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

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# 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.

## **Ethics** approval

University of Sydney human research ethics committee.

#### Acknowledgements

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#### Introduction

Age-related macular degeneration (AMD) is a chronic and progressive disorder of the macula<sup>1</sup> and is the leading cause of blindness and low vision in Australia, directly affecting more than 1 million persons<sup>2,3</sup>. 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<sup>4,5</sup>. 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<sup>6,7</sup>. 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<sup>8,9</sup>. 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<sup>5,10</sup>.

Clearly, the impacts of AMD are far-reaching, with significant influence on family, friends and carers, as well as substantial cost to society<sup>3,11</sup>. 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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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 report 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. 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.

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#### 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;

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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 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, 2=high amount of help given, 3=not applicable). Additional information on family carers was determined by administering several validated instruments and scales as detailed below:

(*i*) Carer burden. The Caregiver Burden Scale (CBS) is a 22-item questionnaire originally developed for assessment of perceived family carer burden in caring for patients with dementia<sup>12,13</sup>. Each question was scored on a 5-point Likert-type scale (0=never, 1=rarely, 2=sometimes, 3=quite frequently, 4=always), reflecting the frequency of family carers' feelings when taking care of their family member. The total burden score calculated for each family carer was used to stratify levels of burden into 3 categories, with higher scores indicating

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higher levels of burden  $(0-20=no/little burden, 21-40=mild burden, \geq 41=moderate-severe burden).$ 

(*ii*) *Depressive symptoms*. The short form of the Centre for Epidemiologic Studies Depression (CESD-10) scale is a 10-item questionnaire and was used to screen for symptoms of depression<sup>14</sup>. Each question gauges the frequency of a family carer experiencing certain symptoms of depression per week and is scored on a 4-point Likert-type scale (0 = rarely or none of the time (<1 day), 1=some or a little of the time (1-2 days), 2=occasionally or a moderate amount of the time (3-4 days), 3=most or all of the time (5-7 days)). A total CESD-10 score of 10 or more indicates significant presence of depressive symptoms, as reported by previous research evaluating the validity of the CESD-10 scale<sup>14</sup>. The CESD-10 is a validated and reliable measure<sup>14</sup>.

*(iii) Fatigue.* The Fatigue Severity Scale (FSS) is a 9-item questionnaire used frequently to assess the degree of impact that fatigue has on an individual's activities and physical functioning<sup>15</sup>. Participants were asked to respond to statements about how much fatigue impacted their ability to function on a scale of 1 *(disagree)* to 7 *(agree)*. Previous studies have shown mean (SD) FSS scores for healthy individuals to be 2.3 (0.7) (ref. 15). Mean FSS scores of 4 or more were categorised as having problematic fatigue. The FSS is a validated and reliable measure<sup>15</sup>.

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*(iv) Self-efficacy.* The General self-efficacy (GSE) scale is a 10-item questionnaire shown to be effective at measuring one's beliefs of overall ability to succeed in specific situations<sup>16</sup>. The degree of how much a family carer agreed with each statement was measured using a 4-point

Likert-type scale (*0=not true, 1=hardly true, 2=moderately true, 3=exactly true*). Higher total GSE scores indicate higher self-efficacy.

(v) Dependency. Carers were asked to quantify the level of dependence their family member with AMD had on them since their diagnosis using a 4-point Likert-type scale (1=not at all dependent, 2=somewhat dependent, 3=moderately dependent, 4 = very dependent, 5 = extremely dependent). Scores 3 or more were interpreted as an indication of high dependency on the family carer (1-2 = low dependency, 3-5 = high dependency).

(vi) Quality of life. Carer's rated their general quality of life (GQL) on a linear scale from 0 (poor quality of life) to 10 (excellent quality of life).

#### 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 conditions<sup>17</sup>. 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 visionrelated 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 health<sup>17</sup>. 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 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 of dependency on the 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.

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#### 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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content in their lives (13%), feeling happier than ever before (13%), feeling more optimistic (8%) and feeling more determined (7%). Family carers played a considerable role in helping their relatives access medical care, with 91% accompanying their relatives to their ophthalmology appointments where the majority of relatives with AMD (79%) were receiving anti-VEGF injections. In terms of how often help was provided to relatives with AMD, 61% of family carers reported providing help for 7 days a week on average, with 45% reporting either spending >8 hours per day with them or living together with the care recipient. The main caregiving duties where carers provided moderate to high amounts of help included cooking (57%), cleaning (60%) and help with leaving the house (70%).

Substantial amounts of fatigue were experienced by 36% of family carers as indicated by scores of 4 or higher on the fatigue severity scale, and a considerable degree of general health comorbidities was reported by 29% of family carers. The mean quality of life and general selfefficacy scores among the family carers in this study were: 7.3 (SD 2.0) and 32.5 (SD 4.9), ier respectively.

#### Burden analysis

More than half of family carers reported experiencing mild (35%) and moderate-severe (22%) burden due to their caregiving experience (Table 1). Family carers of highly dependent relatives with AMD were more likely to experience moderate-severe and mild burden after multivariable adjustment: OR 8.42 (95% CI 1.88-37.60) and 4.26 (95% CI 1.35-13.43), respectively (Table 2). Marginally significant associations were observed between the age and visual functioning of the care recipient with AMD and the level of burden experienced by family carers (Table 2). Table 3 shows that younger carer age, older care recipient age, higher fatigue severity, high level of dependency on the carer and lower NEI VFQ-25 scores were significantly correlated with more carer burden. No statistically significant correlations were

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observed between carer burden scores and carer sex, patient sex, carer GQL scores, carer and patient GHS scores, and carer GSE scores (data not shown).

#### Depressive symptoms

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

#### 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 AMD<sup>18</sup>. 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<sup>19,20</sup>. 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

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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<sup>18,21</sup>.

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

The level of dependency of patients with AMD had on their family carers was independently associated with carer burden. This is in agreement with prior research by our group showing that family carers of patients with AMD that had high levels of dependency on them experience negative impacts such as high levels of emotional distress, as well as disruptions to their lifestyle and retirement plans<sup>5</sup>. Moreover, a systematic review of depression and burden among caregivers of patients with visual impairment found that greater hours of

Page 15 of 27

#### **BMJ** Open

supervision required and greater limitations in the patients' ability to carry out their activities of daily living, to be among the factors commonly associated with caregiver burden<sup>26</sup>, a finding reflected in our study. It is likely that a high level of dependency on family carers may negatively impact the relationship between the carer and care recipient. This could be reflected in the considerable proportion of family carers of relatives with AMD in this study that report feeling frustrated, down and sad during their caregiving experience. Higher levels of dependency by the care recipient could be linked to loss of independence in the family carer due to a lack of time for one's own needs and leisure activities and this in turn could lead to feelings of burden<sup>10</sup>. Moreover, carers have previously reported feelings of guilt from inability to provide the constant and necessary care, with some carers experiencing feelings of being manipulated by the care recipient<sup>5,10</sup>. These feelings of burden due to the AMD caregiving experience can have profound implications on family carer health and well-being.

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

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Over one in five family carers of relatives with AMD experienced elevated depressive symptoms in our study, and this is substantially higher that the global prevalence rates of ~6% (ref. 29). Higher rates of depressive symptoms (~35%) have also been demonstrated in previous studies of family carers of patients with vision loss, along with significant associations between depressive symptoms and younger carer age and poorer patient visual acuity<sup>30</sup>. High rates (40%) of caregivers reporting depressive symptoms were found in a study on family carers of patients with Alzheimer's disease<sup>31</sup>. Higher levels of fatigue were shown to be predictive of family carers experiencing depressive symptoms in our study. This is perhaps unsurprising, given that fatigue and its symptoms are well-known symptoms/predictors of major depressive disorder in the general population<sup>32</sup>. Studies on the emotional well-being of carers of patients with AMD have previously reported increased rates of emotional distress, feelings of frustration, isolation and sadness<sup>5,33,34</sup>.

Furthermore, poorer family carer quality of life was significantly associated with depressive symptoms. This association between quality of life and depressive symptoms is consistent with other cross-sectional and longitudinal studies involving older adults<sup>35</sup>. Poor quality of life limits one's ability to carry out their social and occupational activities<sup>36,37</sup>. Previous studies on caregiver quality of life have suggest that financial burden, lack of family/social support, distress and unmet needs are among the factors purportedly increasing the risk of depression and poor mental health outcomes<sup>38-40</sup>. In this way, demonstrable levels of distress and morbidity experienced by family carers of patients with AMD make them "hidden patients" at greater risk of poor health. As such, it is clear that there is a need for evidence-based interventions and education to help increase support for family carers of patients with AMD, thereby minimising their risk of poor health outcomes.

Strengths of this study include the collection of rich and extensive outcome and covariate data from patients with AMD and their family carers, as well as the use of several validated

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scales for the assessment of carer and patient variables such as burden, depression, fatigue and visual functioning. However, findings of this study should be interpreted with caution. Due to the relatively small sample size, it is likely that the study was underpowered to detect modest associations. Also, we cannot discount residual confounding from factors that were not measured in our study such as the quality/ strength of the carer-care recipient relationship and other psychosocial measures such as spirituality and carer resilience. Moreover, the cross-sectional study design implemented was useful for investigating the relationships between various factors and health outcomes. However, this design limits our ability to draw conclusions about causality. Future longitudinal studies utilising larger population sets would be useful to affirm the findings of this study.

#### Conclusion

A substantial proportion of family carers of relatives with AMD experience significant burden and depressive symptoms. Higher levels of dependency and fatigue, as well as lower quality of life were independently associated with higher levels of burden and/or greater odds of depressive symptoms in family carers. These findings underscore the urgent need for evidencebased interventions tailored to family carers of patients with AMD to alleviate their distress and burden, by targeting factors such as fatigue and quality of life, in a timely and effective manner. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

#### References

- Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. Lancet 2018;392(10153): 1147-1159.
- Wang JJ, Rochtchina E, Lee AJ, Chia EM, Smith W, Cumming RG, et al. Ten-year incidence and progression of age-related maculopathy: the blue Mountains Eye Study. Ophthalmology 2007;114(1): 92-98.
- 3. Deloitte Access Economics, Mitchell P. Eyes on the future: A clear outlook on Age-related Macular Degeneration. Macular Degeneration Foundation Australia, 2011. 144 p.
- Ranmuthugala G, Nepal B, Brown L, Percival R. Impact of home based long term care on informal carers. Aust Fam Physician 2009;38(8): 618-620.
- 5. Gopinath B, Liew G, Burlutsky G, Mitchell P. Age-related macular degeneration and 5-year incidence of impaired activities of daily living. Maturitas 2014;77(3): 263-266.
- Berman K, Brodaty H. Psychosocial effects of age-related macular degeneration. Int Psychogeriatr 2006;18(3): 415-428.
- Gehrs KM, Anderson DH, Johnson LV, Hageman GS. Age-related macular degeneration emerging pathogenetic and therapeutic concepts. Ann Med 2006;38(7): 450-471.
- 8. Goldberg A, Rickler KS. The role of family caregivers for people with chronic illness. Med Health R I 2011;94(2): 41-42.
- Bialon LN, Coke S. A study on caregiver burden: stressors, challenges, and possible solutions. Am J Hosp Palliat Care 2012;29(3): 210-218.

