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REVIEW

Comparison Between Burden of Care Partners of Individuals with Alzheimer's Disease Versus Individuals with Other Chronic Diseases

Murat Demirbas · Julie H. Hahn-Pedersen · Henrik L. Jørgensen

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ABSTRACT

Background: Caregiving in Alzheimer's disease (AD) is often provided by informal care partners, who spend more hours per week on average than care partners of individuals with conditions other than AD. However, the burden of care in partners of individuals with AD has not been systematically compared to that of other chronic diseases.

Objective: The current study therefore aims to compare the care partner burden of AD to that of other chronic diseases through a systematic literature review.

Methods: Data was collected from journal articles published in the last 10 years, using two unique search strings in PubMed and analysed using pre-defined patient-reported outcome measures (PROMs) including the EQ-5D-5L, GAD-7, GHQ-12, PHQ-9, WPAI and the ZBI. The data was grouped according to the included PROMs and the diseases studied. The number of participants in the studies reporting burden of caregiving in AD was adjusted to reflect the number of participants in studies reporting care partner burden in other chronic diseases.

Results: All results in this study are reported as a mean value and standard deviation (SD). The ZBI measurement was the most frequently used PROM to collect care partner burden (15 studies) and showed a moderate burden (mean 36.80, SD 18.35) on care partners of individuals with AD, higher than most of the other included diseases except for those characterized by psychiatric symptoms (mean scores 55.92 and 59.11). Other PROMs such as PHQ-9 (six studies) and GHQ-12 (four studies) showed a greater burden on care partners of individuals with other chronic diseases such as heart failure, haematopoietic cell transplantations, cancer and depression compared to AD. Likewise, GAD-7 and EQ-5D-5L measurements showed a lesser burden on care partners of individuals with AD compared to care partners of individuals with anxiety, cancer, asthma and chronic obstructive pulmonary disease. The current study suggests that care partners of individuals with AD experience a moderate burden, but

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M. Demirbas (✉)
Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
e-mail: muratdemirbas@hotmail.dk

J. H. Hahn-Pedersen
Novo Nordisk A/S, Søborg, Denmark

H. L. Jørgensen
Department of Clinical Biochemistry, Copenhagen University Hospital, Hvidovre, Denmark

H. L. Jørgensen
Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

with some variations depending on the PROMs used.

Conclusion: The results of this study were mixed with some PROMs indicating a greater burden for care partners of individuals with AD versus other chronic diseases, and other PROMs showing a greater burden for care partners of individuals with other chronic diseases. Psychiatric disorders imposed a greater burden on care partners compared to AD, while somatic diseases in the musculoskeletal system resulted in a significantly smaller burden on care partners compared to AD.

Keywords: Alzheimer's disease; Care partner burden; Chronic diseases; Patient-reported outcome measure

Key Summary Points

The care of individuals with chronic diseases can often be a challenging and demanding task, particularly for those who act as informal care partners.

This study examines the care partner burden of Alzheimer's disease and compares it to that of other chronic diseases.

The most important patient-reported outcome measure (PROM) showed a higher care partner burden for Alzheimer's disease: 36.8 scale points compared to a range of 0.8–28.9 for other chronic diseases, the exception being psychiatric diseases with 59.11 scale points. The other PROMS studied showed mixed results.

INTRODUCTION

The care of individuals with chronic diseases can often be a challenging and demanding task, particularly for those who act as informal care partners. Informal care partners often provide physical, emotional and logistical support to individuals with chronic diseases. The burden of care can negatively impact the well-being and quality of life (QoL) of both the care partner and the individual with the chronic disease [1]. Most research has focused on the QoL of the patients. Less is known about the impact of chronic diseases on the QoL of relatives and informal care partners [2].

Alzheimer's disease (AD) is a chronic and progressive neurological disease characterized by the deterioration of cognitive functions causing neuropsychiatric symptoms, impairments in activities of daily living with multiple social and individual consequences [3]. AD is the most frequent cause of dementia, accounting for 60% to 70% of cases [4]. The accumulation of beta-amyloid plaques and tau tangles induces neurodegeneration which impairs cognitive function and manifests as the symptoms of AD [5]. The progression of AD follows a three-stage continuum, beginning with the preclinical disease, in which the beta-amyloid is abnormal, but cognition is unaffected. This can progress into mild cognitive impairment (MCI) which can ultimately evolve into clinically apparent AD dementia [6]. More than 400 million people are affected across the AD continuum on a global scale, costing more than a trillion US dollars annually [7]. In addition, dementia is the most prevalent chronic neurological disease that requires caregiving [3]. As with many other chronic diseases, caregiving in AD is often provided by informal care partners, and a recent study has shown that care partners of individuals living with AD spend more hours per week on average than care partners of individuals with conditions other than AD [8].

There is an increased focus on the care of individuals with AD and a reduction of the burden of care in partners has become a public focus area [9, 10]. One way of measuring the care partner burden is through patient-reported outcome measures (PROMs) as they provide a standardized way to measure the perceptions and experiences of the care partners [11].

In addition to the PROMs themselves, it is relevant to look at the minimal clinically important difference (MCID). The concept pertains to the smallest quantifiable alteration in a score that is deemed clinically significant and is perceived by patients as a noteworthy

improvement or deterioration in their health status. It is important to recognize that a statistical variation does not necessarily correspond to a clinically relevant modification, particularly when evaluating PROMs [12].

