Costs and Healthcare Resource Utilization Associated with Posterior Capsule Opacification After Cataract Surgery with Five Different Intraocular Lenses: An Economic Analysis for Spain

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Purpose: To estimate the economic impact of neodymium-doped yttrium aluminum garnet (Nd:YAG) laser capsulotomy and its related complications for five different intraocular lenses (IOLs) from the payer and hospital perspectives in Spain.

Materials and Methods: The three-year incidence rates of Nd:YAG laser capsulotomy after cataract surgery with five different single-piece acrylic monofocal IOLs (AcrySof IOLs, AJL LLASY60, IOL Tech Stabibag, Medicontur Bi-flex, Zeiss Asphina) for 8293 patients were derived from odds ratios of multivariate analysis adjusted for age, gender, and diabetic retinopathy. A cost-consequence model for a hypothetical cohort of 2000 eyes was then developed to quantify the potential impact of Nd:YAG capsulotomy in terms of costs and time for each of the included IOLs, from the payer and hospital perspectives.

Results: The adjusted three-year Nd:YAG laser capsulotomy incidence was 5.0% (95% CI 3.9 to 6.1) for AcrySof and ranged from 26.0% to 44.0% for the other four IOLs. The average costs of Nd:YAG treatment and related complications were €261.90 for payers and €19.99 for hospitals. The average time needed for Nd:YAG treatment and related complications was 32.82 minutes. Model estimates based on 2000 hypothetical cataract surgeries showed that AcrySof IOLs could lead to cost savings between €110,259.90 and €205,591.50 for payers. For hospitals, time, and cost savings with AcrySof ranged from 230.29 hours and €8415.79 compared to Zeiss Asphina to 429.40 hours and €15,692.15 compared to AJL LLASY60 IOLs.

Conclusion: Post cataract surgery, AcrySof IOLs were associated with a significantly lower incidence of Nd:YAG treatment and its subsequent complications compared to other IOLs. Our analysis shows that IOL choice is an important factor that can reduce the burden for patients, payers, and hospitals.

Keywords: cost, resources, Nd:YAG capsulotomy, cataract, PCO, IOL

Plain Language Summary

Why carry out this study?

- Neodymium-doped yttrium aluminum garnet (Nd:YAG) laser capsulotomy is used to treat Posterior Capsule Opacification, however, can cause complications that increase the burden for patients and healthcare systems.
- Real world evidence (RWE) informed cost consequence analysis of Nd:YAG laser capsulotomy can support intraocular lens (IOL) choice to lower economic costs and burden to patients.
- RWE insights are still limited and prior economic studies mostly focused on the economic cost for payers, but did not consider
 additional time required to care for patients with complications from the perspective of hospitals, which is vital with respect to
 planning of healthcare resources.

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 This study brings new RWE insights into the economic burden associated with post-operative Nd:YAG capsulotomy treatment outcomes associated with five commonly used IOLs from both the perspective of payers and hospitals in Spain.

What was learned from the study?

- AcrySof IOLs were associated with a significantly lower incidence of Nd:YAG laser capsulotomy and subsequent complications compared to four different IOLs.
- Among the investigated IOLs, AcrySof IOLs were the most cost effective for both payers and hospitals.

Introduction

The global leading cause of partial and complete blindness is cataract. ^{1,2} The most commonly performed procedure for the medical treatment of cataracts is a surgery with lens replacement.^{3,4} In 2019, there were 450,247 cataract surgeries performed in Spain, making it the most frequently performed surgical procedure nationally. While safe and effective.⁶ the cataract surgery may cause posterior capsule opacification (PCO), which can lead to impaired contrast sensitivity, glare disabilities and reduced visual acuity. 7,8 PCO is treated with neodymium-doped yttrium aluminum garnet (Nd: YAG) laser capsulotomy. This treatment, in turn, can be associated with further complications, including cystoid macular oedema (CME), late onset endophthalmitis, posterior vitreous detachment, reduction in vision, retinal detachment (RD), or uveitis, 9-11 all of which affect patients' function of vision and quality of life. Thus, PCO increases the burden to patients and healthcare systems due to the necessary Nd:YAG treatment and possible complications that require further specialist consultation and treatment.^{7,12} Given the sheer volume of cataract surgeries being performed annually,⁵ even small differences in costs per patient add up to significant overall costs to the healthcare system. 13 It is therefore important for patients and for healthcare systems more generally to minimize PCO.