- Vukicevic M, Heraghty J, Cummins R, Gopinath B, Mitchell P. Caregiver perceptions about the impact of caring for patients with wet age-related macular degeneration. Eye (Lond) 2016;30(3): 413-421.
  - 11. Wong WL, Su X, Li X, Cheung CMG, Klein R, Cheng C-Y, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health 2014;2(2): 106-116.
  - Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist 1980;20(6): 649-655.
  - 13. Bedard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The Zarit Burden Interview: a new short version and screening version. Gerontologist 2001;41(5): 652-657.
  - 14. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). Am J Prev Med 1994;10(2): 77-84.

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- 15. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46(10): 1121-1123.
- 16. Schwarzer R, Jerusalem M. Generalized Self-Efficacy scale. In Weinman J, Wright S, Johnston M. Measures in health psychology: A user's portfolio. Causal and control beliefs. NFER-Nelson: Windsor, England, 1995, pp 35-37.
- Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol 2001;119(7): 1050-1058.

- 18. Gohil R, Crosby-Nwaobi R, Forbes A, Burton B, Hykin P, Sivaprasad S. Caregiver Burden in Patients Receiving Ranibizumab Therapy for Neovascular Age Related Macular Degeneration. PLoS One 2015;10(6): e0129361.
- 19. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. JAMA 1999;282(23): 2215-2219.
- 20. Vitaliano PP, Schulz R, Kiecolt-Glaser J, Grant I. Research on physiological and physical concomitants of caregiving: where do we go from here? Ann Behav Med 1997;19(2): 117-123.
- 21. Cain CJ, Wicks MN. Caregiver attributes as correlates of burden in family caregivers coping with chronic obstructive pulmonary disease. J Fam Nurs 2000;6(1): 46–68.
- 22. Genc F, Yuksel B, Tokuc FEU. Caregiver Burden and Quality of Life in Early and Late Stages of Idiopathic Parkinson's Disease. Psychiatry Investig 2019;16(4): 285-291.
- 23. Hu P, Yang Q, Kong L, Hu L, Zeng L. Relationship between the anxiety/depression and care burden of the major caregiver of stroke patients. Medicine (Baltimore) 2018;97(40): e12638.
- 24. Riffin C, Van Ness PH, Wolff JL, Fried T. Multifactorial Examination of Caregiver Burden in a National Sample of Family and Unpaid Caregivers. J Am Geriatr Soc 2019;67(2): 277-283.
- 25. Liu S, Li C, Shi Z, Wang X, Zhou Y, Liu S, et al. Caregiver burden and prevalence of depression, anxiety and sleep disturbances in Alzheimer's disease caregivers in China. J Clin Nurs 2017;26(9-10): 1291-1300.
- 26. Kuriakose RK, Khan Z, Almeida DRP, Braich PS. Depression and burden among the caregivers of visually impaired patients: a systematic review. Int Ophthalmol 2017;37(3): 767-777.

#### **BMJ** Open

- 27. Quinn C, Clare L, Woods B. The impact of the quality of relationship on the experiences and wellbeing of caregivers of people with dementia: a systematic review. Aging Ment Health 2009;13(2): 143-154.
  - 28. Tough H, Brinkhof MW, Siegrist J, Fekete C. Subjective Caregiver Burden and Caregiver Satisfaction: The Role of Partner Relationship Quality and Reciprocity. Arch Phys Med Rehabil 2017;98(10): 2042-2051.
  - 29. Malhi GS, Mann JJ. Depression. Lancet. 2018;392(10161): 2299-2312.
  - 30. Bambara JK, Owsley C, Wadley V, Martin R, Porter C, Dreer LE. Family caregiver social problem-solving abilities and adjustment to caring for a relative with vision loss. Invest Ophthalmol Vis Sci 2009;50(4): 1585-1592.
  - 31. Mausbach BT, Chattillion EA, Roepke SK, Patterson TL, Grant I. A comparison of psychosocial outcomes in elderly Alzheimer caregivers and noncaregivers. Am J Geriatr Psychiatry 2013;21(1): 5-13.
  - 32. Corfield EC, Martin NG, Nyholt DR. Co-occurrence and symptomatology of fatigue and depression. Compr Psychiatry 2016;71: 1-10.
  - 33. Pinquart M, Sorensen S. Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. Psychol Aging 2003;18(2): 250-267.
  - 34. Braich PS, Lal V, Hollands S, Almeida DR. Burden and depression in the caregivers of blind patients in India. Ophthalmology 2012;119(2): 221-226.
  - 35. Sivertsen H, Bjorklof GH, Engedal K, Selbaek G, Helvik AS. Depression and Quality of Life in Older Persons: A Review. Dement Geriatr Cogn Disord 2015;40(5-6): 311-339.
  - 36. Shumye, S., Belayneh, Z. & Mengistu, N. Health related quality of life and its correlates among people with depression attending outpatient department in Ethiopia: a cross sectional study. Health Qual Life Outcomes 2019;17(169): 1-9.

- 37. Evans S, Banerjee S, Leese M, Huxley P. The impact of mental illness on quality of life: a comparison of severe mental illness, common mental disorder and healthy population samples. Qual Life Res 2007;16(1): 17-29.
- 38. Song JI, Shin DW, Choi JY, Kang J, Baik YJ, Mo H, Park MH, Choi SE, Kwak JH, Kim EJ. Quality of life and mental health in family caregivers of patients with terminal cancer. Support Care Cancer. 2011;19(10): 1519-26.
- 39. Butow PN, Price MA, Bell ML, Webb PM, deFazio A; Australian Ovarian Cancer Study Group; Australian Ovarian Cancer Study Quality Of Life Study Investigators, Friedlander M. Caring for women with ovarian cancer in the last year of life: a longitudinal study of caregiver quality of life, distress and unmet needs. Gynecol Oncol 2014;132(3): 690-697.
- 40. Price MA, Butow PN, Costa DS, King MT, Aldridge LJ, Fardell JE, DeFazio A, Webb PM; Australian Ovarian Cancer Study Group; Australian Ovarian Cancer Study Group Quality of Life Study Investigators. Prevalence and predictors of anxiety and depression in women with invasive ovarian cancer and their caregivers. Med J Aust 2010;193(S5): S52-S57.

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Table 1. Study characteristics of	f family carers stratified by degree of	burden experienced as me	asured by Ecarer sex, age, gen	eral health st
FSS scores, CESD-10 score	s, GSE scores, GQL scores, and care	recipient sex, age, general	health stortus and NEI VFQ	25 scores (n=
		Degree of	burden es eigen	
	No/little burden	Mild burden	Mode and severe burder	1
Population characteristics	(n=41)	(n=33)	to text and the second	<i>P</i> -valu
Carer variables	( Do		nd dat	
Female sex, $n$ (%)	28 (68.3)	28 (84.9)		0.15
Age, yrs, mean (SD)	66.5 (15.6)	63.1 (13.1)	ية. 25 1 (10.4)	0.14
General health status			mjoper I trainin	
Substantial comorbidi	ty, <i>n</i> (%) 15 (36.6)	11 (33.3)	g, and (9.5)	0.07
Fatigue severity scale sc	ore		om/ or simila	
Problematic fatigue (≥	24), <i>n</i> (%) 11 (26.8)	11 (33.3)	rec <u>5</u> (57.1)	0.06
CESD-10 score			nologi	
Presence of depressive	2		)25 at /	
symptoms (≥10), <i>n</i> (%	6 (14.6) b)	7 (21.2)	20 (47.6)	0.01
			ibliograp	
		22	hique	

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Total general self-efficacy scores,	33.0 (5.4)	32.7 (4.1)	t. 04 04 04 05 05 0 0 0 (4.5)	0.32
mean (SD)			Septern En for use	
Total general quality of life scores, mean (SD)	7.6 (1.7)	7.5 (1.8)	s seignem related 021	0.09
Patient variables			. Downlo ent Supe to text <i>a</i>	
Female sex, <i>n</i> (%)	25 (61.0)	20 (60.6)	nd dat (81.0)	0.23
Age, yrs, mean (SD)	81.0 (10.1)	84.5 (7.2)	a Arran MBR 4 (11.1) ni s	0.15
General health status			ttp://bi ) . ng, Al	
Substantial comorbidity, n (%)	19 (46.3)	15 (45.5)	trainin <b>6</b> 4 (66.7)	0.25
Total NEI VFQ-25 scores, mean	62 7 (21 0)	53 6 (53 6)	$\frac{1}{9}$ and $\frac{1}{9}$ 6 (20.9)	<0 0001
(SD)	02.7 (21.0)		similar t	
SS – Fatigue Severity Scale; CESD-10 – Centre for Epidemiologic	Studies Depression-10; GSE – gener	alised self-efficacy; GQL – General Qualit	y of Life NE VFQ-25 – National Ey	e Institute Visual Functioning
Questionnaire-25			3, 2025 logies.	
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Page 25 of	27		BMJ Open	ıjopen-202 1 by copyr
1 2 3 4 5 6 7	3	Table 2. Association between selected family c as adjusted odds ratios (OR) and 95% confider	carer and care recipient with AMD variables nce intervals (CI).	ight, inclusion among family carers, presented with level of adding for a Sept
8 9			Level of burden	, OR (95% CISEs be
10 11 12		Factors	Moderate-severe	and the memory of the memory o
13 14 15 16 17		Care recipient age (each 1-unit increase)	0.99 (0.92-1.07)	Superieur (A. 1097–1.09) st and data
18 19 20 21		NEI VFQ-25 score (each 1-unit increase)	0.96 (0.93-0.99)	mining, 200 (0.98–1.02)
22 23 24 25 26 27		High level of dependency on carer	8.42 (1.88-37.60)	and simi
28 29 20	)	*Logistic regression model used the burden gro	oup 0-20 (no/little burden) as the reference ca	ategory
31 32 <sup>11</sup>	1			13, 202
33 34 12 35	2			s. 5 at Ag
36 13 37 38 39 40	3			jence Bibliograp
41 42 43 44 45 46		For peer	24 <sup>-</sup> review only - http://bmjopen.bmj.com/site/about/g	guidelines.xhtml <b>e</b>

