


RESEARCH ARTICLE

Dementia and caregiver burden: A three-year longitudinal study

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Objectives: Dementia, with its progressive cognitive and functional decline and associated neuropsychiatric symptoms, places a large burden on caregivers. While frequently studied, longitudinal findings about the overall trajectory of burden are mixed. The study sought to characterize caregiver burden over a 3-year period and identify predictors of this burden.

Methods: Seven-hundred-and-eighty-one patients with dementia were recruited from nine memory clinics around Australia. Measures of caregiver burden, cognition, function, and neuropsychiatric symptoms were completed with patients and their caregivers at regular intervals over a 3-year period. Patients' level of services and medication use were also recorded.

Results: Of the 720 patients with measures of caregiver burden at baseline, 47.4% of caregivers had clinically significant levels of burden. This proportion increased over time, with 56.8% affected at 3 years. Overall levels of burden increased for caregivers of patients without services, though did not change for caregivers of patients receiving services or residential care after controlling for other variables. Patient characteristics—including greater neuropsychiatric symptoms, lower functional ability, fewer medications, lack of driving ability—and female sex of caregivers were associated with greater burden.

Conclusions: High levels of caregiver burden are present in a large proportion of caregivers of people with dementia and this increases over time for those without services. Clinical characteristics of patients (including neuropsychiatric symptoms, function, overall health, driving status), level of services, and caregiver sex appear to be the best predictors of this burden. These characteristics may help identify caregivers at greater risk of burden to target for intervention.

KEYWORDS

Alzheimer's disease, caregiver burden, carer burden, dementia, longitudinal, neuropsychiatric symptoms, vascular dementia

1 | INTRODUCTION

Dementia, with its progressive cognitive and functional decline and associated neuropsychiatric symptoms, places a considerable burden on caregivers.^{1,2} Caregivers face both instrumental challenges—

attending to the needs and symptoms of patients—and emotional challenges—coping with a loved one's ongoing deterioration, as well as their own loss of independence, increased social isolation, and financial pressures. As a result, caregivers typically exhibit higher levels of stress and depression, poorer physical health, and reduced

levels of employment than the general population.³⁻⁵ Given the prevalence of dementia—5% of people over the age of 60—this represents a significant issue at a population level.⁶ Caregivers, however, can vary considerably in their level of burden. As a result, an important goal is to identify caregivers at particular risk of high levels of burden to target for clinical intervention.

Previous cross-sectional research has identified several variables that predict burden. One set of variables is patients' clinical characteristics. These represent primary stressors for caregivers and include patients' neuropsychiatric symptoms and cognitive and functional impairments. Of these, neuropsychiatric symptoms have been noted to be particularly burdensome.⁷⁻¹⁰ Patients' cognitive and functional impairments have also been associated with greater burden, though not consistently.^{8,9} In a related manner, driving cessation, which occurs as a result of these impairments, has been indirectly associated with greater burden, with caregivers of patients who stop driving having higher burden at an earlier assessment than those who did not.¹¹ A second set of variables that predict burden is caregiver characteristics and background contextual variables. Spousal relationships,¹² female sex of caregiver,³ living at home,¹³ and cohabiting with the patient¹⁴ have been associated with greater caregiver burden.

Longitudinal findings are more mixed as to the overall trajectory of burden. Some studies suggest that burden remains relatively stable over time;¹⁵⁻¹⁷ others suggest burden increases;¹⁸⁻²⁰ while others suggest that burden may even decrease.²¹ These findings are relevant given competing accounts of caregiving as either "wear-and-tear"—in which caregivers gradually become more overwhelmed with the ongoing toll of caregiving—or "adaptation"—in which caregivers become accustomed to the demands placed on them.²² Given these mixed findings, research has attempted to identify drivers of burden. Neuropsychiatric symptoms, in particular, have been identified as a key predictor of subsequent caregiver burden.^{16,23-25} By contrast, nursing home placement has been associated with a reduction in burden.²⁶ Other variables, such as caregiver relationship,²⁷ may also affect longitudinal trends. A limitation of some previous research, however, is that it has not controlled for the severity of patients' clinical symptoms when reporting the overall effect of time or considered the impact of patient attrition. Many studies have also been limited by a relatively short follow-up duration (typically only 1-2 years) and some have only considered two data points. Given the importance of neuropsychiatric symptoms to burden, a further issue is the limited longitudinal data on the relationship between individual neuropsychiatric symptoms and caregiver burden.²⁸⁻³⁰

