The association of vision loss and dimensions of depression over 12 years in older

adults: findings from the Three City Study

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Abstract

Background: The established relationship between vision impairment and depression is limited by the examination of depression only as a unidimensional construct. The present study explores the vision-depression relationship using a dimensional approach.

Methods: 9036 participants aged 65 years and above enrolled in the Three-City study were included. Relationships between baseline near Vision Impairment (VI) or self-reported distance Visual Function (VF) loss with trajectory of four dimensions of depression – depressed affect, positive affect, somatic symptoms and interpersonal problems - over 12 years were examined using mixed-effects models. Depression dimensions were determined using the four-factor structure of the Centre for Epidemiology Studies-Depression Scale (CESD).

Results: In the fully adjustment models, mild near VI predicted poorer depressed affect (b= 0.04, p = .002) and positive affect (b = -0.06, p <.001) over time, with evidence of longer term adjustment. Distance VF loss was associated with poorer depressed affect (b = 0.27, p = <.001), positive affect (b = -0.15, p = .002), and somatic symptoms (b = 0.18, p = <.001) at baseline, although only the association with depressed affect was significant longitudinally (b = 0.01, p = .001). Neither near VI nor distance VF loss were associated with interpersonal problems.

Limitations: This paper uses a well-supported model of depression dimensions, however, there remains no definite depression dimension model. Distance VF loss was self-reported, which can be influenced by depression symptoms.

Conclusions: Vision impairment in older adults is primarily associated with affective dimensions of depression. A reduction in social connectedness and ability to engage in pleasurable activities may underlie the depression-vision relationship. Older adults with vision loss may benefit from targeted treatment of affective symptoms, and pleasant event scheduling.

Vision impairment (VI) is common in older adults, with an estimated prevalence of 25% in those aged over 70 (Stevens et al., 2013); and VI substantially contributes to burden of disease in Europe (Mathers & Loncar, 2006). An association between VI and depression in the elderly population is well established (Carriere et al., 2013; Court, McLean, Guthrie, Mercer, & Smith, 2014; Hong et al., 2015), with prevalence of comorbid depression in older adults with VI estimated to be around 30% (Hayman et al., 2007; Hong et al., 2015). Comorbid depression leads to marked reductions in quality of life, increased disability, and increased mortality risk (Eisele et al., 2015; Hernandez Trillo & Dickinson, 2012; Zheng et al., 2012), underscoring the need to better understand the relationship between VI and depression and the long-term trajectory of depression symptoms in VI.

To date, when examining the association with VI, depression has been examined as a single disorder-based category; a methodology with substantial limitations. Major depressive disorder (MDD) is a polythetic disorder, characterized by a number of combinations of different symptoms (Vrieze et al., 2014). A unidimensional approach to depression fails to capture the substantial heterogeneity seen between individuals with depression (Basso, Combs, Purdie, Candilis, & Bornstein, 2013; Watson, 2009). Emerging evidence highlights the utility of a dimensional approach, which explores symptom dimensions rather than dichotomizing depression. Divergent prognoses, treatment needs, and quality of life outcomes have been reported for varying depression dimensions (Shafer, 2006; Soskin, Carl, Alpert, & Fava, 2012; Uher et al., 2012; Wardenaar, Monden, Conradi, & de Jonge, 2015). Moreover, different depression dimensions have been shown to differentially correlate with other mental and physical conditions (Watson, 2009) and may have different neurobiological substrates (Basso et al., 2013). Thus analyses using disorder-based categories may result in a substantial loss of valuable information (Brown & Barlow, 2009). By contrast, a dimensional approach is better suited to understanding the pathogenesis and course of psychiatric disorders and meeting the mental health needs of the elderly population (Bryant et al., 2013; Prisciandaro & Roberts, 2009).

Currently a dimensional approach to depression has not been applied in VI research, limiting understanding of the VI-depression association and the related needs of older adults with VI. This study therefore aims to examine the longitudinal relationship between near VI and distance Visual Function (VF) loss in older adults with depression dimension symptoms over 12 years.

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Method

This study forms part of the SENSE-Cog multi-phase research programme, funded by European Union Horizon 2020 programme. SENSE-Cog aims to promote mental well-being in older adults with sensory and cognitive impairments (www.sense-cog.eu/). The first work package of this project aims to better understand the links between sensory, cognitive and mental ill-health in older Europeans.

Sample

Participants were recruited as part of the multi-centre Three-City (3C) study (The 3C Study Group, 2003), a prospective cohort study of community-dwelling French adults aged 65 years and over. A total of 9294 participants were recruited from electoral rolls in three cities (Bordeaux, Dijon and Montpellier) between 1999 and 2001. A standardized evaluation including a face-to-face interview and clinical examinations were undertaken at baseline. Participants were followed up at 2-3 year intervals for up to 12 years. The study protocol was approved by the Ethics Committees of the University–Hospitals and written informed consent was obtained from each participant.

