Direct costs of glaucoma and severity of the disease: a multinational long term study of resource utilisation in Europe


Background: Resource utilisation and direct costs associated with glaucoma progression in Europe are unknown. As population progressively ages, the economic impact of the disease will increase.

Methods: From a total of 1655 consecutive cases, the records of 194 patients were selected and stratified by disease severity. Record selection was based on diagnoses of primary open angle glaucoma, glaucoma suspect, ocular hypertension, or normal tension glaucoma; 5 years minimum follow up were required. Glaucoma severity was assessed using a six stage glaucoma staging system based on static threshold visual field parameters. Resource utilisation data were abstracted from the charts and unit costs were applied to estimate direct costs to the payer. Resource utilisation and estimated direct cost of treatment, per person year, were calculated.

Results: A statistically significant increasing linear trend ($p = 0.018$) in direct cost as disease severity worsened was demonstrated. The direct cost of treatment increased by an estimated €86 for each incremental step ranging from €455 per person year for stage 0 to €969 per person year for stage 4 disease. Medication costs ranged from 42% to 56% of total direct cost for all stages of disease.

Conclusions: These results demonstrate for the first time in Europe that resource utilisation and direct medical costs of glaucoma management increase with worsening disease severity. Based on these findings, managing glaucoma and effectively delaying disease progression would be expected to significantly reduce the economic burden of this disease. These data are relevant to general practitioners and healthcare administrators who have a direct influence on the distribution of resources.

Glaucoma is a leading cause of blindness worldwide and is the second most frequent cause of legal blindness in industrialised countries. In glaucoma the optic nerve is progressively damaged causing defects in the visual field, usually asymptomatic until the central vision is affected. The goal of glaucoma management is to preserve the patient’s quality of life. The only treatment option proved to prevent the loss of vision is to lower the intraocular pressure to a level deemed safe for the eye. The recommended steps for lowering the intraocular pressure in primary open angle glaucoma (POAG) are topical medications first, followed by laser trabeculoplasty and, lastly, incisional surgery. The global prevalence of glaucoma was estimated at 67 million people in 2001; a projection of these data to European countries estimates 9.25 million glaucoma patients in Europe, of which 4.6 to 6.9 million were undiagnosed and untreated.

In 2000, the prevalence of glaucoma in the United Kingdom was estimated to be as high as 3.3% in people over 40 years of age and up to 5% in those aged 80 and over. In Italy, approximately 50,000 people are visually handicapped by glaucoma, while an estimated 540,000 people over 40 years had glaucoma, half of which are undiagnosed. In Germany, glaucoma was reported as the third leading cause of blindness (1.6/100,000); an estimated one fifth of all cases of legal blindness in people aged 75 and older were the result of glaucoma (22.8/100,000). Approximately 500,000 patients in France are followed and treated for POAG with a similar number of cases undiagnosed.

Glaucoma costs the US healthcare system an estimated $2.5 billion annually: $1.9 billion in direct costs and $0.6 billion in indirect costs. The annual direct medical cost of treating newly diagnosed open angle glaucoma was estimated at $1055 based on a retrospective analysis conducted in 1998. A cost effectiveness analysis estimated average annual cost for standard therapy in treatment of glaucoma at FFr2389 (US$398) per patient in France and £380 (US$627) per patient in the United Kingdom (US$1 = FFr6.60; £0.61).

Several international retrospective chart reviews have considered the economic burden of the management of glaucoma, particularly in the first 2 years after diagnosis. However, few data exist on the resource consumption as a function of disease severity and, in particular, of treating advanced stage disease. A study in Canada showed an increase in direct costs with more severe damage. The aims of this study were to estimate resource utilisation and direct medical costs associated with the long term management of glaucoma of different severities in five European countries (Austria, France, Germany, Italy, and the United Kingdom), and to test the hypothesis that resource consumption and direct costs increase as disease severity worsens.

