1 **DEPRESSIVE SYMPTOMS AND QUALITY OF LIFE IN PEOPLE WITH**

2 **AGE- RELATED MACULAR DEGENERATION**

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1   **ABSTRACT**

2   **Purpose:** To examine quality of life and associated factors in people with Age-Related Macular

3   Degeneration (AMD).

4   **Methods:** 145 AMD participants (mean age 78.0 ±7.7 years) and 104 age- and gender- matched

5   controls (mean age 78.1 ± 5.8 years) comprised the study populations for this case-control study.

6   Depressive symptoms were measured with the Goldberg Anxiety and Depression (GAD) scale;

7   general health and daily functioning was assessed with the Medical Outcomes Study Short Form 36

8   and questions relating to assistance required for daily living activities.

9   **Results:** People with AMD performed more poorly than controls on the GAD depression scale, and

10   physical functioning subscale of SF-36. 44.4% of people with AMD had clinically significant

11   depressive symptoms compared to 17.5% of controls (p<0.001). Multiple regression analysis

12   revealed that AMD was independently associated with depressive symptoms and a path model

13   indicated that AMD led to depressive symptoms both directly and indirectly via reduced general

14   health and social functioning.

15   **Conclusion:** Psychological and functional outcome measures are reduced in people with AMD.

16   Earlier recognition and treatment of depressive symptoms in people with AMD may be crucial to

17   maintaining quality of life in this group.

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1 **INTRODUCTION**

2 Age Related Macular Degeneration (AMD) is the most common cause of visual loss in the elderly

3 and one of the most daunting conditions for older people. In developed countries, it affects 10% of

4 those in the age group 65-74 years and 30% of those 75 years and above[1]. AMD has been reported as

5 the leading cause of blindness in people aged over 40 years [2, 3].

6 Previous studies have examined the quality of life implications of AMD. Some have shown

7 that the presence of AMD is associated with difficulties in performing daily tasks and emotional

8 distress[4,5,7- 9]. Depression, in particular, has many adverse consequences if left untreated including

9 decreased functioning and increased rates of institutionalisation and mortality[11, 12]. However, one

10 study suggests that people with AMD report good life satisfaction despite difficulties with mobility

11 and daily living activities as the condition challenged them to find new coping strategies[6]. These

12 conflicting findings indicate that further study is required to determine the extent to which AMD can

13 adversely affect emotional health and quality of life.

14 In this study we assessed the presence of depressive symptoms and its relationship to

15 comorbidities, physical activity levels, physical and social functioning and requirements for

16 assistance with daily living related activities in large samples of people with AMD and age- and

17 gender-matched controls. This information is important for understanding the full impact of AMD on

18 psychosocial measures with implications for service provision.

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21 **METHODS**

22 249 participants were recruited from a retinal clinic, the Macular Degeneration Foundation,

23 Neuroscience Research Australia (previously the Prince of Wales Medical Research Institute) and

24 the School of Optometry and Vision Science Clinic located within Sydney, Australia. The

25 participants were divided into two groups: participants diagnosed with AMD, and participants

without reported ocular diseases (controls). At the Sydney Retina and Sydney Eye Clinics, staff provided potential subjects study information sheets with instructions to contact the primary researcher if they were interested in taking part in the study. Recruitment at the MD Foundation involved identifying potential subjects from the database and sending them information sheets and contact details of the researcher by mail. The data for the control subjects were collected by random selection matching for age and gender from the database for normal subjects of the Falls and Balance Research Group at Neuroscience Research Australia, which comprised 500 people aged 65 years and older. Inclusion criteria for the AMD group were people aged over 55 years, and with clinical evidence of AMD of at least AREDS Category 3[13] and visual acuity better than or equal to 6/60 and no ocular co-morbidities. The control group were those without self-reported ocular diseases (including cataract, macular degeneration, diabetic retinopathy, glaucoma etc) and age- and gender-matched to the AMD group. This study was conducted with approval from the Human Research Ethics Committee, University of New South Wales, and followed the tenets of the Declaration of Helsinki.

The nine Depression items from the Goldberg Anxiety and Depression (GAD) scale were used to screen for depressive symptoms. One point on this scale is given for every positive response and a score of 2 or greater indicates clinically significant symptomatology[14]. The GAD has excellent validity within an aged population[14, 15] with a sensitivity of 86% and overall specificity of 91% in relation to diagnosed depression[14]. General health was assessed using the Medical Outcomes Study Short Form 36 (SF-36), The SF-36 represents multiple measures of physical and emotional health[16]. It comprises eight subscales: physical functioning, role-physical, role-emotional, bodily pain, general health, social functioning, mental health and vitality. It is scored on a range of 1 to 5 and transformed in accordance to the guidelines provided by Ware et al[16] to a range of 0-100 where 0 correlates with worst possible score/function and 100 correlates with best possible score/function. The SF-36 has excellent validity (internal consistency α ~0.8)[17]. As a measure of comorbidity, the presence of each

