

A Systematic Literature Review of the Economic Burden of Leber Hereditary Optic Neuropathy (LHON)

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Poster
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Introduction

- Leber Hereditary Optic Neuropathy (LHON) is a rare, inherited mitochondrial disorder that leads to severe, irreversible vision loss¹
- It predominantly affects males, with onset usually occurring in early adulthood. Left untreated, affected patients remain visually disabled and blind in most cases for the rest of their lives¹
- The economic impact of LHON is not well-characterized

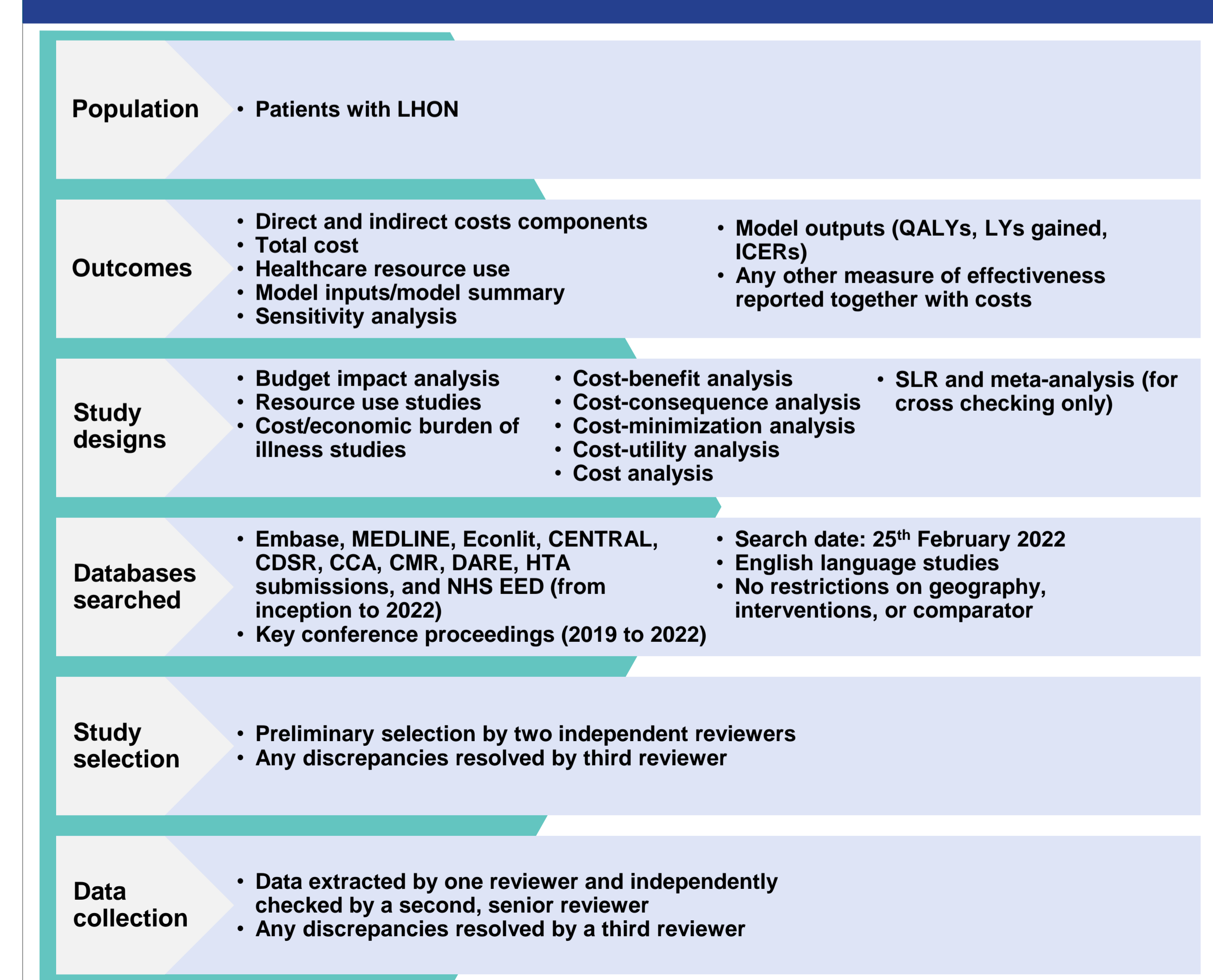
Objective

- This review aimed to comprehensively explore the economic burden of LHON, including healthcare resource utilization, costs, and findings from economic models