Prior studies reported that the incidence of PCO was associated with patient characteristics, such as age and ocular comorbidities, and with factors related to surgical procedures and technique, as well as IOL material and design characteristics. 14,15 There have been a number of studies examining the effects of different IOL types on the incidence rate of PCO following cataract surgery. ¹⁶ Across these studies lower Nd:YAG capsulotomy rates after cataract surgery were consistently associated with hydrophobic acrylic IOLs compared to hydrophilic acrylic IOLs. Recent studies conducted in Scandinavia and the UK showed that AcrySof hydrophobic IOLs were associated with lower PCO incidence and Nd:YAG laser capsulotomy compared to other hydrophobic or hydrophilic acrylic IOLs during three to five years after IOL placement. 17-20 It has been suggested that superior outcomes could be due to the IOL material composition and the edge design of hydrophobic acrylic IOLs. 14,15,21-23

While there are numerous studies examining the association between IOL type and incidence rate of PCO and Nd: YAG laser capsulotomy, real world evidence (RWE) insights into costs related to the placement of different IOLs are still limited. One study that followed up the patients for approximately 3.5 years after cataract surgery, showed that the average costs were significantly lower for hydrophobic IOLs compared to the hydrophilic IOLs, due to the decreased PCO risk.²⁰ Several health economic studies from European countries that followed patients up for three to five years after cataract surgery found that AcrySof IOLs were generally most cost-effective compared to other IOLs, and could save millions of Euros in costs.^{24–26}

Most of these previous studies focused on the economic costs for the payers and did not consider additional time and resources required to care for patients with complications from the perspective of hospitals. Such insights are vital with respect to the planning of healthcare resources.

More RWE from different perspectives is therefore needed to understand economic costs and resource use associated with different IOLs. Furthermore, while previous work has been published which compares PCO related costs associated with hydrophobic and hydrophilic IOLs, ²⁰ this analysis adds comparative evidence relating to IOLs with a lens material classified as hydrophilic with a hydrophobic surface (Zeiss Asphina).

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Adding to this, there are only limited previous investigations in Spain, where the most recent study, which focused on the cost only, was conducted more than ten years ago.²⁵ We therefore conducted a study that extends our previous RWE investigation on Nd:YAG incidence after cataract surgery and provides an economic assessment of the financial costs and time investment for payers and hospitals in Spain.²⁷ The objective was to estimate the health economic impact of five different single-piece, acrylic monofocal IOLs (Alcon AcrySof (hydrophobic), AJL LLASY60, Medicontur Bi-flex, IOL Tech Stabibag (all hydrophilic) and Zeiss Asphina (hydrophilic with a hydrophobic surface) and the costs associated with PCO and the Nd:YAG procedure, as well subsequent complications from both the perspective of payers and hospitals in Spain.

Materials and Methods

Patient Population

The original study (Belda et al, 2021) was conducted in two large Spanish regional hospitals of the Ribera Salud group in the Torrevieja-Vinalopó healthcare area, which are the primary providers of ophthalmic procedures in this Alicante region.²⁷ We followed 14,519 eyes from 9545 patients (47% male, mean age = 75± 5.9 years) up for three years after cataract surgery to monitor Nd:YAG capsulotomy events. Of these, a total of 1647 further eyes were followed for up to six months to assess subsequent complications following Nd:YAG capsulotomy treatment. The data were fully anonymized and compliant with the Spanish data protection rules governing use of patient-level healthcare data, including anonymization of physician names in the dataset (as defined in the newly enforced EU General Data Protection Regulation, 25 May 2018). The study received ethical approval from Ribera Salud's Clinical Research Ethics Committee (CEIC) and was in compliance with the Declaration of Helsinki. Due to anonymization of all patient level data at the participating sites prior to analysis and the retrospective nature of the study, informed consent was not required from the institution's ethics committee. The details of the study population have been described elsewhere.²⁷ The modelling analysis assumed a hypothetical cohort of 2000 annual cataract procedures, conducted in the Spanish National Health System.

