Economic Burden And Changing Treatment Landscape In Stargardt Disease: A Literature And Database Review

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Introduction

- Stargardt Disease (SD) is a rare disease, occurring in 1 person in 8,000-10,000 population[1].
- Onset is commonly seen in childhood, and patients present with bilateral central visual loss, with loss of retinal function over time[1].
- SD is caused by mutations in the *ABCA4* gene and is the most common form of inherited macular dystrophy[1].
- Currently there is no cure for SD[2]. However, vision loss can be slowed through patient actions that include wearing a hat and sunglasses, not smoking, and not over consuming vitamin A supplements[3].
- In anticipation of future therapies becoming available[4], it is important to understand the current economic burden of disease.
- To inform understanding of the disease landscape of SD, this study investigated the current healthcare resource utilisation (HCRU) and direct/indirect costs of SD alongside a review of registered clinical trials to identify potential upcoming treatments.

Methods and Searches

- A broad systematic literature review (SLR) was conducted in Embase in March 2023 to identify any data relating to the economic burden of SD.
- Eligible articles were full-text papers published 2008-2023 and conference proceedings published 2020-2023 that presented data relating to direct/indirect costs and HCRU in SD.
- A clinicaltrials.gov search was then conducted in June 2023 using the search term SD to identify potential future treatments for SD.
- Clinical trials of interest were those registered as Phase 2 or Phase 3, with a status of completed, active not recruiting, recruiting, or enrolling by invitation.

Embase hits: 16

clincialtrials.gov hits: 42

Costs and HCRU studies: 3

Included clinical trials: 8

Results

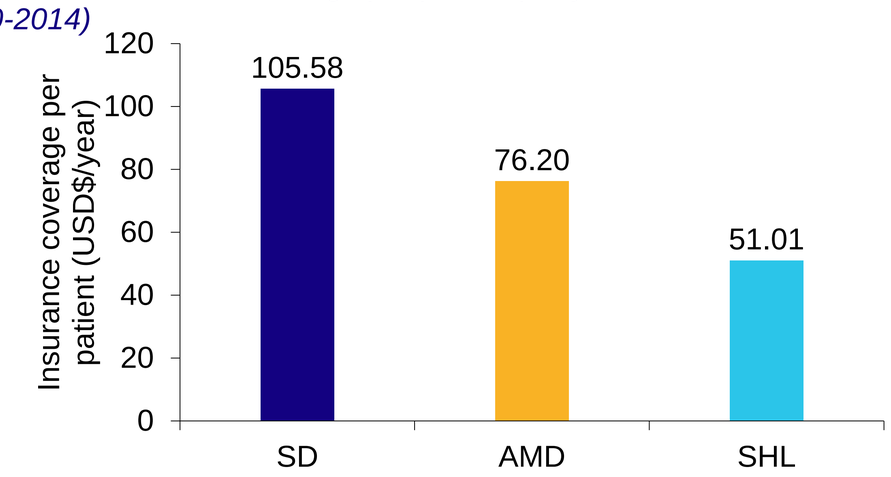
The SLR yielded 3 papers that were included in this review. These studies included data on HCRU and direct costs related to SD. No indirect cost data were identified.

Direct healthcare costs and HCRU

A claims data analysis conducted in the US in 2010-2014 compared SD with age-related macular degeneration (AMD) and bilateral sensorineural hearing loss (SHL)[5]:

- SD had the highest payment per year for insurance coverage, with an annual per-patient cost to the insurer of $105.58 (Figure 1). Female patients with SD were associated with higher costs than males (p=0.03).
- SD had highest median number of insurance claims per year at 0.51 (SHL: 0.40; AMD: 0.50).
- The most common healthcare services utilised for SD were fundus photography (11.98%), medical examination and evaluation (10.74%), and diagnostic imaging (9.14%).

Figure 1: Annual insurance coverage per patient per year for SD, AMD, and SHL (US, 2010-2014)



Note: costs were for the utilisation of disease-specific services. Therefore, most healthcare encounters were visits to the specialists, such as ophthalmologists, optometrists, otolaryngologists or audiologists.

Diagnostic costs

- SD is often misdiagnosed due to the absence of flecks or macular atrophy and normal fundus early in the disease. This has led to a diagnosis delay of 3 years in 50%-90% of SD cases[6]. Therefore, the identification of disease-causing mutations improves the accuracy of SD diagnosis[1].
- One study described a new resequencing chip with a 99% detection rate for 90 retinal diseases, including SD, costing €1500 – reportedly 5-10 times cheaper than conventional sequencing methods (Europe, 2009)[7].
- A second study identified that the main reason why patients with SD did not undergo diagnostic testing was due to the high cost to the patient (US, 2009-2018)[8].

The clinicaltrials.gov database search identified 8 Phase 2 or 3 trials in SD:

- 3 trials had been completed, 3 were recruiting, 1 was active, not recruiting, and 1 was enrolling by invitation (Table 1).
- 7 trials investigated drug interventions (emixustat, STG-001, avacincaptad pegol, ALK-001, tinlarebant) and 1 trial investigated a gene therapy (MCO-010) (Table 1).

Negative news

- STG-001 was withdrawn from the European Medicines Agency (EMA) orphan designation status at the Sponsor's request in 2023[9].

Positive news

- Emixustat received orphan designation status from the EMA in 2019[10] and announced positive post-hoc analysis results from Phase 3 in 2022[11].
- MCO-010 received fast track designation from the US Food and Drug Administration (FDA)[12] and released positive trial results[13] in 2023.
- ALK-001 was granted US FDA breakthrough designation in 2021, and Alkeus plan to submit a New Drug Application for approval in SD in 2024[14].
- Avacincaptad pegol has been granted FDA and EMA approval for the treatment of geographic atrophy, a form of AMD, in 2023[15]. No updates have been released from the sponsor regarding the indication in SD.
- Tinlarebant received EMA orphan designation in 2018,[16] and released 18-month intermin data from a 24-month Phase 2 trial showing tinlarebant was safe and well tolerated[17].

Table 1: Registered clinical trials investigating drug intervention for the treatment of SD

Status	Intervention	Phase	Sponsor	Completion Date	Study Location	NCT Number
Completed	Emixustat	2	Kubota Vision	Dec 2017	US only	NCT03033108
Completed	STG-001	2	Stargazer	Apr 2021	US only	NCT04489511
Completed	Emixustat	3	Kubota Vision	Jun 2022	Global	NCT03772665
Active, not recruiting	MCO-010	2	Nanoscope	Oct 2023	US only	NCT05417126
Enrolling by invitation	ALK-001	2	Alkeus	Dec 2024	US only	NCT04239625
Recruiting	ALK-001	2	Alkeus	Mar 2025	US only	NCT02402660
Recruiting	Avacincaptad pegol	2	Astellas (Iveric Bio)	Apr 2025	Global	NCT03364153
Recruiting	Tinlarebant	3	Belite Bio	Oct 2025	Global	NCT05244304

Conclusions

- The current healthcare costs associated with SD are not well established.
- With the likely launch of new pharmacologic treatments aiming to delay disease progression and the potential for a curable single-injection gene therapy, the treatment landscape is shifting.
- With uncertainty around the current economic burden of SD, it will be difficult to determine the economic impact of any new treatment options when making access decisions.
- With no data on indirect costs and limited data on direct costs, future analysis of SD cost related data would prove beneficial in determining the economic burden to the patient and caregiver for SD.
- In the absence of SD-specific economic data, other ocular degeneration disorders may prove useful as a source of economic data when making assessments for the current burden of SD.

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