1   medical condition was given 1 point from a list of nine system-related conditions (cardiovascular,

2   respiratory, musculoskeletal, endocrine, urogenital, cancer, neurological, mental health, and eye

3   diseases). Physical activity was measured using the Incidental and Planned Exercise Questionnaire

4   (IPEQ) that was designed for use with older people[18]. IPEQ measures the number of self-reported

5   hours of exercise including both planned and incidental activities and has good psychometric

6   properties (test-retest reliability 0.77, and internal consistency 0.6)[18]. Total time spent is summed

7   across all components and expressed as hours per week[18]. Assistance required for everyday tasks was

8   assessed with questions relating to dependence on others (relatives, friends and community services)

9   for basic tasks involved in daily living activities such as cooking, cleaning, and shopping. It was

10   scored in a binary fashion with any assistance for any task being given a score of 1.

11   Statistical analyses were performed using SPSS (Version 16.0). Several variables were

12   transformed due to non-normal distributions based on a method suggested by Tabachnik and Fidell

13   [19]. A square root transformation was used for general health, physical functioning, mental health and

14   IPAQ; a logmarithmic transformation was used for Role-physical, Role-emotional and social

15   functioning subscales of the SF-36; FES-I; and an inverse transformation was used for the depression

16   subscale of the GAD scale. Differences between people with AMD and controls were evaluated

17   using independent t-tests. Associations among the quality of life measures were assessed with

18   Pearson correlations, and a linear regression analysis was used to elucidate the impact of AMD

19   (entered separately as the first block) and physical, health and lifestyle factors (entered together in

20   the second block) on depressive symptoms, excluding all the subscales associated with psychological

21   domains. Path analysis was performed using SPSS in conjunction with Analysis of Moment

22   Structures (AMOS 18.0) Graphics. AMOS was used to examine whether the impact of AMD on

23   depressive symptoms was direct or indirect over associated poor general health. Goodness-of-fit[20] of

24   the model was investigated by chi-square, Goodness-of-Fit Index (GFI) and Comparative Fit Index

25   (CFI). Chi-square (χ^2) is a statistical test of lack of fit resulting from over-identifying restrictions

1   placed on a model, and should not be significant. GFI should be high (>0.90) as it assesses the extent

2   to which the model provides a better fit compared with no model at all [35]. CFI represents relative

3   reduction in lack of fit as estimated by comparing the existing model with a null model that assumes

4   latent variables in the model to be uncorrelated; high values (CFI>0.90) reflect a good model fit.

5   Finally, standardized regression coefficients (rc), which are analogous to correlation coefficients, and

6   explained variances were calculated.

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9   **RESULTS**

10   The mean ages of the AMD and control groups were comparable: 78.0 + 7.7 years and 78.1 +

11   5.8 years respectively ($t_{1,247}$=0.68, p=0.95). Both groups comprised similar proportions of men with

12   53 (36.6%) in the AMD group and 30 (29.1%) in the controls (χ2= 1.49, df=1, p=0.22). Of a possible

13   nine common medical conditions, the AMD group had a mean of 1.7 ± 1.0 and the control group 1.7

14   ± 0.9 (t_1, 247=0.54, p=0.59). In the AMD group, 62 people (43.1%) lived alone compared with 54

15   (52.4%) of the controls (χ2= 2.11, df=1, p=0.15) (Table 1).

16   Table 2 shows the GAD depressive symptoms, SF36 and IPEQ scale scores for the AMD and

17   control groups. People with AMD performed significantly worse than the controls for the GAD

18   depression scale and the SF-36 general health, physical functioning, social functioning and mental

19   health subscales. For those with AMD, 63 (44.4 %) met the criteria for a clinically significant

20   symptomatology compared with 18 (17.5%) of the controls (χ2= 19.5, df=1, p<0.001). Depressive

21   symptoms were rare in the control population (3.3%) unless individuals had significant

22   comorbidities. In the presence of a comorbidity score of >1, a control patient had a 30% chance of

23   having depressive symptoms; a patient with AMD but no comorbidity, had a 36% chance of having

24   depressive symptoms, and a patient with AMD and a comorbidity score >1 had a 62% chance of

25   having depressive symptoms. The AMD group had higher physical activity levels but required more

1   assistance with activities of daily living. 56 (38.6%) of those with AMD required assistance with one

2   or more activities of daily living compared with 5 (4.9%) of the controls (χ2= 37.0, df=1, p<0.001).

3   Table 3 shows the bivariate correlations among the depressive symptoms, physical activity

4   and quality of life scales for the AMD group. Depressive symptoms were significantly associated

5   with the mental health, physical functioning, social functioning, and vitality subscales of the SF-36.