Abbreviations: CLV, corrected loss variance; CP, corrected pattern standard deviation; GSS, glaucoma staging system; IOP, intraocular pressure; LSS, loss variance; MD, mean defect or mean deviation; POAG, primary open angle glaucoma; PSD, pattern standard deviation
### Table 1: Visual field based glaucoma staging system

<table>
<thead>
<tr>
<th>Stage</th>
<th>MD Score</th>
<th>CPSD or CLV</th>
<th>PSD or LV</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0, early glaucoma</td>
<td>0.00</td>
<td>No</td>
<td>No</td>
<td>Does not meet any criteria for stage 1</td>
</tr>
<tr>
<td>1, moderate glaucoma</td>
<td>0.01 to 2</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>Points below 5%</td>
</tr>
<tr>
<td>2, advanced glaucoma</td>
<td>2 to 6</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>Points below 3% in both hemifields</td>
</tr>
<tr>
<td>3, severe glaucoma</td>
<td>6 to 15</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>Points below 1% in both hemifields</td>
</tr>
<tr>
<td>4, end stage glaucoma</td>
<td>15 to 20</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>Points below 1% in both hemifields</td>
</tr>
<tr>
<td>5, end stage glaucoma/blind</td>
<td>20 or worse</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>Points below 1% in both hemifields</td>
</tr>
</tbody>
</table>

**Notes:**
- MD (mean defect or mean deviation): This is the mean difference between the normal sensitivity and the retinal sensitivity for the subject (calculated from all the points tested). MD increases with the following: media opacities, diffuse loss, or severe localised loss.
- CPSD or CLV (corrected pattern standard deviation or corrected loss variance): This indicates the extent of focal loss in the visual field, taking short term fluctuation into account.
- PSD or LV (pattern standard deviation or loss variance): This is the standard deviation or variance of the deviations, and is thus a measure of the degree to which the shape of a patient's field differs from a normal, age corrected, reference field. Thus, the PSD or LV indicates the extent of focal loss in the visual field. The PSD or LV can be normal in cases where there is diffuse loss and they are not good indices for the follow up of advanced glaucoma.

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### PATIENTS AND METHODS

**Recruitment and sampling**

Sites within the participating countries were recruited based on the availability of patient records spanning a minimum of 5 years between 1995 and 2003. At each site, approval was obtained from the ethics committee and/or institutional review board according to local and national policy.

Patients with diagnoses of POAG (ICD-9 code 365.11), normal tension glaucoma (ICD-9 code 365.12), ocular hypertension (ICD-9 code 365.04), or glaucoma suspect (ICD-9 code 365.0), and at least 5 years of continuous follow up were selected. Patients with concomitant ocular diseases likely to affect glaucoma treatment related resource consumption and those enrolled at any time in a clinical trial were excluded.

A glaucoma staging system (GSS) based on visual field defects was used to classify patients into categories of severity. A number of existing GSSs were reviewed. The Bascom Palmer (Hodapp-Anderson-Parrish) GSS was chosen for use in this study as it allows structured severity stage assignment based on visual field parameters, in a manner that is easily applicable to a retrospective chart review since it is based on the most widely available automated threshold testing technology. Patients were allocated to six disease severity categories adopting this GSS (table 1).

**Chart review**

Data collected included patient demographics, glaucoma risk factors, number of ophthalmologist visits, number and type of glaucoma medications and surgeries, and visual field results. All clinical tests documented in the charts were recorded. Both essential examinations, such as intraocular pressure (IOP) assessments, optic nerve assessments, retinal or macular examinations, slit lamp examinations, gonioscopy, as well as more specialised tests, such as diurnal curves of IOP measurements, retinal nerve fibre thickness assessments, and optic disc photographs were considered.

“Study entry” was defined by the date on which the first binocular set of static threshold visual fields was documented in the chart at least 5 years previously. This set of visual fields was used to assign a baseline stage based on the GSS. For stage 5 (end stage) patients, visual acuity at study entry was also used to determine their initial staging. The cases were staged and selected for chart abstraction until a minimum of two per stage (stages 0 to 5) was identified for each site (that is, a minimum of 12 charts per site). Patients were staged on the basis of the worse eye visual field score. A total of 1655 consecutive charts were reviewed to obtain the study sample of 194 charts.

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**Figure 1** Patient distribution by sex and age.
For each country health economists were consulted to provide publicly available unit costs associated with diagnostic tests, surgical procedures, and medication data abstracted from the charts.  

The annual direct cost of treatment per person year, including a breakdown of costs attributed to office visits, diagnostic procedures, glaucoma surgeries, cataract extractions, and glaucoma medications was calculated per stage of disease. For all patients, all direct costs were assumed to be ophthalmology costs and included costs associated with ophthalmologist visits, glaucoma surgeries, Hemifield visual field testing, medications, and other glaucoma services, such as gonioscopies, optic disc photographs, nerve fibre thickness analysis, and IOP diurnal testing. For patients in stage 5, non-physician costs, as low vision care/vision rehabilitation services, were not included since they were not recorded on the hospital charts.