Few studies report direct comparisons of the burden of care in partners of individuals with AD with the burden of care in partners of individuals with other chronic diseases, and no studies have systematically compared AD with numerous other chronic diseases in the same study.

The current study therefore aimed to compare the care partner burden of AD to that of other chronic diseases through a systematic literature review including studies investigating care partner burden of individual chronic diseases through PROMs.

METHODS

Two search strings were created to identify relevant data on care partner burden of AD and other chronic diseases (Supplementary Table 1). The two searches were conducted on PubMed in September and October 2022 to identify data on care partner burden for AD and other chronic diseases from the last decade. One researcher screened titles and abstracts to determine if they met the eligibility criteria.

Eligibility Criteria

Journal articles published during the last 10 years were included in both searches. No geographical restrictions were imposed on the search in this study. The inclusion criteria were:

- Care partners of individuals with AD or another chronic disease
- Completion of one or more PROMs in the article
- Studies in English language only

Exclusion criteria for the screened articles were:

- Studies not reporting either mean or standard deviation (SD) of the PROM values
- Another type of dementia than AD
- Studies reporting PROM values based on more than one disease (comorbidities)
- Randomized clinical trials and method papers

Data Extraction and Analysis

Data about diseases, PROMs and study results, including mean and SD, if reported, were entered into a data extraction table. Data collection was grouped according to the PROMs employed and the diseases studied. The number of participants in the studies reporting burden of caregiving in AD was adjusted according to the number of participants in the studies reporting care partner burden in other chronic diseases. This was done to obtain an estimate of the total and to obtain the correct weight of the respective studies for each PROM. All values are reported as mean and standard deviation (SD) in this study.

Review Manager (RevMan 5.4, Cochrane Collaboration, Oxford, England) was used to create forest plots, illustrating comparisons between burden of caregiving in AD and burden of caregiving in other chronic diseases. Mean differences and SD were calculated across studies to allow for comparisons between AD and other chronic diseases.

Patient-Reported Outcome Measures

The included PROMs were pre-defined as EuroQol-5 Domain-5 Level (EQ-5D-5L), General Anxiety Disorder-7 (GAD-7), General Health Questionnaire-12 (GHQ-12), Patient Health Questionnaire-9 (PHQ-9), Work Productivity and Activity Impairment (WPAI) and Zarit Burden Interview (ZBI). These measurements allowed for comparisons to be made across studies and provided a nuanced perspective on the burden in care partners of individuals with AD and care partners of individuals with other chronic diseases.

Minimal Clinically Important Difference

MCID in each unique PROM is defined as the smallest change in a score that is perceived as meaningful by the patient or care partner [12, 13].

EuroQol-5 Domain-5 Level

EQ-5D-5L is a standardized measure of QoL consisting of five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has five levels of severity: no problems, slight problems, moderate problems, severe problems and unable to perform or extreme severity. The measurement was conducted with a visual analogue scale and provided a single value of the global QoL ranging from 0 (worst imaginable health) to 1 (perfect health) [14, 15]. The MCID for the EQ-5D-5L was defined as 0.1 based on a single study of patients with stroke [13].

General Anxiety Disorder-7

GAD-7 is a self-report questionnaire used to assess the generalized anxiety in adults. It consists of seven questions about anxiety symptoms and their frequency in the past 2 weeks. The frequency is rated on a four-point scale ranging from not at all (1 point), several days (2 points), more than half the days (3 points) to nearly every day (4 points). The point range for the GAD-7 is from 0 to 21 points [16]. The MCID for GAD-7 ranges from 1.5 to 3.8 and is based on individuals with comorbid depression and anxiety symptoms [17, 18].

General Health Questionnaire-12

GHQ-12 is a self-report questionnaire consisting of 12 statements regarding mental health symptoms, sleeping troubles and feelings of being unable to cope. It uses a four-point scale to rate the severity of these common mental health symptoms, ranging from not at all (0 points), no more than usual (1 point), somewhat more than usual (2 points), to much more than usual (3 points). The total score ranges from 0 to 36 points with a higher score indicating increased psychological distress [19]. The MCID has yet to be defined for the GHQ-12.

Patient Health Questionnaire-9

PHQ-9 is a self-administered 9-item questionnaire measuring the severity of depression. The sum of scores determines the severity of depression, where a score of 1 to 4 indicates no depression severity, a score of 5–9 indicates mild depression, a score of 10–14 indicates moderate, a score of 15–19 indicates moderately severe depression and a score of more than 20 indicates severe depression. The total score ranges from 0 to 27 points [20]. The MCID for PHQ-9 ranged from 1.7 to 4.78 in depression [17, 21].

Work Productivity and Activity Impairment

WPAI is a self-report questionnaire assessing the impact of health conditions on work productivity and activity impairment. The sum of score captures the impact of a health condition on overall productivity and functioning, including absenteeism and presenteeism. It covers the following domains, all affected as a result of the health condition: absence from work, reduction in work productivity while at work, impairment in daily activities, impairment in leisure activities and overall impairment in work productivity and activity. The responses are used to calculate a percentage of work productivity and activity impairment, thus having a total score ranging from 0 to 100, with higher scores indicating a greater impairment [22]. The MCID for WPAI was defined for each domain: absenteeism ranged from 6.3 [23] to 8.9 [24], presenteeism ranged from 32.4 [24] to 37 [23], work productivity loss ranged from 20 [25] to 41.3 [23] and activity impairment ranged from 20 [25] to 47.5 [23].