# BMJ Open Table 3. Spearman correlation coefficients between burden group and carer age, FSS scores, and dependence of the state of the score of the vn 8 Septemilier ding for usestie Differ *VFQ-25 scores among family carers of relatives with AMD (n=95)* Variable Carer age Patient age Fatigue severity scale NEI VFQ-25 related to r 2024) Down Igner Superier Igner Superier Iated to text and Carer burden - 0.22 0.22 - 0.26 - 0.45 r 0.0115 0.0349 0.0082 < 0.0001 scores p .suonnaire-25 led from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de .ur (ABES) . data mining, Al training, and similar technologies. FSS - Fatigue Severity Scale; NEI VFQ-25 - National Eye Institute Visual Functioning Questionnaire-25 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Page 27	of 27
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ge 27 of 27	BMJ Op	en by copyri.
17	Table 4. Associations between selected family carer and care recipient with	th AMD variables and presence of depressive symptoms among fami
18	carers, presented as adjusted odds ratios (OR) and 95% confidence intervo	uls (CI).
	Factor	Presence of depressive semptoms, OR (95% CI)
	Family Carer	ated to
	Age (each 1-unit increase)	0.98 (0.99) 0.98 (0.99) 0.98 (0.99)
	Female sex	전 등 : 월 0.58 융위퇴원—2.60)
	General quality of life (each 1-unit increase)	
	Fatigue severity scale score (each 1-unit increase)	ق ق 3.47 (≱.00 12.05)
	General self-efficacy (each 1-unit increase)	0.97 (0.97 (0.97))
	Care recipients with AMD	bmj.cc
	Age (each 1-unit increase)	0.98 a).99-1.05)
	Female sex	1.29 8.25-6.25)
	General health status (each 1-unit increase)	1.84 gg. 5 gg-6.40)
	NEI VFQ-25 (each 1-unit increase)	0.98 (0.9 <b>5</b> –1.01)
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20 21	Table 5. Pearson and care recipient	correl t NEI \	ation coefficients between pro VFQ-25 scores among family	esence of depressive symptoms carers of relatives with AMD (	s and carer variables $G_{n=96}^{-048650}$ for	ores, FSS scores, GSE scores)
	Variable		General quality of life	Fatigue severity scale	General self-effector	NEI VFQ-25
		r	- 0.46	0.34	- 0.21 dement	- 0.26
	CESD-10	р	<0.0001	0.0008	0.0391 text and text	0.0121
22	CESD-10 – Centre for Epi	demiolog	c Studies Depression-10; GQL – General Q	uality of Life; FSS – Fatigue Severity Scale;	GSE – generalised self-efficace	5 – National Eye Institute Visual Functioning
23	Questionnaire-25				n http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliograph ES) . nining, Al training, and similar technologies.	
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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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# Cross-sectional study evaluating burden and depressive symptoms in family carers of persons with age-related macular degeneration in 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.

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### 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 macula<sup>1</sup> and is the leading cause of blindness and low vision in Australia, directly affecting more than 1 million persons<sup>2,3</sup>. 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<sup>4,5</sup>. 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<sup>6,7</sup>. 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<sup>8,9</sup>. 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<sup>5,10</sup>. 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 sclerosis<sup>11</sup>. 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 dementia<sup>12</sup>. 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 depression<sup>13</sup>. 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 distress<sup>14</sup>.

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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<sup>3,15</sup>. 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.

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# 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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2=high amount of help given, 3=not applicable). Furthermore, carers were surveyed to provide details about the impact of providing care to a family member with AMD, including: the impact of carer on the carer's state of mind; ability to manage their own existing health conditions; and impact and change on work, volunteer and recreational activities. Additional information on family carers was determined by administering several validated instruments and scales as detailed below:

(*i*) Carer burden. The Caregiver Burden Scale (CBS) is a 22-item questionnaire originally developed for assessment of perceived family carer burden in caring for patients with dementia<sup>16,17</sup>. Each question was scored on a 5-point Likert-type scale (0=never, 1=rarely, 2=sometimes, 3=quite frequently, 4=always), reflecting the frequency of family carers' feelings when taking care of their family member. The total burden score calculated for each family carer was used to stratify levels of burden into 3 categories, with higher scores indicating higher levels of burden (0-20=no/little burden, 21-40=mild burden,  $\geq$ 41=moderate-severe burden). The CBS is a reliable measure with a Cronbach's alpha of  $0.92^{18}$ .

(*ii*) *Depressive symptoms*. The short form of the Centre for Epidemiologic Studies Depression (CESD-10) scale is a 10-item questionnaire and was used to screen for symptoms of depression<sup>19</sup>. Each question gauges the frequency of a family carer experiencing certain symptoms of depression per week and is scored on a 4-point Likert-type scale (0 = rarely or none of the time (<1 day), 1=some or a little of the time (1-2 days), 2=occasionally or a moderate amount of the time (3-4 days), 3=most or all of the time (5-7 days)). A total CESD-10 score of 10 or more indicates significant presence of depressive symptoms, as reported by previous research evaluating the validity of the CESD-10 scale<sup>19</sup>. The CESD-10 is a validated and reliable measure with a Cronbach's alpha of  $0.80^{19,20}$ .

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*(iii) Fatigue*. The Fatigue Severity Scale (FSS) is a 9-item questionnaire used frequently to assess the degree of impact that fatigue has on an individual's activities and physical functioning<sup>21</sup>. Participants were asked to respond to statements about how much fatigue impacted their ability to function on a scale of 1 *(disagree)* to 7 *(agree)*. Previous studies have shown mean (SD) FSS scores for healthy individuals to be 2.3  $(0.7)^{21}$ . Mean FSS scores of 4 or more were categorised as having problematic fatigue. The FSS is a validated and reliable measure with a Cronbach's alpha of  $0.88^{21}$ .

(*iv*) Self-efficacy. The General self-efficacy (GSE) scale is a 10-item questionnaire shown to be effective at measuring one's beliefs of overall ability to succeed in specific situations<sup>22</sup>. The degree of how much a family carer agreed with each statement was measured using a 4-point Likert-type scale (0=not true, 1=hardly true, 2=moderately true, 3=exactly true). Higher total GSE scores indicate higher self-efficacy.

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(v) Dependency. Carers were asked to quantify the level of dependence their family member with AMD had on them since their diagnosis using a 4-point Likert-type scale (1=not at all dependent, 2=somewhat dependent, 3=moderately dependent, 4 = very dependent, 5 = extremely dependent). Scores 3 or more were interpreted as an indication of high dependency on the family carer (1-2 = low dependency, 3-5 = high dependency).

(vi) Quality of life. Carer's rated their general quality of life (GQL) on a linear scale from 0 (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 conditions<sup>23</sup>. 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 visionrelated 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 health<sup>23</sup>. 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 variable<sup>24</sup>. 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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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. Checks for multicollinearity did not return any confirmation of multicollinearity occurring.

# 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 content in their lives (13%), feeling happier than ever before (13%), feeling more optimistic (8%) and feeling more determined (7%). Family carers played a considerable role in helping their relatives access medical care, with 91% accompanying their relatives to their ophthalmology appointments where the majority of relatives with AMD (79%) were receiving anti-VEGF injections. In terms of how often help was provided to relatives with AMD, 61% of family carers reported providing help for 7 days a week on average, with 45% reporting either spending >8 hours per day with them or living together with the care recipient. The main caregiving duties where carers provided moderate to high amounts of help included cooking (57%), cleaning (60%) and help with leaving the house (70%).

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Substantial amounts of fatigue were experienced by 36% of family carers as indicated by scores of 4 or higher on the fatigue severity scale, and a considerable degree of general health comorbidities was reported by 29% of family carers. The mean quality of life and general self-efficacy scores among the family carers in this study were: 7.3 (SD 2.0) and 32.5 (SD 4.9), respectively.

# Burden analysis

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

# Depressive symptoms

Over one in five family carers (24%) demonstrated a significant presence of depressive symptoms as determined by the CESD-10 scale. Table 3 shows that family carers with higher levels of fatigue were more likely to experience depressive symptoms: OR 3.47 (95% CI 1.00-12.05). Conversely, each unit increase in family carer GQL scores was associated with 40%

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reduced odds of experiencing depressive symptoms: OR 0.60 (95% CI 0.41-0.88). Statistically significant negative correlations between carer CESD-10 scores and carer GQL and GSE scores and care recipient NEI VFQ-25 scores were observed, and a significant positive correlation was shown between CESD-10 and carer FSS (supplementary table 2). No statistically significant correlations were observed between CESD-10 and carer age and sex, patient age and sex, carer and patient GHS scores, and level of dependency on the carer (data not shown).

# 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 AMD<sup>11</sup>. 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<sup>25,26</sup>. 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<sup>11,27</sup>.

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> 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  $\geq$ 41 on the CBS (91.8%), that is, demonstrating substantial amounts of moderate to severe burden<sup>28</sup>. 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 burden<sup>28</sup>.

> When compared with burden experienced by caregivers of patients with idiopathic Parkinson's disease, a greater proportion of family carers of patients with AMD experience moderate-severe burden (22%) than carers supporting family with early (10%) and late (~12%) stages of idiopathic Parkinson's disease<sup>29</sup>. In contrast, studies on caregivers for patients with stroke report higher levels of moderate-severe burden (~68%)<sup>30</sup>. Interestingly, a recent study on family and unpaid carers of older persons revealed that carers were at greater risk of experiencing burden when caring for patients with dementia with or without substantial disability, but not for those patients with substantial disability in the absence of dementia<sup>31</sup>. While patient functional impairment has been shown to be associated with higher levels of caregiver burden, this suggests that the additional challenges of caring for patients with AMD<sup>32</sup>.