6   Linear regression analysis revealed that AMD could explain 7.2% of the variance in depressive

7   symptoms when entered alone at an initial step. Three health and activity measures: poorer general

8   health, higher levels of bodily pain, lower levels of social functioning and number of comorbidities,

9   met the inclusion criteria at second step. Combined, these variables plus AMD explained 31% of the

10   variance in AMD. The standardised beta weights were -0.27 for AMD, -0.17 for general health, -0.21

11   for social functioning, -0.17 for bodily pain and 0.13 for comorbidity. The path analysis further

12   examined the relationship between AMD and depressive symptoms (Figure 1). The results showed

13   that 27% of the variance in the depressive symptoms was explained by the variables in this model,

14   and that AMD led to depressive symptoms both directly and indirectly by reduced general health and

15   social functioning. Goodness-of-fit indicators revealed that the model had a good fit ($\chi^2(6)$=22.45,

16   p=0.001, GFI=0.97, CFI=0.93).

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19   **DISCUSSION**

20   The current study confirms the high prevalence of depressive symptoms in older people with

21   AMD, with nearly half of the AMD group having clinically significant depressive symptoms. Brody

22   et al[8], using previous studies of community samples, suggested that AMD was responsible for

23   doubling the prevalence of depressive symptoms. Our study however indicates a much greater effect,

24   where the presence of AMD may increase the risk of depressive symptoms in a person without

25   comorbidity by 10 fold.

1   The study findings also indicate that people with AMD differ from their age-matched peers in

2   measures of general health, physical and social functioning and requirements for assistance to

3   undertake daily living activities - measures that are all associated with diminished quality of life[21]. It

4   has been previously reported that people with AMD have a reduced quality of life as assessed with

5   the SF-12[22]. The current study builds on this by more extensively assessing aspects of mood and

6   quality of life. We found that people with AMD had significantly reduced physical and social

7   functioning subscale scores even though they reported that their physical and emotional health did

8   not interfere with their functioning (Role - Physical and Social). The AMD group also reported

9   reduced mental health and general health scores even though there were no significant differences in

10   reported comorbidities between the AMD and control groups.

11   The linear regression analysis revealed that AMD was independently associated with

12   depressive symptoms and that with the addition of three health and activity measures: poorer general

13   health, higher levels of bodily pain, lower levels of social functioning and number of comorbidities,

14   these measure could account for 31% of the variance in depressive symptoms. The path analysis

15   provided a complementary analysis of "causal" pathways underlying depressive symptoms and

16   showed that AMD led to depressive symptoms both directly and indirectly via reduced general health

17   and social functioning.

18   We acknowledge that the study has certain limitations. Firstly, data on the occurrence of

19   recent major life events were not recorded. Therefore assumptions about the impact of this factor on

20   depressive symptoms cannot be inferred from this study. Secondly, people with severe AMD were

21   excluded, however we assume that people with more severe AMD would present with further

22   reduced function and increased emotional distress. Thirdly, since all the patients were from semi-

23   urban and urban areas, the findings may not be generalizable to rural areas, where interactions

24   between the level of social support and access to the health services may be different. Finally, we

25   acknowledge that as we did not collect visual acuity data we are unable to determine whether AMD

1   directly causes depressive symptoms or causes depressive symptoms by reducing visual acuity.

2   None-the-less we feel that the strong association found between AMD and depressive symptoms is

3   clinically important and requires further research to elucidate underlying mechanisms and

4   intervention possibilities.

5   Consistent with previous studies[23-26] our findings suggest that people with AMD have more

6   depressive symptoms and a reduced quality of life. The current study adds to this work by

7   delineating possible health and lifestyle mechanisms by which AMD may lead to these psychological

8   and health conditions. Screening people with AMD with respect to depressive symptoms and their

9   ability to perform everyday tasks, with subsequent referral for further evaluation and support

10   services, could assist in maintaining the quality of life in this group [27].

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13   **ACKNOWLEDGEMENTS**

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Table 1: Demographics of the study sample: AMD and control

	AMD (n=145) Mean (SD)	Controls (n=104) Mean (SD)
Age	78.01 (7.73)	78.07 (5.8)
Gender Male	53	31
Female	92	73
Comorbidity	1.53 (1.21)	1.54 (1.07)
Socioeconomic status Above average Below Average	111* 29*	102* 1*
Living arrangements Alone With Spouse Spouse and children Children Relatives Other	62 54 8 13 2 5	54 31 7 5 3 3

3   Chi-square test was performed for Gender, socioeconomic status and living arrangements and

4   ANOVA was done for age difference between the two groups; *p<0.01, statistically significant.

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1 **Table 2: Depression, SF-36 and IPAQ scale scores: AMD and control comparisons**