Zarit Burden Interview

ZBI is a structured interview specifically assessing the burden of caring for a person with a

chronic illness. It consists of 22 questions that elicit information about the physical, emotional and social impact of caregiving on the care partner. A five-point scale is used to rate the frequency of specific tasks and responsibilities for the care partner: never (0 points), rarely (1 point), sometimes (2 points), often (3 points) and almost always (4 points). The overall score of the ZBI ranges from 0 to 88 points [11, 26] and has four levels of burden: no or little burden (0–20 points), mild to moderate burden (21–40 points), moderate to severe burden (41–60 points) and severe burden (61–88 points) [27]. There is no defined MCID value for the ZBI.

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

RESULTS

The search string for AD resulted in 542 studies and the search string for other chronic diseases resulted in 636 studies totalling 1178 published articles. Of these, 860 studies and six duplicates were excluded on the basis of title and abstract screening. The resulting 312 studies were screened. This led to the inclusion of 15 studies relating to the care partner burden in AD and 39 studies relating to the care partner burden in other chronic diseases (Fig. 1).

The 15 studies relating to AD reported data from a total of 2277 care partners of individuals with AD at any stage. A majority of the included care partners of individuals with AD, 1860 individuals, belonged to studies using the ZBI. The number of participants in the studies reporting data on care partner burden in AD ranged from 12 to 454 participants per study. Six studies reported data from Europe, five studies reported data from Asia, two studies reported data from North America, one study reported data from South America and one study reported data from Australia and Oceania (Table 1).

Data from a total of 7957 care partners of individuals with other chronic diseases were reported in the 39 studies. Again, a majority of studies utilised ZBI to assess the care partner burden, comprising data from a total of 4331 participants. The sample size ranged from 26 to 1380 in the studies reporting data on care partner burden in other chronic diseases. Eighteen studies reported data from Asia, nine studies reported data from North America, 11 studies reported data from Europe, two studies reported data from Australia and Oceania, two studies reported data from Africa while one study reported data from South America (Table 2).

In total, 10,234 care partners were included in this study, of which 2919 were care partners of individuals with AD and 7957 were care partners of individuals with various other chronic diseases.

ZBI was the most frequently utilized PROM in both searches to capture care partner burden (12 studies in AD and 26 studies in other chronic diseases), reporting a mean value of 36.80 with a SD of 18.35 indicating a moderate burden of care of individuals with AD (Table 3). The burden of care experienced by care partners of individuals with AD as measured by ZBI was higher for most of the other included diseases, although not higher for bipolar affective disorder (mean 59.11, SD 17.8), schizophrenia (mean 55.92, SD 17.43) and motor neuron disease (mean 37.43, SD 18.75). Across diseases, the highest value reported for ZBI was 59.11 (bipolar affective disorder) [28], while the lowest value reported was 0.77 (chronic musculoskeletal pain) [29] (Fig. 2). The total mean difference from the meta-analysis (Fig. 3) with 95% confidence interval was 13.68 [12.78, 14.58] for a greater care partner burden of AD.

According to the PHQ-9 (one study in AD and five studies in other chronic diseases), the burden of care in partners of individuals with AD (mean 4.7, SD 4.7) was found to be greater in comparison to care partners of individuals with heart failure (mean 3.53, SD 4.9) and individuals receiving haematopoietic cell transplantations (mean 2.4, SD 1.8) [30, 31], while caring for individuals with cancer (mean 6.47, SD 6.07) and depression (mean 10.26, SD

