

Enzyme replacement therapy for late-onset Pompe disease: a systematic review

Guilherme I. P. S. Gertsenchtein^{a,b}, Ida V. D. Schwartz^{a,b}

^aHospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; ^bFederal University of Rio Grande do Sul, Porto Alegre, Brazil.

Introduction

Pompe disease (PD) is an inherited disorder characterized by deficiency of acid alpha-glucosidase, leading to progressive glycogen accumulation in the body's organs and tissues.

Previous systematic reviews (SR) on enzyme replacement therapy (ERT) for late-onset PD (LOPD) haven't evaluated important endpoints as quality of life (QOL) and safety, creating the need for reassessing clinical outcomes.

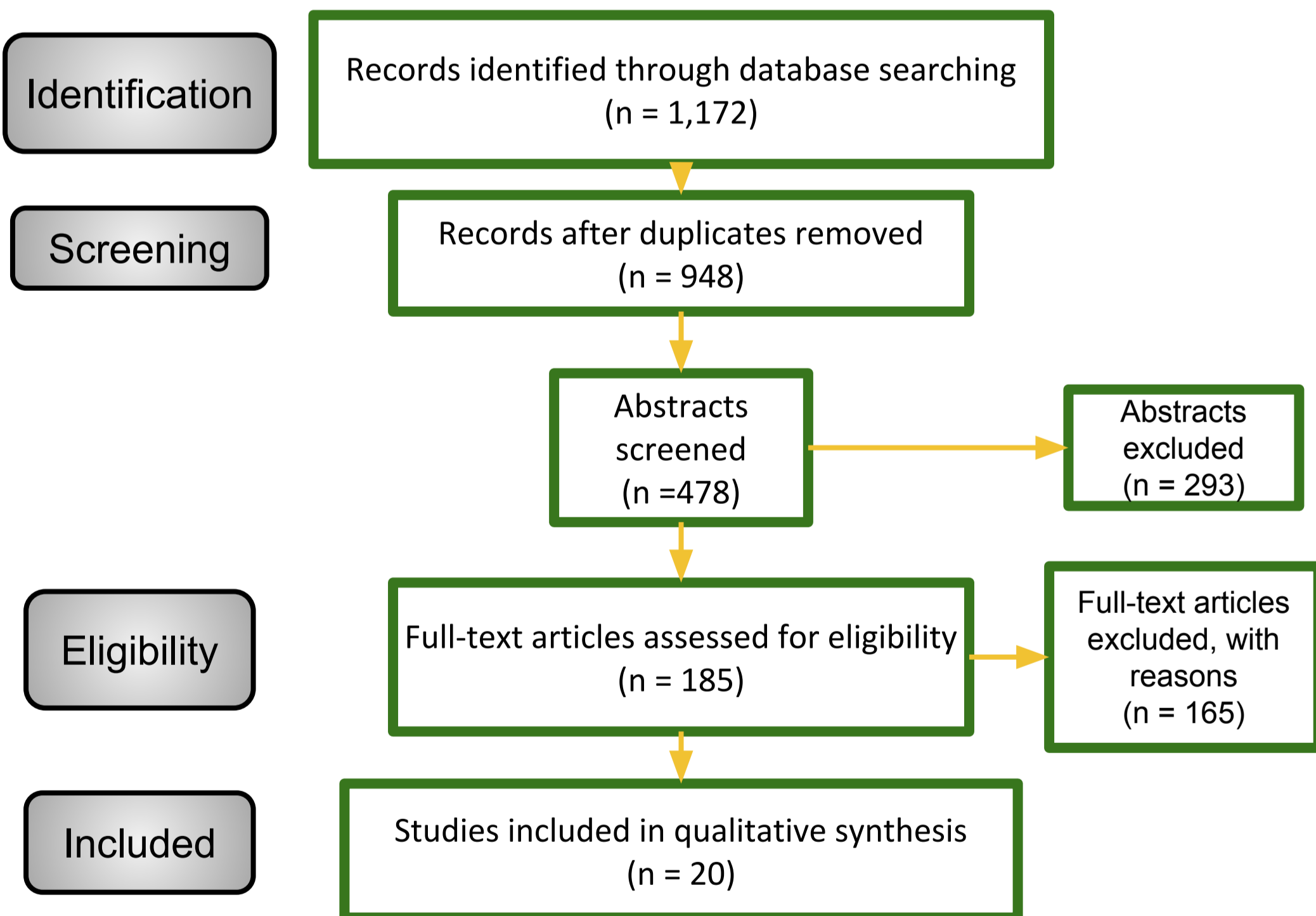
Objective

To evaluate evidence available on the efficacy and safety of ERT for LOPD.

Methods

We systematically searched PubMed and Embase for prospective clinical studies published until May, 2017 evaluating ERT for LOPD.

Outcomes of interest were defined *a priori*. Only studies with $n > 5$ were included. Assessment of quality of evidence (QOE) was performed according to the GRADE criteria.



Results

A total of 1172 articles were identified, 185 studies were eligible for abstract and full text reading and 25 articles were included in our analysis.

From a total of 10 endpoints evaluated, 4 had moderate or high GRADE Score: QOL, 6MWT, Muscle strength and AE.

Two endpoints defined a priori was not assessed by any of the studies: Sleep quality and Swallowing.

Quality of life outcome was evaluated in 6/25 studies and 5/6 used the SF-36 questionnaire, which measures physical and mental components. In spite of heterogeneous results across studies, GRADE score was moderate and the final results favors ERT.

Table 1. QOE according to GRADE criteria

Muscle Strength: High
Quality of life (QOL): Moderate
6MWT: High
WGMS: Very low
FVC : Very low
Survival : Very low
Adverse events (AE): Moderate
Ventilation hours/day: Low

Table 2 - Search Strategies

Research Data Base	Search Strategy