Data Extraction

Data were extracted from medical records for patients who had cataract surgery with five different IOLs, including Alcon AcrySof, AJL LLASY60, Medicontur Bi-flex, IOL Tech Stabibag and Zeiss Asphina.²⁷ The specific of intra- and post-Nd:YAG capsulotomy procedure complications that were extracted are illustrated in Table 1. All data were coded using system wide Ribera Salud proprietary procedure codes, along with procedure descriptors and International Classification of Disease-10 diagnosis codes. 27,28

Analysis

We first computed odds ratios (OR) and three-year incidence rates of Nd:YAG capsulotomy by IOL type. Subsequently, a similar cost-consequence model to the one reported by Dhariwal et al (2019)²⁶ was used to quantify the health care resource utilization and cost impact of Nd:YAG capsulotomy by IOL type (AcrySof, LLASY60, Bi-flex, Stabibag and CT Asphina). Costs associated with Nd:YAG treatment and its related complications up to three years after cataract surgery were analyzed from the perspective of payers. Efficiency gains and potential costs associated with time spent carrying out Nd:YAG treatment and other PCO related procedures were also estimated from a hospital perspective. In our analysis it was assumed that the five included IOLs shared the same prices, because in the Spanish National Healthcare System the cataract surgery tariff include the IOL costs. Thus, the general costs of cataract surgery are equivalent regardless of the type of IOL that is used. All analyses were performed using Microsoft Excel.

Cost-Consequence Model Analysis

Clinical Inputs

The incidence rates of Nd:YAG capsulotomy three years after cataract surgery with 95% confidence intervals (CIs) were attained from the data available from the previously published original RWE study, where ORs were adjusted for age, gender and diabetic retinopathy in multivariate analysis for each IOL with AcrySof as the reference group.²⁷ The

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Table I Average Time and/or Cost Required from Payers and Hospitals for the Nd:YAG Treatment and Related Complications ^a

| Procedure Type | Total Events | Cost for Payer (EUR) | Time for Hospital HCP (mins) | Cost for Hospital HCP (EUR) ^b | | | |
|---|-----------------|-------------------------|---------------------------------|--|--|--|--|
| Nd:YAG treatment only | | | | | | | |
| Total for Nd:YAG treatment only | 1647 | € 399,364.56 ° | 49,410 ^d | € 30,091.00 ° | | | |
| Nd:YAG related complications within 6 months after Nd:YAG treatment | | | | | | | |
| Cystoid macular oedema | П | € 7,351.63 | 660 | € 401.94 | | | |
| Endophthalmitis | 2 | € 2,277.08 | 160 | € 97.44 | | | |
| Hyphaema | I | € 80.04 | 40 | € 24.36 | | | |
| IOL decentered/subluxed | 4 | € 4,554.16 | 440 | € 267.96 | | | |
| Macular hole | 5 | € 6,242.45 | 550 | € 334.95 | | | |
| Posterior vitreous detachment | 36 | € 2,881.44 | 1440 | € 876.96 | | | |
| Raised Intraocular pressure | 5 | € 400.20 | 200 | € 121.80 | | | |
| Reduction in vision | 10 | € 800.40 | € 800.40 400 | | | | |
| Retinal detachment | 6 | € 7,029.12 | 660 | € 401.94 | | | |
| Retinal tear | I | € 217.48 | 50 | € 30.45 | | | |
| Uveitis (Iridocyclitis) | I | € 149.97 | 40 | € 24.36 | | | |
| Total for all complications | 82 | € 31,984.00 | 4640 | € 2825.76 | | | |
| Nd:YAG treatment and related complications | | | | | | | |
| Average costs | Per case | €261.90 | 32.82 | € 19.99 | | | |