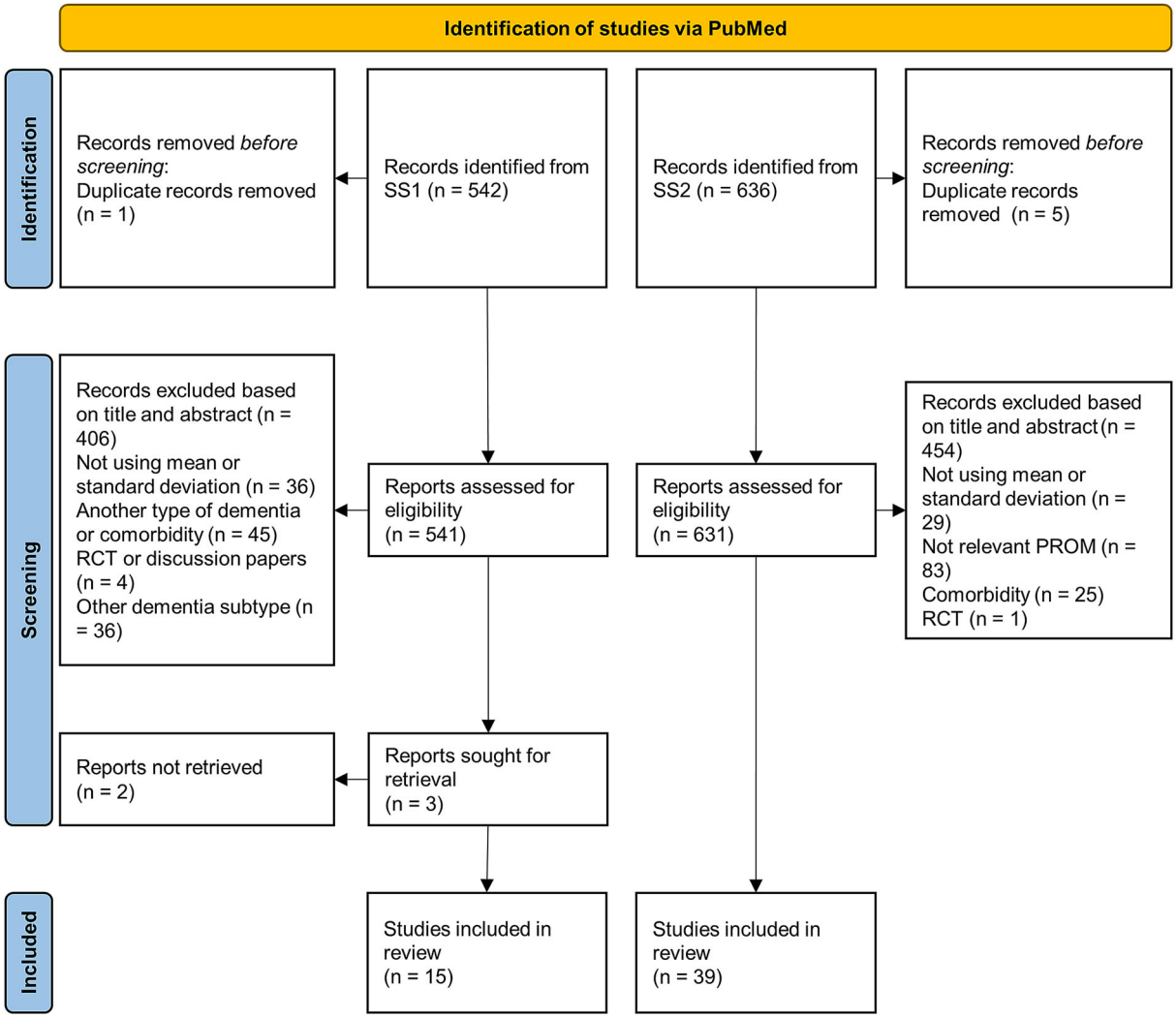

Fig. 1 Study flowchart. The study flowchart shows the structured and transparent methodology for identifying literature pertaining to care partner burden in relation to AD and other chronic diseases

5.35) led to a greater burden compared to caring for individuals with AD [32, 33]. Overall, there was no significant difference between AD and the other diseases in this PROM with a mean difference of − 0.74 [− 3.76, 2.28] (Table 3).

GHQ-12 measurements (one study in AD and three studies in other chronic diseases) showed a much higher burden of care in partners of individuals with thalassaemia (mean 32, SD 4.25) compared to care partners of individuals with AD (mean 13.23, SD 6.85) [34]. A mean value for the burden on care partners of individuals with rare lung diseases such as cystic fibrosis, interstitial lung disease and primary ciliary dyskinesia (mean 13.1, SD 4.1) was calculated, and was similar to that for the care partners of individuals with AD [35]. Finally, a greater burden was reported among the care partners of individuals with AD than both care partners of individuals with acquired brain injuries (mean 9.3, SD 5.9) and care partners of individuals with chronic developmental diseases (mean 8.1, SD 5.3) [36]. The combined result was not significant with a wide 95% confidence interval due to a high level of heterogeneity and a relatively low number of patients in the studies (Table 3).

Table 1 Alzheimer's disease

Study (reference)	*n*	PROM	Region
Dixit et al. [27]	26	ZBI	Europe
Huang et al. [57]	244	ZBI	Asia
Igarashi et al. [58]	321	EQ-5D, WPAI, ZBI	Asia
Kumfor et al. [59]	12	ZBI	Australia and Oceania
Lee et al. [60]	454	ZBI	Asia
Lima-Silva et al. [61]	30	ZBI	South America
Martinez et al. [62]	25	ZBI	North America
Mougias et al. [63]	194	ZBI	Europe
Mougias et al. [64]	161	ZBI	Europe
Sinha et al. [65]	32	ZBI	Asia
Goncalves-Pereira et al. [66]	61	ZBI	Europe
Yin et al. [94]	300	ZBI	Asia
Jennings et al. [67]	254	PHQ	North America
Avargues-Navarro et al. [68]	96	GHQ	Europe
Alexopoulos et al. [69]	67	GAD-7	Europe

Summary of AD studies including the number of participants in each study, the PROMs used and the region of the conducted study

The GAD-7 (one study in AD and three studies in other chronic diseases) showed that care partners of individuals with AD experienced generalized anxiety (mean 5.18, SD 4.9) to a lesser degree than care partners of individuals with anxiety (mean 8.55, SD 5.03) [32] and cancer (mean 13.36, SD 5.93) [33, 37] with a total mean difference of − 5.82 [− 10.53, − 1.11] (Table 3). This was significant and the mean difference was notably bigger than the reported MCID value range.

The EQ-5D-5L (one study in AD and one study in other chronic diseases) compared the QoL in care partners of individuals with AD (mean 0.885, SD 0.126) to that of care partners of individuals with asthma (mean 0.88, SD 0.13) and chronic obstructive pulmonary disease (mean 0.85, SD 0.17) [38]. The QoL assessed by the EQ-5D-5L showed no overall difference between the care partners of the different conditions (Table 3).