Medline (via PubMed)	"Glycogen Storage Disease Type II"[Mesh] AND "alpha-Glucosidases"[Mesh]
Cochrane (via Bireme)	('glycogen storage disease type 2'/exp) AND ('recombinant glucan 1, 4 alpha glucosidase'/exp or 'recombinant glucan 1, 4 alpha glucosidase')

6MWT is a substitute outcome for cardiopulmonary system evaluation. In all 12 studies assessing 6MWT, patients under ERT showed improvement, with high QOE .

Muscle strength (MS) was evaluated in 8/25 included studies and only 2/8 were unable to show improvement after ERT, also with high QOE. Strength was graded according to the grading scale of the Medical Research Council (MRC) and was measured with dynamometer and quantitative muscle testing (QMT).

Most AE were considered to be mild or moderate symptoms, such as urticarial rashes, flu-like symptoms, pruritus and hyperhidrosis. None of these AE caused discontinuation of the treatment.

In AE evaluation, one concern is antibody formation. In 4/5 studies, antibody anti-aglucosidase was analyzed and although all patients developed antibodies there was no correlation with severe AE and infusion-associated reactions (IARs) nor with treatment efficacy. Most IARs were mild to moderate in severity. The results suggest that ERT is safe in patients with PD.

Other outcomes had low or very low QOE, such as WGMS, Survival, Ventilation hours/day. In all 5 studies evaluating WGMS there was no improvement shown, however more data has to be assessed considering the very low QOE.

Table 3 - Outcomes and number of articles that evaluated it

Outcomes	Number of articles
6MWT	12
FVC (Forced vital capacity)	12
Adverse events (AE)	12
Muscle strength	8
Quality of life (QOL)	6
WGMS (Walton Gardner Medwin Score)	5
Ventilation hours/day	3
Survival	1
Sleep quality	0
Swallowing	0

Discussion

Our results corroborate previously published SR on ERT impact on 6MWT and show positive effect of ERT on QOL and MS.

Our findings also suggest that ERT is safe in LOPD, once most AEs were mild to moderate and antibody formation did not seem to interfere with any outcome evaluated.