Notes: HCP, healthcare personnel, ^avalues are based on the 1647 YAG eyes within three years. ²⁶ ^bCost of hospital specialist per minute is €0.609, ²⁹ therefore Cost for hospital HCP = Time for hospital HCP × 0.609. ^cEach Nd:YAG treatment costs €242.48. ^dEach Nd:YAG treatment on average takes the hospital HCP 30 mins. ^eEach Nd: YAG treatment on average costs the hospital HCP €18.27 per case.

different types of complications, with their associated costs, and consultation time among 1647 cases were analysed based on RWE data.27

Cost Inputs

The costs were estimated from the payer and hospital perspectives. All the analyses took the direct treatment costs into account. For payers these included Nd:YAG laser capsulotomy costs and costs for the treatment of related complications (Table 2), expressed in euros (€). The direct costs were sourced from publically available healthcare costs statistics for the Valencian Community.²⁹

For hospitals, we analysed specialist staff consultation time (expert clinical opinion) for Nd:YAG laser capsulotomy and its related complications. We estimated the total cost savings for hospitals depending on IOL type, based on the costs of a specialist per minute.³⁰

Table 2 Adjusted Nd:YAG Capsulotomy Incidence Rates for Different IOL Groups at Three Years Post-Cataract Surgery (Derived from Odd Ratios)²⁶

| Production | Odd Ratio | LCI (95%) | UCI (95%) | Incidence Rate | LCI (95%) | UCI (95%) |
|---------------|-----------|-----------|-----------|----------------|-----------|-----------|
| AcrySof | Reference | NA | NA | 5.00% | 3.90% | 6.10% |
| Zeiss Asphina | 5.21 | 4.07 | 6.66 | 26.05% | 20.35% | 33.30% |
| IOL Tech | 5.74 | 3.37 | 9.78 | 28.70% | 16.85% | 48.90% |
| Medicontur | 5.86 | 4.5 | 7.62 | 29.30% | 22.50% | 38.10% |
| AJL LLASY60 | 8.85 | 6.82 | 11.47 | 44.25% | 34.10% | 57.35% |

Abbreviations: LCI, lower confidence interval; UCI, upper confidence interval.

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Model Outputs

We report the estimated reduction in Nd:YAG capsulotomy events, costs and specialist staff time spent in relation to Nd: YAG capsulotomy with 95% CIs. The estimated incidence rate of Nd:YAG capsulotomy procedures was utilized for calculating the lower and upper values of number reduction between AcrySof and the four other IOLs. The total cost savings were assessed with respect to reduction in Nd:YAG laser capsulotomy events with the AcrySof IOL compared to the other IOLs, from the payer and hospital perspectives. Moreover, total time savings were estimated only considering the hospital perspective.

Sensitivity Analysis

A sensitivity analysis was conducted to obtain the minimum and maximum savings for the comparisons between AcrySof and the other four IOLs to evaluate the robustness of the economic analysis. The lower and upper values for Nd:YAG capsulotomy event reduction was derived from the available CI values. A $\pm 10\%$ variation in costs was applied to the lower and upper values of all events to derive the minimum and maximum cost differences between AcrySof and the other four IOLs.

Results

Clinical Results

Table 2 shows the ORs and three-year incidence rates of Nd:YAG capsulotomy by IOL type from the original clinical research which underpinned the economic analysis.²⁷ The multivariate analysis showed that odds for Nd:YAG laser capsulotomy were significantly higher for AJL LLASY60, Medicontur Bi-flex, IOL Tech Stabibag and Zeiss Asphina compared to Alcon AcrySof, with ORs of 8.85, 5.86, 5.74, and 5.21 respectively. Using the OR, the three-year incidence of Nd:YAG after cataract surgery was estimated to be 5% (95% CI 3.9 to 6.1) for Alcon AcrySof, while it ranged from 21.2% to 31.1% for the other four IOLs.