The WPAI (one study in AD and five studies in other chronic diseases) showed that care partners of individuals with depression (mean 41.72, SD 32.03) had the highest levels of overall impairment in work productivity and activity [39]. Care partners of individuals with asthma (mean 30.75, SD 23.13) and cystic fibrosis (mean 32.8, SD 37.8) also showed slightly higher levels of overall impairment compared to care partners of individuals with AD (mean 28.9, SD 32.8) [38, 40], while care partners of individuals with chronic obstructive pulmonary disease (mean 12.69, SD 8.4) showed the lowest levels [38, 41]. Finally, the overall impairment in work productivity and activity was found to be similar between care partners of individuals with AD and care partners of individuals with rheumatoid arthritis (mean 29, SD 26) [42]. The combined result was not significant.

Minimal Clinically Important Difference

The MCID has been established for four of the health measures included in the study (namely EQ-5D-5L, GAD-7, PHQ-9 and WPAI), however it has yet to be defined for the remaining two measures (GHQ-12 and ZBI). In the EQ-5D-5L, the MCID values were determined to be 0.1 measured on patients with stroke [13]. The MCID values for depression as measured by the GAD-7 scale ranged between 1.5 [17] and 3.8 [18]. The PHQ-9 MCID values revealed a modestly low score in depression [17, 43]. The MCID values of the WPAI were only evaluated in the context of dermatological and rheumatoid diseases and indicated that absenteeism was lower

Table 2 Other chronic diseases

Study (reference)	*n*	PROM	Region	Disease
Akkus et al. [37]	250	GAD-7, ZBI	Europe/Asia	Cancer
Al Qadire et al. [70]	264	ZBI	Asia	Cancer
Arshad et al. [71]	98	ZBI	Asia	Renal disease
Bucak et al. [72]	29	ZBI	Europe/Asia	Celiac disease
Caro et al. [73]	30	ZBI	South America	Stroke
Hasuo et al. [74]	152	ZBI	Asia	Cancer
Hasuo et al. [75]	320	ZBI	Asia	Cancer
Intas et al. [76]	310	ZBI	Europe	Renal disease
Jeong et al. [77]	238	ZBI	Asia	Stroke
Kang et al. [78]	44	ZBI	Asia	Renal disease
Kellner et al. [79]	57	ZBI	North America	Essential tremor
Lithin et al. [80]	60	ZBI	Asia	Motor neuron disease, Parkinson's disease
Macchi et al. [81]	175	ZBI	North America	PD
Mohammadi et al. [29]	184	ZBI	Europe	Chronic musculoskeletal pain
Monarrez-Espino et al. [82]	137	ZBI	North America	Renal disease
Morgan et al. [83]	55	ZBI	North America	Essential tremor
Nagarathnam et al. [84]	150	ZBI	Asia	Renal disease
Ogunmodede et al. [85]	100	ZBI	Africa	Type 2 diabetes mellitus
Parekh et al. [86]	162	ZBI	North America	Inflammatory bowel disease
Rady et al. [87]	70	ZBI	Africa	Heart failure, mental illness
Ramos-Campos et al. [88]	60	ZBI	Europe	Cancer
Roy et al. [89]	94	ZBI	North America	Celiac disease
Semere et al. [90]	441	ZBI	North America	Cancer
Shamsaei et al. [91]	225	ZBI	Asia	Schizophrenia
Tanna [28]	210	ZBI	Asia	Bipolar disorder, schizophrenia
Toledano-Toledano et al. [92]	416	ZBI	North America	Chronic diseases
Batmaz et al. [32]	168	GAD-7, PHQ	Europe/Asia	Anxiety, depression
Durante et al. [30]	50	PHQ	Europe	Heart failure
Gupta et al. [31]	944	PHQ	North America	Haematopoietic cell transplantation
Jeyagurunathan et al. [93]	339	PHQ	Asia	Mental illness

Table 2 continued

Study (reference)	*n*	PROM	Region	Disease
Levesque et al. [33]	36	GAD-7, PHQ	Australia and Oceania	Cancer
Ademhan Tural et al. [35]	113	GHQ	Europe/Asia	Rare pulmonary diseases
Moradabadi et al. [34]	140	GHQ	Asia	Thalassaemia
Silberg et al. [36]	72	GHQ	Asia	Acquired brain injury, developmental chronic diseases
Majellano et al. [38]	157	EQ-5D, WPAI	Australia and Oceania	Asthma, COPD
Balkaran et al. [39]	1380	WPAI	Europe	Depression
Galloway et al. [42]	26	WPAI	Europe	Rheumatoid arthritis
Rehman et al. [41]	113	WPAI	Asia	COPD
Suthoff et al. [40]	88	WPAI	Europe & North America	Cystic fibrosis

Summary of studies on other chronic diseases including the number of participants in each study, the PROMs used and the region of the conducted study

in rheumatoid arthritis [23] compared to psoriatic arthritis [24], presenteeism was higher in rheumatoid arthritis [23], work productivity loss was lower in psoriasis [25], and activity impairment was lower in psoriasis [25] in comparison to the aforementioned diseases. For further information, see Supplementary Table 2. The results obtained from the MCID analysis were restricted by the paucity of available data. There is no available information on MCID values in GHQ-12 and ZBI, and the current information is not based on dementia.