The level of dependency that patients with AMD had on their family carers was independently associated with carer burden. This is in agreement with prior research by our group showing that family carers of patients with AMD that had high levels of dependency on them experience negative impacts such as high levels of emotional distress, as well as disruptions to their lifestyle and retirement plans<sup>5</sup>. Moreover, a systematic review of depression and burden among caregivers of patients with visual impairment found that greater hours of

Page 15 of 32

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supervision required and greater limitations in the patients' ability to carry out their activities of daily living, to be among the factors commonly associated with caregiver burden<sup>33</sup>, a finding reflected in our study. It is likely that a high level of dependency on family carers may negatively impact the relationship between the carer and care recipient. This could be reflected in the considerable proportion of family carers of relatives with AMD in this study that report feeling frustrated, down and sad during their caregiving experience. Higher levels of dependency by the care recipient could be linked to loss of independence in the family carer due to a lack of time for one's own needs and leisure activities and this in turn could lead to feelings of burden<sup>10</sup>. Moreover, carers have previously reported feelings of guilt from inability to provide the constant and necessary care, with some carers experiencing feelings of being manipulated by the care recipient<sup>5,10</sup>. These feelings of burden due to the AMD caregiving experience can have profound implications on family carer health and well-being. Previous research conducted on the caregiving experience for elderly patients with chronic illnesses has demonstrated negative impacts on the carer's physical and psychological well-being, such as experiencing increased psychological distress, reduced engagement with preventative health behaviours, and disruptions to employment and increased financial stress<sup>5, 10, 34</sup>

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In contrast, around one in ten family carers of relatives with AMD in this study experienced positive impacts of providing care, including feeling happier and more content with their lives, as well as feeling more optimistic and determined. It is possible that these differences of the caregiving experience among family carers may be related to pre-existing strong familial ties and/or relationships, or otherwise relationships that have strengthened since the need for family caregiving. Indeed, research into the role of partner relationship quality and reciprocity (that is, a mutual sense of fair exchange) has demonstrated benefits on caregiver wellbeing<sup>35,36</sup>. Another study examining the role of reciprocity in providing care for persons with dementia, chronic physical disability/illness, frailty from aging, and intellectual disability

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showed an inverse relationship between reciprocity and self-esteem to caregiver burden<sup>36</sup>. These high-quality relationships may in fact provide the resources and means to alleviate the stress and burden that would otherwise be present during the provision of care<sup>36</sup>. As such, understanding the factors that determine relationship strength and how they can be targeted may be a potential area to address when aiming to improve equity in the family carer-care recipient dynamic.

Over one in five family carers of relatives with AMD demonstrated a significant presence of depressive symptoms in our study, and this is substantially higher that the global prevalence rates of ~6%<sup>37</sup>. Higher rates of depressive symptoms (~35%) have also been demonstrated in previous studies of family carers of patients with vision loss, along with significant associations between depressive symptoms and younger carer age and poorer patient visual acuity<sup>38</sup>. High rates (40%) of caregivers reporting depressive symptoms were found in a study on family carers of patients with Alzheimer's disease<sup>39</sup>. Higher levels of fatigue were shown to be predictive of family carers experiencing depressive symptoms in our study. This is perhaps unsurprising, given that fatigue and its symptoms are well-known symptoms/predictors of major depressive disorder in the general population<sup>40</sup>. Studies on the emotional well-being of carers of patients with AMD have previously reported increased rates of emotional distress, feelings of frustration, isolation and sadness<sup>5,13,34</sup>.

Furthermore, poorer family carer quality of life was significantly associated with depressive symptoms. This association between quality of life and depressive symptoms is consistent with other cross-sectional and longitudinal studies involving older adults<sup>41</sup>. Poor quality of life limits one's ability to carry out their social and occupational activities<sup>42,43</sup>. Previous studies on caregiver quality of life have suggest that financial burden, lack of family/social support, distress and unmet needs are among the factors purportedly increasing the risk of depression and poor mental health outcomes<sup>44-46</sup>.

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

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# Conclusion

A substantial proportion of family carers of relatives with AMD experience significant burden and depressive symptoms. Family carers played a considerable role in the care of relatives with AMD, including aiding with access to medical care and assistance with care-recipient's ADLs.

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Many carers self-reported experiencing feeling frustrated, depressive and sad. Levels of dependency and fatigue, as well as lower quality of life were independently associated with higher levels of burden and/or greater odds of depressive symptoms in family carers. Further research is required to affirm these conclusions regarding these predictors of burden and depressive symptoms in family carers of relatives with AMD.

# a. 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.

# **b.** Competing interests

None of the authors declared a conflict of interest.

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Australia.

# d. Data sharing statement

Data are available upon reasonable request.

# References

- 1. Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. Lancet 2018;392(10153): 1147-1159.
- Wang JJ, Rochtchina E, Lee AJ, Chia EM, Smith W, Cumming RG, et al. Ten-year incidence and progression of age-related maculopathy: the blue Mountains Eye Study. Ophthalmology 2007;114(1): 92-98.
- 3. Deloitte Access Economics, Mitchell P. Eyes on the future: A clear outlook on Age-related Macular Degeneration. Macular Degeneration Foundation Australia, 2011. 144 p.
- Ranmuthugala G, Nepal B, Brown L, Percival R. Impact of home based long term care on informal carers. Aust Fam Physician 2009;38(8): 618-620.
- 5. Gopinath B, Liew G, Burlutsky G, Mitchell P. Age-related macular degeneration and 5-year incidence of impaired activities of daily living. Maturitas 2014;77(3): 263-266.
- Berman K, Brodaty H. Psychosocial effects of age-related macular degeneration. Int Psychogeriatr 2006;18(3): 415-428.
- Gehrs KM, Anderson DH, Johnson LV, Hageman GS. Age-related macular degeneration emerging pathogenetic and therapeutic concepts. Ann Med 2006;38(7): 450-471.
- 8. Goldberg A, Rickler KS. The role of family caregivers for people with chronic illness. Med Health R I 2011;94(2): 41-42.
- Bialon LN, Coke S. A study on caregiver burden: stressors, challenges, and possible solutions. Am J Hosp Palliat Care 2012;29(3): 210-218.
- Vukicevic M, Heraghty J, Cummins R, Gopinath B, Mitchell P. Caregiver perceptions about the impact of caring for patients with wet age-related macular degeneration. Eye (Lond) 2016;30(3): 413-421.

- 11. Gohil R, Crosby-Nwaobi R, Forbes A, Burton B, Hykin P, Sivaprasad S. Caregiver Burden in Patients Receiving Ranibizumab Therapy for Neovascular Age Related Macular Degeneration. PLoS One 2015;10(6): e0129361.
- 12. Lindt, N., van Berkel, J. and Mulder, B.C. 2020. Determinants of overburdening among informal carers: a systematic review. BMC Geriatr 20(1) 304.
- Braich PS, Lal V, Hollands S, Almeida DR. Burden and depression in the caregivers of blind patients in India. Ophthalmology 2012;119(2): 221-226.
- 14. Gopinath, B., Kifley, A., Cummins, R. et al. 2015. Predictors of psychological distress in caregivers of older persons with wet age-related macular degeneration. Aging Ment Health 19(3) 239-246.
- 15. Wong WL, Su X, Li X, Cheung CMG, Klein R, Cheng C-Y, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health 2014;2(2): 106-116.
- Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist 1980;20(6): 649-655.
- 17. Bedard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The Zarit Burden Interview: a new short version and screening version. Gerontologist 2001;41(5): 652-657.
- 18. Hébert, R., Bravo, G. and Préville, M. 2010. Reliability, Validity and Reference Values of the Zarit Burden Interview for Assessing Informal Caregivers of Community-Dwelling Older Persons with Dementia. Canadian Journal on Aging / La Revue canadienne du vieillissement 19(4) 494-507.
- 19. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). Am J Prev Med 1994;10(2): 77-84.

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- 20. Irwin, M., Artin, K.H. and Oxman, M.N. 1999. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). Arch Intern Med 159(15) 1701-1704.
- 21. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46(10): 1121-1123.
- 22. Schwarzer R, Jerusalem M. Generalized Self-Efficacy scale. In Weinman J, Wright S, Johnston M. Measures in health psychology: A user's portfolio. Causal and control beliefs. NFER-Nelson: Windsor, England, 1995, pp 35-37.
- 23. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol 2001;119(7): 1050-1058.
- 24. Elkin, E. Beyong Binary Outcomes: Proc Logistic to Model Ordinal and Nominal Dependent Variables. ICON Late Phase & Outcomes Research; San Francisco, CA, USA 2012.

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- 25. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. JAMA 1999;282(23): 2215-2219.
- 26. Vitaliano PP, Schulz R, Kiecolt-Glaser J, Grant I. Research on physiological and physical concomitants of caregiving: where do we go from here? Ann Behav Med 1997;19(2): 117-123.
- 27. Cain CJ, Wicks MN. Caregiver attributes as correlates of burden in family caregivers coping with chronic obstructive pulmonary disease. J Fam Nurs 2000;6(1): 46–68.
- 28. Khare, S., Rohatgi, J., Bhatia, M.S. et al. 2016. Burden and depression in primary caregivers of persons with visual impairment. Indian J Ophthalmol 64(8) 572-577.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

# **BMJ** Open

1	29. Genc F, Yuksel B, Tokuc FEU. Caregiver Burden and Quality of Life in Early and Late
2	Stages of Idiopathic Parkinson's Disease. Psychiatry Investig 2019;16(4): 285-291.
3	30. Hu P, Yang Q, Kong L, Hu L, Zeng L. Relationship between the anxiety/depression and
4	care burden of the major caregiver of stroke patients. Medicine (Baltimore)
5	2018;97(40): e12638.
6	31. Riffin C, Van Ness PH, Wolff JL, Fried T. Multifactorial Examination of Caregiver Burden
7	in a National Sample of Family and Unpaid Caregivers. J Am Geriatr Soc 2019;67(2):
8	277-283.
9	32. Liu S, Li C, Shi Z, Wang X, Zhou Y, Liu S, et al. Caregiver burden and prevalence of
10	depression, anxiety and sleep disturbances in Alzheimer's disease caregivers in China.
11	J Clin Nurs 2017;26(9-10): 1291-1300.
12	33. Kuriakose RK, Khan Z, Almeida DRP, Braich PS. Depression and burden among the
13	caregivers of visually impaired patients: a systematic review. Int Ophthalmol
14	2017;37(3): 767-777.
15	34. Pinquart M, Sorensen S. Differences between caregivers and noncaregivers in
16	psychological health and physical health: a meta-analysis. Psychol Aging 2003;18(2):
17	250-267.
18	35. Hirschfeld, M. 2003. Home care versus institutionalization: family caregiving and senile
19	brain disease. International Journal of Nursing Studies 40(5) 463-469.
20	36. Reid, C.E., Moss, S. and Hyman, G. 2007. Caregiver Reciprocity: The effect of reciprocity,
21	carer self-esteem and motivation on the experience of caregiver burden. Australian Journal
22	of Psychology 57(3) 186-196.
23	37. Malhi GS, Mann JJ. Depression. Lancet. 2018;392(10161): 2299-2312.