Cost Results

Table 1 illustrates costs and time associated with Nd:YAG treatment with related complications for 1647 Nd:YAG eyes within three years from the payer and hospital perspectives. The cost of each Nd:YAG treatment was €242.48, which comprised a specialist's consultation fee and Nd:YAG laser capsulotomy cost. From the payer's perspective, the cost of each Nd:YAG treatment with related complications was €261.90. From the hospital's perspective, the estimated specialist time for each Nd:YAG treatment with related complications was 32.82 minutes. The cost for hospital HCP per Nd:YAG treatment with related complications amounted to €19.99. The detailed estimates for staff time for Nd:YAG treatment and its subsequent complications are shown in <u>Supplementary Table 1</u>.

The cost-consequence analysis results from the payer and hospital perspectives are presented in Tables 3 and 4, respectively. For the hypothetical cohort of 2000 cataract eyes the estimation from the payer perspective shows that the cost savings estimates ranged from €110,259 (AcrySof compared to Zeiss Asphina) to €205,591 (AcrySof compared to LLASY60). Similarly, for the hospital HCP the estimation shows that time and costs savings with AcrySof IOLs could range from 230.29 hours and €8,415.79 compared to CT Asphina up to 429.40 hours and €15,692.15 compared to AJL LLASY60 (Table 4).

Table 3 Cost Savings per 2000 Cataract Eyes for the IOL Groups from the Payer Perspective

| Comparison | Cost Savings (EUR) | Lower Value | Upper Value | |
|--------------------------|--------------------|--------------|--------------|--|
| AcrySof vs Zeiss Asphina | € 110,259.90 | € 67,177.35 | € 169,396.92 | |
| AcrySof vs IOL Tech | € 124,140.60 | € 50,677.65 | € 259,281.00 | |
| AcrySof vs Medicontur | € 127,283.40 | € 77,312.88 | € 197,053.56 | |
| AcrySof vs AJL LLASY60 | € 205,591.50 | € 131,997.60 | € 307,968.21 | |

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Table 4 Time and Cost Savings per 2000 Cataract Eyes for the IOL Groups from the Hospital Perspective

| Comparison | Time Savings (Hours) | Lower Value | Upper Value | Cost Savings (EUR) | Lower Value | Upper Value |
|--------------------------|-------------------------|----------------|----------------|-----------------------|----------------|----------------|
| AcrySof vs Zeiss Asphina | 230.29 | 140.31 | 353.80 | € 8,415.79 | € 5,127.44 | € 12,929.53 |
| AcrySof vs IOL Tech | 259.28 | 105.84 | 541.53 | € 9,475.26 | € 3,868.07 | € 19,790.10 |
| AcrySof vs Medicontur | 265.84 | 161.47 | 411.56 | € 9,715.14 | € 5,901.05 | € 15,040.48 |
| AcrySof vs AJL LLASY60 | 429.40 | 275.69 | 643.22 | € 15,692.15 | € 10,074.96 | € 23,506.24 |

Discussion

To our knowledge our study is the first economic analysis based on a longitudinal cohort study that investigated the economic impact of Nd:YAG capsulotomy after cataract surgery with five different single-piece, monofocal, acrylic IOLs from a Spanish healthcare perspective. When considering not only the cost of the cataract surgery but also its related complications over three years, we estimated that AcrySof IOLs could substantially reduce the economic burden for payers (from €110,259.90 to €205,591.50) and save the health care resources in terms of time and money for hospitals (from 230.29 to 429.40 hours and €8415 to €15,692), when compared to four other IOLs, including AJL LLASY60, IOL Tech Stabibag, Medicontur Bi-flex and Zeiss Asphina. In line with previous work, 20,24-26 our findings highlight the importance of IOL choice with respect to economic costs and resources for both payers and hospitals.

