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Cross-sectional study evaluating burden and depressive symptoms in family carers of persons with age-related macular degeneration in Australia

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3 **Cross-sectional study evaluating burden and depressive symptoms in**
4 **family carers of persons with age-related macular degeneration in**
5 **Australia**
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Abstract

Objectives: We aimed to quantify the degree of carer burden and depressive symptoms in family carers of persons with age-related macular degeneration (AMD) and establish the factors independently associated with carer burden and depressive symptoms.

Methods: Cross-sectional study using self- and interviewer-administered surveys, involving 96 family carer-care recipient pairs. Participants were identified from tertiary ophthalmology clinics in Sydney, Australia, as well as the Macular Disease Foundation of Australia database. Logistic regression, Pearson and Spearman correlation analyses were used to investigate associations of explanatory factors, (family caregiving experience, carer fatigue, carer quality of life and care recipient level of dependency) with study outcomes - carer burden and depressive symptoms.

Results: Over one in two family carers reported experiencing mild or moderate-severe burden. More than one in five and more than one in three family carers experienced depressive symptoms and substantial fatigue, respectively. High level of care recipient dependency was associated with greater odds of moderate-severe and mild carer burden, multivariable-adjusted OR 8.42 (95% CI 1.88-37.60) and OR 4.26 (95% CI 1.35-13.43) respectively. High levels of fatigue were associated with 3-fold greater odds of the carer experiencing depressive symptoms, multivariable-adjusted OR 3.47 (95% CI 1.00-12.05).

Conclusions: A substantial degree of morbidity is observed in family carers during the caregiving experience for patients with AMD. Level of dependency on the family carer and fatigue were independently associated with family carer burden and depressive symptoms.

Strengths and limitations of this study

- The study design and method of surveying allowed for the collection of rich and extensive data from patients with AMD and their family carers.
- Several validated scales for the assessment of both carer and patient variables were used, including those for burden, depression, fatigue and visual functioning.
- Study participants were recruited from only one state in Australia
- Due to the relatively small sample size, the study is likely to be underpowered for detecting modest associations

Contributors

All authors—IJ, DT, GB, JG, KNP, AC, GL, PM and BG—provided inputs in study design. IJ, DT, JG, GB, PM and BG were involved in data collection and data analysis. IJ, JG and BG were responsible for publication writing. All authors reviewed and approved the final version of this manuscript.

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Competing interests

None of the authors declared a conflict of interest.

Patient consent

Obtained.

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3 **Ethics approval**
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5 University of Sydney human research ethics committee.
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10 **Acknowledgements**
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12 The authors thank all individuals for their time and participation in the study.
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Introduction

Age-related macular degeneration (AMD) is a chronic and progressive disorder of the macula¹ and is the leading cause of blindness and low vision in Australia, directly affecting more than 1 million persons^{2,3}. The effects of vision impairment in AMD are not limited to declining visual function, with several studies showing that AMD affects multiple health domains and leads to significant emotional distress, poorer quality of life and reduced functional independence^{4,5}. For many patients, the ongoing nature of a chronic illness like AMD is such that it requires the provision of continuous physical and emotional care beyond the scope of what can be currently provided by hospitals or other institutions^{6,7}. Family carers of relatives with AMD are often expected to provide a high standard of care despite not receiving formal training and adequate support for this role^{8,9}. Surveys on the perceptions of family carers of relatives with AMD in their role as informal carers, demonstrate experiences of significant psychological distress, with the negative impacts of caring extending to increased financial stress, disruptions to lifestyle and retirement plans, and added strain on the relationship between carer and care recipient^{5,10}.

Clearly, the impacts of AMD are far-reaching, with significant influence on family, friends and carers, as well as substantial cost to society^{3,11}. However, currently there exists little literature reporting on the level and factors of burden and depressive symptoms experienced by family carers of relatives with AMD. As such, the key aims of this cross-sectional study were to: 1) Quantify the degree of carer burden and depressive symptoms in family carers of persons with AMD; and 2) Establish the factors that were independently associated with carer burden and depressive symptoms.

Methods

Participants

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3 Participants for this study were recruited as a part of a randomised controlled trial
4 implementing a novel multi-component intervention targeting the drivers of stress and burden
5 in family carers of patients with AMD. This report analysed a total of 96 patients with AMD
6 and 96 of their family carers who were examined at baseline (pre-intervention). Recruitment
7 of participants occurred between January 2017 to May 2020 across multiple ophthalmology
8 practices in Sydney, Australia, as well as via the Macular Disease Foundation Australia
9 (MDFA) database of members. The inclusion criteria for eligible family carers participating in
10 this study were: adults aged more than 18 years old; family carer of a relative with AMD;
11 willing to engage in a 10-week cognitive behavioural therapy intervention over a 3-month
12 period; and sufficient English fluency to effectively engage in the intervention. All participants
13 in this study gave written informed consent. Ethics approval was obtained from The University
14 of Sydney Human Research Ethics Committee (ID# - 2016/793). Information on baseline study
15 participant characteristics were obtained via surveys of family carers and their relatives with
16 AMD, completed on-site during clinic visits or at home either independently or with help from
17 the study coordinator e.g. due to limitations imposed by poor vision.
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40 *Patient and Public Involvement*

41 It was not appropriate or possible to involve patients or the public in the design, or conduct, or
42 reporting, or dissemination plans of our research.
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49 *Sociodemographic information and medical history*

50 All participants (carers and care recipients with AMD) provided sociodemographic
51 information including: age, sex, education level and marital status. They also self-reported any
52 medical conditions such as: heart attacks; angina (without myocardial infarction); any other
53 cardiac conditions; strokes or transient ischaemic attacks; high blood pressure; high cholesterol;
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3 diabetes or prediabetes; kidney disease; arthritis; hearing loss; and visual impairment. This
4 information was used to assess the general health status (GHS) of each participant. Participants
5 who reported 3 or more health conditions were considered as having substantial comorbidity
6 and received a score of 1, whereas those with fewer than 3 health conditions received a score
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17 *Carer variables*

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19 Family carers were asked to provide details about the patient with AMD that they cared for
20 such as whether they were the sole caregiver of the patient; the type of caregiving duties
21 performed and the hours of care they provided to the care recipient with AMD. This comprised
22 of 21 questions detailing caregiving duties as they applied to typical activities of daily living
23 and instrumental activities of daily living for the patient with AMD, including exercise and/or
24 sport, cooking and preparing food, cleaning, reading, personal grooming, using public transport,
25 driving and more. Each question was scored reflecting the degree of help given for each activity
26 (*0=no help or little help given, 1=moderate amount of help given, 2=high amount of help given,*
27 *3=not applicable*). Additional information on family carers was determined by administering
28 several validated instruments and scales as detailed below:
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45 (i) *Carer burden*. The Caregiver Burden Scale (CBS) is a 22-item questionnaire originally
46 developed for assessment of perceived family carer burden in caring for patients with
47 dementia^{12,13}. Each question was scored on a 5-point Likert-type scale (*0=never, 1=rarely,*
48 *2=sometimes, 3=quite frequently, 4=always*), reflecting the frequency of family carers'
49 feelings when taking care of their family member. The total burden score calculated for each
50 family carer was used to stratify levels of burden into 3 categories, with higher scores indicating
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3 higher levels of burden (0-20=no/little burden, 21-40=mild burden, ≥ 41 =moderate-severe
4 burden).
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10 (ii) *Depressive symptoms.* The short form of the Centre for Epidemiologic Studies Depression
11 (CESD-10) scale is a 10-item questionnaire and was used to screen for symptoms of
12 depression¹⁴. Each question gauges the frequency of a family carer experiencing certain
13 symptoms of depression per week and is scored on a 4-point Likert-type scale (0 = rarely or
14 none of the time (<1 day), 1=some or a little of the time (1-2 days), 2=occasionally or a
15 moderate amount of the time (3-4 days), 3=most or all of the time (5-7 days)). A total CESD-
16 10 score of 10 or more indicates significant presence of depressive symptoms, as reported by
17 previous research evaluating the validity of the CESD-10 scale¹⁴. The CESD-10 is a validated
18 and reliable measure¹⁴.
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33 (iii) *Fatigue.* The Fatigue Severity Scale (FSS) is a 9-item questionnaire used frequently to
34 assess the degree of impact that fatigue has on an individual's activities and physical
35 functioning¹⁵. Participants were asked to respond to statements about how much fatigue
36 impacted their ability to function on a scale of 1 (*disagree*) to 7 (*agree*). Previous studies have
37 shown mean (SD) FSS scores for healthy individuals to be 2.3 (0.7) (ref. 15). Mean FSS scores
38 of 4 or more were categorised as having problematic fatigue. The FSS is a validated and reliable
39 measure¹⁵.
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51 (iv) *Self-efficacy.* The General self-efficacy (GSE) scale is a 10-item questionnaire shown to
52 be effective at measuring one's beliefs of overall ability to succeed in specific situations¹⁶. The
53 degree of how much a family carer agreed with each statement was measured using a 4-point
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3 Likert-type scale (*0=not true, 1=hardly true, 2=moderately true, 3=exactly true*). Higher total
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5 GSE scores indicate higher self-efficacy.
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11 *(v) Dependency.* Carers were asked to quantify the level of dependence their family member
12 with AMD had on them since their diagnosis using a 4-point Likert-type scale (*1=not at all*
13 *dependent, 2=somewhat dependent, 3=moderately dependent, 4 = very dependent, 5 =*
14 *extremely dependent*). Scores 3 or more were interpreted as an indication of high dependency
15 on the family carer (*1-2 = low dependency, 3-5 = high dependency*).
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24 *(vi) Quality of life.* Carer's rated their general quality of life (GQL) on a linear scale from 0
25 (*poor quality of life*) to 10 (*excellent quality of life*).
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31 *Care recipients with AMD*

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33 The National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) was completed
34 by care recipients, and is a reliable and validated tool used to measure status of vision-related
35 health impairment most relevant to patients with chronic eye conditions¹⁷. Questions in the
36 NEI VFQ-25 were used to determine the extent of how visual disability and symptoms
37 negatively impacts the patient's ability to function, well-being and efficacy in achieving vision-
38 related tasks. The NEI VFQ-25 is comprised of 12 subscales, assessing general vision, near
39 and distance vision, vision-related difficulty with activities, vision-related driving problems,
40 eye pain, colour vision, dependency, impact on social functioning, mental health and general
41 health¹⁷. Scores recorded in the original response category for each question were recoded to a
42 scale between 0-100 in accordance with the NEI VFQ-25 scoring algorithm, with higher scores
43 indicating greater vision-related well-being.
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Statistical analysis

SAS statistical software (SAS Institute, NC, v9.4) was used for the statistical analysis, including t-tests, chi-squared tests and logistical regression. A stepwise logistical regression analysis utilising a forward selection procedure was performed to assess potential predictors of study outcomes - carer burden and depressive symptoms. Predictor variables assessed for both these study outcomes were: carer age, carer sex, carer general quality of life, carer general health status, fatigue severity, general self-efficacy, level of dependency on the carer, patient age, patient sex, patient general health status and patient NEI VFQ-25 scores. The CORR procedure was used to compute the Pearson correlations and Spearman rank-order correlations between presence of depressive symptoms (CESD-10 score) and the following variables: patient age and sex, and carer variables (age, sex, general quality of life scores, fatigue severity scale scores, carer and patient general health status, general self-efficacy, level of dependency on the carer and NEI VFQ-25 scores). The significance level was <0.05 .