Methods

- A systematic literature review (SLR) was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify studies reporting on the economic burden in LHON as described in Figure 1

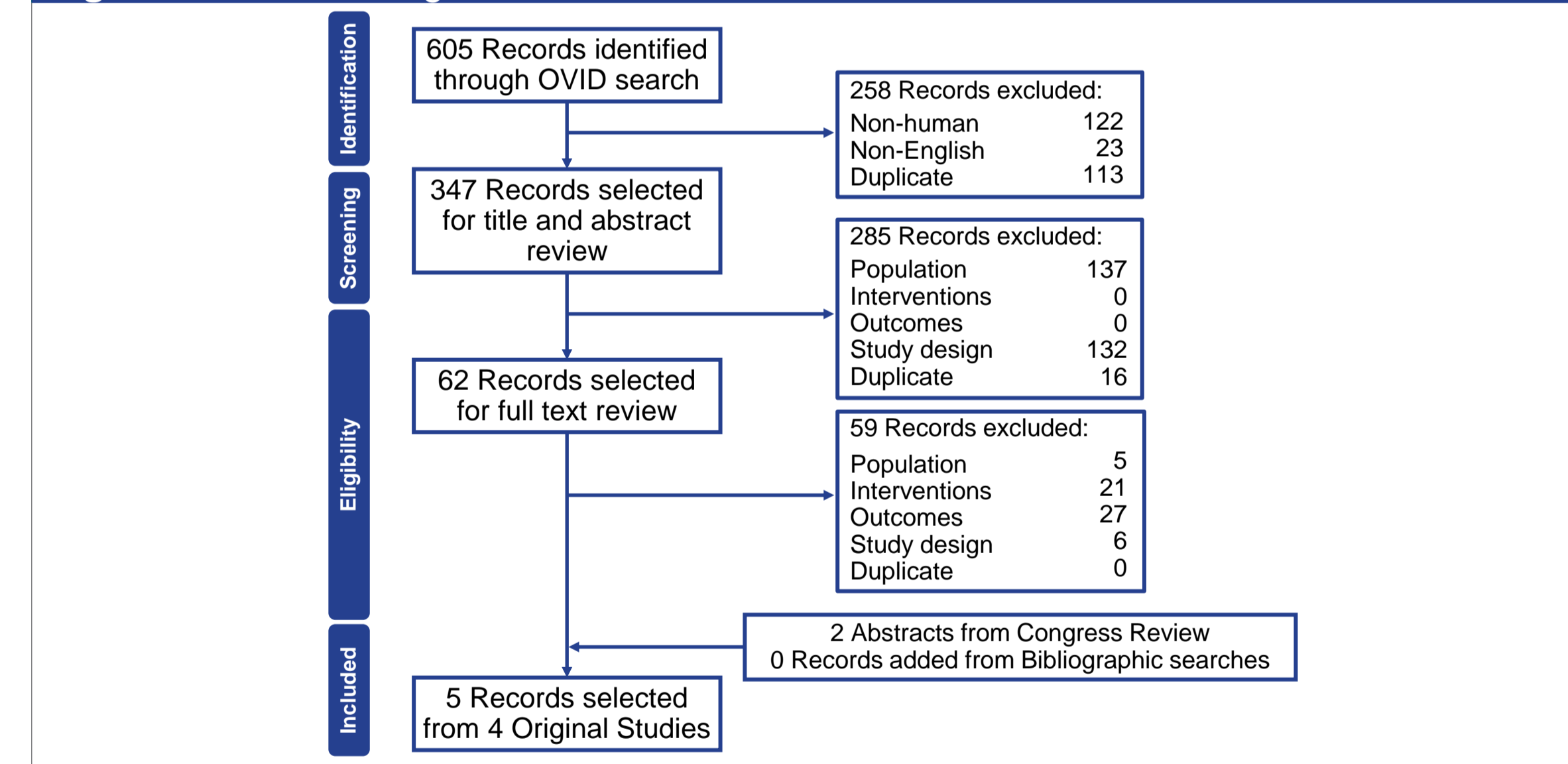
Figure 1. Economic SLR in LHON methods



Results

- Among 269 records identified in the SLR, five publications²⁻⁶ from four original studies met the inclusion criteria (Figure 2)
- The study designs included:
 - Targeted literature search combined with a patient and caregiver survey^{2,3}
 - Retrospective review of reimbursement decisions⁴
 - Retrospective chart review^{5,6}
- The target populations reported by studies included: patients with inherited retinal disease (IRD) including LHON^{2,3} and patients undergoing genetic testing including LHON^{5,6}
- There were two studies from North America (US/Canada),^{2,3,6} one from the UK,⁵ and one from Finland⁴
- No health economic models were identified

Figure 2. PRISMA diagram of included studies



Total overall costs

- The estimated total financial and non-financial costs of LHON in the US and Canada in 2019 ranged from \$84 million to \$200 million (USD) and from \$10 million to \$42 million (CAD), respectively (Figure 3)²
- The breakdown of total costs is reported for the overall IRD population only:
 - Loss of wellbeing accounted for the largest share of total costs in both the US and Canada (Figure 4)^{2,3}
 - Other costs included productivity losses (second largest), informal care, deadweight losses, health system (primary and secondary care, diagnostic tests, pharmaceuticals, vitamins and supplements, and medical research), and other costs (Figure 4)^{2,3}
- Limited economic data was available for Europe:
 - A retrospective analysis of conditional reimbursement decisions by the Finnish Pharmaceutical Pricing Board on 23 medicines reported the reimbursement decision concerning a treatment for LHON fell within the annual cost range of €20,000 to €60,000 (based on list price)⁴