DISCUSSION

The aim of this systematic literature review was to compare the care partner burden of AD to that of other chronic diseases. Two search strings were conducted for care partners of AD and care partners of other chronic diseases, respectively. Data was extracted from six predefined PROMs from which mean values and SD were calculated and compared.

The findings from this review were mixed. The results of the published literature, as measured by the EQ-5D-5L, WPAI and the ZBI, indicate a greater burden of care in partners of individuals with AD. Conversely, the results from the GAD-7 and GHQ-12 suggest that care partners of individuals with other chronic diseases experience a greater burden. Lastly, the PHQ-9 shows the same burden experienced in care partners of individuals with AD and care partners of individuals with other chronic diseases.

The results of multiple PROMs have indicated a greater burden among care partners of individuals diagnosed with psychiatric disorders as compared to those diagnosed with AD. Specifically, the ZBI revealed a higher experienced burden in care partners of individuals diagnosed with bipolar affective disorder and schizophrenia, while the PHQ-9 and the WPAI revealed heightened levels of impairment in care partners of individuals diagnosed with depression. In general, neuropsychiatric diseases demonstrated a greater burden in the ZBI compared to somatic diseases. Furthermore, the

Table 3 Comparison of PROMs

PROM	AD (number of studies, [number of patients])	Comparator (number of studies, [number of patients])	Comparator	Mean difference	Greater burden in
EQ-5D-5L	1 [321]	2 [137]	Asthma and COPD	0.01 [− 0.01,0.04]	AD
GAD-7	1 [67]	3 [454]	Anxiety and cancer	− 5.82 [− 10.53, − 1.11]	Other chronic diseases
GHQ-12	1 [96]	4 [325]	Acquired brain injury, developmental chronic disease, rare pulmonary diseases and thalassaemia	− 2.49 [− 15.03, 10.05]	Other chronic diseases
PHQ-9	1 [254]	5 [1537]	Cancer, depression, heart failure, mental illness and stem cell transplantation	− 0.74 [− 3.76, 2.28]	Same
WPAI	1 [321]	6 [1744]	Asthma, COPD, cystic fibrosis, depression, rheumatoid arthritis	− 0.83 [− 14.68, 13.03]	AD
ZBI	12 [1860]	26 [4331]	Bipolar affective disorder, cancer, celiac disease, chronic conditions, chronic musculoskeletal pain, essential tremor, heart failure, IBD, motor neuron disease, Parkinson's disease, renal disease, schizophrenia, stroke, type 2 diabetes mellitus	12.13 [4.90, 19.36]	AD

Summary of PROMs and their respective comparators in random effects meta-analyses. The disease(s) imposing the greatest burden on the care partner of the given disease, here listed as either "AD" or "Other chronic diseases". The result in EQ-5D-5L is shifted towards AD, but this indicates, contrary to the other results, that the smallest burden is in AD and thus a greater life quality in care partners of individuals with AD. The point system in EQ-5D-5L is reversed

GAD-7 revealed a greater burden in care partners of individuals diagnosed with anxiety disorders.

However, it is important to note that the results of the PROMs for heart failure, as measured by the ZBI and the PHQ-9, suggested a lesser burden and fewer depressive symptoms in care partners. Additionally, the results for PROMs measuring cancer were found to be divergent in comparison to AD. The values in ZBI suggested that cancer imposed a lesser burden on care partners than AD but led to more frequent depressive symptoms and greater anxiety. The discrepancy may be attributed to the various subtypes of cancer and the differing symptomatology and associated burden on care partners.

Tu et al. [8] conducted a similar, but not identical, systematic review of 15 PROMs focusing on four PROMs: the ZBI, the Screen for Caregiver Burden (SCB), the Caregiver Burden Inventory (CBI) and the Burden Scale for Family Caregivers (BSFC). These PROMs were developed to assess the burden experienced by care