Based on the number of drops per bottle, a 5 ml bottle of an ocular medication prescribed twice daily or its equivalent (for example, a 2.5 ml bottle of a medication prescribed once daily) was assumed to represent a 1 month supply for any given patient. Data on medication usage were collected at every visit and patients were assumed to adhere fully to medication regimens unless otherwise noted in the chart.

Statistical analyses
To calculate the number of resources consumed per person time by stage, the total number of each resource consumed in each stage of glaucoma was added and then divided by the total of all patients' follow up time in that stage. As visits occurred frequently and visual fields were assessed regularly, the number of these resources consumed per person year was calculated. Surgical procedures were performed with less frequency, and therefore reported per 100 person years. Conversely, as there was extensive medication use in this population, with frequent prescription changes, these costs were calculated on a daily basis. The person time values were multiplied by unit costs for each country to calculate the direct cost by stage over time (for example, €/person year).

RESULTS
Demographics
From the 1665 consecutive cases examined, a total of 194 charts (47.9% female) met the review criteria. An equal number of patients from each stage were selected (mean 32.5, median 32, range 31–34); the demographics are presented in figure 1. The mean age of the study sample was 64.7 years (SD 12.1), and was significantly lower (p < 0.01) for stage 0 (57.6 for stage 0, 65.7 for stage 1, 64.1 for stage 2, 66.0 for stage 3, 67.5 years for stage 4, and 67.7 for stage 5).

Resource utilisation
The use of resources increased with the worsening of disease (table 2). The number of ophthalmologist visits per person year increased with each worsened stage with a significant linear trend (p = 0.001). The number of visual fields performed increased from stage 0 to stage 3 and decreased from stage 4 to 5. Laser trabeculoplasty was most common in early stages (stage 2 with 8.1 surgeries per 100 person years), while trabeculectomy was most common in more advanced stages (stage 4 with 8.9 per 100 person years). A statistically significant increasing linear trend (p = 0.008) was observed in the number of glaucoma medications per person month used from stage 0 to stage 5. As expected, cataract extractions did not show any specific trend.

<table>
<thead>
<tr>
<th>Table 2 Number of resources utilised per person time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resource (per person time unit)</td>
</tr>
<tr>
<td>Disease stage (n)</td>
</tr>
<tr>
<td>0 (33) 1 (32) 2 (34) 3 (33) 4 (31) 5 (31)</td>
</tr>
<tr>
<td>Office visits (per 1 person year)</td>
</tr>
<tr>
<td>Visual fields (per 1 person year)</td>
</tr>
<tr>
<td>Trabeculoplasties (per 100 person years)</td>
</tr>
<tr>
<td>Trabeculectomies (per 100 person years)</td>
</tr>
<tr>
<td>Glaucoma medications (per 1 person month)</td>
</tr>
</tbody>
</table>

| Table 3 Direct healthcare cost of glaucoma treatment per person year by stage |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Disease stage | France | Germany* | Italy | United Kingdom |
| 0             | €414   | €918    | €153  | €457   |
| 1             | €718   | €814    | €386  | €595   |
| 2             | €820   | €986    | €421  | €870   |
| 3             | €601   | €928    | €689  | €533   |
| 4             | €1002  | €1194   | €791  | €829   |
| 5             | €812   | €952    | €712  | €1065  |

*Includes data of 12 charts from Austria.
Direct costs
Table 3 depicts the annual direct cost of glaucoma treatment by stage. A statistically significant linear trend (p = 0.018), showing an increase in direct cost as disease severity worsened, is demonstrated. Direct ophthalmology costs were estimated at €455 per person year for stage 0 patients and increased as disease severity worsened to an estimated €969 per person year for patients with stage 4.

Annual direct costs of treatment were also calculated for each participating country, stratified by stage of disease, based on the corresponding utilisation of resources (table 2). While the exception of Germany, an increase in direct cost from stage 0 to stage 4 was observed in all countries, and was significant for Italy (p = 0.026) and the United Kingdom (p = 0.037). Stage 5 costs were lower than stage 4 costs, except in the United Kingdom. A statistically significant increasing trend (p = 0.037) in direct cost was observed in Italy from stage 0 to stage 5, where medications and glaucoma surgery accounted for the majority of cost. The resource consumption peaked for stage 4 with €791 per person year and slightly decreased for stage 5 patients. A statistically significant increasing trend (p = 0.026) in direct cost was observed in the United Kingdom from stage 0 to stage 5. Medications and outpatient clinic visits accounted for the majority of these costs (fig 2).

