Exploring the Impact of a Rare Disease (RD) Diagnosis on Work Productivity and Social Activity Impairment: A Systematic Literature Review (SLR)

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Introduction and Objective

- A RD is defined by the US Orphan Drug Act as a condition that affects fewer than 200,000 people[1], with RD in Europe defined as diseases that affect fewer than 1 in 2,000 people[2].
- While RD individually have a low prevalence, the large number of RD being diagnosed means over 30 million Americans[1] and 30 million Europeans[2] are affected in total.
- Since each RD presents unique challenges for the patient, the way in which each disease affects a patient's work and social activity likely varies. Receiving a RD diagnosis could impact work by resulting in missed days, reduced productivity while at work, career changes, or early retirement, depending on the specific disease manifestations experienced.
- Therefore, this study aimed to explore the impact on work productivity and social activity impairment in six RD: Huntington's disease (HD), dystrophic epidermolysis bullosa (DEB), hereditary angioedema (HAE), transthyretin amyloidosis (ATTR), Stargardt disease (SD), and alpha-1 antitrypsin deficiency (A1AT).

Methods

- A broad SLR was conducted in Embase in March 2023 to evaluate the direct and indirect costs associated with the six RD.
- Studies of interest were full text papers published 2008-2023 or conference proceedings published 2020-2023 presenting data on healthcare resource utilization or disease-related direct or indirect costs. This sub-analysis was focused on data relating to work and social activity impairment.
- Studies were screened by two reviewers and reconciled by a third. Data was extracted by a single reviewer, with data number-checked by a second reviewer.
- Costs were converted from the published currency into USD using April 2024 currency rates using: https://www.google.com/finance/ (1 Euro = 1.09 USD).

Embase hits: 1,238
(HD: 238, DEB: 63, HAE: 622, ATTR: 128, SD: 16; A1AT: 171)

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Included economic studies: 189
(HD: 62, DEB: 14, HAE: 55, ATTR: 25, SD: 3, A1AT: 31)

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Work impairment studies: 39
(HD: 12, DEB: 2, HAE: 18, ATTR: 4, SD: 0, A1AT: 3)

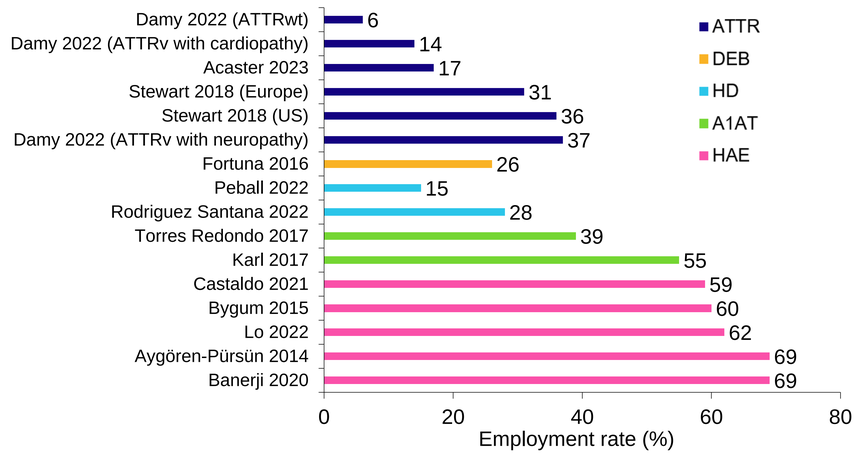
Results

The SLR yielded 36 papers with data on the impact on RD on work. No data on the impact of an SD diagnosis on work were identified, leaving 5 RD for comparison. Full citations of all papers are included in the supplementary document.

Patient employment rates

- Employment rate varied substantially across RD, highest in HAE (59%-69%) and A1AT (39%-55%) and lowest in DEB (26%), HD (15%-28%), and ATTR (6%-37%; Figure 1)[2-14].

Figure 1: Average employment rates in patients by RD (%)[2-14]



- For patients with ATTR, employment rates was lowest for wild type ATTR (ATTRwt) compared to hereditary ATTR (ATTRv)[2] (Figure 1). Moreover, patients with ATTRv with cardiopathy reported lower employment rates than patients with ATTRv with neuropathy[2].
- For hospitalized patients with HD, a group who potentially had more severe disease, lower employment rates were reported (15%)[7] compared with a study where all disease stages of HD were included (early, mid, advanced; 28%[8]).
- Discrepancies observed in the employment rates for patients with A1AT may be due to variance in sample sizes (Torres Redondo 2017[9] [n=26]; Karl 2017[10] [n=131]).

Work productivity and social activity impairment by RD

- HD is associated with the highest overall work impairment, activity impairment, and presenteeism (Table 2).
- A1AT showed the highest absenteeism due to sick days (67%)[10] and reported the greatest number of missed days per patient per year (25 days)[10], associated with annual costs of $4,777 (€4,395)[10].
- HAE reported the highest annual cost for lost productivity ($14,243)[10] (DEB: $513 [€471][15]; not reported for other RD) but the least impact on activity impairment.
- The range in work impairment values observed in ATTR is attributed to lower values in Spain vs US, although both locations report considerable activity impairment[4].

Table 2: Work impairment by RD

Disease area	Absenteeism (% range)	Presenteeism (% range)	Overall work impairment (% range)	Activity impairment (% range)
HAE[16, 18-20]	6 - 8	20 - 25	22 - 27	28 - 34
HD[7,21]	12 - 20	42 - 60	48 - 61	58 - 79
ATTR[5]	0 - 22	5 - 41	5 - 47	33 - 56
A1AT[10]	67*	NR	NR	NR

Abbreviations: NR: not reported; **Note:** *Karl 2017 only reported percentage of patients with sick days compared to absenteeism overall.

Impact on career

- Impact on career due to RD diagnosis was described in Table 3.
- Annual costs per patient due to early retirement were higher in A1AT ($13,129)[10] compared to DEB ($6,298 [€5,794])[15] (not reported for other RD).

Table 3: RD impact on careers

RD	Impact on career
HAE	• Prevented career advancement in **36%** of patients[14] • Prevented **40%** of patients from applying to certain jobs[14] • Average lost earnings per year was **$3,818**[11]
HD (with chorea)	• **45%** of patients changed their workplace[22] • **33%** of patients adopted flexible working hours[22]
ATTR	• Up to **14%** stopped work due to RD diagnosis[3]
A1AT	• **35%** reported premature retirement[10]

Conclusions

- Substantial work/activity impairment and low employment rates were observed in HD, likely linked to the motor and cognitive decline that occurs as the disease progresses. Given the substantial impact of this RD on patient work productivity and social involvement, this should be a key area of focus for improvement when assessing future treatments.
- The high absenteeism burden observed in A1AT may be due in part to the management of the disease, as treatment includes augmentation therapy involving weekly infusions of purified alpha-1 antitrypsin, which may cause patients to be away from work. A therapy with a less intensive treatment schedule would be beneficial for this patient group in order to improve work-related outcomes.
- Although ATTR has a later onset and more patients may be retired, considerable social activity exists and for those who remain employed work impairment is observed.
- In contrast, the lower activity impairment in HAE may reflect recent advances in treatment, since novel gene therapies provide promising opportunities in the management of HAE[23].
- Lack of data suggests that productivity may be overlooked and poorly understood in some RD (e.g. SD).

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