Results

AMD caregiving experience and health-related variables

The majority of family carers (91%) were aged 50 years and over, with family carers aged 65 years or older making up 54% of the sample. The proportion of females was 78% and 66% among family carers and care recipients with AMD, respectively. Of the 96 family carers in this study, 75% were the sole carer of the patients with AMD, with 43% reporting that the family member they cared for was highly dependent on them. Responses to questions about the impact of providing care to a family member with AMD on the carer's state of mind showed that many carers experienced feeling frustrated (43%), depressive (31%) and sad (27%). Some carers reported feeling no different (26%), with a relatively smaller proportion of carers reporting positive impacts in relation to their caregiving experience, such as feeling more

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3 content in their lives (13%), feeling happier than ever before (13%), feeling more optimistic
4 (8%) and feeling more determined (7%). Family carers played a considerable role in helping
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6 their relatives access medical care, with 91% accompanying their relatives to their
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8 ophthalmology appointments where the majority of relatives with AMD (79%) were receiving
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10 anti-VEGF injections. In terms of how often help was provided to relatives with AMD, 61%
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12 of family carers reported providing help for 7 days a week on average, with 45% reporting
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14 either spending >8 hours per day with them or living together with the care recipient. The main
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16 caregiving duties where carers provided moderate to high amounts of help included cooking
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18 (57%), cleaning (60%) and help with leaving the house (70%).
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24 Substantial amounts of fatigue were experienced by 36% of family carers as indicated by
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26 scores of 4 or higher on the fatigue severity scale, and a considerable degree of general health
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28 comorbidities was reported by 29% of family carers. The mean quality of life and general self-
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30 efficacy scores among the family carers in this study were: 7.3 (SD 2.0) and 32.5 (SD 4.9),
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32 respectively.
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38 *Burden analysis*

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40 More than half of family carers reported experiencing mild (35%) and moderate-severe (22%)
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42 burden due to their caregiving experience (Table 1). Family carers of highly dependent
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44 relatives with AMD were more likely to experience moderate-severe and mild burden after
45
46 multivariable adjustment: OR 8.42 (95% CI 1.88-37.60) and 4.26 (95% CI 1.35-13.43),
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48 respectively (Table 2). Marginally significant associations were observed between the age and
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50 visual functioning of the care recipient with AMD and the level of burden experienced by
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52 family carers (Table 2). Table 3 shows that younger carer age, older care recipient age, higher
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54 fatigue severity, high level of dependency on the carer and lower NEI VFQ-25 scores were
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56 significantly correlated with more carer burden. No statistically significant correlations were
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3 observed between carer burden scores and carer sex, patient sex, carer GQL scores, carer and
4 patient GHS scores, and carer GSE scores (data not shown).
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10 *Depressive symptoms*

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12 Over one in five family carers (24%) experienced elevated depressive symptoms as determined
13 by the CESD-10 scale. Table 4 shows that family carers with higher levels of fatigue were
14 more likely to experience depressive symptoms: OR 3.47 (95% CI 1.00-12.05). Conversely,
15 each unit increase in family carer GQL scores was associated with 40% reduced odds of
16 experiencing depressive symptoms: OR 0.60 (95% CI 0.41-0.88). Statistically significant
17 negative correlations between carer CESD-10 scores and carer GQL and GSE scores and care
18 recipient NEI VFQ-25 scores were observed, and a significant positive correlation was shown
19 between CESD-10 and carer FSS (Table 5). No statistically significant correlations were
20 observed between CESD-10 and carer age and sex, patient age and sex, carer and patient GHS
21 scores, and level of dependency on the carer (data not shown).
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40 **Discussion**

41 This novel study shows that family carers experience substantial levels of burden, depressive
42 symptoms and fatigue when caring for relatives with AMD. The findings from this study are
43 consistent with other studies that demonstrated poorer well-being of family carers of relatives
44 with AMD¹⁸. Older carers of relatives with chronic disease are themselves biologically
45 vulnerable to disease and are at substantial risk of developing health problems themselves, with
46 studies showing family carers who experienced strain during their experience of providing care
47 to be at greater risk of increased psychiatric morbidity^{19,20}. This is also reflected by the finding
48 that nearly a third of family carers in this study were providing care for their relatives with
49 AMD while experiencing significant medical morbidity themselves including, cardiovascular
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3 disease, cerebrovascular disease, kidney disease, arthritis and diabetes. The continuous nature
4 and stresses of providing care, together with burdensome physical and emotional demands on
5 a population already at risk of declining health outcomes is a significant area of concern, not
6 only due to declining health associated with the strain of providing care, but also because any
7 compromise of carer health may in effect lead to inadequate provision of optimal care to the
8 relative with AMD^{18,21}.

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17 More than half of family carers of relatives with AMD reported experiencing mild or
18 moderate-severe burden. When compared with burden experienced by caregivers of patients
19 with idiopathic Parkinson's disease, a greater proportion of family carers of patients with AMD
20 experience moderate-severe burden (22%) than carers supporting family with early (10%) and
21 late (~12%) stages of idiopathic Parkinson's disease²². In contrast, studies on caregivers for
22 patients with stroke report higher levels of moderate-severe burden (~68%) (ref. 23).
23 Interestingly, a recent study on family and unpaid carers of older persons revealed that carers
24 were at greater risk of experiencing burden when caring for patients with dementia with or
25 without substantial disability, but not for those patients with substantial disability in the
26 absence of dementia²⁴. While patient functional impairment has been shown to be associated
27 with higher levels of caregiver burden, this suggests that the additional challenges of caring for
28 patients with dementia may be an issue that is not as relevant for the provision of care to
29 patients with AMD²⁵.

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47 The level of dependency of patients with AMD had on their family carers was
48 independently associated with carer burden. This is in agreement with prior research by our
49 group showing that family carers of patients with AMD that had high levels of dependency on
50 them experience negative impacts such as high levels of emotional distress, as well as
51 disruptions to their lifestyle and retirement plans⁵. Moreover, a systematic review of depression
52 and burden among caregivers of patients with visual impairment found that greater hours of
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3 supervision required and greater limitations in the patients' ability to carry out their activities
4 of daily living, to be among the factors commonly associated with caregiver burden²⁶, a finding
5 reflected in our study. It is likely that a high level of dependency on family carers may
6 negatively impact the relationship between the carer and care recipient. This could be reflected
7 in the considerable proportion of family carers of relatives with AMD in this study that report
8 feeling frustrated, down and sad during their caregiving experience. Higher levels of
9 dependency by the care recipient could be linked to loss of independence in the family carer
10 due to a lack of time for one's own needs and leisure activities and this in turn could lead to
11 feelings of burden¹⁰. Moreover, carers have previously reported feelings of guilt from inability
12 to provide the constant and necessary care, with some carers experiencing feelings of being
13 manipulated by the care recipient^{5,10}. These feelings of burden due to the AMD caregiving
14 experience can have profound implications on family carer health and well-being.

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17 In contrast, around one in ten family carers of relatives with AMD in this study
18 experienced positive impacts of providing care, including feeling happier and more content
19 with their lives, as well as feeling more optimistic and determined. It is possible that these
20 differences of the caregiving experience among family carers may be related to pre-existing
21 strong familial ties and/or relationships, or otherwise relationships that have strengthened since
22 the need for family caregiving. Indeed, recent research into the role of partner relationship
23 quality and reciprocity (that is, a mutual sense of fair exchange) has shown lower subjective
24 carer burden and higher satisfaction in carers of partners with spinal cord injury, provided the
25 initial relationship quality was high^{27,28}. These high-quality relationships may in fact provide
26 the resources and means to alleviate the stress and burden that would otherwise be present
27 during the provision of care²⁸. As such, understanding the factors that determine relationship
28 strength and how they can be targeted may be a potential area to address when aiming to
29 improve equity in the family carer-care recipient dynamic.

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3 Over one in five family carers of relatives with AMD experienced elevated depressive
4 symptoms in our study, and this is substantially higher than the global prevalence rates of ~6%
5 (ref. 29). Higher rates of depressive symptoms (~35%) have also been demonstrated in previous
6 studies of family carers of patients with vision loss, along with significant associations between
7 depressive symptoms and younger carer age and poorer patient visual acuity³⁰. High rates (40%)
8 of caregivers reporting depressive symptoms were found in a study on family carers of patients
9 with Alzheimer's disease³¹. Higher levels of fatigue were shown to be predictive of family
10 carers experiencing depressive symptoms in our study. This is perhaps unsurprising, given that
11 fatigue and its symptoms are well-known symptoms/predictors of major depressive disorder in
12 the general population³². Studies on the emotional well-being of carers of patients with AMD
13 have previously reported increased rates of emotional distress, feelings of frustration, isolation
14 and sadness^{5,33,34}.

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17 Furthermore, poorer family carer quality of life was significantly associated with
18 depressive symptoms. This association between quality of life and depressive symptoms is
19 consistent with other cross-sectional and longitudinal studies involving older adults³⁵. Poor
20 quality of life limits one's ability to carry out their social and occupational activities^{36,37}.
21 Previous studies on caregiver quality of life have suggested that financial burden, lack of
22 family/social support, distress and unmet needs are among the factors purportedly increasing
23 the risk of depression and poor mental health outcomes³⁸⁻⁴⁰. In this way, demonstrable levels
24 of distress and morbidity experienced by family carers of patients with AMD make them
25 "hidden patients" at greater risk of poor health. As such, it is clear that there is a need for
26 evidence-based interventions and education to help increase support for family carers of
27 patients with AMD, thereby minimising their risk of poor health outcomes.

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30 Strengths of this study include the collection of rich and extensive outcome and covariate
31 data from patients with AMD and their family carers, as well as the use of several validated
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3 scales for the assessment of carer and patient variables such as burden, depression, fatigue and
4 visual functioning. However, findings of this study should be interpreted with caution. Due to
5 the relatively small sample size, it is likely that the study was underpowered to detect modest
6 associations. Also, we cannot discount residual confounding from factors that were not
7 measured in our study such as the quality/ strength of the carer-care recipient relationship and
8 other psychosocial measures such as spirituality and carer resilience. Moreover, the cross-
9 sectional study design implemented was useful for investigating the relationships between
10 various factors and health outcomes. However, this design limits our ability to draw
11 conclusions about causality. Future longitudinal studies utilising larger population sets would
12 be useful to affirm the findings of this study.
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28 **Conclusion**

29
30 A substantial proportion of family carers of relatives with AMD experience significant burden
31 and depressive symptoms. Higher levels of dependency and fatigue, as well as lower quality
32 of life were independently associated with higher levels of burden and/or greater odds of
33 depressive symptoms in family carers. These findings underscore the urgent need for evidence-
34 based interventions tailored to family carers of patients with AMD to alleviate their distress
35 and burden, by targeting factors such as fatigue and quality of life, in a timely and effective
36 manner.
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3 Table 1. Study characteristics of family carers stratified by degree of burden experienced as measured by carer sex, age, general health status,
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1 Table 1. Study characteristics of family carers stratified by degree of burden experienced as measured by carer sex, age, general health status,
2 FSS scores, CESD-10 scores, GSE scores, GQL scores, and care recipient sex, age, general health status and NEI VFQ-25 scores (n=96)