To address these issues, we examined caregiver burden longitudinally in a sample of patients with dementia recruited from memory clinics. Patients with dementia and their caregivers were assessed regularly over 3 years. We used linear mixed models to analyze the data; these have the advantage of being able to handle missing data, including attrition, without the need for imputation.³¹ Based on previous research, we expected that a range of patient characteristics—such as higher levels of neuropsychiatric symptoms, greater cognitive and functional impairments, and poorer health—and background features—such as longer duration of symptoms, level of services,

Key points

- Dementia, with its associated cognitive and functional impairments and frequent neuropsychiatric symptoms, can place a large burden on caregivers.
- In a 3-year longitudinal study of nine memory clinics, we found that around half of caregivers had clinically significant levels of burden with this increasing over time, particularly for those at home without services.
- Patient characteristics—including neuropsychiatric symptoms, severity of functional impairment, inability to drive, and fewer medications—and level of services and caregiver sex predicted overall burden.

spousal relationships, and cohabitation—would predict caregiver burden. We also expected that burden would increase over time with the worsening of patients' impairments and symptoms.

2 | METHODS

2.1 | Design

Participants were drawn from the Prospective Research in MEemory Clinics (PRIME) study,^{32,33} a 3-year observational study of patients attending memory clinics. Of 964 patients recruited, 779 had dementia and 185 had mild cognitive impairment. All patients received specialist assessment or treatment at one of nine memory clinics around Australia. These memory clinics were in four of the eight states and territories of Australia and included both regional and capital centers (for more information about dementia services in Australia, see Brodaty & Cumming³⁴). Patients, together with their caregiver as their informant, had annual follow-ups with a research nurse/psychologist or specialist clinician, with additional visits at 3 and 6 months. Ethics approvals were obtained from institutional ethics committees associated with individual referring centers (National-Institute-of-Health-clinical-trials-registry-number: NCT00297271).

2.2 | Patients

The current analyses focused on patients with dementia. All had received a diagnosis from a specialist clinician according to DSM-IV criteria.³⁵ Patients were included in the PRIME study if they lived in the community, had less than 40 h/week care, were fluent in English, had a caregiver consent to the study, and provided written informed consent either themselves or through a legal guardian/proxy. Patients with acute or life-threatening illness or requiring high-level residential care at baseline were excluded.

2.3 | Instruments and methods

Assessments were completed by a specialist clinician or trained research nurse/psychologist. Demographic and diagnostic data were collected at baseline. All other measures were completed at each visit. Caregiver burden was assessed with the 22-item Zarit Burden Interview (ZBI);³⁶ higher scores indicate greater burden (range 0-88), with a cut-off score of 24 indicating clinically significant burden.³⁷ Dementia severity was assessed using the Clinical Dementia Rating (CDR) scale³⁸ and scored using the sum of boxes method;³⁹ higher scores indicate greater severity (range 0-18). Cognition was assessed using the mini-mental state examination (MMSE);⁴⁰ higher scores indicate better cognition (range 0-30). Function was assessed using the functional autonomy measurement system (SMAF);⁴¹ higher scores indicate better function (range -87 to 0). Neuropsychiatric symptoms were assessed using the total score of the 12-item Neuropsychiatric Inventory NPI;⁴² higher scores indicate greater frequency and severity of symptoms (range 0-144). Patients' level of services (no services, home services, low-level residential care, high-level residential care) was recorded at each visit. A list of medications that patients were taking at each visit was compiled.