Page 23 of 32

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77 10	
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49 50	
50	
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52	
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54	
55	
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57	
58	
59	
60	

38. Bambara JK, Owsley C, Wadley V, Martin R, Porter C, Dreer LE. Family caregiver social
 problem-solving abilities and adjustment to caring for a relative with vision loss. Invest
 Ophthalmol Vis Sci 2009;50(4): 1585-1592.

# 39. Mausbach BT, Chattillion EA, Roepke SK, Patterson TL, Grant I. A comparison of psychosocial outcomes in elderly Alzheimer caregivers and noncaregivers. Am J Geriatr Psychiatry 2013;21(1): 5-13.

40. Corfield EC, Martin NG, Nyholt DR. Co-occurrence and symptomatology of fatigue and
 depression. Compr Psychiatry 2016;71: 1-10.

41. Sivertsen H, Bjorklof GH, Engedal K, Selbaek G, Helvik AS. Depression and Quality of
 Life in Older Persons: A Review. Dement Geriatr Cogn Disord 2015;40(5-6): 311-339.

- 42. Shumye, S., Belayneh, Z. & Mengistu, N. Health related quality of life and its correlates
  among people with depression attending outpatient department in Ethiopia: a cross
  sectional study. Health Qual Life Outcomes 2019;17(169): 1-9.
- 43. Evans S, Banerjee S, Leese M, Huxley P. The impact of mental illness on quality of life: a
  comparison of severe mental illness, common mental disorder and healthy population
  samples. Qual Life Res 2007;16(1): 17-29.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

44. Song JI, Shin DW, Choi JY, Kang J, Baik YJ, Mo H, Park MH, Choi SE, Kwak JH, Kim
EJ. Quality of life and mental health in family caregivers of patients with terminal
cancer. Support Care Cancer. 2011;19(10): 1519-26.

45. Butow PN, Price MA, Bell ML, Webb PM, deFazio A; Australian Ovarian Cancer Study
Group; Australian Ovarian Cancer Study Quality Of Life Study Investigators,
Friedlander M. Caring for women with ovarian cancer in the last year of life: a
longitudinal study of caregiver quality of life, distress and unmet needs. Gynecol Oncol
2014;132(3): 690-697.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

46. Price MA, Butow PN, Costa DS, King MT, Aldridge LJ, Fardell JE, DeFazio A, Webb PM; Australian Ovarian Cancer Study Group; Australian Ovarian Cancer Study Group Quality of Life Study Investigators. Prevalence and predictors of anxiety and depression in women with invasive ovarian cancer and their caregivers. Med J Aust 2010;193(85): S52-S57.

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Page 25 of 3	32	BMJ	Open	njopen-202 1 by copyri	
1 2 3 5 5 3	Table 1. Study characteristics of family carers st	tratified by degree of bu	rden experienced as mea	ght, in ceaser sex, age, gene sured by Ecarer sex, age, gene	eral health status,
<b>6</b> 54	FSS scores, CESD-10 scores, GSE scores, G	QL scores, and care red	cipient sex, age, general l	health statuswand NEI VFQ-2	5 scores (n=96)
7 8 9			Degree of b	urden ze	
10 11		No/little burden	Mild burden	Moderate - severe burden	
12 13 14	Population characteristics	(n=41)	(n=33)	to text and contact of the second sec	<i>P</i> -value
15 16	Carer variables	Da		nd da	
17 18	Female sex, $n$ (%)	28 (68.3)	28 (84.9)	ta (A from MBE 88 (85.7)	0.15
19 20	Age, yrs, mean (SD)	66.5 (15.6)	63.1 (13.1)		0.14
21 22 23	General health status			mjope trainir	
23 24 25	Substantial comorbidity, n (%)	15 (36.6)	11 (33.3)	ig, and 22 (9.5)	0.07
26 27	Fatigue severity scale score			l simila	
28 29	Problematic fatigue ( $\geq$ 4), <i>n</i> (%)	11 (26.8)	11 (33.3)	tech <u><u><u></u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u></u>	0.06
30 31 32	CESD-10 score			nologi	
33 34	Presence of depressive			925 at /	
35 36 37	symptoms (≥10), <i>n</i> (%)	6 (14.6)	7 (21.2)	47.6)	0.01
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	Total general self-efficacy scores,	33.0 (5.4)	32.7 (4.1)	uding 33.0 (4.5)	0.32
mean (SD)				Septer EI	
	Total general quality of life scores,	7.6 (1.7)	7.5 (1.8)	s reign relance: s reign	0.09
	mean (SD)			021. D ement ted to	
	Patient variables			ownlo: Super text ar	
	Female sex, $n$ (%)	25 (61.0)	20 (60.6)	nd data teur (81.0)	0.23
	Age, yrs, mean (SD)	81.0 (10.1)	84.5 (7.2)		0.15
	General health status			p://bm g, Al ti	
	Substantial comorbidity, <i>n</i> (%)	19 (46.3)	15 (45.5)	aining <b>5</b> 4 (66.7)	0.25
	Total NEI VFQ-25 scores, mean	62.7 (21.0)	53.6 (53.6)	and $36.6(20.9)$	<0.0001
	(SD)			similar on	
55 56	Unadjusted <i>P</i> values from test of heterogeneity GSE – generalised self-efficacy; GQL – General Quality of Life; NEI	v across the three burden VFQ-25 – National Eye Institute Vis	categories. FSS – Fatigue Severity S sual Functioning Questionnaire-25	Scale; C SD- H – Centre for Epidemi	ologic Studies Depression-10;
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 Table 3. Associations between selected variables and presence of depressive symptoms among family arons and care recipients with AMD, presented as adjusted odds ratios (OR) and 95% confidence intervals (CI).
 Image: Confidence intervals (CI).

Factor	Presence of depressive semptoms, OR (95% CI)
Family Carer	ated to
Age (each 1-unit increase)	0.98 (0.99) 0.98 (0.99) 0.99 (0.94)
Female sex	西 (1) (1) (1) (1) (1) (1) (1) (1)
General quality of life (each 1-unit increase)	0.60
Fatigue severity scale score (each 1-unit increase)	3.47 ( <b>≱</b> .00 12.05)
General self-efficacy (each 1-unit increase)	0.97
Care recipients with AMD	, and s
Age (each 1-unit increase)	0.98 ( .96 - 1.05)
Female sex	1.29 8.25-6.25)
General health status (each 1-unit increase)	1.84 <b>9</b> .5 <b>8</b> –6.40)
NEI VFQ-25 (each 1-unit increase)	0.98 (0.95 - 1.01)
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	bliogra
27	hiqu.
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Page 29 of 32				BN	ЛЈ Open	njopen-202 1 by copyr	
1 2 3 4 5	Supplementary tab Table 1. Spearma	les n correlc	ation coefficients betw	ween burden group an	nd carer age, FSS scores, and	ight, including t depetede <b>n</b> cy, and car	e recipient age and NEI
7 8 9	VFQ-25 scores am	ong fami	ily carers of relatives	s with AMD ( $n=95$ )		eptember Enseig or uses re	1 0
10 11	Variable		Carer age	Patient age	Fatigue severity scale	Dere Hency	NEI VFQ-25
12 13 14	Carer burden	r	- 0.26	- 0.22	0.22	text a	- 0.45
15 16	scores	р	0.0115	0.0349	0.0082	nd et	<0.0001
20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43			For peer r	review only - http://bmior		//bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique d Al training, and similar technologies.	
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Supplementary ta	able 2			048658 or ht, includi		
Table 2. Pearson	i correl	lation coefficients between pr	resence of depressive symptoms	s and carer variables $\vec{a}(G \tilde{\vec{a}})$ s	ores, FSS scores, GSE scores)	
and care recipien	nt NEI	VFQ-25 scores among family	carers of relatives with AMD (	(n=96) uses a use		
Variable		General quality of life	Fatigue severity scale	General self-eff	NEI VFQ-25	
	r	- 0.46	0.34	- 0.21	- 0.26	
CESD-10	р	<0.0001	0.0008	0.0391 dated	0.0121	
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		For peer review	v only - http://bmjopen.bmj.com/site	sibliographique e/about/guidelines.xhtml de d		