Figure 3. Total annual costs attributable to LHON in the US and Canada²

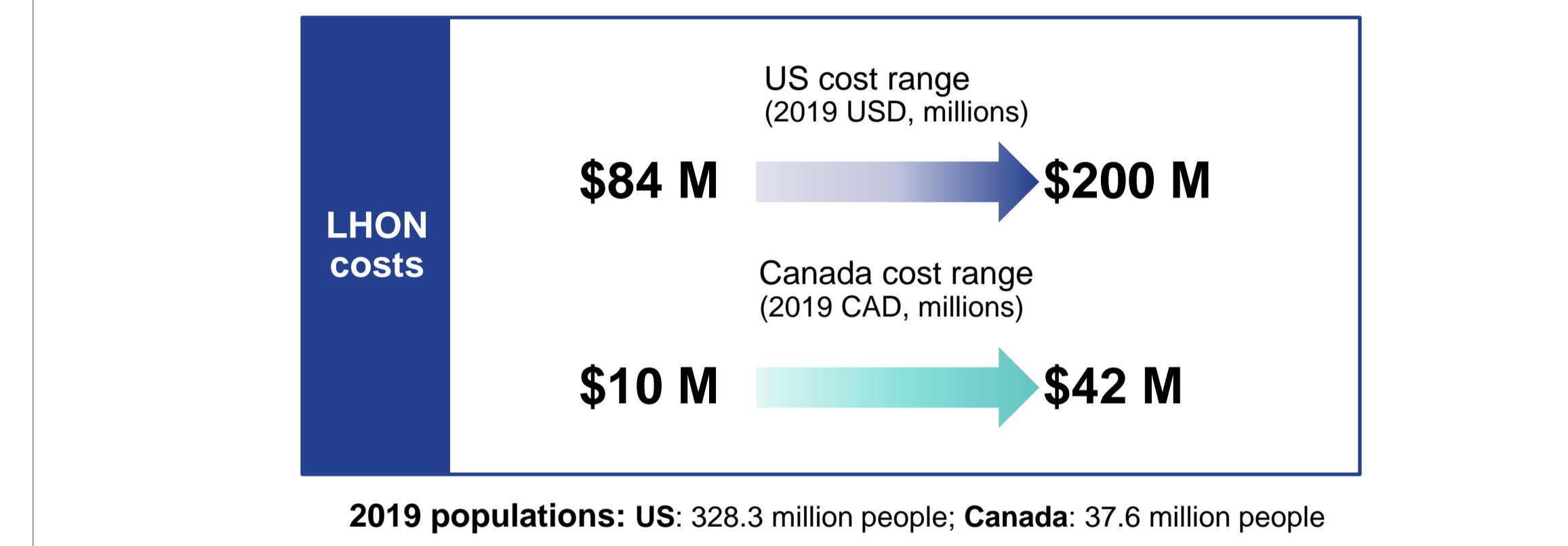
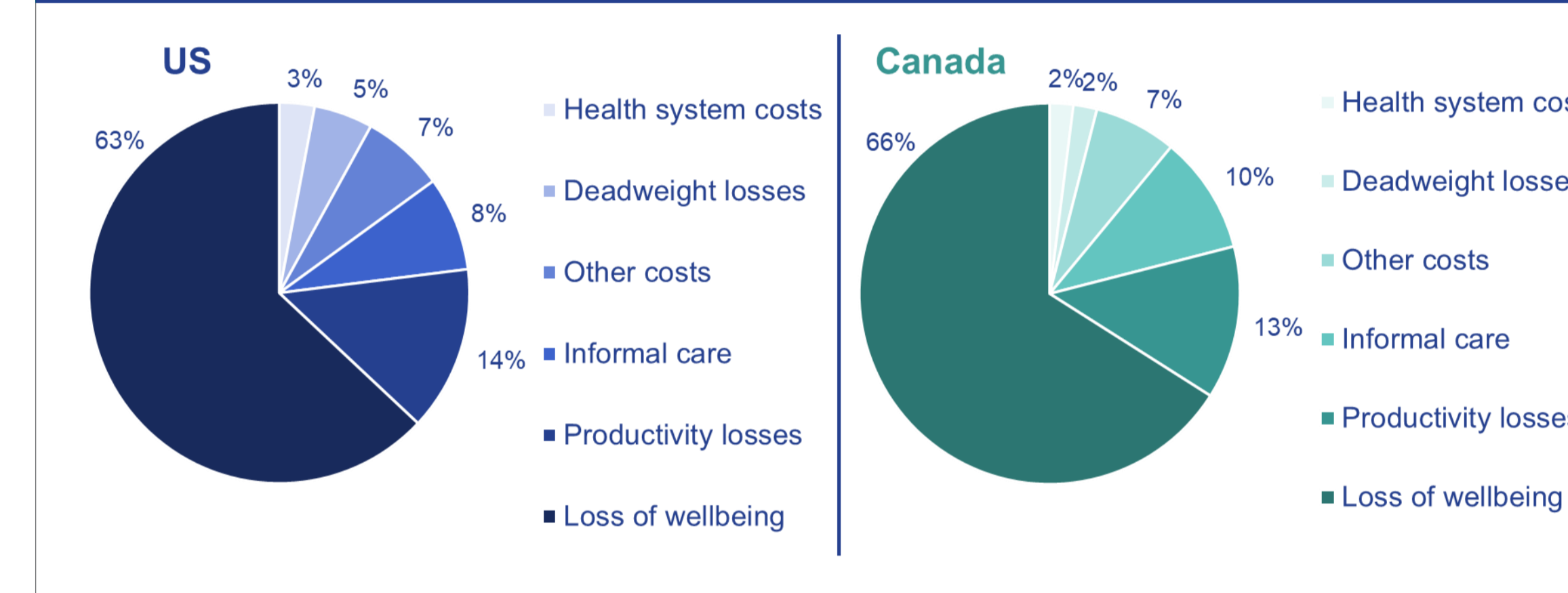


Figure 4. Breakdown of total IRD costs^{2,3}



Loss of wellbeing

- Loss of wellbeing, defined as reduced quality of life, was estimated using disability-adjusted life years²
- For patients with IRD, loss of wellbeing accounted for the largest share of total costs, ranging from \$51 million to \$120 million (USD) in the US and from \$6 million to \$26 million (CAD) in Canada (Table 1)²