2.4 | Statistical analyses

Continuous variables at baseline were reported by mean and SD; categorical variables were reported as frequencies (%). Patients who had complete ZBI data at baseline were compared to those who did not using logistic regression controlling for time from clinical diagnosis. Patients who had complete ZBI data at the 3-year follow-up were also compared to those who did not have this follow-up data in terms of their characteristics at baseline in the same manner. Patients whose caregiver changed over the study were compared to the rest of the sample in the same way.

Longitudinal data across all time points were analyzed using linear mixed models with normally distributed random intercepts and random effects for time. As patients varied in the duration with which they had dementia at baseline, time was measured in years from patients' dementia diagnosis. This allowed estimates of burden and its predictors across the whole course of dementia, rather than only the three year period of the study. The outcome measure across time was caregiver burden (ZBI score) as a continuous measure. For patients, the following predictors were included in the model: at baseline—age, sex, type of dementia—and at each time point—cognition (MMSE), function (SMAF), dementia severity (CDR), neuropsychiatric symptoms (NPI total), driving status, level of services (no services, home services, low-level residential care, high-level residential care), and total number of medications (as a proxy for physical health).⁴³ For caregivers, the following variables were included: sex, caregiver relationship (spouse vs other relationship), living arrangement (lives with patient vs lives separately), and employment status at baseline. An interaction between level of services and time was tested and retained in the model if $P < .10$. Given

the previously reported relationships between sex and driving status in older age,⁴⁴⁻⁴⁶ interactions between patient sex and driving and between caregiver sex and driving were also tested. Models were selected based on the Akaike information criterion.

To examine the contribution of individual neuropsychiatric symptoms on caregiver burden, an analysis was conducted in which individual NPI sub-scores (delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behavior, night-time behavior, and appetite) were included as predictors while controlling for age, sex, function, number of medications, antipsychotic medication, and level of services. To reduce the impact of change in caregiver on the results, both analyses were repeated excluding patients who changed caregivers after the change in caregiver occurred. All analyses were completed with SPSS (version 25).

3 | RESULTS

3.1 | Baseline characteristics

Of the 779 patients with dementia, 720 (92.4%) had the ZBI completed by a caregiver. Patients who had the ZBI completed were taking more medications (OR = 1.16, 95% CI 1.05-1.28) than patients who did not, but did not differ in age, sex, or any other clinical and demographic variables. Patients who had ZBI data completed at the 3-year follow-up were younger (OR = 0.95, 95% CI 0.93-0.97); had higher cognition scores (OR = 1.10, 95% CI 1.07-1.13), higher functioning scores (OR = 1.06, 95% CI 1.05-1.08), lower dementia severity scores (OR = 0.84, 95% CI 0.80-0.88), lower neuropsychiatric symptom scores (OR = 0.98, 95% CI 0.97-0.99), and lower caregiver burden scores (OR = 0.98, 95% CI 0.97-0.99). They were also more likely to be driving (OR = 2.44, 95% CI 1.78-3.34) and have a spouse as a caregiver (OR = 1.40, 95% CI 1.02-1.93), but did not differ in sex, number of medications, or other characteristics at baseline from those who did not have 3-year follow-up data. Caregivers changed for 19 patients during the study. These patients were more likely to have caregivers who were working (OR = 3.70, 95% CI 1.12-12.28), but did not differ from other patients in the study in any other clinical or demographic variables in logistic regression analyses.

Demographic features of patients and their caregivers are summarized in Table 1. Of the 720 patients with completed ZBI data, 633 (87.9%) did not receive services; 71 (9.9%) accessed home services; and 16 (2.2%) were living in low-level residential care (patients requiring high-level residential care at baseline were excluded).