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or	1.2
		the abstract	-,_
		We have indicated in the title and abstract that this is a cross-	
		sectional study.	
		(b) Provide in the abstract an informative and balanced summary of	2
		what was done and what was found	
		This is done.	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation	5
		being reported	
		This is done.	
Objectives	3	State specific objectives, including any prespecified hypotheses	6
		This is done.	
Methods			
Study design	4	Present key elements of study design early in the paper	6
		This is done.	
Setting	5	Describe the setting, locations, and relevant dates, including periods of	6
-		recruitment, exposure, follow-up, and data collection	
		This is done.	
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and	6
		methods of selection of participants. Describe methods of follow-up	
		Case-control study—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	
		Cross-sectional study—Give the eligibility criteria, and the sources and	
		methods of selection of participants	
		This is shown in the ' <i>Participants</i> ' section of manuscript.	
		(b) Cohort study—For matched studies, give matching criteria and	
		number of exposed and unexposed	
		Case-control study—For matched studies, give matching criteria and the	
		number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential	7, 8, 9, 10
		confounders, and effect modifiers. Give diagnostic criteria, if applicable	
		This information is provided in the Methods section.	
Data sources/	8*	For each variable of interest, give sources of data and details of	7, 8, 9, 10
measurement		methods of assessment (measurement). Describe comparability of	
		assessment methods if there is more than one group	
		This information is provided in the Methods section.	
Bias	9	Describe any efforts to address potential sources of bias	
		N/A	
Study size	10	Explain how the study size was arrived at	6
		This is described in the Methods section	
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 method	ls	12 ( <i>a</i> ) Describe all statistical methods, including those used to control for confounding	10, 11		
		This information is provided in the Methods section			
		(b) Describe any methods used to examine subgroups and interactions	10 11		
		(b) Describe any methods used to examine subgroups and interactions	10, 11		
		(c) Explain how missing data were addressed			
		(d) Cohort study—If applicable, explain how loss to follow-up was			
		Case-control study—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			
		( <u>e</u> ) Describe any sensitivity analyses			
		N/A			
Results					
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	6		
		potentially eligible, examined for eligibility, confirmed eligible, included in			
		the study, completing follow-up, and analysed			
		This is described in the Methods section			
		(b) Give reasons for non-participation at each stage	6		
		This is described in the Methods			
		(c) Consider use of a flow diagram			
		N/A			
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical,	25		
data		social) and information on exposures and potential confounders			
		See Table 1			
		(b) Indicate number of participants with missing data for each variable of			
		interest			
		N/A			
		(c) Cohort study —Summarise follow-up time (eg, average and total amount)			
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures			
		over time			
		Case-control study-Report numbers in each exposure category, or summary			
		measures of exposure			
		Cross-sectional study	11, 12, 13, 2		
		This is reported in the Tables and Results section	26, 27, 28		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted	11, 12, 13, 2		
		estimates and their precision (eg, 95% confidence interval). Make clear	26, 27, 28		
		which confounders were adjusted for and why they were included			
		See Tables 2-3 and Results section			
		(b) Report category boundaries when continuous variables were categorized			
		N/A			

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

\*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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# Cross-sectional study evaluating burden and depressive symptoms in family carers of persons with age-related macular degeneration in 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.

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# 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 macula<sup>1</sup> and is the leading cause of blindness and low vision in Australia, directly affecting more than 1 million persons<sup>2,3</sup>. 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<sup>4,5</sup>. 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<sup>6,7</sup>. 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<sup>8,9</sup>. 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<sup>5,10</sup>. 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 sclerosis<sup>11</sup>. 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 dementia<sup>12</sup>. 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 depression<sup>13</sup>. 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 distress<sup>14</sup>.

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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<sup>3,15</sup>. 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.

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# 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*,
2=high amount of help given, 3=not applicable). Additional information on family carers was determined by administering several validated instruments and scales as detailed below:

(*i*) Carer burden. The Caregiver Burden Scale (CBS) is a 22-item questionnaire originally developed for assessment of perceived family carer burden in caring for patients with dementia<sup>16,17</sup>. Each question was scored on a 5-point Likert-type scale (0=never, 1=rarely, 2=sometimes, 3=quite frequently, 4=always), reflecting the frequency of family carers' feelings when taking care of their family member. The total burden score calculated for each family carer was used to stratify levels of burden into 3 categories, with higher scores indicating higher levels of burden (0-20=no/little burden, 21-40=mild burden,  $\geq$ 41=moderate-severe burden). <sup>16</sup> The CBS is a reliable measure with a Cronbach's alpha of  $0.92^{18}$ .

(*ii*) *Depressive symptoms*. The short form of the Centre for Epidemiologic Studies Depression (CESD-10) scale is a 10-item questionnaire and was used to screen for symptoms of depression<sup>19</sup>. Each question gauges the frequency of a family carer experiencing certain symptoms of depression per week and is scored on a 4-point Likert-type scale (0 = rarely or none of the time (<1 day), 1=some or a little of the time (1-2 days), 2=occasionally or a moderate amount of the time (3-4 days), 3=most or all of the time (5-7 days). A total CESD-10 score of 10 or more indicates significant presence of depressive symptoms, as reported by previous research evaluating the validity of the CESD-10 scale<sup>19</sup>. The CESD-10 is a validated and reliable measure with a Cronbach's alpha of  $0.80^{19,20}$ .

*(iii) Fatigue.* The Fatigue Severity Scale (FSS) is a 9-item questionnaire used frequently to assess the degree of impact that fatigue has on an individual's activities and physical functioning<sup>21</sup>. Participants were asked to respond to statements about how much fatigue

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impacted their ability to function on a scale of 1 *(disagree)* to 7 *(agree)*. Previous studies have shown mean (SD) FSS scores for healthy individuals to be 2.3  $(0.7)^{21}$ . Mean FSS scores of 4 or more were categorised as having problematic fatigue. The FSS is a validated and reliable measure with a Cronbach's alpha of  $0.88^{21}$ .

*(iv)* Self-efficacy. The General self-efficacy (GSE) scale is a 10-item questionnaire shown to be effective at measuring one's beliefs of overall ability to succeed in specific situations<sup>22</sup>. The degree of how much a family carer agreed with each statement was measured using a 4-point Likert-type scale (0=not true, 1=hardly true, 2=moderately true, 3=exactly true). Higher total GSE scores indicate higher self-efficacy.

(v) Dependency. Carers were asked to quantify the level of dependence their family member with AMD had on them since their diagnosis using a 5-point Likert-type scale (1=not at all dependent, 2=somewhat dependent, 3=moderately dependent, 4 = very dependent, 5 = extremely dependent). Scores 3 or more were interpreted as an indication of high dependency on the family carer (1-2 = low dependency, 3-5 = high dependency).

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(vi) Quality of life. Carer's rated their general quality of life (GQL) on a linear scale from 0 (poor quality of life) to 10 (excellent quality of life).

### 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 conditions<sup>23</sup>. Questions in the

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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 health<sup>23</sup>. 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. We analysed caregiver burden as a categorical variable based on the previous literature by Zarit et al.<sup>16</sup> and the generalised logits model was used for carer burden, given that it is a three-level categorical variable<sup>24</sup>. 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, 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

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significance level was <0.05. Checks for multicollinearity did not return any confirmation of multicollinearity occurring.

# **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. Family carers played a considerable role in helping their relatives access medical care, with 91% accompanying their relatives to their ophthalmology appointments where the majority of relatives with AMD (79%) were receiving anti-VEGF injections. In terms of how often help was provided to relatives with AMD, 61% of family carers reported providing help for 7 days a week on average, with 45% reporting either spending >8 hours per day with them or living together with the care recipient. The main caregiving duties where carers provided moderate to high amounts of help included cooking (57%), cleaning (60%) and help with leaving the house (70%).

Substantial amounts of fatigue were experienced by 36% of family carers as indicated by scores of 4 or higher on the fatigue severity scale, and a considerable degree of general health comorbidities was reported by 29% of family carers. The mean quality of life and general selfefficacy scores among the family carers in this study were: 7.3 (SD 2.0) and 32.5 (SD 4.9), respectively.

Burden analysis

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

### Depressive symptoms

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

# 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 AMD<sup>11</sup>. 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<sup>25,26</sup>. 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<sup>11,27</sup>.

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  $\geq$ 41 on the CBS (91.8%), that is, demonstrating substantial amounts of moderate to severe burden<sup>28</sup>. 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 burden<sup>28</sup>. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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When compared with burden experienced by caregivers of patients with idiopathic Parkinson's disease, a greater proportion of family carers of patients with AMD experience moderate-severe burden (22%) than carers supporting family with early (10%) and late (~12%) stages of idiopathic Parkinson's disease<sup>29</sup>. In contrast, studies on caregivers for patients with stroke report higher levels of moderate-severe burden (~68%)<sup>30</sup>. Interestingly, a recent study on family and unpaid carers of older persons revealed that carers were at greater risk of experiencing burden when caring for patients with dementia with or without substantial disability, but not for those patients with substantial disability in the absence of dementia<sup>31</sup>. While patient functional impairment has been shown to be associated with higher levels of caregiver burden, this suggests that the additional challenges of caring for patients with AMD<sup>32</sup>.

The level of dependency that patients with AMD had on their family carers was independently associated with carer burden. This is in agreement with prior research by our group showing that family carers of patients with AMD that had high levels of dependency on them experience negative impacts such as high levels of emotional distress, as well as disruptions to their lifestyle and retirement plans<sup>5</sup>. Moreover, a systematic review of depression and burden among caregivers of patients with visual impairment found that greater hours of supervision required and greater limitations in the patients' ability to carry out their activities of daily living, to be among the factors commonly associated with caregiver burden<sup>33</sup>, a finding reflected in our study. It is likely that a high level of dependency on family carers may negatively impact the relationship between the carer and care recipient. Higher levels of dependency by the care recipient could be linked to loss of independence in the family carer due to a lack of time for one's own needs and leisure activities and this in turn could lead to feelings of burden<sup>10</sup>. Moreover, carers have previously reported feelings of guilt from inability to provide the constant and necessary care, with some carers experiencing feelings of being

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manipulated by the care recipient<sup>5,10</sup>. These feelings of burden due to the AMD caregiving experience can have profound implications on family carer health and well-being. Previous research conducted on the caregiving experience for elderly patients with chronic illnesses has demonstrated negative impacts on the carer's physical and psychological well-being, such as experiencing increased psychological distress, reduced engagement with preventative health behaviours, and disruptions to employment and increased financial stress<sup>5, 10, 34</sup>

In contrast, around one in ten family carers of relatives with AMD in this study experienced positive impacts of providing care, including feeling happier and more content with their lives, as well as feeling more optimistic and determined. It is possible that these differences of the caregiving experience among family carers may be related to pre-existing strong familial ties and/or relationships, or otherwise relationships that have strengthened since the need for family caregiving. Indeed, research into the role of partner relationship quality and reciprocity (that is, a mutual sense of fair exchange) has demonstrated benefits on caregiver wellbeing<sup>35,36</sup>. Another study examining the role of reciprocity in providing care for persons with dementia, chronic physical disability/illness, frailty from aging, and intellectual disability showed an inverse relationship between reciprocity and self-esteem to caregiver burden<sup>36</sup>. These high-quality relationships may in fact provide the resources and means to alleviate the stress and burden that would otherwise be present during the provision of care<sup>36</sup>. As such, understanding the factors that determine relationship strength and how they can be targeted may be a potential area to address when aiming to improve equity in the family carer-care recipient dynamic.