The three-year incidence of Nd:YAG capsulotomy in this expanded RWE study showed the overall incidence rate after cataract surgery was approximately 14%, and rates were significantly lower for AcrySof IOLs (5%) compared to the other included IOLs (for a detailed report see²⁷). Our subsequent cost-consequence analysis estimated that IOL choice also reduces the burden on resources for health care providers. This is important, particularly seen through the prism of the COVID-19 pandemic:³¹ avoidance of PCO means that patients will have fewer hospital visits and as such, resources can be liberated to elsewhere in eye-care services, 32 as well as reducing the risk of infection for patients and healthcare professionals.

Our study showed cost and time savings for the hydrophobic compared to the hydrophilic IOLs. The savings were the largest for AcrySof compared to AJL LLASY60 IOLs, which had the highest risk for Nd:YAG incidence among the investigated IOLs.²⁷ Our findings are in line with a previous study which was conducted in UK, Italy and Denmark which showed that hydrophobic IOLs were associated with a lower risk of PCO and Nd:YAG capsulotomy, resulting in a lower costs in total compared to hydrophilic IOLs. 26 Economic studies comparing costs related to cataract surgery with hydrophobic and hydrophilic IOLs in Poland, Germany and Netherlands showed similar results. 33-35 In the current study the difference in Nd:YAG incidence rate between hydrophilic IOLs with hydrophobic surface and without hydrophobic surface was slightly lower. This is reflected in comparatively smaller cost and time savings for AcrySof vs Zeiss Asphina. Previous research indicates that hydrophobic IOLs are associated with a substantially lower incidence of Nd:YAG compared to other IOL material types. 17-20,36,37 Our work and the work of others 25,26 suggests that they will be associated with substantially lower costs. It has been hypothesized that a lower water content and higher fibronectin bioadhesion properties of hydrophobic acrylic IOLs may account for the beneficial effects with respect to PCO incidence and related complications. 16

The current results need to be interpreted in the light of some methodological considerations. Firstly, we assumed the price is the same for AcrySof IOLs and other IOLs. However, in a healthcare system where service is not universally provided for free, the prices of the IOLs may differ from each other and become an important factor in selecting IOLs for the hospital.³³ Under such a scenario, our assumption may not hold and the surcharge caused by different IOLs may need to be taken into account. Furthermore, while our study quantified direct costs for the IOLs, as well as for subsequent complications associated with the IOLs, other costs to patients, their relatives and health care systems have not been considered. 38,39 For example, indirect costs might arise due to the challenges related to loss of full binocular vision, that are associated with a reduced quality of vision and life, and with an increased risk of falling and traffic accidents. 40-43 Future studies could include such indirect costs in the evaluation of the economic impact of PCO, to produce more

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holistic cost estimates. Future studies should also consider the direct and indirect costs associated with IOL choice and PCO over longer follow-up durations to gain better insights into the long-term economic effects.

Conclusion

This study is the first to report on Nd:YAG capsulotomy treatment related economic impact and to report costs in relation to five different IOL types harnessing RWE data from Spain. Our study showed that from the payer and hospital perspectives IOL choice is an important economic factor. AcrySof IOLs are associated with lower costs for both payers and hospital HCP, due to substantial lower Nd:YAG capsulotomy rates and a lower risk for complications in three years after cataract surgery.

Abbreviations

DRG, diagnosis-related groups; HCP, healthcare personnel; IOLs, intraocular lenses; Nd:YAG, neodymium-doped yttrium aluminum garnet; OR, odds ratio; PCO, Posterior Capsule Opacification; RWE, real-world evidence.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Disclosure

JIB reports grants from Alcon, during the conduct of the study. JP reports personal fees from AVI (Allergan) for presentation/Webinar, outside the submitted work. DOB, XP, and CPV are employees of Alcon. MZ, JY and SS are employees of IQVIA. The authors report no other conflicts of interest in this work.

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