3.2 | Caregiver burden during the study

Numbers of patients across the study are shown in Figure 1. Reported caregiver burden increased over the study. Mean levels of caregiver burden were 24.0 (SD = 15.8) at baseline, 25.6 (SD = 17.0) at 3 months, 26.1 (SD = 17.1) at 6 months, 27.4 (SD = 18.9) at 1 year, 28.9

TABLE 1 Baseline characteristics of patients (n = 720)

Characteristic	Baseline Value
<i>Demographics</i>	
Age	78.0 (7.5)
Sex (female)	338 (46.9%)
Education (postsecondary)	250 (34.7%)
Partnered	553 (76.8%)
Living alone	87 (12.1%)
Driving	225 (31.3%)
<i>Clinical characteristics</i>	
Cognition (MMSE)	21.5 (5.3)
Function (SMAF)	-18.1 (11.2)
Neuropsychiatric symptoms (NPI)	14.5 (16.1)
Number of medications	6.6 (3.6)
<i>Dementia type</i>	
Alzheimer's disease	521 (66.9%)
Vascular dementia	51 (6.5%)
Mixed dementia	129 (16.6%)
Lewy body dementia	16 (2.1%)
Frontotemporal dementia	31 (4.0%)
Other	31 (5.0%)
<i>Caregiver characteristics</i>	
Caregiver burden (ZBI)	24.0 (15.8)
<i>Relationship to patient</i>	
Spouse	515 (71.5%)
Child	150 (20.8%)
Sibling	10 (1.4%)
Other	45 (6.3%)
Sex (female)	479 (66.5%)
Employed	152 (21.1%)
<i>Level of services</i>	
No services	633 (87.9%)
Home services	71 (9.9%)
Low-level residential care	16 (2.2%)
High-level residential care	0 (0.0%)

(SD = 19.0) at 2 years, and 30.7 (SD = 21.3) at 3 years. Clinically significant levels—indicated by scores of 24 or more—were present in 47.4% of the sample at baseline, 49.1% at 3 months, 49.8% at 6 months, 51.6% at 1 year, 52.5% at 2 years, and 56.8% at 3 years. At 3 years, 283 (76.9%) of the patients remaining in the study had no services, 41 (11.1%) had home services, 18 (4.9%) had low-level residential care, and 26 (7.1%) had high-level residential care.

Regression analysis from the linear mixed models showed an interaction between time and level of services (see Table 2). At time of diagnosis, caregivers of patients receiving home services had 7.9 points greater burden relative to caregivers of those at home without services, while caregivers of patients in low-level residential care had 8.9 points less burden relative to caregivers of those at home without

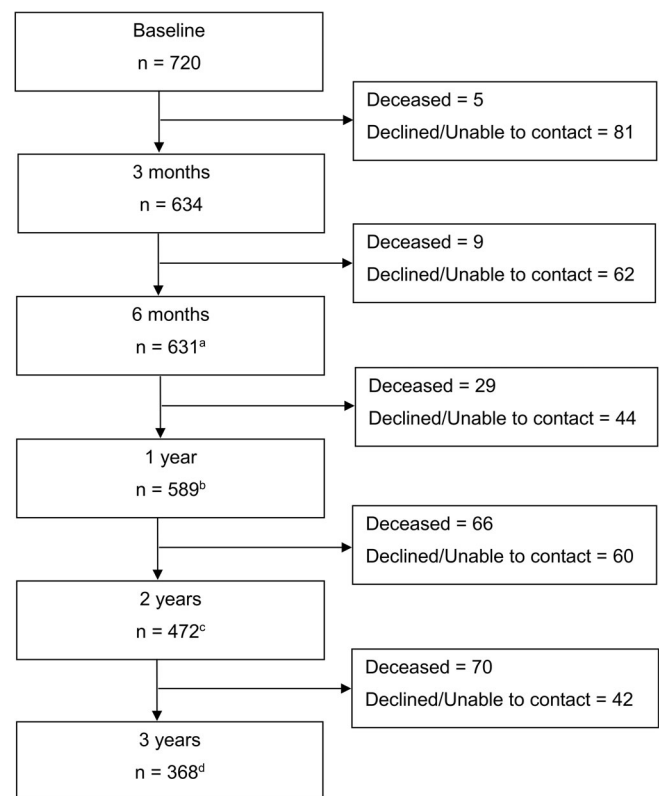


FIGURE 1 Number of patient-caregiver dyads with completed Zarit Burden Interview data at each time point. ^aSixty-eight participants completed the 6-month follow-up but not 3-month follow-up. ^bThirty-one participants completed the 12-month follow-up but not 6-month follow-up. ^cNine participants completed 2-year follow-up but not the 1-year follow-up. ^dEight participants completed 3-year follow-up but not the 2-year follow-up