Population characteristics	Degree of burden			P-value
	No/little burden (n=41)	Mild burden (n=33)	Moderate-severe burden (n=21)	
Carer variables				
Female sex, <i>n</i> (%)	28 (68.3)	28 (84.9)	18 (85.7)	0.15
Age, yrs, <i>mean</i> (<i>SD</i>)	66.5 (15.6)	63.1 (13.1)	59.1 (10.4)	0.14
General health status				
Substantial comorbidity, <i>n</i> (%)	15 (36.6)	11 (33.3)	2 (9.5)	0.07
Fatigue severity scale score				
Problematic fatigue (≥ 4), <i>n</i> (%)	11 (26.8)	11 (33.3)	5 (23.8)	0.06
CESD-10 score				
Presence of depressive symptoms (≥ 10), <i>n</i> (%)	6 (14.6)	7 (21.2)	10 (47.6)	0.01

Total general self-efficacy scores, <i>mean (SD)</i>	33.0 (5.4)	32.7 (4.1)	31.0 (4.5)	0.32
Total general quality of life scores, <i>mean (SD)</i>	7.6 (1.7)	7.5 (1.8)	7.6 (2.0)	0.09
Patient variables				
Female sex, <i>n (%)</i>	25 (61.0)	20 (60.6)	27 (81.0)	0.23
Age, yrs, <i>mean (SD)</i>	81.0 (10.1)	84.5 (7.2)	80.4 (11.1)	0.15
General health status				
Substantial comorbidity, <i>n (%)</i>	19 (46.3)	15 (45.5)	14 (66.7)	0.25
Total NEI VFQ-25 scores, <i>mean (SD)</i>	62.7 (21.0)	53.6 (53.6)	30.6 (20.9)	<0.0001

3 FSS – Fatigue Severity Scale; CESD-10 – Centre for Epidemiologic Studies Depression-10; GSE – generalised self-efficacy; GQL – General Quality of Life; NEI VFQ-25 – National Eye Institute Visual Functioning

4 Questionnaire-25

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For peer review only

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Table 2. Association between selected family carer and care recipient with AMD variables with level of burden among family carers, presented as adjusted odds ratios (OR) and 95% confidence intervals (CI).

Factors	Level of burden, OR (95% CI)*	
	Moderate-severe	Mild
Care recipient age (each 1-unit increase)	0.99 (0.92-1.07)	1.03 (0.97–1.09)
NEI VFQ-25 score (each 1-unit increase)	0.96 (0.93-0.99)	1.00 (0.98–1.02)
High level of dependency on carer	8.42 (1.88-37.60)	4.26 (1.35–13.43)

*Logistic regression model used the burden group 0-20 (no/little burden) as the reference category

14 *Table 3. Spearman correlation coefficients between burden group and carer age, FSS scores, and dependency, and care recipient age and NEI*
 15 *VFQ-25 scores among family carers of relatives with AMD (n=95)*

Variable		Carer age	Patient age	Fatigue severity scale	Dependency	NEI VFQ-25
Carer burden	<i>r</i>	- 0.26	- 0.22	0.22	0.57	- 0.45
scores	<i>p</i>	0.0115	0.0349	0.0082	<0.001	<0.0001

16 FSS – Fatigue Severity Scale; NEI VFQ-25 – National Eye Institute Visual Functioning Questionnaire-25

17 *Table 4. Associations between selected family carer and care recipient with AMD variables and presence of depressive symptoms among family*
 18 *carers, presented as adjusted odds ratios (OR) and 95% confidence intervals (CI).*

Factor	Presence of depressive symptoms, OR (95% CI)
Family Carer	
Age (each 1-unit increase)	0.98 (0.9—1.04)
Female sex	0.58 (0.1—2.60)
General quality of life (each 1-unit increase)	0.60 (0.4—0.88)
Fatigue severity scale score (each 1-unit increase)	3.47 (1.0—12.05)
General self-efficacy (each 1-unit increase)	0.97 (0.8—1.10)
Care recipients with AMD	
Age (each 1-unit increase)	0.98 (0.9—1.05)
Female sex	1.29 (0.2—6.25)
General health status (each 1-unit increase)	1.84 (0.5—6.40)
NEI VFQ-25 (each 1-unit increase)	0.98 (0.9—1.01)

Table 5. Pearson correlation coefficients between presence of depressive symptoms and carer variables (GQL scores, FSS scores, GSE scores) and care recipient NEI VFQ-25 scores among family carers of relatives with AMD (n=96)

Variable	General quality of life	Fatigue severity scale	General self-efficacy	NEI VFQ-25
	<i>r</i>	- 0.46	0.34	- 0.21
CESD-10	<i>p</i>	<0.0001	0.0008	0.0391

CESD-10 – Centre for Epidemiologic Studies Depression-10; GQL – General Quality of Life; FSS – Fatigue Severity Scale; GSE – generalised self-efficacy; NEI VFQ-25 – National Eye Institute Visual Functioning Questionnaire-25

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Cross-sectional study evaluating burden and depressive symptoms in family carers of persons with age-related macular degeneration in Australia

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3 **Cross-sectional study evaluating burden and depressive symptoms in**
4 **family carers of persons with age-related macular degeneration in**
5 **Australia**
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Abstract

Objectives: We aimed to analyse the degree of carer burden and depressive symptoms in family carers of persons with age-related macular degeneration (AMD) and explore the factors independently associated with carer burden and depressive symptoms.

Methods: Cross-sectional study using self- and interviewer-administered surveys, involving 96 family carer-care recipient pairs. Participants were identified from tertiary ophthalmology clinics in Sydney, Australia, as well as the Macular Disease Foundation of Australia database. Logistic regression, Pearson and Spearman correlation analyses were used to investigate associations of explanatory factors, (family caregiving experience, carer fatigue, carer quality of life and care recipient level of dependency) with study outcomes - carer burden and depressive symptoms.

Results: Over one in two family carers reported experiencing mild or moderate-severe burden. More than one in five and more than one in three family carers experienced depressive symptoms and substantial fatigue, respectively. High level of care recipient dependency was associated with greater odds of moderate-severe and mild carer burden, multivariable-adjusted OR 8.42 (95% CI 1.88-37.60) and OR 4.26 (95% CI 1.35-13.43) respectively. High levels of fatigue were associated with 3-fold greater odds of the carer experiencing depressive symptoms, multivariable-adjusted OR 3.47 (95% CI 1.00-12.05).

Conclusions: A substantial degree of morbidity is observed in family carers during the caregiving experience for patients with AMD. Level of dependency on the family carer and fatigue were independently associated with family carer burden and depressive symptoms.

Strengths and limitations of this study

- The study design and method of surveying allowed for the collection of rich and extensive data from patients with AMD and their family carers.
- Several validated scales for the assessment of both carer and patient variables were used, including those for burden, depression, fatigue and visual functioning.
- Study participants were recruited from only one state in Australia
- Due to the relatively small sample size, the study is likely to be underpowered for detecting modest associations

Patient consent

Obtained.

Ethics approval

Ethics approval was obtained from The University of Sydney Human Research Ethics Committee (ID# - 2016/793).

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Introduction

Age-related macular degeneration (AMD) is a chronic and progressive disorder of the macula¹ and is the leading cause of blindness and low vision in Australia, directly affecting more than 1 million persons^{2,3}. The effects of vision impairment in AMD are not limited to declining visual function, with several studies showing that AMD affects multiple health domains and leads to significant emotional distress, poorer quality of life and reduced functional independence^{4,5}. For many patients, the ongoing nature of a chronic illness like AMD is such that it requires the provision of continuous physical and emotional care beyond the scope of what can be currently provided by hospitals or other institutions^{6,7}. Family carers of relatives with AMD are often expected to provide a high standard of care despite not receiving formal training and adequate support for this role^{8,9}. Surveys on the perceptions of family carers of relatives with AMD in their role as informal carers, demonstrate experiences of significant psychological distress, with the negative impacts of caring extending to increased financial stress, disruptions to lifestyle and retirement plans, and added strain on the relationship between carer and care recipient^{5,10}. Moreover, previous studies based in the UK have shown that caregivers of patients with AMD experience burden levels comparable to those caring for persons with rheumatoid arthritis and multiple sclerosis¹¹. Additionally, comorbidity has been shown to be associated with a higher degree of caregiver burden, as demonstrated in other caregiving settings such as for patients with dementia¹². Furthermore, a significant degree of psychological distress has been reported in caregivers of legally blind patients, with one such study reporting more than a third of caregivers experiencing depression¹³. Previous research conducted by our group on caregiving for AMD have demonstrated that the level of caregiver dependence and the presence of multiple chronic illnesses in the care-recipient were independent predictors of psychological distress¹⁴.

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Clearly, the impacts of AMD are far-reaching, with significant influence on family, friends and carers, as well as substantial cost to society^{3,15}. However, currently there exists little literature reporting on the level and factors of burden and depressive symptoms experienced by family carers of relatives with AMD. As such, the key aims of this cross-sectional study were to: 1) Analyse the degree of carer burden and depressive symptoms in family carers of persons with AMD; and 2) Explore the factors that were independently associated with carer burden and depressive symptoms.

Methods

Participants

Participants for this study were recruited as a part of a randomised controlled trial implementing a novel multi-component intervention targeting the drivers of stress and burden in family carers of patients with AMD. This study analysed a total of 96 patients with AMD and 96 of their family carers who were examined at baseline (pre-intervention). Recruitment of participants occurred between January 2017 to May 2020 across multiple ophthalmology practices in Sydney, Australia, as well as via the Macular Disease Foundation Australia (MDFA) database of members. The inclusion criteria for eligible family carers participating in this study were: adults aged more than 18 years old; family carer of a relative with AMD; willing to engage in a 10-week cognitive behavioural therapy intervention over a 3-month period; and sufficient English fluency to effectively engage in the intervention. All participants in this study gave written informed consent. Ethics approval was obtained from The University of Sydney Human Research Ethics Committee (ID# - 2016/793). Information on baseline study participant characteristics were obtained via surveys of family carers and their relatives with AMD, completed on-site during clinic visits or at home either independently or with help from the study coordinator e.g. due to limitations imposed by poor vision.

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Sociodemographic information and medical history

All participants (carers and care recipients with AMD) provided sociodemographic information including: age, sex, education level and marital status. They also self-reported any medical conditions such as: heart attacks; angina (without myocardial infarction); any other cardiac conditions; strokes or transient ischaemic attacks; high blood pressure; high cholesterol; diabetes or prediabetes; kidney disease; arthritis; hearing loss; and visual impairment. This information was used to assess the general health status (GHS) of each participant. Participants who reported 3 or more health conditions were considered as having substantial comorbidity and received a score of 1, whereas those with fewer than 3 health conditions received a score of 0.

