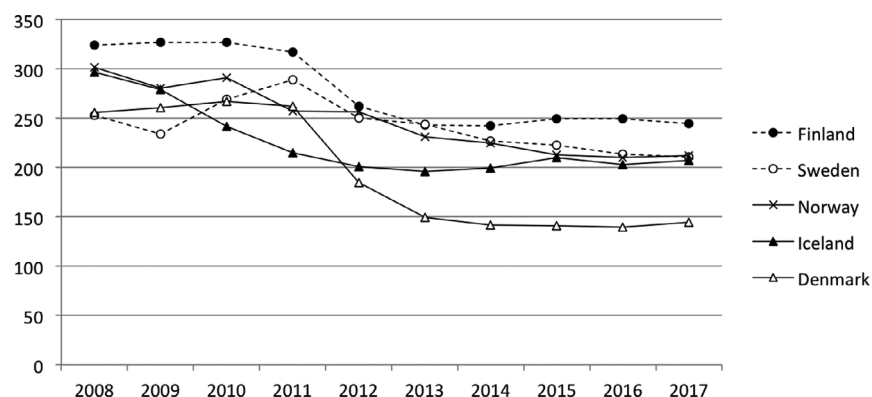


Fig. 4. Annual cost (Euro) per patient with topical ocular hypotensive treatment in the Nordic countries between 2008 and 2017.

treatment within the specified 5-year age categories will remain similar as in 2017, the number of patients with topical ocular hypotensive treatment is estimated to be 633 000 in 2040 (Table 1, Fig. 5). This is an increase of 51%

compared with 2017. Using the same calculation, the yearly cost for ocular hypotensive treatment in the Nordic region is estimated to increase from 87 million Euro in 2017 to 131 million Euro in 2040 (Table 1).

Discussion

This study on trends in dispensation of glaucoma medications in the Nordic region during the last decade revealed an increase in medications in the population from 17 to 21 DDD/1000 inhabitants ($\approx 17\%$). This was mainly caused by an increased number of patients with topical ocular hypotensive treatment from 14 to 16 patients/1000 inhabitants ($\approx 13\%$), but also due to more medications per treated patient from 1.2 to 1.3 DDD/patients ($\approx 4\%$). Based on population projections, in 2040, the increase in the number of patients with topical ocular hypotensive treatment in the Nordic region is estimated to over 50%.

In this study, we found PGA as the most common monotherapy. This is consistent with recommendations in Europe, where treatment is initiated with monotherapy such as PGA followed by combination therapies in cases where the target IOP is not reached (EGS 2017). As shown in previous studies, the proportion of dispensed combination drugs for glaucoma has increased (Kolko et al. 2015). However, the proportion of beta-blocker combinations in the Nordic region of 30%, it is still lower than the 55% reported in English health care (Hogg & Connor 2020).

Even though the total number of DDD increased between 2008 and 2017, the total cost of glaucoma medications in the Nordic region decreased by 9% (Fig. 4). The decrease is likely caused by the increase in the number of generic IOP-lowering eye drops, mainly by the introduction of latanoprost eye drops around 2012. This has considerably lowered the cost for PGAs, and the conclusion is consistent with previous research in other regions (Heng et al. 2016).

Our result of a 51% increase of the number of glaucoma patients between 2017 and 2040 conforms well to the global estimates of a 49% increase between 2020 and 2040 (Tham et al. 2014). Worldwide, some regions will be affected more than others, as the change in the number of elderly subjects is likely to increase more substantially in Asia and Africa compared with Europe and North America.