services. Over time, however, caregivers of patients living at home without services had significant increases in burden by an average 0.7 points on the ZBI annually while controlling for other variables. By contrast, caregivers of patients at home with services and those with low-level and high-level residential care showed no significant changes in burden over time. There was also substantial variability in longitudinal trends: The SD of 2.5 for the random effect of time indicates that the change in caregiver burden for patients at home without services varied from -4.2 (percentile 2.5) to 5.6 (percentile 97.5) points on the ZBI each year. There were no significant interactions between driving status and either patient sex or caregiver sex, so these terms were removed from the model.

Patients' function, neuropsychiatric symptoms, driving status, number of medications, level of services, and caregiver sex predicted caregiver burden (see Table 2). For functional impairment, each point worsening in function on the SMAF scale was associated with a 0.2 point increase in caregiver ZBI score, as shown in Table 2. Likewise, each point increase in neuropsychiatric symptoms on the NPI scale was associated with a 0.3 point increase in caregiver ZBI score. Each additional medication was associated with 0.3 less burden and caregiver's female sex was associated with 5.3 points greater burden

TABLE 2 A linear mixed model analysis examining the relationship between caregiver burden and patient and caregiver characteristics

Parameter	Effect estimate	95% CI	Sig
<i>Effect of time</i>			
Time effect for no services ^{a,b}	0.7	0.1, 1.3	.034
Time effect for home services ^{a,c}	-0.6	-1.8, 0.6	.305
Time effect for low-level residential care ^{a,d}	1.5	-0.5, 3.5	.148
Time effect for high-level residential care ^{a,e}	-1.0	-4.3, 2.3	.546
<i>Level of services</i>			
No services (at time of diagnosis) ^f	Ref		
Home services (at time of diagnosis) ^f	7.9	4.4, 11.5	<.001
Low-level residential care (at time of diagnosis) ^f	-8.9	-14.8, -3.1	.003
High-level residential care (at time of diagnosis) ^f	-5.8	-18.0, 6.3	.346
<i>Patient variables</i>			
Age at baseline	-0.2	-0.3, 0.0	.053
Sex (female)	1.1	-2.4, 4.6	.551
Drivers (vs non-drivers)	-2.5	-4.4, -0.6	.011
Cognition	0.1	0.0, 0.3	.131
Function	-0.2	-0.3, -0.1	<.001
Dementia severity	0.1	-0.2, 0.3	.623
Neuropsychiatric symptoms	0.3	0.3, 0.4	<.001
Number of medications	-0.3	-0.6, 0.0	.046
<i>Type of dementia</i>			
Vascular dementia ^g	1.8	-3.7, 7.2	.523
Dementia with Lewy Bodies ^g	-2.5	-11.6, 6.5	.583
Frontotemporal dementia ^g	4.3	-3.1, 11.7	.253
Mixed dementia ^g	-0.1	-3.6, 3.4	.947
Other dementias ^g	-5.8	-12.2, 0.6	.075
<i>Caregiver variables</i>			
Caregiver sex (female)	-5.3	-8.9, -1.7	.004
Caregiver relationship (spouse)	-3.6	-7.3, 0.2	.064
Living status (lives with patient)	3.7	-0.1, 7.5	.054
Caregiver employed	-0.9	-3.8, 2.1	.574

Note: For sex of patient and caregiver, estimates of effect are given for females relative to males. For education, estimates of effect are given for those who completed some postsecondary education compared to those who did not. For caregiver relationship, estimates of effect are given for spouses compared to other relationships (other family members, friends). For driving, estimates of effects are given for those driving compared to those not driving. Numbers in bold indicate P -values $<.05$.