Scale	AMD (n=145) Mean (SD)	Controls (n=104) Mean (SD)
Depression	2.8 (2.1)*	1.7 (1.4)
General health	59.42 (20.6)	63.42 (21.5)
Physical functioning	52.27 (29.94)*	63.19 (24.42)
Role- Physical	53.68 (40.82)	56.79 (40.32)
Role – Emotional	71.27 (37.7)	74.66 (32.68)
Vitality	52.84 (19.99)	55.27 (23.10)
Bodily pain	60.76 (25.34)	62.37 (24.49)
Mental health	73.87 (17.73)	79.80 (18.0)
Social functioning	74.75 (25.66)	70.61 (21.72)
IPAQ†	29.87 (13.19)*	22.23 (10.54)

2   †Total hours of planned and incidental physical activity/week

3   * p<0.01; ANOVA.

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Table 3: AMD Group: Pearson's correlation co-efficients (R) for GAD depression, SF 36 and IPAQ scales

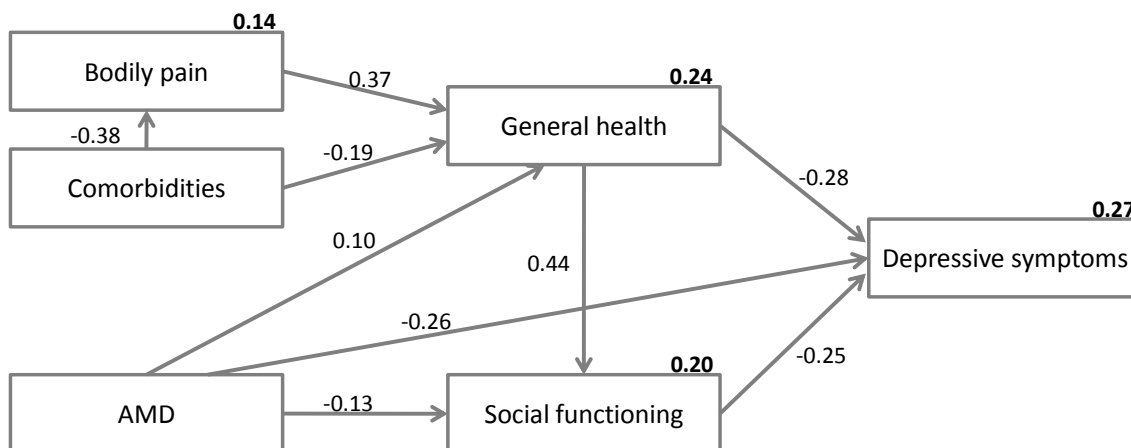|	2	3	4	5	6	7	8	9	10	11	12	13
1	0.20*	0.28**	-0.29**	-0.21*	-0.41**	-0.25**	-0.09	-0.32	-0.20	0.41	-0.35**	-0.33**
2	-	0.65**	-0.53**	-0.65**	-0.27**	-0.42**	-0.19**	-0.49**	-0.32**	0.37**	-0.35**	0.59**
3	-	-	-0.53**	-0.54**	-0.43**	-0.53**	-0.29**	-0.61**	-0.33**	0.38**	-0.38**	-0.55**
4	-	-	-	0.55**	-0.38**	0.45**	0.18*	0.55**	0.31**	-0.39**	0.48**	-0.51**
5	-	-	-	--	0.19*	0.35**	0.82	0.56**	0.24**	-0.24**	0.31**	0.50**
6	-	-	-	-	-	0.43**	0.35**	0.46**	0.35**	-0.48**	0.41**	0.24**
7	-	-	-	-	-	-	0.25**	0.57**	0.44**	-0.28**	0.41**	0.32**
8	-	-	-	-	-	-	-	0.31**	0.22**	-0.26**	0.18**	0.19**
9	-	-	-	-	-	-	-	-	0.42**	-0.33**	0.47**	0.50**
10	-	-	-	-	-	-	-	-	-	-0.16*	0.38**	0.24**
11	-	-	-	-	-	-	-	-	-	-	-0.25**	-0.26**
12	-	-	-	-	-	-	-	-	-	-	-	0.56**
13	-	-	-	-	-	-	-	-	-	-	-	-

1 = ADLA: Assistance with Daily Living Activities; 2 = Anxiety; 3 = Depression; 4 = Social functioning; 5 = Mental health; 6 = Physical functioning; 7 = General health; 8 = IPAQ; 9 = Vitality; 10 = Body pain; 11 = MFES; 12 = Role − physical; 13 = Role − emotional

* p<0.05, **p< 0.01

1 **Figure 1. Output of the path analysis. Values shown are standardized regression coefficients.**

2 **Direct effects are provided next to each arrow and explained variances are provided in bold**

3 **above each variable.**

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