Carer variables

Family carers were asked to provide details about the patient with AMD that they cared for such as whether they were the sole caregiver of the patient; the type of caregiving duties performed and the hours of care (per day) they provided to the care recipient with AMD. This comprised of 21 questions detailing caregiving duties as they applied to typical activities of daily living and instrumental activities of daily living for the patient with AMD, including exercise and/or sport, cooking and preparing food, cleaning, reading, personal grooming, using public transport, driving and more. Each question was scored reflecting the degree of help given for each activity (*0=no help or little help given, 1=moderate amount of help given,*

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3 2=*high amount of help given*, 3=*not applicable*). Furthermore, carers were surveyed to provide
4 details about the impact of providing care to a family member with AMD, including: the impact
5 of carer on the carer's state of mind; ability to manage their own existing health conditions;
6 and impact and change on work, volunteer and recreational activities. Additional information
7 on family carers was determined by administering several validated instruments and scales as
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19 (i) *Carer burden*. The Caregiver Burden Scale (CBS) is a 22-item questionnaire originally
20 developed for assessment of perceived family carer burden in caring for patients with
21 dementia^{16,17}. Each question was scored on a 5-point Likert-type scale (0=*never*, 1=*rarely*,
22 2=*sometimes*, 3=*quite frequently*, 4=*always*), reflecting the frequency of family carers'
23 feelings when taking care of their family member. The total burden score calculated for each
24 family carer was used to stratify levels of burden into 3 categories, with higher scores indicating
25 higher levels of burden (0-20=*no/little burden*, 21-40=*mild burden*, ≥ 41 =*moderate-severe*
26 *burden*). The CBS is a reliable measure with a Cronbach's alpha of 0.92¹⁸.
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40 (ii) *Depressive symptoms*. The short form of the Centre for Epidemiologic Studies Depression
41 (CESD-10) scale is a 10-item questionnaire and was used to screen for symptoms of
42 depression¹⁹. Each question gauges the frequency of a family carer experiencing certain
43 symptoms of depression per week and is scored on a 4-point Likert-type scale (0 = *rarely or*
44 *none of the time (<1 day)*, 1=*some or a little of the time (1-2 days)*, 2=*occasionally or a*
45 *moderate amount of the time (3-4 days)*, 3=*most or all of the time (5-7 days)*). A total CESD-
46 10 score of 10 or more indicates significant presence of depressive symptoms, as reported by
47 previous research evaluating the validity of the CESD-10 scale¹⁹. The CESD-10 is a validated
48 and reliable measure with a Cronbach's alpha of 0.80^{19,20}.
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6 (iii) *Fatigue*. The Fatigue Severity Scale (FSS) is a 9-item questionnaire used frequently to
7 assess the degree of impact that fatigue has on an individual's activities and physical
8 functioning²¹. Participants were asked to respond to statements about how much fatigue
9 impacted their ability to function on a scale of 1 (*disagree*) to 7 (*agree*). Previous studies have
10 shown mean (SD) FSS scores for healthy individuals to be 2.3 (0.7)²¹. Mean FSS scores of 4
11 or more were categorised as having problematic fatigue. The FSS is a validated and reliable
12 measure with a Cronbach's alpha of 0.88²¹.
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24 (iv) *Self-efficacy*. The General self-efficacy (GSE) scale is a 10-item questionnaire shown to
25 be effective at measuring one's beliefs of overall ability to succeed in specific situations²². The
26 degree of how much a family carer agreed with each statement was measured using a 4-point
27 Likert-type scale (*0=not true, 1=hardly true, 2=moderately true, 3=exactly true*). Higher total
28 GSE scores indicate higher self-efficacy.
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38 (v) *Dependency*. Carers were asked to quantify the level of dependence their family member
39 with AMD had on them since their diagnosis using a 4-point Likert-type scale (*1=not at all*
40 *dependent, 2=somewhat dependent, 3=moderately dependent, 4 = very dependent, 5 =*
41 *extremely dependent*). Scores 3 or more were interpreted as an indication of high dependency
42 on the family carer (*1-2 = low dependency, 3-5 = high dependency*).
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51 (vi) *Quality of life*. Carer's rated their general quality of life (GQL) on a linear scale from 0
52 (*poor quality of life*) to 10 (*excellent quality of life*).
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Care recipients with AMD

The National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) was completed by care recipients, and is a reliable and validated tool used to measure status of vision-related health impairment most relevant to patients with chronic eye conditions²³. Questions in the NEI VFQ-25 were used to determine the extent of how visual disability and symptoms negatively impacts the patient's ability to function, well-being and efficacy in achieving vision-related tasks. The NEI VFQ-25 is comprised of 12 subscales, assessing general vision, near and distance vision, vision-related difficulty with activities, vision-related driving problems, eye pain, colour vision, dependency, impact on social functioning, mental health and general health²³. Scores recorded in the original response category for each question were recoded to a scale between 0-100 in accordance with the NEI VFQ-25 scoring algorithm, with higher scores indicating greater vision-related well-being.

Statistical analysis

SAS statistical software (SAS Institute, NC, v9.4) was used for the statistical analysis, including t-tests, chi-squared tests, F-test and logistical regression. The generalised logits model was used for carer burden, given that it is a three-level categorical variable²⁴. A binary logistic regression was used for the study outcome of depressive symptoms as it is a two-level variable. For all models, a stepwise selection method was used.

Predictor variables assessed for both these study outcomes were: carer age, carer sex, carer general quality of life, carer general health status, fatigue severity, general self-efficacy, level of dependency on the carer, patient age, patient sex, patient general health status and patient NEI VFQ-25 scores. The CORR procedure was used to compute the Pearson correlations and Spearman rank-order correlations between presence of depressive symptoms (CESD-10 score) and the following variables: patient age and sex, and carer variables (age,

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3 sex, general quality of life scores, fatigue severity scale scores, carer and patient general health
4 status, general self-efficacy, level of dependency on the carer and NEI VFQ-25 scores). The
5 significance level was <0.05 . Checks for multicollinearity did not return any confirmation of
6 multicollinearity occurring.
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16 **Results**

17 *AMD caregiving experience and health-related variables*

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20 The majority of family carers (91%) were aged 50 years and over, with family carers aged 65
21 years or older making up 54% of the sample. The proportion of females was 78% and 66%
22 among family carers and care recipients with AMD, respectively. Of the 96 family carers in
23 this study, 75% were the sole carer of the patients with AMD, with 43% reporting that the
24 family member they cared for was highly dependent on them. Responses to questions about
25 the impact of providing care to a family member with AMD on the carer's state of mind showed
26 that many carers experienced feeling frustrated (43%), depressive (31%) and sad (27%). Some
27 carers reported feeling no different (26%), with a relatively smaller proportion of carers
28 reporting positive impacts in relation to their caregiving experience, such as feeling more
29 content in their lives (13%), feeling happier than ever before (13%), feeling more optimistic
30 (8%) and feeling more determined (7%). Family carers played a considerable role in helping
31 their relatives access medical care, with 91% accompanying their relatives to their
32 ophthalmology appointments where the majority of relatives with AMD (79%) were receiving
33 anti-VEGF injections. In terms of how often help was provided to relatives with AMD, 61%
34 of family carers reported providing help for 7 days a week on average, with 45% reporting
35 either spending >8 hours per day with them or living together with the care recipient. The main
36 caregiving duties where carers provided moderate to high amounts of help included cooking
37 (57%), cleaning (60%) and help with leaving the house (70%).
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3 Substantial amounts of fatigue were experienced by 36% of family carers as indicated by
4 scores of 4 or higher on the fatigue severity scale, and a considerable degree of general health
5 comorbidities was reported by 29% of family carers. The mean quality of life and general self-
6 efficacy scores among the family carers in this study were: 7.3 (SD 2.0) and 32.5 (SD 4.9),
7 respectively.
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17 *Burden analysis*

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19 More than half of family carers reported experiencing mild (35%) and moderate-severe (22%)
20 burden due to their caregiving experience (Table 1). Family carers of highly dependent
21 relatives with AMD were more likely to experience moderate-severe and mild burden after
22 multivariable adjustment: OR 8.42 (95% CI 1.88-37.60) and 4.26 (95% CI 1.35-13.43),
23 respectively (Table 2). Marginally significant associations were observed between the age and
24 visual functioning of the care recipient with AMD and the level of burden experienced by
25 family carers (Table 2). Younger carer age, older care recipient age, higher fatigue severity,
26 high level of dependency on the carer and lower NEI VFQ-25 scores were significantly
27 correlated with more carer burden (supplementary table 1). No statistically significant
28 correlations were observed between carer burden scores and carer sex, patient sex, carer
29 general quality of life scores (quality of life), carer and patient GHS scores (general health
30 status, and carer GSE scores (general self-efficacy) (data not shown).
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49 *Depressive symptoms*

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51 Over one in five family carers (24%) demonstrated a significant presence of depressive
52 symptoms as determined by the CESD-10 scale. Table 3 shows that family carers with higher
53 levels of fatigue were more likely to experience depressive symptoms: OR 3.47 (95% CI 1.00-
54 12.05). Conversely, each unit increase in family carer GQL scores was associated with 40%
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3 reduced odds of experiencing depressive symptoms: OR 0.60 (95% CI 0.41-0.88). Statistically
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5 significant negative correlations between carer CESD-10 scores and carer GQL and GSE
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7 scores and care recipient NEI VFQ-25 scores were observed, and a significant positive
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9 correlation was shown between CESD-10 and carer FSS (supplementary table 2). No
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11 statistically significant correlations were observed between CESD-10 and carer age and sex,
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13 patient age and sex, carer and patient GHS scores, and level of dependency on the carer (data
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15 not shown).
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22 **Discussion**

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24 This novel study shows that family carers experience substantial levels of burden, depressive
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26 symptoms and fatigue when caring for relatives with AMD. The findings from this study are
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28 consistent with other studies that demonstrated poorer well-being of family carers of relatives
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30 with AMD¹¹. Older carers of relatives with chronic disease are themselves biologically
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32 vulnerable to disease and are at substantial risk of developing health problems themselves, with
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34 studies showing family carers who experienced strain during their experience of providing care
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36 to be at greater risk of increased psychiatric morbidity^{25,26}. This is also reflected by the finding
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38 that nearly a third of family carers in this study were providing care for their relatives with
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40 AMD while experiencing significant medical morbidity themselves including, cardiovascular
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42 disease, cerebrovascular disease, kidney disease, arthritis and diabetes. The continuous nature
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44 and stresses of providing care, together with burdensome physical and emotional demands on
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46 a population already at risk of declining health outcomes is a significant area of concern, not
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48 only due to declining health associated with the strain of providing care, but also because any
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50 compromise of carer health may in effect lead to inadequate provision of optimal care to the
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52 relative with AMD^{11,27}.
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3 More than half of family carers of relatives with AMD reported experiencing mild or
4 moderate-severe burden. In comparison, a cross-sectional study on caregiver burden for blind
5 persons in India demonstrated a greater proportion of caregivers scoring ≥ 41 on the CBS
6 (91.8%), that is, demonstrating substantial amounts of moderate to severe burden²⁸. However,
7 it is perhaps unsurprising that higher levels of burden were reported, given the more severe
8 visual impairment of the population studied. Other areas of interest that should be considered
9 for future research are differences in setting, availability of community support, socioeconomic
10 status and cultural attitudes that may also influence perceived caregiver burden²⁸.
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22 When compared with burden experienced by caregivers of patients with idiopathic
23 Parkinson's disease, a greater proportion of family carers of patients with AMD experience
24 moderate-severe burden (22%) than carers supporting family with early (10%) and late (~12%)
25 stages of idiopathic Parkinson's disease²⁹. In contrast, studies on caregivers for patients with
26 stroke report higher levels of moderate-severe burden (~68%)³⁰. Interestingly, a recent study
27 on family and unpaid carers of older persons revealed that carers were at greater risk of
28 experiencing burden when caring for patients with dementia with or without substantial
29 disability, but not for those patients with substantial disability in the absence of dementia³¹.
30 While patient functional impairment has been shown to be associated with higher levels of
31 caregiver burden, this suggests that the additional challenges of caring for patients with
32 dementia may be an issue that is not as relevant for the provision of care to patients with AMD³².
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46 The level of dependency that patients with AMD had on their family carers was
47 independently associated with carer burden. This is in agreement with prior research by our
48 group showing that family carers of patients with AMD that had high levels of dependency on
49 them experience negative impacts such as high levels of emotional distress, as well as
50 disruptions to their lifestyle and retirement plans⁵. Moreover, a systematic review of depression
51 and burden among caregivers of patients with visual impairment found that greater hours of
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3 supervision required and greater limitations in the patients' ability to carry out their activities
4 of daily living, to be among the factors commonly associated with caregiver burden³³, a finding
5 reflected in our study. It is likely that a high level of dependency on family carers may
6 negatively impact the relationship between the carer and care recipient. This could be reflected
7 in the considerable proportion of family carers of relatives with AMD in this study that report
8 feeling frustrated, down and sad during their caregiving experience. Higher levels of
9 dependency by the care recipient could be linked to loss of independence in the family carer
10 due to a lack of time for one's own needs and leisure activities and this in turn could lead to
11 feelings of burden¹⁰. Moreover, carers have previously reported feelings of guilt from inability
12 to provide the constant and necessary care, with some carers experiencing feelings of being
13 manipulated by the care recipient^{5,10}. These feelings of burden due to the AMD caregiving
14 experience can have profound implications on family carer health and well-being. Previous
15 research conducted on the caregiving experience for elderly patients with chronic illnesses has
16 demonstrated negative impacts on the carer's physical and psychological well-being, such as
17 experiencing increased psychological distress, reduced engagement with preventative health
18 behaviours, and disruptions to employment and increased financial stress^{5, 10, 34}