^aThe interaction between time and level of services had a P -value of .068 and was retained in the model. As such, separate time effects for each service level are reported while the intercept term is not reported. The time effect for no services was significantly greater than the time effect for home services ($P = .021$).

^bRandom effect with mean 0.7 and $SD = 2.5$.

^cRandom effect with mean -0.6 and $SD = 2.5$.

^dRandom effect with mean 1.5 and $SD = 2.5$.

^eRandom effect with mean -1.0 and $SD = 2.5$.

^fFor level of services, estimates of effects are given compared to no services.

^gFor type of dementia, estimates of effects are given compared to patients with Alzheimer's disease.

compared to males. Not driving in patients was associated with 2.5 points greater burden than driving. There were also trends for lower patient age, cohabiting with the patient, and non-spousal relationships (correcting for cohabitation) to be associated with greater burden. There was no association between caregiver burden and type of

dementia, patient sex, dementia severity, cognition, or caregiver employment once other variables were controlled for.

A further analysis examined different types of neuropsychiatric symptoms. This found that delusions, hallucinations, agitation, depression, anxiety, euphoria, apathy, irritability, aberrant motor

TABLE 3 A linear mixed model analysis examining the relationship between caregiver burden and individual neuropsychiatric symptoms

Parameter	Effect estimate	95% CI	Sig
<i>Time</i>			
Time effect for no services ^{a,b}	1.2	0.7, 1.7	<.001
Time effect for home services ^{a,c}	−0.1	−1.0, 0.7	.730
Time effect for low-level residential care ^{a,d}	2.9	1.7, 4.1	<.001
Time effect for high-level residential care ^{a,e}	−0.4	−1.9, 1.1	.599
<i>Level of services</i>			
No services (at time of diagnosis) ^f	Ref		
Home services (at time of diagnosis) ^f	7.1	4.5, 9.7	<.001
Low-level residential care (at time of diagnosis) ^f	−10.6	−14.9, −6.2	<.001
High-level residential care (at time of diagnosis) ^f	3.0	−3.4, 9.4	.360
<i>Patient variables</i>			
Age	−0.1	−0.2, 0.1	.398
Sex (female)	−1.3	−3.1, 0.5	.147
Function	−0.2	−0.3, −0.2	<.001
Number of medications	−0.4	−0.7, −0.2	<.001
Antipsychotic medication	−1.6	−3.6, 0.4	.123
<i>Type of dementia</i>			
Vascular dementia ^g	0.4	−3.5, 4.2	.850
Dementia with Lewy Bodies ^g	−1.5	−7.3, 4.3	.605
Frontotemporal dementia ^g	3.7	−0.8, 8.3	.104
Mixed dementia ^g	1.6	−0.8, 4.0	.192
Other dementias ^g	−3.6	−7.9, 0.6	.096
<i>Neuropsychiatric symptoms</i>			
Delusions	0.4	0.1, 0.6	.003
Hallucinations	0.6	0.3, 0.8	<.001
Agitation/aggression	0.6	0.5, 0.8	<.001
Depression	0.6	0.4, 0.8	<.001
Anxiety	0.5	0.3, 0.6	<.001
Euphoria	0.5	0.2, 0.7	.001
Apathy	0.2	0.1, 0.4	<.001
Disinhibition	0.1	−0.1, 0.4	.154
Irritability	0.5	0.4, 0.7	<.001
Aberrant motor	0.3	0.2, 0.5	<.001
Night-time behavior	0.0	−0.2, 0.1	.708
Appetite	0.2	0.1, 0.4	.002

Note: For sex, estimates of effect are given for females relative to males. Numbers in bold indicate P -values < .05.

^aThe interaction between time and level of services had a P -value of <.001 and was retained in the model. As such, separate time effects for each service level are reported while the intercept term is not reported. The time effect for no services was significantly greater than the time effects for home services ($P = .001$) and high-level residential care ($P = .034$) and significantly lower than the time effect for low-level residential care ($P = .006$).

^bRandom effect with mean 1.2 and SD = 2.7.

^cRandom effect with mean −0.1 and SD = 2.7.

