Lumanity

Economic Evaluation and Budget Impact Analysis of ERTs in Patients with Pompe Disease – A Systematic Literature Review

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INTRODUCTION

- Pompe disease (PD), also known as glycogen storage disease type II, is a rare autosomal metabolic disorder that occurs due to deficiency of α-glucosidase – an enzyme responsible for glycogen breakdown.[1] This leads to release of glycogen into the cytoplasm and causes swelling in the organelles, triggering the worsening of cell function and structure and resulting in damage in various tissues like the heart, liver and skeletal muscles[2]
- PD has been traditionally classified according to the age at which it first presents: late-onset PD (LOPD) and infantile-onset PD (IOPD)[1]
- The approximate incidence of PD is 1:40,000 births[3], and the current standard of care for patients with PD is enzyme replacement therapy (ERT) including alglucosidase alfa

OBJECTIVES

The objective of this systematic literature review (SLR) was to identify and summarize model-based economic evaluations and budget impact analyses of ERTs in patients with PD.

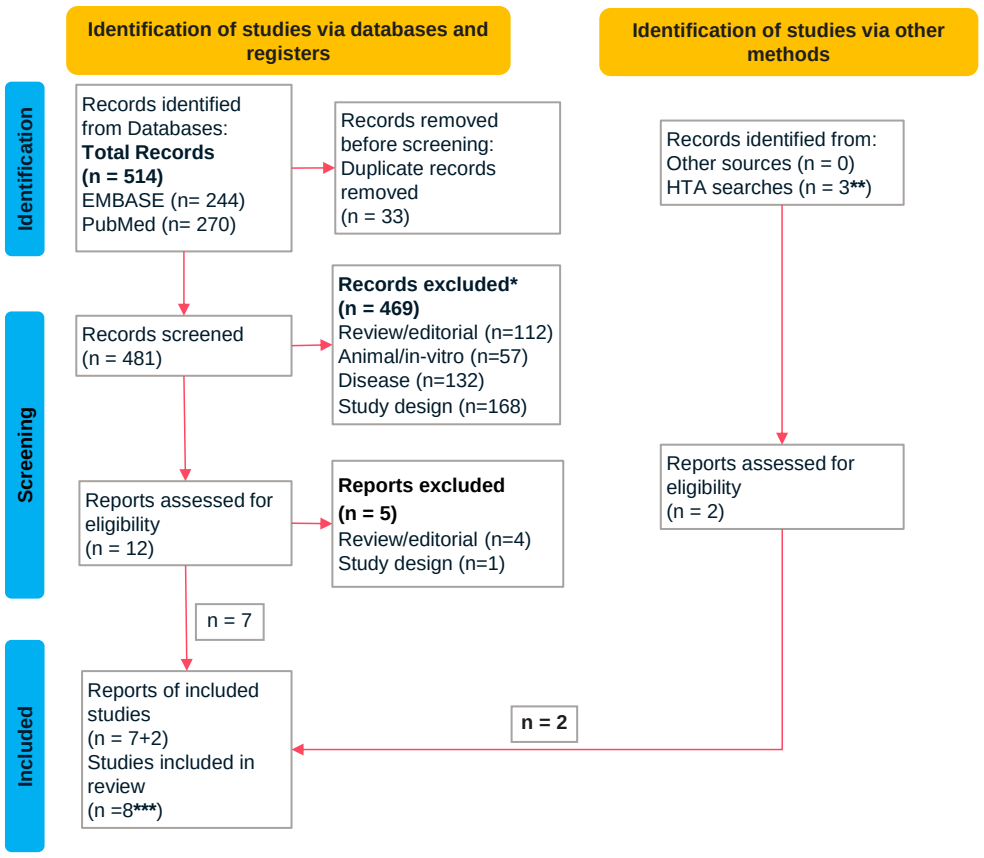
METHODS

- PubMed® and Embase® were systematically searched, according to guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[4], by combining relevant keywords to identify economic evaluation studies. The Population, Intervention, Comparator, Outcome, and Study design (PICOS) criteria were used to identify relevant studies
- Database searches were supplemented by bibliographic searches. The searches were not restricted by timeframe or study country; however, they were confined to English language studies
- The title and abstract of each publication retrieved from the database search were initially screened by two reviewers independently. Any uncertainty regarding the inclusion of a study was checked by a third independent reviewer. Data were extracted by one reviewer and quality checked against the source by another independent reviewer

RESULTS

Of the 514 records identified from the electronic database search, the final review included eight studies with model-based economic evaluations in patients with PD **(Figure 1)**

Figure 1: PRISMA flow diagram



Key: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
Notes: *All records were screened; manually, no automation tools were used.
**A total of three HTAs were identified initially but one HTA not assessed for eligibility as relevant outcome data was redacted.
***One of the study retrieved from the electronic database searches was linked, leaving six unique studies for data extraction.