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40 In contrast, around one in ten family carers of relatives with AMD in this study
41 experienced positive impacts of providing care, including feeling happier and more content
42 with their lives, as well as feeling more optimistic and determined. It is possible that these
43 differences of the caregiving experience among family carers may be related to pre-existing
44 strong familial ties and/or relationships, or otherwise relationships that have strengthened since
45 the need for family caregiving. Indeed, research into the role of partner relationship quality and
46 reciprocity (that is, a mutual sense of fair exchange) has demonstrated benefits on caregiver
47 wellbeing^{35,36}. Another study examining the role of reciprocity in providing care for persons
48 with dementia, chronic physical disability/illness, frailty from aging, and intellectual disability
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3 showed an inverse relationship between reciprocity and self-esteem to caregiver burden³⁶.
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5 These high-quality relationships may in fact provide the resources and means to alleviate the
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7 stress and burden that would otherwise be present during the provision of care³⁶. As such,
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9 understanding the factors that determine relationship strength and how they can be targeted
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11 may be a potential area to address when aiming to improve equity in the family carer-care
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13 recipient dynamic.
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17 Over one in five family carers of relatives with AMD demonstrated a significant presence
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19 of depressive symptoms in our study, and this is substantially higher than the global prevalence
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21 rates of ~6%³⁷. Higher rates of depressive symptoms (~35%) have also been demonstrated in
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23 previous studies of family carers of patients with vision loss, along with significant associations
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25 between depressive symptoms and younger carer age and poorer patient visual acuity³⁸. High
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27 rates (40%) of caregivers reporting depressive symptoms were found in a study on family
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29 carers of patients with Alzheimer's disease³⁹. Higher levels of fatigue were shown to be
30
31 predictive of family carers experiencing depressive symptoms in our study. This is perhaps
32
33 unsurprising, given that fatigue and its symptoms are well-known symptoms/predictors of
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35 major depressive disorder in the general population⁴⁰. Studies on the emotional well-being of
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37 carers of patients with AMD have previously reported increased rates of emotional distress,
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39 feelings of frustration, isolation and sadness^{5,13,34}.
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45 Furthermore, poorer family carer quality of life was significantly associated with
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47 depressive symptoms. This association between quality of life and depressive symptoms is
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49 consistent with other cross-sectional and longitudinal studies involving older adults⁴¹. Poor
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51 quality of life limits one's ability to carry out their social and occupational activities^{42,43}.
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53 Previous studies on caregiver quality of life have suggest that financial burden, lack of
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55 family/social support, distress and unmet needs are among the factors purportedly increasing
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57 the risk of depression and poor mental health outcomes⁴⁴⁻⁴⁶.
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3 Strengths of this study include the collection of rich and extensive outcome and covariate
4 data from patients with AMD and their family carers, as well as the use of several validated
5 scales for the assessment of carer and patient variables such as burden, depression, fatigue
6 and visual functioning. However, findings of this study should be interpreted with caution.
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8 Due to the relatively small sample size, it is likely that the study was underpowered to detect
9 modest associations, as well as limiting the generalisability of the results. Similarly, in the
10 analyses small sample sizes accounted for large confidence intervals, providing less precise
11 estimates of effect. The use of other tools such as the Barthel index for the measurement of
12 care recipient dependency may have been potentially useful in providing a more accurate
13 quantification of dependency. However, while this is a reliable measure of dependency, it is
14 time consuming, given that direct observation of the person performing specific tasks is
15 required. Also, we cannot discount residual confounding from factors that were not measured
16 in our study such as the quality/ strength of the carer-care recipient relationship and other
17 psychosocial measures such as spirituality and carer resilience. Moreover, the cross-sectional
18 study design implemented was useful for investigating the relationships between various
19 factors and health outcomes. However, this design limits our ability to draw conclusions
20 about causality. Longitudinal and experimental analyses would allow for a better
21 understanding of causality and the temporal interactions and relationships between variables
22 in this study. As such, future studies of these types utilising larger population sets would be
23 useful to affirm the findings of this study.
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51 **Conclusion**

52 A substantial proportion of family carers of relatives with AMD experience significant burden
53 and depressive symptoms. Family carers played a considerable role in the care of relatives with
54 AMD, including aiding with access to medical care and assistance with care-recipient's ADLs.
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3 Many carers self-reported experiencing feeling frustrated, depressive and sad. Levels of
4 dependency and fatigue, as well as lower quality of life were independently associated with
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6 higher levels of burden and/or greater odds of depressive symptoms in family carers. Further
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8 research is required to affirm these conclusions regarding these predictors of burden and
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10 depressive symptoms in family carers of relatives with AMD.
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17 **a. Contributors**

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19 All authors—IJ, DT, GB, JG, KNP, AC, GL, PM and BG—provided inputs in study design.
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21 IJ, DT, JG, GB, PM and BG were involved in data collection and data analysis. IJ, JG and
22
23 BG were responsible for publication writing. All authors reviewed and approved the final
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25 version of this manuscript.
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28 **b. Competing interests**

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30 None of the authors declared a conflict of interest.
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34
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36
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38
39 Australia.
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42 **d. Data sharing statement**

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44 Data are available upon reasonable request.
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53 *Table 1. Study characteristics of family carers stratified by degree of burden experienced as measured by carer sex, age, general health status,*
 54 *FSS scores, CESD-10 scores, GSE scores, GQL scores, and care recipient sex, age, general health status and NEI VFQ-25 scores (n=96)*

Population characteristics	Degree of burden			P-value
	No/little burden (n=41)	Mild burden (n=33)	Moderate-severe burden (n=21)	
Carer variables				
Female sex, <i>n</i> (%)	28 (68.3)	28 (84.9)	18 (85.7)	0.15
Age, yrs, <i>mean</i> (<i>SD</i>)	66.5 (15.6)	63.1 (13.1)	59.1 (10.4)	0.14
General health status				
Substantial comorbidity, <i>n</i> (%)	15 (36.6)	11 (33.3)	2 (9.5)	0.07
Fatigue severity scale score				
Problematic fatigue (≥ 4), <i>n</i> (%)	11 (26.8)	11 (33.3)	5 (23.8)	0.06
CESD-10 score				
Presence of depressive symptoms (≥ 10), <i>n</i> (%)	6 (14.6)	7 (21.2)	10 (47.6)	0.01

Total general self-efficacy scores, <i>mean (SD)</i>	33.0 (5.4)	32.7 (4.1)	31.0 (4.5)	0.32
Total general quality of life scores, <i>mean (SD)</i>	7.6 (1.7)	7.5 (1.8)	7.6 (2.0)	0.09
Patient variables				
Female sex, <i>n (%)</i>	25 (61.0)	20 (60.6)	27 (81.0)	0.23
Age, yrs, <i>mean (SD)</i>	81.0 (10.1)	84.5 (7.2)	80.4 (11.1)	0.15
General health status				
Substantial comorbidity, <i>n (%)</i>	19 (46.3)	15 (45.5)	14 (66.7)	0.25
Total NEI VFQ-25 scores, <i>mean (SD)</i>	62.7 (21.0)	53.6 (53.6)	30.6 (20.9)	<0.0001

Unadjusted *P* values from test of heterogeneity across the three burden categories. FSS – Fatigue Severity Scale; CESD-10 – Centre for Epidemiologic Studies Depression-10; GSE – generalised self-efficacy; GQL – General Quality of Life; NEI VFQ-25 – National Eye Institute Visual Functioning Questionnaire-25

60 *Table 2. Association between selected family carer and care recipient with AMD variables with level of burden among family carers, presented*
 61 *as adjusted odds ratios (OR) and 95% confidence intervals (CI).*

Factors	Level of burden, OR (95% CI)*	
	Mild	Moderate-severe
Care recipient age (each 1-unit increase)	1.03 (0.97–1.09)	0.99 (0.92-1.07)
NEI VFQ-25 score (each 1-unit increase)	1.00 (0.98–1.02)	0.96 (0.93-0.99)
High level of dependency on carer	4.26 (1.35–13.43)	8.42 (1.88-37.60)

62 *Logistic regression model (Generalized Logit Model) used the burden group 0-20 (no/little burden) as the reference category.

