PCR105

Identifying Rare Diseases: Do New Therapies Improve Time to Diagnosis?

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Introduction

•**Orphan Disease Impact**: Although rare diseases affect a small population fraction (defined in the US as affecting less than <200,000 individuals), their collective impact extends to millions of individuals globally[1]

•**Historical Challenges**: Due to the small number of patients in given diseases there is minimal incentive for investment in developing treatments, precipitating diagnostic delays and misdiagnoses

•**Legislative Transformation**: The U.S. Orphan Drug Act of 1983 created incentive for the development of treatments for orphan conditions through extended exclusivity periods, tax breaks, and other advantages.[2]

•**Therapy Awareness**: As new treatments become commercially available there may be heightened awareness in patients and providers of symptoms and new treatments

•**Research Aims**: This study sought to evaluate whether the availability of rare disease therapy may be associated with a younger age of diagnosis as a proxy for increasing awareness

Methods

•**Literature Search:** To identify potential trends in time to diagnosis a literature search was conducted to identify outcomes of interest (below) in select rare diseases. PubMed and Google Scholar were queried using search strings built to identify surveys, observational studies, and patient reported results (e.g., "hereditary angioedema patient survey")

•**Diseases Analyzed:** Diseases of interest were identified as hereditary angioedema (HAE), Gaucher's disease (GD), and Fabry's disease (FD) based on recent therapy developments and rare disease status. Treatments were first approved by the FDA in 2001 (GD), 2003 (FD), and 2010 (HAE) (date of regulatory approval used as a proxy for commercial availability)

•**Outcomes** : The following outcomes were abstracted from identified literature

- **Primary outcome:** Mean age of diagnosis as reported in patient surveys, clinical trials, and retrospective/prospective studies that included mean age of diagnosis
- **Secondary outcome**: Mean age of participation in patient surveys, clinical trials, or entry into registry studies

•**Analysis:**

- To evaluate trends, mean patient ages and the year studies were conducted were mapped to a scatter plot and a line fit using linear regression. R^2 statistic detailed the proportion of variability attributable to time since commercial treatment availability (for this analysis, $R^2 > 0.30$ = moderate fit, $R^2 > 0.50$ = excellent fit)
- **Hypothesis for evaluation**: Age of diagnosis reported in recent literature trends downward with >50% of variability attributable to time since commercial availability

Conclusions

•This study did not reveal that commercial availability of rare disease treatments significantly impacted the age of diagnosis.

•Age of participation in disease studies tended to increase in the years following commercial availability, although publication bias may have

•Notably, most studies identified took place within 10 years of commercial availability, suggesting therapy approval attracts interest in conducting and publishing disease research

•A relatively small sample of studies was identified, increasing the impact of outliers. Additionally, participants may not be representative of a given disease or the cohort itself (e.g., subtype) may have introduced confounding factors, despite attempting to control for confounders. HAE is a condition that is primarily diagnosed after a swelling attack, which may impact age of diagnosis. Some studies may have captured the same patients.

•Further research may be warranted to investigate this hypothesis and examine if increased awareness also drives the identification of mild disease in older patients

Age at Diagnosis Results

Studies: 7 studies that reported age of diagnosis were identified for HAE, 3 in GD, and 4 in FD[3,7,8,9,10,12,16,19,20,23,26,27,29,30]

Results: Reported HAE age at diagnosis decreased (R^2=0.03, Figure 1A), while age of diagnosis appeared to increase in GD (R^2=0.29, Figure 1B) and was flat in FD (R^2=0.01, Figure 1C) since treatment availability (pre-treatment availability period shaded light red).