^dRandom effect with mean 2.9 and SD = 2.7.

^eRandom effect with mean −0.4 and SD = 2.7.

^fFor level of services, estimates of effects are given compared to no services.

^gFor type of dementia, estimates of effects are given compared to patients with Alzheimer's disease.

behavior, and appetite disturbances were all predictors of caregiver burden controlling for age, sex, function, antipsychotic medication use, number of medications, level of services, and time

since diagnosis (see Table 3). The largest effects were seen for agitation and depression. Disinhibition and night-time behavior did not predict burden once other variables were controlled for.

All results were unchanged when the 19 patients who switched caregivers were excluded from the analyses (results not shown).

4 | DISCUSSION

A large proportion of caregivers experienced clinically significant levels of caregiver burden in this study. Around half of caregivers exhibited clinically significant levels of burden, with the proportion affected increasing steadily over the 3-year period. While these figures are consistent with previous research, the current study extends previous findings by demonstrating an interaction between time and level of services. In particular, the findings showed that caregiver burden increases over time for patients without services after controlling for patients' clinical symptoms and other characteristics, though may not change to the same degree for caregivers of patients with services at home and in residential care. In addition, the current study confirms that patients' characteristics—specifically neuropsychiatric symptoms, lower function, fewer medications, and inability to drive—and caregiver sex and level of services also predict burden.

The overall increase in burden over time for patients' at home without services is consistent with some^{18,19} though not all previous studies.¹⁵⁻¹⁷ The current study controlled for clinical and demographic variables and showed that the duration of patients' symptoms, independent of their severity, was associated with greater caregiver burden. This suggests that burden may reflect the cumulative toll on caregivers and not just symptoms at a particular time point. Previous authors have argued that persisting demands on caregivers over time are likely to be associated with greater levels of burden than similar demands of shorter duration.⁴⁷ Others²⁴ have also noted that attrition of participants with the most severe symptoms could mask such effects and create the illusion of adaptation, particularly in studies of shorter duration. In this regard, a strength of our approach was the use of linear mixed models, which can provide estimates of trajectories of burden over the course of the disease and handle missing data in the analyses.³¹ Nevertheless, significant variability in changes in burden over time was evident, indicating the need for further research to identify drivers of longitudinal trends.

For patients with services at home or who were living in residential facilities, the study found no changes in caregiver burden over time after controlling for demographic and clinical variables. In addition, caregivers of patients in low-level residential care experienced lower levels of burden at time of diagnosis compared to caregivers of patients living at home without services after controlling for other variables. This suggests that supported accommodation, by alleviating some instrumental demands of caregiving, can help reduce overall levels of burden. By contrast, caregivers of patients with home services experienced greater burden at time of diagnosis than caregivers of patients living at home without services. Greater neuropsychiatric symptoms, which are associated with caregiver burden, could hasten access to home support, as may greater caregiver burden directly. At the same time, home services may be insufficient to meet the needs of many caregivers for patients in the community or there may be a

delay in obtaining nursing home placement when this is warranted, giving rise to the higher levels of burden. While the lack of change of burden over time for these caregivers with different levels of services could suggest a level of adaptation, these analyses were limited by the relatively small numbers of patients in these groups.

The finding that neuropsychiatric symptoms and functional decline are associated with greater caregiver burden is consistent with previous research.^{8,9,28,48} These features represent primary stressors for caregivers and are, not surprisingly, related to the level of caregiver burden.⁴⁹ In the case of neuropsychiatric symptoms, the current study confirmed that almost all neuropsychiatric symptoms assessed by the NPI—delusions, hallucinations, agitation/aggression, depression, anxiety, apathy, irritability, and aberrant motor behavior—were independent predictors of caregiver burden, with agitation and depression having the greatest effects. Previous cross-sectional research has reported mixed findings as to whether certain symptoms are more significant to burden than others, though have noted agitation and depression as among the most troublesome.^{28-30,50} In the case of functional decline, previous research has likewise found such impairments to be associated with burden, though less reliably than neuropsychiatric symptoms. In one previous review, one third of studies demonstrated an association between functional impairment and burden.⁹