SUMMARY OF EVIDENCE

- Of the eight included studies, two were conducted in the Netherlands[5,6], and one study each was conducted in the US[7], England/Colombia[11], Scotland[12], Canada[9], Iran[10] and Taiwan[8] (for details see **Table 1**)
- The evidence included a cost-effectiveness analysis or cost-utility analysis conducted using patient-level simulation model in the Netherlands[5,6]; a cost–utility analysis conducted using a Markov model in England and Colombia[11]; a combination of Markov and decision tree models in Iran[10]; a decision analytic micro-simulation model in the US[7]; and a cost-minimization analysis conducted alongside a trial in Canada[9]. No model details were reported for Taiwan[8] and Scotland[12]
- A payer or healthcare perspective was adopted in four studies[9,10,11,12] and a societal perspective in three studies[5,6,8] and both societal and healthcare perspective in one study[7]
- Three studies assessed ERT versus no ERT, two assessed ERT versus supportive therapy, and one study assessed avalglucosidase alfa versus alglucosidase alfa.[9] Two studies assessed newborn screening programmes, including newborn screening + ERT versus clinical diagnosis + ERT[7] and universal screening versus self-paid screening[8]

BUDGET IMPACT ANALYSIS

- In Scotland[12], the manufacturer estimated the gross drug budget impact of alglucosidase alfa in infants to be £167,000 in Year 1 and £210,000 in Year 5. The respective cost for late onset patients was £1.04 million in Year 1 and £2.6 million in Year 5
- In Canada[9], the budget impact of reimbursing avalglucosidase alfa for patients with LOPD is expected to yield 3-year total budgetary savings of $3,041,419 (or $3,044,660 when dispensing fees and markups are included) when both new and switching patients are considered

Table 1: Key characteristics of the included studies

Study name (Country)	PD classification	Analysis type	Model	Time horizon	Perspective	Cost year	Discounting
Castro-Jaramillo 2012[11] (England and Colombia)	IOPD	CUA	Two Markov models for comparing both countries (state transition model)	20 years	Healthcare	2010	5% for both costs and effects
Chien 2011[8] (Taiwan)	IOPD	CUA	NR	NR	Societal	NR	NR
Hashempour 2020[10] (Iran)	IOPD	CUA; CEA	Markov model and decision tree	Lifetime	Payer	2017	Not used
Kanters 2017[5] (Netherlands)	PD	CUA; CEA	Patient-level simulation model	Lifetime	Societal	2014	Costs discounted at 4.0%; effects at 1.5%
Kanters 2014[6] (Netherlands)	IOPD	CUA; CEA	Patient-level simulation model	Lifetime	Societal	2009	Costs discounted at 4%; effects at 1.5%
Richardson 2021[7] (US)	IOPD	CUA	Decision analytic micro-simulation model	Lifetime	Societal; healthcare	2016	QALYs discounted at 3%
CADTH 2022[9] (Canada)	LOPD	CMA	NA	1 year	Payer	NR	NR
SMC 2007[12] (Scotland)	IOPD	CUA	NR	Lifetime	Payer	NR	NR

Key: CADTH, Canadian Agency for Drugs and Technologies in Health; CEA, cost-effectiveness analysis; CMA, cost-minimization analysis; CUA, cost-utility analysis; IOPD, infantile-onset Pompe disease; LOPD, late-onset Pompe disease; PD, Pompe disease; NA, not applicable; NR, not reported; SMC, Scottish Medicines Consortium.