Table 1. Estimated breakdown of costs for LHON based on overall IRD costs²

2019 Costs		US (USD, M)	Canada (CAD, M)
Financial costs	Health system costs		
	IRD (range)	963.8 to 2,216.8	37.8 to 144.3
	LHON (range)*	5.78 to 13.30	0.23 to 0.87
	Productivity costs		
Non-financial costs	IRD (range)	1,706.2 to 4,056.0	205.2 to 839.2
	LHON (range)*	10.24 to 24.34	1.23 to 5.04
	Loss of wellbeing		
	IRD (range)	8,431.7 to 20,043.6	1,071.4 to 4,381.9
Non-financial costs	LHON (range)*	50.59 to 120.26	6.43 to 26.29
	Deadweight losses		
	IRD (range)	706.0 to 1,662.9	38.3 to 155.7
	LHON (range)*	4.24 to 9.98	0.23 to 0.93

* Costs for LHON comprised 0.6% of the estimated total costs of all IRDs in the US and Canada.² This proportion is used to estimate the financial and non-financial costs associated with LHON

Cost of genetic testing

- A retrospective review of a regional genetics laboratory in the UK reported that among the 107 requests for neurogenetic tests in 82 patients, 6 requests (5.6%) were for LHON⁵
- The median cost per genetic diagnostic test was £225 (range £95 to £950)⁵
- A retrospective review of an Ocular Genetics Clinic in the US reported that up to 46% of patients suspected to have a genetic condition did not undergo genetic testing; approximately 59% of these patients declined to test for financial reasons⁶

Limitations

- There was a paucity of results and the majority of articles identified were abstracts with limited reporting of study methods and results. Both these factors limited the degree to which we could compare and contrast disease and treatment costs associated with LHON
- The SLR was limited to English-language publications. While this is generally considered acceptable for HTA submission, it presents a language bias and risk of exclusion of relevant studies not published in English
- Most of the evidence was generated from a few western countries, possibly limiting insights into the global costs associated with the treatment of LHON

Conclusions

- This SLR revealed that there are various gaps in the evidence regarding the economic burden of LHON
- Further, there are no published health economic models specific to LHON
- Despite limited available data, the indirect economic burden of LHON appears to be substantial, particularly for loss of wellbeing
- For comprehensive health economic evaluations that best support decision-making, a greater understanding of the true economic and humanistic burden of LHON is needed

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Abbreviations: CAD, Canadian dollar; HCRU, healthcare resource utilization; ICER, incremental cost-effectiveness ratio; IRD, Inherited Retinal Disease; LHON, Leber hereditary optic neuropathy; LY, life year; M, million; PICOS, Population, Intervention, Comparator, Outcomes, Study design; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; QALY, quality-adjusted life year; SLR, systematic literature review; USD, US dollar

References: 1) NORD's Rare Disease Database. <https://rarediseases.org/rare-diseases/leber-hereditary-optic-neuropathy/>. 2) Gong J, Cheung S, Fasso-Opie A, et al. The Impact of Inherited Retinal Diseases in the United States of America (US) and Canada from a Cost-of-Illness Perspective. *Clin Ophthalmol.* 2021;15:2855-2866. 3) Daly A, Cheung S, Galvin O. Cost of illness study of inherited retinal diseases in the USA and Canada. presented at: ARVO Annual Meeting Abstract; 2021; 4) Hahl J, Kosunen M, Pudas H, Renlund M. First 27 months of conditional reimbursement in Finland. *Value in Health.* 2013;22(S721). 5) Appleton J, Nicholl D, Fulton P, Macdonald F. Ten years of neurogenetic requests: to test or not to test? presented at: Association of British Neurologists (ABN) joint meeting with the Royal College of Physicians (RCP); 2013. 6) Lowery R, Dehnel J, Schaefer G, Uwaydat S. Rates of diagnostic genetic testing in a tertiary ocular genetics clinic. *Ophthalmic Genet.* 2020 41(3):271-274.