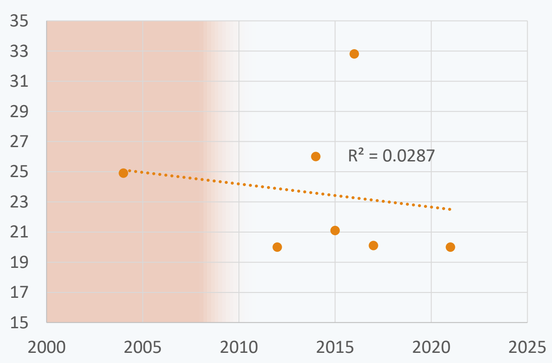
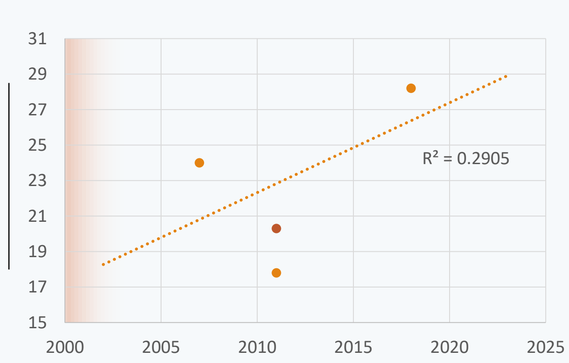
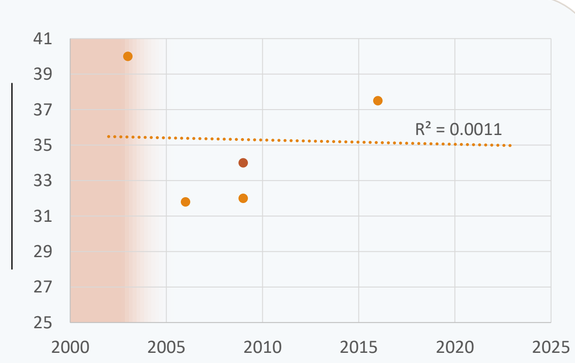


Figure 1. HAE Age of Diagnosis (A)



Gaucher's Disease Age of Diagnosis (B)



Fabry's Disease Age of Diagnosis (C)

Age of Participation Results

Studies: 12 studies that reported age of diagnosis were identified for HAE, 7 in GD, and 5 in FD [3,4,5,6,8,9,10,11,13,14,15,17,18,19, 20,21,22,23,24,25,26,28,29,30]

Results: Age of participation increased in the time since HAE (R^2=0.16, Figure 2A), GD (R^2=0.08, Figure 2B) and FD (R^2=0.25, Figure 2C) treatments became available (pre-treatment availability period shaded light red).

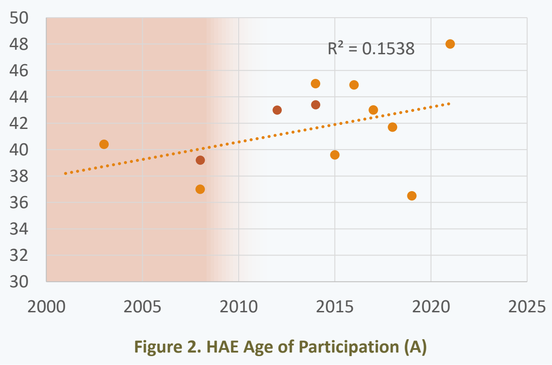
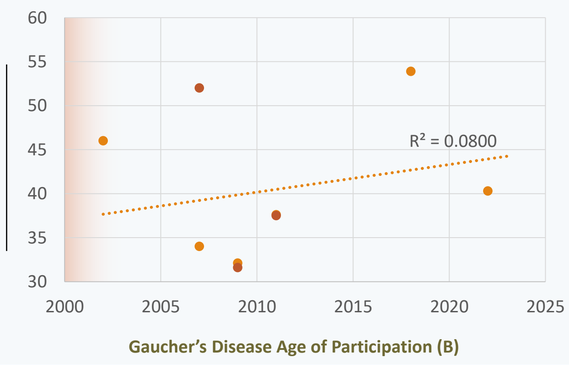
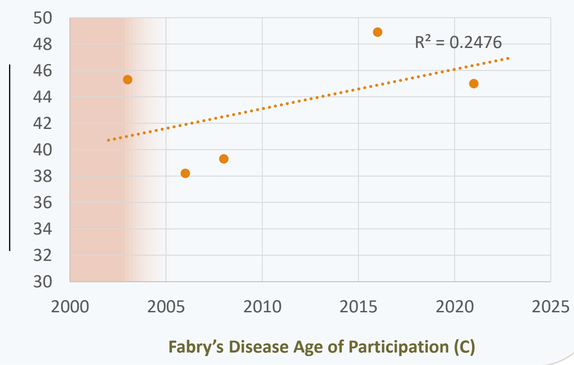


Figure 2. HAE Age of Participation (A)



Gaucher's Disease Age of Participation (B)



Fabry's Disease Age of Participation (C)

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