68 *Table 3. Associations between selected variables and presence of depressive symptoms among family carers and care recipients with AMD,*
 69 *presented as adjusted odds ratios (OR) and 95% confidence intervals (CI).*

Factor	Presence of depressive symptoms, OR (95% CI)
Family Carer	
Age (each 1-unit increase)	0.98 (0.9—1.04)
Female sex	0.58 (0.1—2.60)
General quality of life (each 1-unit increase)	0.60 (0.4—0.88)
Fatigue severity scale score (each 1-unit increase)	3.47 (1.0—12.05)
General self-efficacy (each 1-unit increase)	0.97 (0.8—1.10)
Care recipients with AMD	
Age (each 1-unit increase)	0.98 (0.9—1.05)
Female sex	1.29 (0.2—6.25)
General health status (each 1-unit increase)	1.84 (0.5—6.40)
NEI VFQ-25 (each 1-unit increase)	0.98 (0.9—1.01)

Supplementary tables

Table 1. Spearman correlation coefficients between burden group and carer age, FSS scores, and dependency, and care recipient age and NEI VFQ-25 scores among family carers of relatives with AMD (n=95)

Variable		Carer age	Patient age	Fatigue severity scale	Dependency	NEI VFQ-25
Carer burden	<i>r</i>	- 0.26	- 0.22	0.22	0.07	- 0.45
scores	<i>p</i>	0.0115	0.0349	0.0082	<0.0001	<0.0001

FSS – Fatigue Severity Scale; NEI VFQ-25 – National Eye Institute Visual Functioning Questionnaire-25

Supplementary table 2

Table 2. Pearson correlation coefficients between presence of depressive symptoms and carer variables (GQL scores, FSS scores, GSE scores) and care recipient NEI VFQ-25 scores among family carers of relatives with AMD (n=96)

Variable		General quality of life	Fatigue severity scale	General self-efficacy	NEI VFQ-25
CESD-10	<i>r</i>	- 0.46	0.34	- 0.21	- 0.26
	<i>p</i>	<0.0001	0.0008	0.0391	0.0121

CESD-10 – Centre for Epidemiologic Studies Depression-10; GQL – General Quality of Life; FSS – Fatigue Severity Scale; GSE – generalised self-efficacy; NEI VFQ-25 – National Eye Institute Visual Functioning

Questionnaire-25

STROBE Statement

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract We have indicated in the title and abstract that this is a cross-sectional study.	1, 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found This is done.	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported This is done.	5
Objectives	3	State specific objectives, including any prespecified hypotheses This is done.	6
Methods			
Study design	4	Present key elements of study design early in the paper This is done.	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This is done.	6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants This is shown in the 'Participants' section of manuscript.	6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable This information is provided in the Methods section.	7, 8, 9, 10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group This information is provided in the Methods section.	7, 8, 9, 10
Bias	9	Describe any efforts to address potential sources of bias N/A	
Study size	10	Explain how the study size was arrived at This is described in the Methods section	6
Quantitative	11	Explain how quantitative variables were handled in the analyses. If	7, 8, 9, 10

variables		applicable, describe which groupings were chosen and why This information is provided in the Methods section.	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding This information is provided in the Methods section.	10, 11
		(b) Describe any methods used to examine subgroups and interactions This information is provided in the Methods section.	10, 11
		(c) Explain how missing data were addressed N/A	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy N/A	
		(e) Describe any sensitivity analyses N/A	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed This is described in the Methods section	6
		(b) Give reasons for non-participation at each stage This is described in the Methods	6
		(c) Consider use of a flow diagram N/A	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders See Table 1	25
		(b) Indicate number of participants with missing data for each variable of interest N/A	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> This is reported in the Tables and Results section	11, 12, 13, 25, 26, 27, 28
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included See Tables 2-3 and Results section	11, 12, 13, 25, 26, 27, 28
		(b) Report category boundaries when continuous variables were categorized N/A	

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

N/A

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Included in Tables 2-3 and Supplementary files and Results section	11, 12, 13, 25, 26, 27, 28, Supplementary files 1-2
Discussion			
Key results	18	Summarise key results with reference to study objectives Paragraph 1, 2, 3 and 6 of the Discussion section	13, 14, 15, 16, 17, 18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Strengths and limitations are discussed in Discussion section – page 16 and 17	16, 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence This is provided in the Discussion	16, 17
Generalisability	21	Discuss the generalisability (external validity) of the study results Provided in the Discussion	16, 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based This information is provided on page 3 after the Abstract	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cross-sectional study evaluating burden and depressive symptoms in family carers of persons with age-related macular degeneration in Australia

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3 **Cross-sectional study evaluating burden and depressive symptoms in**
4 **family carers of persons with age-related macular degeneration in**
5 **Australia**
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Abstract

Objectives: We aimed to analyse the degree of carer burden and depressive symptoms in family carers of persons with age-related macular degeneration (AMD) and explore the factors independently associated with carer burden and depressive symptoms.

Methods: Cross-sectional study using self- and interviewer-administered surveys, involving 96 family carer-care recipient pairs. Participants were identified from tertiary ophthalmology clinics in Sydney, Australia, as well as the Macular Disease Foundation of Australia database. Logistic regression, Pearson and Spearman correlation analyses were used to investigate associations of explanatory factors, (family caregiving experience, carer fatigue, carer quality of life and care recipient level of dependency) with study outcomes - carer burden and depressive symptoms.

Results: Over one in two family carers reported experiencing mild or moderate-severe burden. More than one in five and more than one in three family carers experienced depressive symptoms and substantial fatigue, respectively. High level of care recipient dependency was associated with greater odds of moderate-severe and mild carer burden, multivariable-adjusted OR 8.42 (95% CI 1.88-37.60) and OR 4.26 (95% CI 1.35-13.43) respectively. High levels of fatigue were associated with 3-fold greater odds of the carer experiencing depressive symptoms, multivariable-adjusted OR 3.47 (95% CI 1.00-12.05).

Conclusions: A substantial degree of morbidity is observed in family carers during the caregiving experience for patients with AMD. Level of dependency on the family carer and fatigue were independently associated with family carer burden and depressive symptoms.

Strengths and limitations of this study

- The study design and method of surveying allowed for the collection of rich and extensive data from patients with AMD and their family carers.
- Several validated scales for the assessment of both carer and patient variables were used, including those for burden, depression, fatigue and visual functioning.
- Study participants were recruited from only one state in Australia
- Due to the relatively small sample size, the study is likely to be underpowered for detecting modest associations

Patient consent

Obtained.

Ethics approval

Ethics approval was obtained from The University of Sydney Human Research Ethics Committee (ID# - 2016/793).

Acknowledgements

The authors thank all individuals for their time and participation in the study.

Introduction

Age-related macular degeneration (AMD) is a chronic and progressive disorder of the macula¹ and is the leading cause of blindness and low vision in Australia, directly affecting more than 1 million persons^{2,3}. The effects of vision impairment in AMD are not limited to declining visual function, with several studies showing that AMD affects multiple health domains and leads to significant emotional distress, poorer quality of life and reduced functional independence^{4,5}. For many patients, the ongoing nature of a chronic illness like AMD is such that it requires the provision of continuous physical and emotional care beyond the scope of what can be currently provided by hospitals or other institutions^{6,7}. Family carers of relatives with AMD are often expected to provide a high standard of care despite not receiving formal training and adequate support for this role^{8,9}. Surveys on the perceptions of family carers of relatives with AMD in their role as informal carers, demonstrate experiences of significant psychological distress, with the negative impacts of caring extending to increased financial stress, disruptions to lifestyle and retirement plans, and added strain on the relationship between carer and care recipient^{5,10}. Moreover, previous studies based in the UK have shown that caregivers of patients with AMD experience burden levels comparable to those caring for persons with rheumatoid arthritis and multiple sclerosis¹¹. Additionally, comorbidity has been shown to be associated with a higher degree of caregiver burden, as demonstrated in other caregiving settings such as for patients with dementia¹². Furthermore, a significant degree of psychological distress has been reported in caregivers of legally blind patients, with one such study reporting more than a third of caregivers experiencing depression¹³. Previous research conducted by our group on caregiving for AMD have demonstrated that the level of caregiver dependence and the presence of multiple chronic illnesses in the care-recipient were independent predictors of psychological distress¹⁴.

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Clearly, the impacts of AMD are far-reaching, with significant influence on family, friends and carers, as well as substantial cost to society^{3,15}. However, currently there exists little literature reporting on the level and factors of burden and depressive symptoms experienced by family carers of relatives with AMD. As such, the key aims of this cross-sectional study were to: 1) Analyse the degree of carer burden and depressive symptoms in family carers of persons with AMD; and 2) Explore the factors that were independently associated with carer burden and depressive symptoms.

Methods

Participants

Participants for this study were recruited as a part of a randomised controlled trial implementing a novel multi-component intervention targeting the drivers of stress and burden in family carers of patients with AMD. This study analysed a total of 96 patients with AMD and 96 of their family carers who were examined at baseline (pre-intervention). Recruitment of participants occurred between January 2017 to May 2020 across multiple ophthalmology practices in Sydney, Australia, as well as via the Macular Disease Foundation Australia (MDFA) database of members. The inclusion criteria for eligible family carers participating in this study were: adults aged more than 18 years old; family carer of a relative with AMD; willing to engage in a 10-week cognitive behavioural therapy intervention over a 3-month period; and sufficient English fluency to effectively engage in the intervention. All participants in this study gave written informed consent. Ethics approval was obtained from The University of Sydney Human Research Ethics Committee (ID# - 2016/793). Information on baseline study participant characteristics were obtained via surveys of family carers and their relatives with AMD, completed on-site during clinic visits or at home either independently or with help from the study coordinator e.g. due to limitations imposed by poor vision.

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Sociodemographic information and medical history

All participants (carers and care recipients with AMD) provided sociodemographic information including: age, sex, education level and marital status. They also self-reported any medical conditions such as: heart attacks; angina (without myocardial infarction); any other cardiac conditions; strokes or transient ischaemic attacks; high blood pressure; high cholesterol; diabetes or prediabetes; kidney disease; arthritis; hearing loss; and visual impairment. This information was used to assess the general health status (GHS) of each participant. Participants who reported 3 or more health conditions were considered as having substantial comorbidity and received a score of 1, whereas those with fewer than 3 health conditions received a score of 0.

Carer variables

Family carers were asked to provide details about the patient with AMD that they cared for such as whether they were the sole caregiver of the patient; the type of caregiving duties performed and the hours of care (per day) they provided to the care recipient with AMD. This comprised of 21 questions detailing caregiving duties as they applied to typical activities of daily living and instrumental activities of daily living for the patient with AMD, including exercise and/or sport, cooking and preparing food, cleaning, reading, personal grooming, using public transport, driving and more. Each question was scored reflecting the degree of help given for each activity (*0=no help or little help given, 1=moderate amount of help given,*

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3 2=*high amount of help given*, 3=*not applicable*). Additional information on family carers was
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5 determined by administering several validated instruments and scales as detailed below:
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10 (i) *Carer burden*. The Caregiver Burden Scale (CBS) is a 22-item questionnaire originally
11 developed for assessment of perceived family carer burden in caring for patients with
12 dementia^{16,17}. Each question was scored on a 5-point Likert-type scale (0=*never*, 1=*rarely*,
13 2=*sometimes*, 3=*quite frequently*, 4=*always*), reflecting the frequency of family carers'
14 feelings when taking care of their family member. The total burden score calculated for each
15 family carer was used to stratify levels of burden into 3 categories, with higher scores indicating
16 higher levels of burden (0-20=*no/little burden*, 21-40=*mild burden*, ≥ 41 =*moderate-severe*
17 *burden*).¹⁶ The CBS is a reliable measure with a Cronbach's alpha of 0.92¹⁸.
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31 (ii) *Depressive symptoms*. The short form of the Centre for Epidemiologic Studies Depression
32 (CESD-10) scale is a 10-item questionnaire and was used to screen for symptoms of
33 depression¹⁹. Each question gauges the frequency of a family carer experiencing certain
34 symptoms of depression per week and is scored on a 4-point Likert-type scale (0 = *rarely or*
35 *none of the time (<1 day)*, 1=*some or a little of the time (1-2 days)*, 2=*occasionally or a*
36 *moderate amount of the time (3-4 days)*, 3=*most or all of the time (5-7 days)*). A total CESD-
37 10 score of 10 or more indicates significant presence of depressive symptoms, as reported by
38 previous research evaluating the validity of the CESD-10 scale¹⁹. The CESD-10 is a validated
39 and reliable measure with a Cronbach's alpha of 0.80^{19,20}.
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53 (iii) *Fatigue*. The Fatigue Severity Scale (FSS) is a 9-item questionnaire used frequently to
54 assess the degree of impact that fatigue has on an individual's activities and physical
55 functioning²¹. Participants were asked to respond to statements about how much fatigue
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3 impacted their ability to function on a scale of 1 (*disagree*) to 7 (*agree*). Previous studies have
4 shown mean (SD) FSS scores for healthy individuals to be 2.3 (0.7)²¹. Mean FSS scores of 4
5 or more were categorised as having problematic fatigue. The FSS is a validated and reliable
6 measure with a Cronbach's alpha of 0.88²¹.
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15 *(iv) Self-efficacy.* The General self-efficacy (GSE) scale is a 10-item questionnaire shown to
16 be effective at measuring one's beliefs of overall ability to succeed in specific situations²². The
17 degree of how much a family carer agreed with each statement was measured using a 4-point
18 Likert-type scale (*0=not true, 1=hardly true, 2=moderately true, 3=exactly true*). Higher total
19 GSE scores indicate higher self-efficacy.
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28 *(v) Dependency.* Carers were asked to quantify the level of dependence their family member
29 with AMD had on them since their diagnosis using a 5-point Likert-type scale (*1=not at all*
30 *dependent, 2=somewhat dependent, 3=moderately dependent, 4 = very dependent, 5 =*
31 *extremely dependent*). Scores 3 or more were interpreted as an indication of high dependency
32 on the family carer (*1-2 = low dependency, 3-5 = high dependency*).
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42 *(vi) Quality of life.* Carer's rated their general quality of life (GQL) on a linear scale from 0
43 (*poor quality of life*) to 10 (*excellent quality of life*).
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51 *Care recipients with AMD*