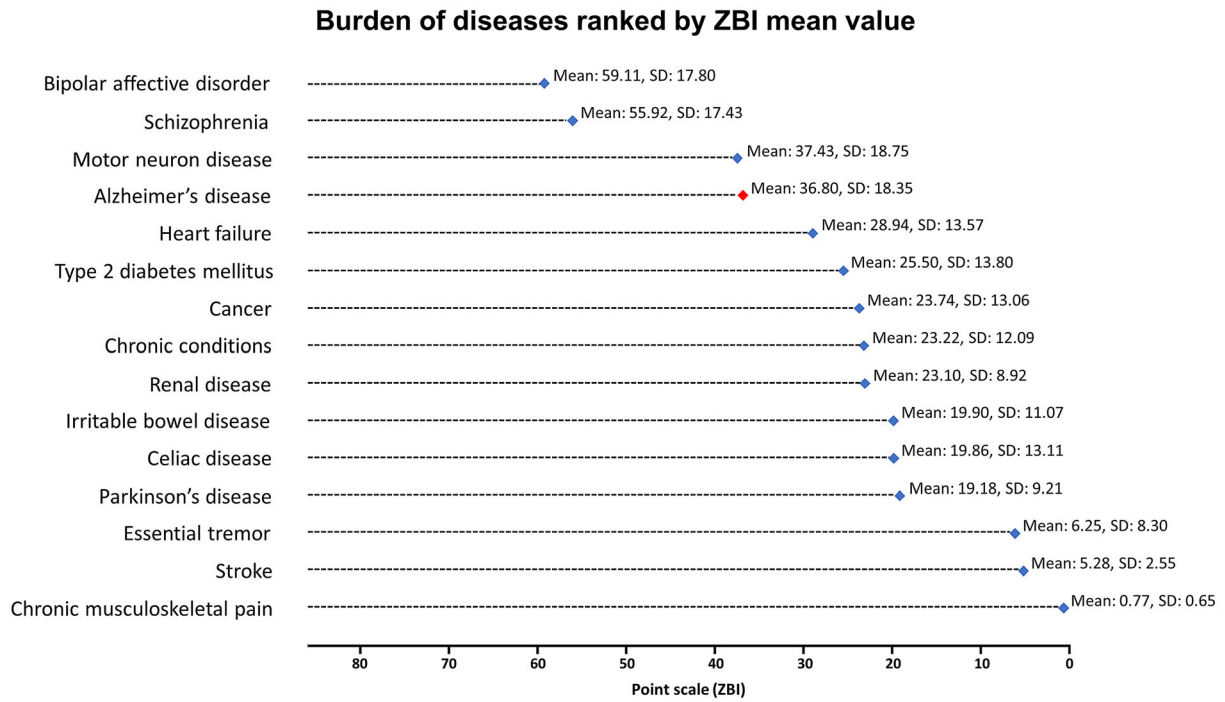

Fig. 2 Listing of diseases. Listing of the burden imposed on care partners by AD and other chronic diseases in descending order based on their mean score using the ZBI

partners of individuals with various conditions. However, the SCB and BSFC are specifically aimed at evaluating the burden of spousal care partners and family care partners of individuals with dementia [8]. According to Tu et al. [8], the ZBI may be the most appropriate PROM for comparing the burden among unpaid family caregivers. Despite this, the SCB offers a more comprehensive examination of the burden and its variations while the CBI, on the other hand, is capable of precisely identifying disparities in the burden of care among care partners [44]. Furthermore, the BSFC has been recognized to possess two important advantages over the ZBI: firstly, it includes 11 items compared to the ZBI's four items, reducing the risk of response bias [45]. Secondly, the BSFC items encompass the care partner's unfulfilled wishes in addition to the interactions between the care receiver and the care partner, whereas the ZBI items are limited to the recipient of care. Future studies could benefit from including these PROMs (SCB, CBI, BSFC and ZBI) to better illuminate the burden of care from all perspectives.

Relevance of Minimal Clinically Important Difference

The use of PROMs and their respective MCID is of great significance for healthcare professionals, who can use the data to deliver better treatment and improve the well-being of both care recipients and care partners. The findings of the MCID are restricted to only a few diseases, highlighting the need for further research in this area to gain a more comprehensive understanding of its utility in clinical practice. More research is needed to assess the MCID of the GHQ-12 and the ZBI.

Limitations

Only studies from 2012 to 2022 were included, of which the pre-specified PROMs were selected and analysed. These PROMs are susceptible to bias and may be influenced by factors such as the emotional state of care partners during the completion of the survey. Missing data such as SD may be due to selection bias or the affected

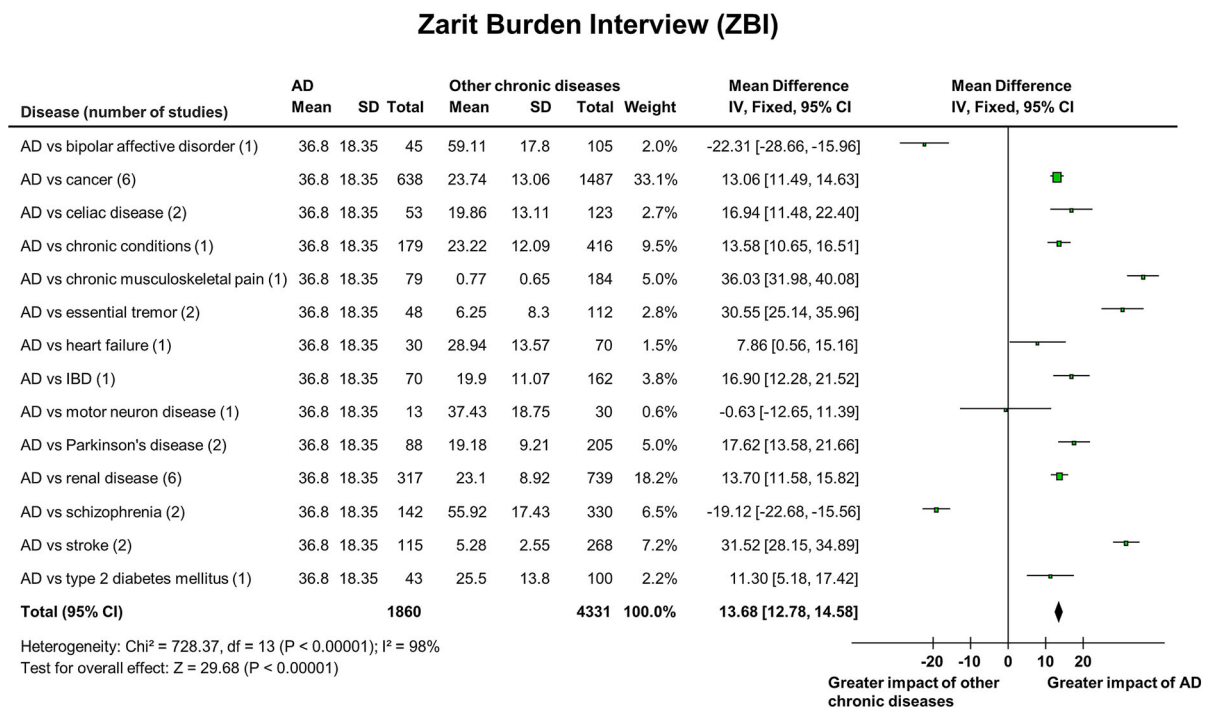

Fig. 3 Comparison of diseases. Comparison of the burden of AD and the burden of other chronic diseases using the ZBI. The comparison was performed by calculating the mean value, standard deviation and total number of individuals with each respective disease. A fixed effect analysis was conducted to perform the comparison