Importantly, the current study also showed that patients' driving status is a significant predictor of caregiver burden, even after controlling for functional impairment and other variables. Driving cessation is another feature representing degree of dependence and is likely to be a primary stressor for caregivers. While the significant impact of driving cessation on patients' and caregivers' lives has been known for some time,⁵¹ comparatively little research has quantified the psychological impact in terms of caregiver burden longitudinally. One previous study noted that the caregivers of patients who ceased driving had higher levels of caregiver burden at an earlier baseline assessment than those who did not.¹¹ As this analysis focused on levels of burden prior to driving cessation, the direction of the relationship remained unclear and could be attributable to associated clinical impairments. The current study, which assessed burden longitudinally and controlled for other variables, provides evidence for a more direct, causal relationship.

Other characteristics were associated with increased burden. Number of medications was negatively associated with burden and there was likewise a trend for patient age to be negatively associated with burden as well. Similar findings for patient age have been reported before.^{52,53} Explanations include the possibility that caregivers of younger patients encounter a greater discrepancy between their life expectations and present experience; have greater competing role demands; and face the prospect that their burden will endure for longer than those of older patients. Similar explanations could potentially be advanced for healthier patients; a greater number of medications could also reflect greater contact with the healthcare system, which could also potentially be associated with less burden. Finally, consistent with previous research,^{3,8} female sex of the caregiver, controlling for cohabitation, was associated with greater burden. Previous authors have noted that women typically provide more personal care, are more likely to complete household tasks at lower levels of patient impairment, and are more likely to report burden

than men.⁵⁴⁻⁵⁶ Other demographic variables and patients' cognition and dementia severity were not related to caregiver burden once other variables were controlled for.

Limitations of the study include the convenience sampling of patients and the limited data collected on caregivers, which did not contain certain demographic information (eg, age, education); caregiving arrangements (eg, number of hours worked, sharing of caregiving responsibilities, informal supports); caregivers' driving status; or measures of mood, coping strategies and comorbidities. Previous research has found that, while more time caregiving is associated with greater burden,⁷ levels of burden may be moderated by caregiver's coping strategies and appraisals of patient's symptoms.⁵⁷ The current study was also limited by the fact that it did not specifically assess caregiving "uplifts"—such as feeling useful or increased closeness with the patient—that are not indexed in the ZBI.⁷ Previous research has shown that such uplifts are associated with lower levels of burden.⁷ Finally, as for all cohort studies, it is possible that attrition, if nonrandom, could affect the study's findings.

5 | CONCLUSION

Despite these limitations, the study further highlights the high levels of caregiver burden associated with dementia and the characteristics of patients and caregivers that predict this. In particular, the study confirms that patients' neuropsychiatric symptoms—especially agitation and mood disturbances—remain a large determinant of burden over time. In addition, the study underscores the significant contribution of other risk factors, such as functional impairment, level of services, time since diagnosis, patients' health and driving status, and caregiver sex, many of which have received less attention. Such characteristics may be useful to identify caregivers with high levels of burden who might benefit from more timely intervention.

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CONFLICT OF INTEREST

In the last 3 years, David Ames has received grants/funds for clinical trials from Eli Lilly and royalties for edited books from Cambridge University Press and Taylor & Francis. Michael Woodward has worked on drug trials funded by pharmaceutical companies including AbbiVie, Astra Zeneca, AZ therapies, Biogen, Buck, Eisai, Janssen, Lilly, Lundbeck, Merck/MSD, Novartis, Pfizer, Roche, Servier, Takeda, Tau Rx, vTv Therapeutics and Zinfandel. He has also received honoraria for consultancy or presentations at meetings organized by CogRx, Lundbeck, Merck Sharp & Dohme, Novartis, and Nutricia. Henry Brodaty is an advisory board member for Nutricia Australia. Michael Connors, Katrin Seeher, and Armando Teixeira-Pinto have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data are available on request from the authors.

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