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53 The National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) was completed
54 by care recipients, and is a reliable and validated tool used to measure status of vision-related
55 health impairment most relevant to patients with chronic eye conditions²³. Questions in the
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3 NEI VFQ-25 were used to determine the extent of how visual disability and symptoms
4 negatively impacts the patient's ability to function, well-being and efficacy in achieving vision-
5 related tasks. The NEI VFQ-25 is comprised of 12 subscales, assessing general vision, near
6 and distance vision, vision-related difficulty with activities, vision-related driving problems,
7 eye pain, colour vision, dependency, impact on social functioning, mental health and general
8 health²³. Scores recorded in the original response category for each question were recoded to a
9 scale between 0-100 in accordance with the NEI VFQ-25 scoring algorithm, with higher scores
10 indicating greater vision-related well-being.
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23 *Statistical analysis*

24 SAS statistical software (SAS Institute, NC, v9.4) was used for the statistical analysis,
25 including t-tests, chi-squared tests, F-test and logistical regression. We analysed caregiver
26 burden as a categorical variable based on the previous literature by Zarit et al.¹⁶ and the
27 generalised logits model was used for carer burden, given that it is a three-level categorical
28 variable²⁴. A binary logistic regression was used for the study outcome of depressive symptoms
29 as it is a two-level variable. For all models, a stepwise selection method was used.
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40 Predictor variables assessed for both these study outcomes were: carer age, carer sex,
41 carer general quality of life, carer general health status, fatigue severity, general self-efficacy,
42 level of dependency on the carer, patient age, patient sex, patient general health status and
43 patient NEI VFQ-25 scores. The CORR procedure was used to compute the Pearson
44 correlations and Spearman rank-order correlations between presence of depressive symptoms
45 (CESD-10 score) and the following variables: patient age and sex, and carer variables (age,
46 sex, general quality of life scores, fatigue severity scale scores, carer and patient general health
47 status, general self-efficacy, level of dependency on the carer and NEI VFQ-25 scores). The
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3 significance level was <0.05 . Checks for multicollinearity did not return any confirmation of
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5 multicollinearity occurring.
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10 11 **Results**

12 *AMD caregiving experience and health-related variables*

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15 The majority of family carers (91%) were aged 50 years and over, with family carers aged 65
16 years or older making up 54% of the sample. The proportion of females was 78% and 66%
17 among family carers and care recipients with AMD, respectively. Of the 96 family carers in
18 this study, 75% were the sole carer of the patients with AMD, with 43% reporting that the
19 family member they cared for was highly dependent on them. Family carers played a
20 considerable role in helping their relatives access medical care, with 91% accompanying their
21 relatives to their ophthalmology appointments where the majority of relatives with AMD (79%)
22 were receiving anti-VEGF injections. In terms of how often help was provided to relatives with
23 AMD, 61% of family carers reported providing help for 7 days a week on average, with 45%
24 reporting either spending >8 hours per day with them or living together with the care recipient.
25 The main caregiving duties where carers provided moderate to high amounts of help included
26 cooking (57%), cleaning (60%) and help with leaving the house (70%).
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43 Substantial amounts of fatigue were experienced by 36% of family carers as indicated by
44 scores of 4 or higher on the fatigue severity scale, and a considerable degree of general health
45 comorbidities was reported by 29% of family carers. The mean quality of life and general self-
46 efficacy scores among the family carers in this study were: 7.3 (SD 2.0) and 32.5 (SD 4.9),
47 respectively.
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54 55 56 57 *Burden analysis*

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3 More than half of family carers reported experiencing mild (35%) and moderate-severe (22%)
4 burden due to their caregiving experience (Table 1). Family carers of highly dependent
5 relatives with AMD were more likely to experience moderate-severe and mild burden after
6 multivariable adjustment: OR 8.42 (95% CI 1.88-37.60) and 4.26 (95% CI 1.35-13.43),
7 respectively (Table 2). Marginally significant associations were observed between the age and
8 visual functioning of the care recipient with AMD and the level of burden experienced by
9 family carers (Table 2). Younger carer age, older care recipient age, higher fatigue severity,
10 high level of dependency on the carer and lower NEI VFQ-25 scores were significantly
11 correlated with more carer burden (supplementary table 1). No statistically significant
12 correlations were observed between carer burden scores and carer sex, patient sex, carer
13 general quality of life scores (quality of life), carer and patient GHS scores (general health
14 status, and carer GSE scores (general self-efficacy) (data not shown).
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33 *Depressive symptoms*

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35 Over one in five family carers (24%) demonstrated a significant presence of depressive
36 symptoms as determined by the CESD-10 scale (i.e. total score 10 or more). Table 3 shows
37 that family carers with higher levels of fatigue were more likely to experience depressive
38 symptoms: OR 3.47 (95% CI 1.00-12.05). Conversely, each unit increase in family carer GQL
39 scores was associated with 40% reduced odds of experiencing depressive symptoms: OR 0.60
40 (95% CI 0.41-0.88). Statistically significant negative correlations between carer CESD-10
41 scores and carer GQL and GSE scores and care recipient NEI VFQ-25 scores were observed,
42 and a significant positive correlation was shown between CESD-10 and carer FSS
43 (supplementary table 2). No statistically significant correlations were observed between
44 CESD-10 and carer age and sex, patient age and sex, carer and patient GHS scores, and level
45 of dependency on the carer (data not shown).
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Discussion

This novel study shows that family carers experience substantial levels of burden, depressive symptoms and fatigue when caring for relatives with AMD. The findings from this study are consistent with other studies that demonstrated poorer well-being of family carers of relatives with AMD¹¹. Older carers of relatives with chronic disease are themselves biologically vulnerable to disease and are at substantial risk of developing health problems themselves, with studies showing family carers who experienced strain during their experience of providing care to be at greater risk of increased psychiatric morbidity^{25,26}. This is also reflected by the finding that nearly a third of family carers in this study were providing care for their relatives with AMD while experiencing significant medical morbidity themselves including, cardiovascular disease, cerebrovascular disease, kidney disease, arthritis and diabetes. The continuous nature and stresses of providing care, together with burdensome physical and emotional demands on a population already at risk of declining health outcomes is a significant area of concern, not only due to declining health associated with the strain of providing care, but also because any compromise of carer health may in effect lead to inadequate provision of optimal care to the relative with AMD^{11,27}.

More than half of family carers of relatives with AMD reported experiencing mild or moderate-severe burden. In comparison, a cross-sectional study on caregiver burden for blind persons in India demonstrated a greater proportion of caregivers scoring ≥ 41 on the CBS (91.8%), that is, demonstrating substantial amounts of moderate to severe burden²⁸. However, it is perhaps unsurprising that higher levels of burden were reported, given the more severe visual impairment of the population studied. Other areas of interest that should be considered for future research are differences in setting, availability of community support, socioeconomic status and cultural attitudes that may also influence perceived caregiver burden²⁸.

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3 When compared with burden experienced by caregivers of patients with idiopathic
4 Parkinson's disease, a greater proportion of family carers of patients with AMD experience
5 moderate-severe burden (22%) than carers supporting family with early (10%) and late (~12%)
6 stages of idiopathic Parkinson's disease²⁹. In contrast, studies on caregivers for patients with
7 stroke report higher levels of moderate-severe burden (~68%)³⁰. Interestingly, a recent study
8 on family and unpaid carers of older persons revealed that carers were at greater risk of
9 experiencing burden when caring for patients with dementia with or without substantial
10 disability, but not for those patients with substantial disability in the absence of dementia³¹.
11 While patient functional impairment has been shown to be associated with higher levels of
12 caregiver burden, this suggests that the additional challenges of caring for patients with
13 dementia may be an issue that is not as relevant for the provision of care to patients with AMD³².
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28 The level of dependency that patients with AMD had on their family carers was
29 independently associated with carer burden. This is in agreement with prior research by our
30 group showing that family carers of patients with AMD that had high levels of dependency on
31 them experience negative impacts such as high levels of emotional distress, as well as
32 disruptions to their lifestyle and retirement plans⁵. Moreover, a systematic review of depression
33 and burden among caregivers of patients with visual impairment found that greater hours of
34 supervision required and greater limitations in the patients' ability to carry out their activities
35 of daily living, to be among the factors commonly associated with caregiver burden³³, a finding
36 reflected in our study. It is likely that a high level of dependency on family carers may
37 negatively impact the relationship between the carer and care recipient. Higher levels of
38 dependency by the care recipient could be linked to loss of independence in the family carer
39 due to a lack of time for one's own needs and leisure activities and this in turn could lead to
40 feelings of burden¹⁰. Moreover, carers have previously reported feelings of guilt from inability
41 to provide the constant and necessary care, with some carers experiencing feelings of being
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3 manipulated by the care recipient^{5,10}. These feelings of burden due to the AMD caregiving
4 experience can have profound implications on family carer health and well-being. Previous
5 research conducted on the caregiving experience for elderly patients with chronic illnesses has
6 demonstrated negative impacts on the carer's physical and psychological well-being, such as
7 experiencing increased psychological distress, reduced engagement with preventative health
8 behaviours, and disruptions to employment and increased financial stress^{5, 10, 34}
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17 In contrast, around one in ten family carers of relatives with AMD in this study
18 experienced positive impacts of providing care, including feeling happier and more content
19 with their lives, as well as feeling more optimistic and determined. It is possible that these
20 differences of the caregiving experience among family carers may be related to pre-existing
21 strong familial ties and/or relationships, or otherwise relationships that have strengthened since
22 the need for family caregiving. Indeed, research into the role of partner relationship quality and
23 reciprocity (that is, a mutual sense of fair exchange) has demonstrated benefits on caregiver
24 wellbeing^{35,36}. Another study examining the role of reciprocity in providing care for persons
25 with dementia, chronic physical disability/illness, frailty from aging, and intellectual disability
26 showed an inverse relationship between reciprocity and self-esteem to caregiver burden³⁶.
27 These high-quality relationships may in fact provide the resources and means to alleviate the
28 stress and burden that would otherwise be present during the provision of care³⁶. As such,
29 understanding the factors that determine relationship strength and how they can be targeted
30 may be a potential area to address when aiming to improve equity in the family carer-care
31 recipient dynamic.
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51 Over one in five family carers of relatives with AMD demonstrated a significant presence
52 of depressive symptoms in our study, and this is substantially higher than the global prevalence
53 rates of ~6%³⁷. Higher rates of depressive symptoms (~35%) have also been demonstrated in
54 previous studies of family carers of patients with vision loss, along with significant associations
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3 between depressive symptoms and younger carer age and poorer patient visual acuity³⁸. High
4 rates (40%) of caregivers reporting depressive symptoms were found in a study on family
5 carers of patients with Alzheimer's disease³⁹. Higher levels of fatigue were shown to be
6 predictive of family carers experiencing depressive symptoms in our study. This is perhaps
7 unsurprising, given that fatigue and its symptoms are well-known symptoms/predictors of
8 major depressive disorder in the general population⁴⁰. Studies on the emotional well-being of
9 carers of patients with AMD have previously reported increased rates of emotional distress,
10 feelings of frustration, isolation and sadness^{5,13,34}.