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Over one in five family carers of relatives with AMD demonstrated a significant presence of depressive symptoms in our study, and this is substantially higher that the global prevalence rates of ~6%<sup>37</sup>. Higher rates of depressive symptoms (~35%) have also been demonstrated in previous studies of family carers of patients with vision loss, along with significant associations

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between depressive symptoms and younger carer age and poorer patient visual acuity<sup>38</sup>. High rates (40%) of caregivers reporting depressive symptoms were found in a study on family carers of patients with Alzheimer's disease<sup>39</sup>. Higher levels of fatigue were shown to be predictive of family carers experiencing depressive symptoms in our study. This is perhaps unsurprising, given that fatigue and its symptoms are well-known symptoms/predictors of major depressive disorder in the general population<sup>40</sup>. Studies on the emotional well-being of carers of patients with AMD have previously reported increased rates of emotional distress, feelings of frustration, isolation and sadness<sup>5,13,34</sup>.

Furthermore, poorer family carer quality of life was significantly associated with depressive symptoms. This association between quality of life and depressive symptoms is consistent with other cross-sectional and longitudinal studies involving older adults<sup>41</sup>. Poor quality of life limits one's ability to carry out their social and occupational activities<sup>42,43</sup>. Previous studies on caregiver quality of life have suggest that financial burden, lack of family/social support, distress and unmet needs are among the factors purportedly increasing the risk of depression and poor mental health outcomes<sup>44-46</sup>.

Strengths of this study include the collection of rich and extensive outcome and covariate data from patients with AMD and their family carers, as well as the use of several validated scales for the assessment of carer and patient variables such as burden, depression, fatigue and visual functioning. However, findings of this study should be interpreted with caution. Due to the relatively small sample size, it is likely that the study was underpowered to detect modest associations, as well as limiting the generalisability of the results. Similarly, in the analyses small sample sizes accounted for large confidence intervals, providing less precise estimates of effect. The use of other tools such as the Barthel index for the measurement of care recipient dependency may have been potentially useful in providing a more accurate quantification of dependency. However, while this is a reliable measure of dependency, it is

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time consuming, given that direct observation of the person performing specific tasks is required. Also, we cannot discount residual confounding from factors that were not measured in our study such as the quality/ strength of the carer-care recipient relationship and other psychosocial measures such as spirituality and carer resilience. Moreover, the cross-sectional study design implemented was useful for investigating the relationships between various factors and health outcomes. However, this design limits our ability to draw conclusions about causality. Longitudinal and experimental analyses would allow for a better understanding of causality and the temporal interactions and relationships between variables in this study. As such, future studies of these types utilising larger population sets would be useful to affirm the findings of this study.

### Conclusion

A substantial proportion of family carers of relatives with AMD experience significant burden and depressive symptoms. Family carers played a considerable role in the care of relatives with AMD, including aiding with access to medical care and assistance with care-recipient's ADLs. Levels of dependency and fatigue, as well as lower quality of life were independently associated with higher levels of burden and/or greater odds of depressive symptoms in family carers. Further research is required to affirm these conclusions regarding these predictors of burden and depressive symptoms in family carers of relatives with AMD. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

# a. 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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# **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.

# References

1. Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. Lancet 2018;392(10153): 1147-1159.

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- Wang JJ, Rochtchina E, Lee AJ, Chia EM, Smith W, Cumming RG, et al. Ten-year incidence and progression of age-related maculopathy: the blue Mountains Eye Study. Ophthalmology 2007;114(1): 92-98.
- 3. Deloitte Access Economics, Mitchell P. Eyes on the future: A clear outlook on Age-related Macular Degeneration. Macular Degeneration Foundation Australia, 2011. 144 p.
- Ranmuthugala G, Nepal B, Brown L, Percival R. Impact of home based long term care on informal carers. Aust Fam Physician 2009;38(8): 618-620.

### **BMJ** Open

5. Gop	binath B, Liew G, Burlutsky G, Mitchell P. Age-related macular degeneration and 5-year
	incidence of impaired activities of daily living. Maturitas 2014;77(3): 263-266.
6. Bei	rman K, Brodaty H. Psychosocial effects of age-related macular degeneration. In
	Psychogeriatr 2006;18(3): 415-428.
7. Geh	nrs KM, Anderson DH, Johnson LV, Hageman GS. Age-related macular degeneration -
	emerging pathogenetic and therapeutic concepts. Ann Med 2006;38(7): 450-471.
8. Gol	dberg A, Rickler KS. The role of family caregivers for people with chronic illness. Mec
	Health R I 2011;94(2): 41-42.
9. Bia	lon LN, Coke S. A study on caregiver burden: stressors, challenges, and possible
	solutions. Am J Hosp Palliat Care 2012;29(3): 210-218.
10. Vi	ukicevic M, Heraghty J, Cummins R, Gopinath B, Mitchell P. Caregiver perceptions
	about the impact of caring for patients with wet age-related macular degeneration. Eye
	(Lond) 2016;30(3): 413-421.
11. Go	ohil R, Crosby-Nwaobi R, Forbes A, Burton B, Hykin P, Sivaprasad S. Caregiver Burder
	in Patients Receiving Ranibizumab Therapy for Neovascular Age Related Macular
	Degeneration. PLoS One 2015;10(6): e0129361.
12. Li	ndt, N., van Berkel, J. and Mulder, B.C. 2020. Determinants of overburdening among
inf	Formal carers: a systematic review. BMC Geriatr 20(1) 304.
13. Br	raich PS, Lal V, Hollands S, Almeida DR. Burden and depression in the caregivers o
	blind patients in India. Ophthalmology 2012;119(2): 221-226.
14. Go	opinath, B., Kifley, A., Cummins, R. et al. 2015. Predictors of psychological distress in
	caregivers of older persons with wet age-related macular degeneration. Aging Ment

- 15. Wong WL, Su X, Li X, Cheung CMG, Klein R, Cheng C-Y, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health 2014;2(2): 106-116.
- Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist 1980;20(6): 649-655.
- 17. Bedard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The Zarit Burden Interview: a new short version and screening version. Gerontologist 2001;41(5): 652-657.
- 18. Hébert, R., Bravo, G. and Préville, M. 2010. Reliability, Validity and Reference Values of the Zarit Burden Interview for Assessing Informal Caregivers of Community-Dwelling Older Persons with Dementia. Canadian Journal on Aging / La Revue canadienne du vieillissement 19(4) 494-507.
- 19. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). Am J Prev Med 1994;10(2): 77-84.
- 20. Irwin, M., Artin, K.H. and Oxman, M.N. 1999. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). Arch Intern Med 159(15) 1701-1704.
- 21. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46(10): 1121-1123.
- 22. Schwarzer R, Jerusalem M. Generalized Self-Efficacy scale. In Weinman J, Wright S, Johnston M. Measures in health psychology: A user's portfolio. Causal and control beliefs. NFER-Nelson: Windsor, England, 1995, pp 35-37.

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- 23. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol 2001;119(7): 1050-1058.
- 24. Elkin, E. Beyong Binary Outcomes: Proc Logistic to Model Ordinal and Nominal Dependent Variables. ICON Late Phase & Outcomes Research; San Francisco, CA, USA 2012.
- 25. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. JAMA 1999;282(23): 2215-2219.
- 26. Vitaliano PP, Schulz R, Kiecolt-Glaser J, Grant I. Research on physiological and physical concomitants of caregiving: where do we go from here? Ann Behav Med 1997;19(2): 117-123.
- 27. Cain CJ, Wicks MN. Caregiver attributes as correlates of burden in family caregivers coping with chronic obstructive pulmonary disease. J Fam Nurs 2000;6(1): 46–68.
- 28. Khare, S., Rohatgi, J., Bhatia, M.S. et al. 2016. Burden and depression in primary caregivers of persons with visual impairment. Indian J Ophthalmol 64(8) 572-577.

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Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

### **BMJ** Open

1	29. Genc F, Yuksel B, Tokuc FEU. Caregiver Burden and Quality of Life in Early and Late
2	Stages of Idiopathic Parkinson's Disease. Psychiatry Investig 2019;16(4): 285-291.
3	30. Hu P, Yang Q, Kong L, Hu L, Zeng L. Relationship between the anxiety/depression and
4	care burden of the major caregiver of stroke patients. Medicine (Baltimore)
5	2018;97(40): e12638.
6	31. Riffin C, Van Ness PH, Wolff JL, Fried T. Multifactorial Examination of Caregiver Burden
7	in a National Sample of Family and Unpaid Caregivers. J Am Geriatr Soc 2019;67(2):
8	277-283.
9	32. Liu S, Li C, Shi Z, Wang X, Zhou Y, Liu S, et al. Caregiver burden and prevalence of
10	depression, anxiety and sleep disturbances in Alzheimer's disease caregivers in China.
11	J Clin Nurs 2017;26(9-10): 1291-1300.
12	33. Kuriakose RK, Khan Z, Almeida DRP, Braich PS. Depression and burden among the
13	caregivers of visually impaired patients: a systematic review. Int Ophthalmol
14	2017;37(3): 767-777.
15	34. Pinquart M, Sorensen S. Differences between caregivers and noncaregivers in
16	psychological health and physical health: a meta-analysis. Psychol Aging 2003;18(2):
17	250-267.
18	35. Hirschfeld, M. 2003. Home care versus institutionalization: family caregiving and senile
19	brain disease. International Journal of Nursing Studies 40(5) 463-469.
20	36. Reid, C.E., Moss, S. and Hyman, G. 2007. Caregiver Reciprocity: The effect of reciprocity,
21	carer self-esteem and motivation on the experience of caregiver burden. Australian Journal
22	of Psychology 57(3) 186-196.
23	37. Malhi GS, Mann JJ. Depression. Lancet. 2018;392(10161): 2299-2312.

Page 23 of 32

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55	
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58	
59	
60	

38. Bambara JK, Owsley C, Wadley V, Martin R, Porter C, Dreer LE. Family caregiver social
 problem-solving abilities and adjustment to caring for a relative with vision loss. Invest
 Ophthalmol Vis Sci 2009;50(4): 1585-1592.

# 39. Mausbach BT, Chattillion EA, Roepke SK, Patterson TL, Grant I. A comparison of psychosocial outcomes in elderly Alzheimer caregivers and noncaregivers. Am J Geriatr Psychiatry 2013;21(1): 5-13.

40. Corfield EC, Martin NG, Nyholt DR. Co-occurrence and symptomatology of fatigue and
 depression. Compr Psychiatry 2016;71: 1-10.