manner of the informal care partners, as some may be cautious when reporting the informal burden for personal reasons (guilty conscience, self-reproach, or sympathy to the care-recipient). Confounding factors such as age, sex, socioeconomic status and lifestyle factors including diet, exercise, smoking and alcohol consumption have not been adjusted for, potentially leading to a biased estimation of the actual burden imposed on care partners. Brandt et al. found a lesser burden in informal care partners with higher socioeconomic status and more resources resulting in a higher QoL score [46].

There is a persistent lack of consistency in the definition and reporting of care partners burden and the characteristics of both the care-recipient and the care partner in the literature [47–50]. It is important to consider the impact of the disease on the care partner burden experienced by the informal care partner in this study. The variability of the disease symptoms and care requirements among the studies should be taken into account when interpreting the results [51, 52]. In this study, diseases are reported without considering their various stages. For instance, AD is reported as a single value despite encompassing mild, moderate and severe dementia, with mild cognitive impairment preceding these stages of AD [53]. It is expected that as the disease progresses, the burden on care partners increases. Similar expectations apply to different types and stages of cancer, as well as different severities of other diseases.

Additionally, the PROMs assess the informal care burden at a single point in time and they do not provide information on changes in burden over time.

The most frequently used PROM in this study, the ZBI, has multiple limitations. It only assesses the care partner burden at a global level and it does not provide information on specific domains of burden, such as physical, emotional

or financial strain and, therefore, the remaining questionnaires were included. Overall, while the ZBI is a useful tool for assessing care partner burden, it is important to consider its limitations and considerations should be given to using it in conjunction with other PROMs to obtain a comprehensive understanding of the care partner's experience of providing care.

The assessment of the burden of care partners in the context of AD and other chronic diseases was performed using instruments measuring anxiety, depression, psychological distress and experienced burden. The PROMs had a comprehensive range of reported data to obtain the most informative result.

The study may have included care partners of individuals with other subtypes, as there are few studies that confirm the diagnosis of AD using biomarkers in accordance with the NINCDS-ADRDA (National Institute of Neurological Disorders and Stroke–Alzheimer's Disease and Related Disorders Association) criteria. Care partners may not be able to make the differentiation between dementia subtypes, hence the burden may be perceived as similar from a care partners perspective [3]. The use of biomarkers allows AD to be distinguished from other dementia subtypes with higher sensitivity and specificity [54]. The clinical diagnosis of AD is thus supported by biological markers according to the NINCDS-ADRDA criteria, but access to the use of biological markers in clinical settings is often limited [55]. However, with the development of blood biomarkers instead of cerebrospinal fluid markers, this will be greatly facilitated as described by Karikari et al., who measured tau-biomarkers in blood [54]. In the present study, the inclusion of other subtypes of dementia could result in an overestimation or an underestimation of the combined effect. Future research is needed to assess how different subtypes of dementia may affect care partners differently.

Lastly, a limitation in the comparisons of AD and the chronic diseases is that they vary in severity and duration. The progressive nature of the different diseases is very heterogeneous, but it has not been possible to correct for this as the data in the included articles did not provide these details.

Perspectives

The utilization of PROMs is of great significance in comprehending the cultural and societal patterns associated with the caregiving experience. These PROMs provide a systematic and quantifiable means of capturing the experience of burden in partners of individuals with chronic diseases, while also preserving meaningful insights into the experience [8].

For healthcare professionals, PROMs collected from informal care partners are essential to attaining a deeper comprehension of the disease's dynamics and ensuring the delivery of optimal treatment. The assessment of burden of care in partners can not only enhance the psychological well-being of the care partner but also that of the care receiver. Hence, the completion of PROMs is beneficial to both the care receiver and the care partner [8].

PROMs are of benefit to the public as one of their purposes of measuring caregiving burden is to facilitate the development of services and interventions based on empirical evidence [56]. A more comprehensive understanding of caregiving burden can guide the focus areas of the health sector towards inclusiveness of both individuals with dementia and their care partners. However, researchers must exercise caution in the assessment of burden using PROMs as care partners may be hesitant or even unwilling to openly acknowledge their caregiving burden [45].

CONCLUSION

The results of this study were mixed, with some PROMs indicating a greater burden for care partners of individuals with AD versus other chronic diseases and other PROMs showing a greater burden for care partners of individuals with other chronic diseases. Psychiatric disorders imposed a greater burden on care partners compared to AD, while somatic diseases in the musculoskeletal system resulted in a significantly smaller burden on care partners compared to AD.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability. The data used in this meta-analysis is derived from original papers freely available in the public domain.

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