KEY FINDINGS

- In the Netherlands, cost-effectiveness analyses among patients with IOPD and adult patients with PD estimated an incremental cost-effectiveness ratio (ICER) of €1.0 million[6] and €3.2 million[5] per quality-adjusted life year (QALY) gained, respectively, with ERT compared with supportive therapy. This was primarily due to the high ERT cost[5]
- The cost per QALY remained very high for ERT compared with no ERT in high-income countries like England (£234,308; cost year: 2010) and middle-income countries like Colombia (£109,991; cost year: 2010) in patients with IOPD[11]
- ERT was not considered cost-effective in Iran (ICER was US$96,809 for ERT with human acid alpha-glucosidase over no ERT)[10], and the Scottish Medicines Consortium (SMC)[12] reiterated that ERT is associated with an extremely high cost for health gain
- Newborn screening can result in substantial health gains for patients with IOPD, but with additional costs, as reported in a study in the US.[7] Furthermore, a universal screening programme showed savings of US$133 per QALY versus self-paid screening in patients with IOPD in Taiwan[8] (for details see **Table 2**)

Table 2: Results of included studies

Study name	Intervention Comparator	Increment-al QALY	Incremental LYG	Incremental costs	ICER
Castro-Jaramillo 2012[11]	ERT with alglucosidase alfa No ERT (England)	5.07	NR	£1187,940	£234,308/QALY gained
	ERT with alglucosidase alfa No ERT (Colombia)	5.07	NR	£557,653	£109,991/QALY gained
Chien 2011[8]	Universal screening Self-paid screening	NR	NR	NR	US$133/QALY gained
Hashempour 2020[10]	ERT with human acid alpha-glucosidase No ERT	3.79	4.92787	US$366,777	US$96,809/QALY gained US$74,429/LYG
Kanters 2017[5]	ERT with alglucosidase alfa ST	2.04	1.89	€6,466,827	€3,167,914/QALY gained € 3,417,713/LYG
Kanters 2014[6]	ERT with alglucosidase alfa ST	6.75	13.39	€7,000,028	~€1,000,000/QALY gained ~€500,000/LYG
Richardson 2021[7]	NBS with ERT Clinical identification with ERT	466	NR	Healthcare sector: US$190,043,216 Societal: US$176,660,800	Healthcare sector: US$408,000/QALY Societal: US$379,000/QALY
CADTH[9] (Reimbursed with conditions[d])	Avalglucosidase alfa	NR	NR	CA$27,292 per patient per year	NR
	Alglucosidase alfa	NR	NR		NR
SMC[12] (Not recommended[e])	Alglucosidase alfa	NR	NR	NR	£244,450/QALY[a] £244,450/QALY[b] £819,806/QALY[c]
	No ERT	NR	NR	NR	

Key: CADTH, Canadian Agency for Drugs and Technologies in Health; ERT, enzyme replacement therapy; ICER, incremental cost-effectiveness ratio; LYG, life years gained; NBS, newborn screen; NR, not reported; QALY, quality-adjusted life year; SMC, Scottish Medicines Consortium; ST, supportive treatment.
Note: [a]Infants who receive their first dose of alglucosidase alfa before the age of six months; [b]Infants who receive their first dose of alglucosidase alfa between the ages of six months; [c]People with severe late-onset Pompe disease; [d]CADTH recommends that avalglucosidase alfa be reimbursed by public drug plans for the long-term treatment of patients with late-onset Pompe disease if certain conditions are met; [e]Alglucosidase alfa is not recommended for use within NHS Scotland for the treatment of Pompe disease.

CONCLUSIONS

- This SLR suggests that ERTs can provide substantial benefits in terms of life expectancy but at higher incremental costs, impacting its overall cost-effectiveness
- Considerable budgetary savings have been reported with the use of ERTs in patients with LOPD when both new and switching patients are considered
- Newborn screening results in considerable health gains for patients with IOPD and may be cost-effective when considering the fact that PD is a rare disease
- Therefore, exploring more cost-effective treatment options and screening methods is warranted in the future to overcome the persistent and lifelong economic burden of PD
- However, the results of this SLR should be interpreted with caution because there is a dearth of economic evaluations assessing individual treatments/screening activities in patients with Pompe disease. Only nine economic evaluation studies were retrieved in this review, the majority of which focused on cost utility/cost-effectiveness of the only currently approved treatment – the ERTs
- Further research with more cost minimization and budget impact analysis studies are needed for better understanding of the benefits in cost-effectiveness for healthcare decision-making purposes

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