DISCUSSION
In examining medical resource consumption associated with a chronic, potentially blinding disease, such as glaucoma, one may postulate that as disease severity worsens, greater medical effort will be prompted by physicians’ goals to slow disease progression as well as by increased patient concern. In particular, being glaucoma asymptomatic in the early phases resulting most often in delayed diagnosis, a reactively increased medical vigilance is afterwards likely as disease progresses. This study supports this hypothesis in chronic glaucoma patients, showing that resource utilisation and direct medical treatment costs increase as disease severity worsens.

Patients with end stage disease, stage 5 for our study, typically have failed to adequately respond to conventional ocular hypotensive medications and may have already undertaken numerous surgical procedures with suboptimal results.

Direct ophthalmology resource utilisation, including physician visits, glaucoma surgeries, and medications, was lower for patients with stage 5 compared to stage 4 in all countries except the United Kingdom. This may be explained by the fact that ophthalmologists have less to offer to such severely visually impaired patients in terms of therapy to preserve vision, compared with patients with less severe disease. Moreover, low vision care, vision rehabilitation services, and non-physician resources where patients with end stage disease may be referred to for further management were not calculated as direct medical costs.

When full compliance with medications is assumed, medication costs represent a minimum of 42% of total direct cost at any disease stage. Since topical ocular hypotensive medications are as effective as early surgery in delaying the rates of progression, the majority of physicians are likely to offer medication therapy before advising surgery. In general, preventing patients progressing from stage 0 or 1 to stage 4 or 5 will project a decrease between 30–50% of the costs.

The overall results from this study appear to be within the range of similar glaucoma resource utilisation studies, but there are methodological limitations. Glaucoma progression may be measured by ophthalmologists using visual field examination, optic nerve head clinical assessment, or both. Visual field examination is the standard of care to evaluate disease progression, and for clinicians it represents the driver for adjusting the management of the patient. Since the study retrospectively collected patient data from the previous 5–7 years, the number of years a patient may have been in his/her baseline stage before the study entry could not be controlled. Patients with at least 5 years of follow up data may differ from patients who do not seek persistent care for glaucoma for the same period, thus creating a potential selection bias. Data on patients in end stage disease who may have been referred to low vision care and vision rehabilitation centres were not captured and the total medical and societal costs associated with end stage disease were not fully estimated. Examining costs from a societal perspective, as opposed to a payer perspective, may have an impact on treatment cost of end stage glaucoma; in particular, as costs for low vision care and vision rehabilitation centres are likely to be borne by the patient or society, such resources are inherently excluded from medical costing methods. The relatively small number of charts reviewed may limit the generalisability of the results.

Data on ocular hypotensive medication use were collected at every ophthalmic visit and for cost calculations it was assumed that patients fully adhered to medication regimens; this may overestimate real life resource utilisation and costs associated with medication use. Medication costs are distributed over periods of months to several years while surgical costs are incurred at a single point in time and are represented in the analysis as costs divided over the period that patients remain categorised within a given stage. For example, the relatively high unit cost of an incisional surgery will be divided by the number of years of follow up and may therefore be reported as a lower yearly cost. This costing approach still represents the best approximation of actual surgical costs given sample size and timelines. The possibility of surgery to control the IOP for years in the majority of patients is well documented. Our study demonstrates a significant linear trend in resource consumption and total direct cost, both increasing with worsening of disease severity. The direct cost of treatment increased by an estimated €86 for each incremental increase in stage. The costs ranged from €455 per person year for early stage (stage 0) to €969 per person year for late stage (stage 4) disease across Europe; similar trends were observed across each analysed countries. Health policy models have been constructed for other conditions, such as stroke, to allow for investigation of policy issues and options; similar analyses in glaucoma are warranted. According to our results, glaucoma management strategies aimed at slowing or stopping disease progression, if effective, would be expected to significantly reduce the health economic burden of this chronic disease over many years.

Ophthalmologists, general practitioners, and health administrators now have a European based set of data demonstrating that managing glaucoma effectively, preventing progression beyond the early to moderate stages of the disease, will result in a decrease in direct costs. This should be used to offset the constraints on resource delivery to manage patients with an unquestionable diagnosis of progressive glaucoma.

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