Consistent with our results, earlier studies of glaucoma medication sales statistics have shown large

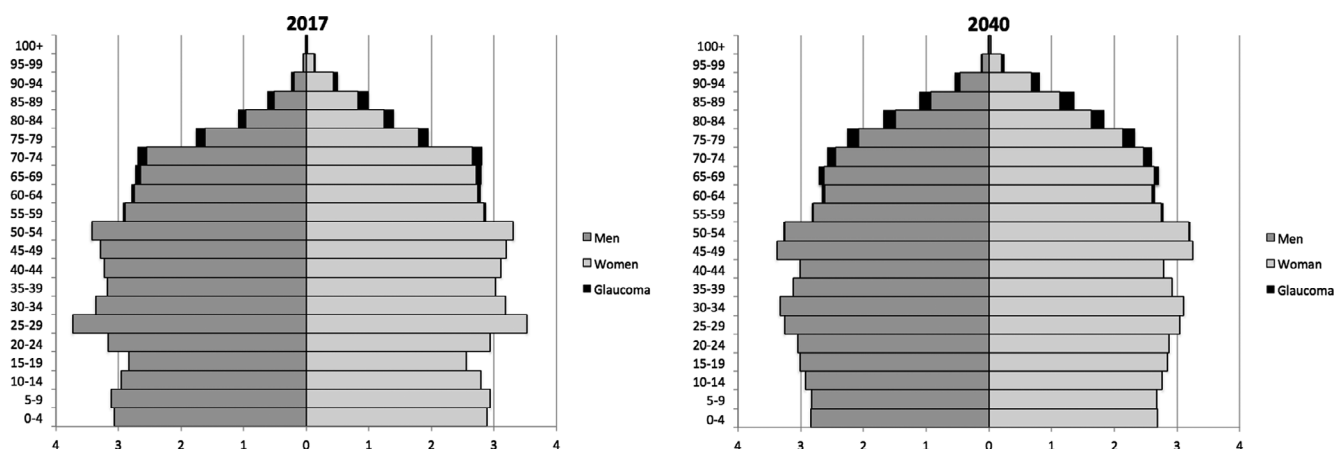


Fig. 5. Projection of glaucoma burden in 2040, an example from Sweden. The proportions of subjects in each age group were calculated for each country as of the year 2017.

discrepancies between the Nordic countries with Denmark having both the lowest glaucoma prevalence and drug consumption (Goldschmidt et al. 1989; Calissendorff 2001). The estimated number of patients with topical ocular hypotensive treatment of 11.5% of the population over 80 years in Finland conforms well to earlier data of glaucoma prevalence (Uusitalo et al. 2014). The corresponding Danish number of patients of 8.1% differs somewhat compared with a recent that estimated a prevalence of 10% in 2011 (Kolko et al. 2015). The latter study included all individuals with dispensed glaucoma medication at any time during their lifetime, while the current study only included individuals treated over the defined time period. This may explain our lower prevalence.

Differences in the number of drug dispensations between countries may be due to several reasons. For example, the use of other IOP-lowering treatments might vary. The number of trabeculectomy procedures for glaucoma has been reported to 18 per 100 000 inhabitants per year in Iceland (Tryggvadottir et al. 2020) compared with 7 in 100 000 inhabitants in Sweden (Socialstyrelsen) in 2019. Comparisons of the use of other surgical procedures for glaucoma between the other Nordic countries are yet not published, but a possible subject for future research. Furthermore, the prevalence of exfoliation syndrome, a risk factor for glaucoma that may increase the incentive to initiate treatment, is also less common in Denmark compared with Finland (Alyahya et al. 2005). Disparities in therapeutic traditions, especially the

approach towards treatment of ocular hypertension and normal tension glaucoma, might also differ. Finally, differences in reimbursement systems may be another cause. Even if all Nordic countries have systems for generic substitution to encourage dispense of the product with the lowest price (Icelandic Health Insurance Centre 2019; The Dental and Pharmaceutical Benefits Agency 2019), the price out of pocket for the patient shows considerable variability. Apart from a lower service fee, in Finland, medical costs for glaucoma are fully reimbursed from the first package (Finnish Medicines Agency Fimea & Social Insurance Institution 2018). In Norway, more than half of the actual cost is reimbursed already from start of therapy (Felleskatalogen AS 2020). In the remaining Nordic countries, the patient needs to pay the full price up to approximately 120 euro (Icelandic Health Insurance Centre 2019; Danish Medicines Agency 2020; The Dental & Pharmaceutical Benefits Agency 2020). The price out of pocket for a glaucoma patient with no other medications and a total yearly drug cost of 250 euro could therefore vary between 0 Euro in Finland, 98 Euro in Norway and 179–190 Euro in Denmark, Iceland and Sweden. An important question – if countries using more drugs and/or spending more money have better glaucoma care – is an important issue for future research and imply for the need to collect and evaluate real-world data outcomes. However, a comparison of a higher-spending and a lower-spending region in Finland could find no significant difference in quality-of-