41. Sivertsen H, Bjorklof GH, Engedal K, Selbaek G, Helvik AS. Depression and Quality of
 Life in Older Persons: A Review. Dement Geriatr Cogn Disord 2015;40(5-6): 311-339.

- 42. Shumye, S., Belayneh, Z. & Mengistu, N. Health related quality of life and its correlates
  among people with depression attending outpatient department in Ethiopia: a cross
  sectional study. Health Qual Life Outcomes 2019;17(169): 1-9.
- 43. Evans S, Banerjee S, Leese M, Huxley P. The impact of mental illness on quality of life: a
  comparison of severe mental illness, common mental disorder and healthy population
  samples. Qual Life Res 2007;16(1): 17-29.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

44. Song JI, Shin DW, Choi JY, Kang J, Baik YJ, Mo H, Park MH, Choi SE, Kwak JH, Kim
EJ. Quality of life and mental health in family caregivers of patients with terminal
cancer. Support Care Cancer. 2011;19(10): 1519-26.

45. Butow PN, Price MA, Bell ML, Webb PM, deFazio A; Australian Ovarian Cancer Study
Group; Australian Ovarian Cancer Study Quality Of Life Study Investigators,
Friedlander M. Caring for women with ovarian cancer in the last year of life: a
longitudinal study of caregiver quality of life, distress and unmet needs. Gynecol Oncol
2014;132(3): 690-697.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

46. Price MA, Butow PN, Costa DS, King MT, Aldridge LJ, Fardell JE, DeFazio A, Webb PM; Australian Ovarian Cancer Study Group; Australian Ovarian Cancer Study Group Quality of Life Study Investigators. Prevalence and predictors of anxiety and depression in women with invasive ovarian cancer and their caregivers. Med J Aust 2010;193(85): S52-S57.

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1 2 3 5 5 3	Table 1. Study characteristics of family carers st	tratified by degree of bu	rden experienced as mea	ght, in ceaser sex, age, gene sured by Ecarer sex, age, gene	eral health status,
<b>6</b> 54	FSS scores, CESD-10 scores, GSE scores, G	QL scores, and care red	cipient sex, age, general l	health statuswand NEI VFQ-2	5 scores (n=96)
7 8 9			Degree of b	urden ze	
10 11		No/little burden	Mild burden	Moderate - severe burden	
12 13 14	Population characteristics	(n=41)	(n=33)	to text and contact of the second sec	<i>P</i> -value
15 16	Carer variables	Da		nd da	
17 18	Female sex, $n$ (%)	28 (68.3)	28 (84.9)	ta (A from MBE 88 (85.7)	0.15
19 20	Age, yrs, mean (SD)	66.5 (15.6)	63.1 (13.1)		0.14
21 22 23	General health status			mjope trainir	
23 24 25	Substantial comorbidity, n (%)	15 (36.6)	11 (33.3)	ig, and 22 (9.5)	0.07
26 27	Fatigue severity scale score			l simila	
28 29	Problematic fatigue ( $\geq$ 4), <i>n</i> (%)	11 (26.8)	11 (33.3)	tech <u><u><u></u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u></u>	0.06
30 31 32	CESD-10 score			nologi	
33 34	Presence of depressive			925 at /	
35 36 37	symptoms (≥10), <i>n</i> (%)	6 (14.6)	7 (21.2)	47.6)	0.01
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43 44 45	For peer r	eview only - http://bmjoper	n.bmj.com/site/about/guideli	nes.xhtml	

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	Total general self-efficacy scores,	33.0 (5.4)	32.7 (4.1)	uding 33.0 (4.5)	0.32
	mean (SD)			Septer EI	
	Total general quality of life scores,	7.6 (1.7)	7.5 (1.8)	s reign relance: s reign	0.09
	mean (SD)			021. D ement ted to	
	Patient variables			ownlo: Super text ar	
	Female sex, $n$ (%)	25 (61.0)	20 (60.6)	d at (81.0)	0.23
	Age, yrs, mean (SD)	81.0 (10.1)	84.5 (7.2)		0.15
	General health status			p://bm g, Al ti	
	Substantial comorbidity, <i>n</i> (%)	19 (46.3)	15 (45.5)	aining <b>5</b> 4 (66.7)	0.25
	Total NEI VFQ-25 scores, mean	62.7 (21.0)	53.6 (53.6)	and $36.6(20.9)$	<0.0001
	(SD)			similar on	
55 56	Unadjusted <i>P</i> values from test of heterogeneity GSE – generalised self-efficacy; GQL – General Quality of Life; NEI	v across the three burden VFQ-25 – National Eye Institute Vis	categories. FSS – Fatigue Severity S sual Functioning Questionnaire-25	Scale; C SD- H – Centre for Epidemi	ologic Studies Depression-10;
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 Table 3. Associations between selected variables and presence of depressive symptoms among family arons and care recipients with AMD, presented as adjusted odds ratios (OR) and 95% confidence intervals (CI).
 Image: Confidence intervals (CI).

Factor	Presence of depressive semptoms, OR (95% CI)
Family Carer	ated to
Age (each 1-unit increase)	
Female sex	西 (1) (1) (1) (1) (1) (1) (1) (1)
General quality of life (each 1-unit increase)	0.60
Fatigue severity scale score (each 1-unit increase)	3.47 ( <b>≱</b> .00 12.05)
General self-efficacy (each 1-unit increase)	0.97
Care recipients with AMD	, and s
Age (each 1-unit increase)	0.98 ( .96 - 1.05)
Female sex	1.29 8.25-6.25)
General health status (each 1-unit increase)	1.84 <b>9</b> .5 <b>8</b> –6.40)
NEI VFQ-25 (each 1-unit increase)	0.98 (0.95 - 1.01)
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1 2 3 4	Supplementary tab	oles				:1-048658 on ight, includir	
5 6	Table 1. Spearma	n correla	tion coefficients betw	veen burden group an	d carer age, FSS scores, and	d dependency, and car	e recipient age and NEI
7 8 9	VFQ-25 scores am	ıong fami	ly carers of relatives	with AMD $(n=95)$		tembei Enseijuses re	
10 11	Variable		Carer age	Patient age	Fatigue severity scale	Depentiency	NEI VFQ-25
12 13 14	Carer burden	r	- 0.26	- 0.22	0.22		- 0.45
15 16	scores	р	0.0115	0.0349	0.0082	nd date add at (0)01	< 0.0001
19         20         21         22         23         24         25         26         27         28         29         30         31         32         33						ttp://bmjopen.bmj.com/ on June 13, 2025 ng, Al training, and similar technologies.	
34 35 36 37 38 39 40 41						at Agence Bibliograph	
42 43 44 45 46			For peer r	eview only - http://bmjop	en.bmj.com/site/about/guideline	es.xhtml de	

			BMJ Open	open-2021 by copyrig		Page
Supplementary ta	ble 2			-048658 or jht, includi		
Table 2. Pearson	correl	ation coefficients between pr	resence of depressive symptom.	and carer variables $G_{\mathbf{g}}^{\mathbf{g}}$	L scores, FSS scores, GSE scores)	
and care recipier	nt NEI V	/FQ-25 scores among family	carers of relatives with AMD (	n=96) uses r		
Variable		General quality of life	Fatigue severity scale	General self-eff	NEI VFQ-25	
	r	- 0.46	0.34	- 0.21 are	- 0.26	
CESD-10	р	<0.0001	0.0008	0.0391 dat	0.0121	
				nd similar technologies.		

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or	1.2
		the abstract	-,_
		We have indicated in the title and abstract that this is a cross-	
		sectional study.	
		(b) Provide in the abstract an informative and balanced summary of	2
		what was done and what was found	
		This is done.	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation	5
		being reported	
		This is done.	
Objectives	3	State specific objectives, including any prespecified hypotheses	6
		This is done.	
Methods			
Study design	4	Present key elements of study design early in the paper	6
		This is done.	
Setting	5	Describe the setting, locations, and relevant dates, including periods of	6
-		recruitment, exposure, follow-up, and data collection	
		This is done.	
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and	6
		methods of selection of participants. Describe methods of follow-up	
		Case-control study—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	
		Cross-sectional study—Give the eligibility criteria, and the sources and	
		methods of selection of participants	
		This is shown in the ' <i>Participants</i> ' section of manuscript.	
		(b) Cohort study—For matched studies, give matching criteria and	
		number of exposed and unexposed	
		Case-control study—For matched studies, give matching criteria and the	
		number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential	7, 8, 9, 10
		confounders, and effect modifiers. Give diagnostic criteria, if applicable	
		This information is provided in the Methods section.	
Data sources/	8*	For each variable of interest, give sources of data and details of	7, 8, 9, 10
measurement		methods of assessment (measurement). Describe comparability of	
		assessment methods if there is more than one group	
		This information is provided in the Methods section.	
Bias	9	Describe any efforts to address potential sources of bias	
		N/A	
Study size	10	Explain how the study size was arrived at	6
		This is described in the Methods section	
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 method	ls	12 ( <i>a</i> ) Describe all statistical methods, including those used to control for confounding	10, 11
		This information is provided in the Methods section	
		(b) Describe any methods used to examine subgroups and interactions	10 11
		(b) Describe any methods used to examine subgroups and interactions	10, 11
		(c) Explain how missing data were addressed	
		(d) Cohort study—If applicable, explain how loss to follow-up was	
		Case-control study—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	
		( <u>e</u> ) Describe any sensitivity analyses	
		N/A	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	6
		potentially eligible, examined for eligibility, confirmed eligible, included in	
		the study, completing follow-up, and analysed	
		This is described in the Methods section	
		(b) Give reasons for non-participation at each stage	6
		This is described in the Methods	
		(c) Consider use of a flow diagram	
		N/A	
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical,	25
data		social) and information on exposures and potential confounders	
		See Table 1	
		(b) Indicate number of participants with missing data for each variable of	
		interest	
		N/A	
		(c) Cohort study —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures	
		over time	
		Case-control study-Report numbers in each exposure category, or summary	
		measures of exposure	
		Cross-sectional study	11, 12, 13, 2
		This is reported in the Tables and Results section	26, 27, 28
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted	11, 12, 13, 2
		estimates and their precision (eg, 95% confidence interval). Make clear	26, 27, 28
		which confounders were adjusted for and why they were included	
		See Tables 2-3 and Results section	
		(b) Report category boundaries when continuous variables were categorized	
		N/A	

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

\*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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