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12 Furthermore, poorer family carer quality of life was significantly associated with
13 depressive symptoms. This association between quality of life and depressive symptoms is
14 consistent with other cross-sectional and longitudinal studies involving older adults⁴¹. Poor
15 quality of life limits one's ability to carry out their social and occupational activities^{42,43}.
16 Previous studies on caregiver quality of life have suggest that financial burden, lack of
17 family/social support, distress and unmet needs are among the factors purportedly increasing
18 the risk of depression and poor mental health outcomes⁴⁴⁻⁴⁶.

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20 Strengths of this study include the collection of rich and extensive outcome and covariate
21 data from patients with AMD and their family carers, as well as the use of several validated
22 scales for the assessment of carer and patient variables such as burden, depression, fatigue
23 and visual functioning. However, findings of this study should be interpreted with caution.
24 Due to the relatively small sample size, it is likely that the study was underpowered to detect
25 modest associations, as well as limiting the generalisability of the results. Similarly, in the
26 analyses small sample sizes accounted for large confidence intervals, providing less precise
27 estimates of effect. The use of other tools such as the Barthel index for the measurement of
28 care recipient dependency may have been potentially useful in providing a more accurate
29 quantification of dependency. However, while this is a reliable measure of dependency, it is
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3 time consuming, given that direct observation of the person performing specific tasks is
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5 required. Also, we cannot discount residual confounding from factors that were not measured
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7 in our study such as the quality/ strength of the carer-care recipient relationship and other
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9 psychosocial measures such as spirituality and carer resilience. Moreover, the cross-sectional
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11 study design implemented was useful for investigating the relationships between various
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13 factors and health outcomes. However, this design limits our ability to draw conclusions
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15 about causality. Longitudinal and experimental analyses would allow for a better
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17 understanding of causality and the temporal interactions and relationships between variables
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19 in this study. As such, future studies of these types utilising larger population sets would be
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21 useful to affirm the findings of this study.
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28 **Conclusion**

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30 A substantial proportion of family carers of relatives with AMD experience significant burden
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32 and depressive symptoms. Family carers played a considerable role in the care of relatives with
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34 AMD, including aiding with access to medical care and assistance with care-recipient's ADLs.
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36 Levels of dependency and fatigue, as well as lower quality of life were independently
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38 associated with higher levels of burden and/or greater odds of depressive symptoms in family
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40 carers. Further research is required to affirm these conclusions regarding these predictors of
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42 burden and depressive symptoms in family carers of relatives with AMD.
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49 **a. Contributors**

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51 All authors—IJ, DT, GB, JG, KNP, AC, GL, PM and BG—provided inputs in study design.
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53 IJ, DT, JG, GB, PM and BG were involved in data collection and data analysis. IJ, JG and
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55 BG were responsible for publication writing. All authors reviewed and approved the final
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57 version of this manuscript.
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b. Competing interests

None of the authors declared a conflict of interest.

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d. Data sharing statement

Data are available upon reasonable request.

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53 *Table 1. Study characteristics of family carers stratified by degree of burden experienced as measured by carer sex, age, general health status,*
 54 *FSS scores, CESD-10 scores, GSE scores, GQL scores, and care recipient sex, age, general health status and NEI VFQ-25 scores (n=96)*

Population characteristics	Degree of burden			P-value
	No/little burden (n=41)	Mild burden (n=33)	Moderate-severe burden (n=21)	
Carer variables				
Female sex, <i>n</i> (%)	28 (68.3)	28 (84.9)	18 (85.7)	0.15
Age, yrs, <i>mean</i> (<i>SD</i>)	66.5 (15.6)	63.1 (13.1)	59.1 (10.4)	0.14
General health status				
Substantial comorbidity, <i>n</i> (%)	15 (36.6)	11 (33.3)	2 (9.5)	0.07
Fatigue severity scale score				
Problematic fatigue (≥ 4), <i>n</i> (%)	11 (26.8)	11 (33.3)	5 (23.8)	0.06
CESD-10 score				
Presence of depressive symptoms (≥ 10), <i>n</i> (%)	6 (14.6)	7 (21.2)	10 (47.6)	0.01

Total general self-efficacy scores, <i>mean (SD)</i>	33.0 (5.4)	32.7 (4.1)	31.0 (4.5)	0.32
Total general quality of life scores, <i>mean (SD)</i>	7.6 (1.7)	7.5 (1.8)	7.6 (2.0)	0.09
Patient variables				
Female sex, <i>n</i> (%)	25 (61.0)	20 (60.6)	27 (81.0)	0.23
Age, yrs, <i>mean (SD)</i>	81.0 (10.1)	84.5 (7.2)	80.4 (11.1)	0.15
General health status				
Substantial comorbidity, <i>n</i> (%)	19 (46.3)	15 (45.5)	14 (66.7)	0.25
Total NEI VFQ-25 scores, <i>mean (SD)</i>	62.7 (21.0)	53.6 (53.6)	30.6 (20.9)	<0.0001

Unadjusted *P* values from test of heterogeneity across the three burden categories. FSS – Fatigue Severity Scale; CESD-10 – Centre for Epidemiologic Studies Depression-10; GSE – generalised self-efficacy; GQL – General Quality of Life; NEI VFQ-25 – National Eye Institute Visual Functioning Questionnaire-25

60 *Table 2. Association between selected family carer and care recipient with AMD variables with level of burden among family carers, presented*
 61 *as adjusted odds ratios (OR) and 95% confidence intervals (CI).*

Factors	Level of burden, OR (95% CI)*	
	Mild	Moderate-severe
Care recipient age (each 1-unit increase)	1.03 (0.97–1.09)	0.99 (0.92-1.07)
NEI VFQ-25 score (each 1-unit increase)	1.00 (0.98–1.02)	0.96 (0.93-0.99)
High level of dependency on carer	4.26 (1.35–13.43)	8.42 (1.88-37.60)

62 *Logistic regression model (Generalized Logit Model) used the burden group 0-20 (no/little burden) as the reference category.

68 *Table 3. Associations between selected variables and presence of depressive symptoms among family carers and care recipients with AMD,*
 69 *presented as adjusted odds ratios (OR) and 95% confidence intervals (CI).*

Factor	Presence of depressive symptoms, OR (95% CI)
Family Carer	
Age (each 1-unit increase)	0.98 (0.9—1.04)
Female sex	0.58 (0.1—2.60)
General quality of life (each 1-unit increase)	0.60 (0.4—0.88)
Fatigue severity scale score (each 1-unit increase)	3.47 (1.0—12.05)
General self-efficacy (each 1-unit increase)	0.97 (0.8—1.10)
Care recipients with AMD	
Age (each 1-unit increase)	0.98 (0.9—1.05)
Female sex	1.29 (0.2—6.25)
General health status (each 1-unit increase)	1.84 (0.5—6.40)
NEI VFQ-25 (each 1-unit increase)	0.98 (0.9—1.01)

Supplementary tables

Table 1. Spearman correlation coefficients between burden group and carer age, FSS scores, and dependency, and care recipient age and NEI VFQ-25 scores among family carers of relatives with AMD (n=95)

Variable		Carer age	Patient age	Fatigue severity scale	Dependency	NEI VFQ-25
Carer burden	<i>r</i>	- 0.26	- 0.22	0.22	0.07	- 0.45
scores	<i>p</i>	0.0115	0.0349	0.0082	<0.0001	<0.0001

FSS – Fatigue Severity Scale; NEI VFQ-25 – National Eye Institute Visual Functioning Questionnaire-25

Supplementary table 2

Table 2. Pearson correlation coefficients between presence of depressive symptoms and carer variables (GQL scores, FSS scores, GSE scores) and care recipient NEI VFQ-25 scores among family carers of relatives with AMD (n=96)

Variable	General quality of life	Fatigue severity scale	General self-efficacy	NEI VFQ-25	
	<i>r</i>	- 0.46	0.34	- 0.21	- 0.26
CESD-10	<i>p</i>	<0.0001	0.0008	0.0391	0.0121

CESD-10 – Centre for Epidemiologic Studies Depression-10; GQL – General Quality of Life; FSS – Fatigue Severity Scale; GSE – generalised self-efficacy; NEI VFQ-25 – National Eye Institute Visual Functioning

Questionnaire-25

STROBE Statement

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract We have indicated in the title and abstract that this is a cross-sectional study.	1, 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found This is done.	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported This is done.	5
Objectives	3	State specific objectives, including any prespecified hypotheses This is done.	6
Methods			
Study design	4	Present key elements of study design early in the paper This is done.	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This is done.	6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants This is shown in the 'Participants' section of manuscript.	6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable This information is provided in the Methods section.	7, 8, 9, 10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group This information is provided in the Methods section.	7, 8, 9, 10
Bias	9	Describe any efforts to address potential sources of bias N/A	
Study size	10	Explain how the study size was arrived at This is described in the Methods section	6
Quantitative	11	Explain how quantitative variables were handled in the analyses. If	7, 8, 9, 10

variables		applicable, describe which groupings were chosen and why This information is provided in the Methods section.	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding This information is provided in the Methods section.	10, 11
		(b) Describe any methods used to examine subgroups and interactions This information is provided in the Methods section.	10, 11
		(c) Explain how missing data were addressed N/A	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy N/A	
		(e) Describe any sensitivity analyses N/A	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed This is described in the Methods section	6
		(b) Give reasons for non-participation at each stage This is described in the Methods	6
		(c) Consider use of a flow diagram N/A	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders See Table 1	25
		(b) Indicate number of participants with missing data for each variable of interest N/A	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> This is reported in the Tables and Results section	11, 12, 13, 25, 26, 27, 28
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included See Tables 2-3 and Results section	11, 12, 13, 25, 26, 27, 28
		(b) Report category boundaries when continuous variables were categorized N/A	

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

N/A

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Included in Tables 2-3 and Supplementary files and Results section	11, 12, 13, 25, 26, 27, 28, Supplementary files 1-2
Discussion			
Key results	18	Summarise key results with reference to study objectives Paragraph 1, 2, 3 and 6 of the Discussion section	13, 14, 15, 16, 17, 18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Strengths and limitations are discussed in Discussion section – page 16 and 17	16, 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence This is provided in the Discussion	16, 17
Generalisability	21	Discuss the generalisability (external validity) of the study results Provided in the Discussion	16, 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based This information is provided on page 3 after the Abstract	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.