life scores among glaucoma patients between the two regions (Hagman 2013).

A major strength in this study is that national prescription data are collected in uniform systems independent of the user and of generally a good quality. However, the study has several limitations. As the prescription data were not linked to diagnose registries, it was not possible to differ dispensations for glaucoma from ocular hypertension. Further, consumption of glaucoma medications is not an accurate estimation of the prevalence of glaucoma. Undetected glaucoma could represent approximately 50% of all glaucoma cases in a population (Heijl et al. 2013). Overtreatment may also be common. A study from Finland has shown that as many as 40% of patients with a diagnosis of glaucoma had no signs of disease even after 11 years of treatment. However, as intraocular pressure was not included in the analysis, the medication could have prevented onset of glaucoma, which would have developed if they had not been treated (Hagman 2013). Switches between treatments might also have been calculated as double prescriptions, and this might have overestimated the extent of treatment. We could further not separate preserved eye drops from more expensive non-preserved drops, which complicates comparisons of costs. Due to Swedish regulations, our data could not separate prescriptions of combinations of sympathomimetics/carbonic anhydrase inhibitors from sympathomimetics. As these classes of medicines never exceeded 3%, it is however not likely to affect the result to any

important extent. For the same reason, it was not possible to separate oral from ocular carbonic anhydrase inhibitors in all countries. As the proportion of acetazolamide tablets of the DDD for glaucoma treatment was below 0.5% in Denmark and Norway during the timeframe, this is probably not significant either. A final important weakness is the inherent uncertainty of population projections. Nevertheless, the proportion of Nordic population aged 65 years or older will most probably increase in the years to come (Nordic Council of Ministers 2018).

Tomorrow is always uncertain, and predictions of the future tend to fail. Medical innovations over the next decades might revolutionize the way glaucoma is diagnosed and treated. New and better methods for diagnosis and detection of progression might give a higher accuracy in which individuals that should be treated to prevent visual disability. New surgical procedures as minimally or micro-invasive glaucoma surgery (MIGS) procedures might also reduce medication use; however, there is a need for high-quality, independently funded and performed, comparative studies on these devices (Rosdahl & Gupta 2020). New research could also reboot interest in existing methods, for example the LiGHT trial that showed that selective laser trabeculoplasty is a cost-efficient first-line treatment (Gazzard et al. 2019). However, the future development of all these factors is impossible to predict today. Due to an increased number of ageing individuals, it is however conceivable that the number of patients requiring ocular hypotensive therapy in the Nordic region will rise in the next twenty years. An increase of patients with an additional 50% in 2040 will not only lead to an increase in prescriptions with a subsequent rise in costs. Additional expenses like consultations, monitoring, surgical procedures and hospitalizations may consist of 25–50% of the total costs for glaucoma care (Lindblom et al. 2006; Hagman 2013). Besides these direct costs, the healthcare system must also plan for and increase the capacity to handle a rise in the number of patients.

In summary, this retrospective study of national pharmacy data on the dispensations of topical ocular hypotensive treatment between 2008 and 2017 shows an increase in both the number of

patients with ocular hypotensive treatment and the DDD per patient and day. Whether or not this has improved clinical outcomes remains to be shown. The total drug cost has however decreased during the study period due to the introduction of generic medications. Due to an increased number of ageing individuals, the number of subjects with ocular hypotensive therapy is likely to increase by a further half by 2040. This will be a challenge for healthcare systems to overcome.

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