Depression Measures

Depression symptoms were examined using the 20-item Centre for Epidemiology Studies-Depression scale (CESD) (Radloff, 1977). A four-factor structure proposed by Radloff is most commonly replicated (Radloff, 1977; Shafer, 2006). The four factors reflect different dimensions of depression symptoms: depressed affect (DA) assessed by 7 items (felt sad, crying spells, could not shake the blues, depressed, lonely, fearful, felt as though life is a failure); positive affect (PA) assessed by 4 items (hope about the future, enjoyed life, felt as good as others, felt happy); somatic symptoms (S) as represented by 7 items (poor appetite, restless sleep, could not get going, concentration difficulties, everything an effort, bothered by things, talked less than usual); and 2 items

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that examine interpersonal problems (IP; people dislike me, people were unfriendly). The four dimensions are reported to be phenomenologically and psychometrically distinct (Devins, Orme, Costello, & Binik, 1988; Leventhal, Ramsey, Brown, LaChance, & Kahler, 2008; Shafer, 2006).The four-factor structure of the CESD has been validated across a number of populations (Shafer, 2006) including community dwelling older adults (Gellis, 2010) and has also been validated in the French version of the CESD in a population of community dwelling French adults (Morin et al., 2011). The scores for each item were summed for the different dimensions. For PA, items were not reverse scored as is required for calculating total CESD scores, thus lower scores indicate more severe depression. For the other dimensions, higher scores are indicative of more severe depression symptomatology.

Vision measures

Binocular near visual acuity was assessed using the Parinaud scale (a Jaeger-like reading test commonly used in France) at all time points. Assessment was undertaken using presenting vision with usual optical correction where applicable. Identical cards were used at each centre with a standardised reading distance of 33 cm. Mild VI was classified as Parinaud 3 or 4 (Snellen equivalent 20/30-20/60) and moderate to severe VI as Parinaud > 4 (Snellen equivalent < 20/60). Distance visual function was assessed in the face-to-face interview. Distance VF loss was classified as self-reported inability or difficulty in recognising a familiar face at 4 metres.

Socio-demographic and health variables

Socio-demographic and health-related information was collected during the standardised interview at baseline. Known covariates of depression and/or vision were assessed, including variables such as education level (elementary schooling, secondary school, higher education), monthly income (low <€760, €760-2280, >€2280, withheld/missing), and marital status. Alcohol consumption (<10 grams, 10-40 grams, >40 grams per day), tobacco use (current-, past -, or non-smoker) and falls during the past 12 months were also assessed. A composite score representing activity limitations was calculated based on scores from the Rosow-Breslau scale, the Lawton-Brody

Instrumental Activities of Daily Living (IADL) scale and the Katz Index of Independence in Activities of Daily Living; activity limitations were (categorised as autonomous; dependent for mobility; mobility and IADL limitations; and dependent in 3 or more areas of functioning; Barberger-Gateau, Rainville, Letenneur, & Dartigues, 2000). During the detailed medical questionnaire history of myocardial infarction and use of psychotropic medication (ATC classification codes: N05A-C, N06A-B) in the past month was obtained. A medical examination assessed diabetes (fasting glycemia≥7mmol/L and/or anti-diabetic treatment), and blood pressure was measured using a digital electronic tensiometer OMRON M4. Hypertension was defined using the 140/90 mmHg threshold or treatment with blood-pressure lowering drugs. Cognitive functioning was also assessed using the Mini Mental State Examination (MMSE; <16, 16-23 or ≥24).

Statistical Analysis

The relationship between baseline near VI and distance VF loss at baseline with the trajectory of depression dimension symptoms over 12 years were assessed using multilevel growth models. Due to few participants reporting any IP symptomatology, the distribution of IP problems was not amenable to linear models, thus only S, DA and PA dimensions were examined using multilevel models (IP was examined using logistic mixed models). Due to non-normal distribution, dimension scores for PA, DA and S were transformed using the estimated link function (Proust-Lima, 2015). Scores were then converted to z-scores for subsequent analyses.

A series of exploratory models (Singer & Willett, 2003) were undertaken separately for each depression dimension (PA, DA, S) to assess the longitudinal effects of vision on depression symptoms over time; with all vision-related variables entered in a single model, thus models adjusted for the effect of VI on VF loss and VF loss on VI. In an initial step, an unconditional growth model adjusted only for time was undertaken to examine if depression dimension symptoms changed significantly over time. Secondly, time and its quadratic trend were entered to establish the trajectory of depression symptomatology. Exploratory analyses indicated that, for each dimension, depression trajectory was curvilinear and the model with a quadratic trend was the best fit of the data. These models then served as the basis for comparison for the subsequent models exploring the association between VI and VF loss with symptom dimensions. In a third step, baseline mild VI, moderate to severe VI, VF loss, and their interactions with time were entered concurrently into the model. A range of variables such as

functional ability, age, gender, education level, income and physical health have been identified as related to depression amongst older adults (see e.g. Blazer, 2003; Pennix, Leveille, Ferrucci, van Eijk, & Guralnik, 1999). Thus, in the final stage, three models were carried out for each dimension which adjusted for such known covariates that have been previously documented in the literature. The first adjusted for age, sex and study centre; the second model additionally adjusted for education level, income, marital status, and use of psychotropic medication; and the third model additionally adjusted for cognitive function (MMSE), activity limitations, falls in past 12 months, hypertension, diabetes, smoking status, alcohol consumption, and history of myocardial infarction, with covariates added as additional explanatory variables in the models.

The IP score was converted to a binary variable: presence of any IP symptomology and absence thereof. A logistic mixed model (Carriere & Bouyer, 2002) was used to explore if those with baseline VI or VF loss had differential odds of experiencing IP symptoms over the twelve years of follow-up. Logistic mixed models take into account within-subject correlation and model the individual time evolutions of the outcome across the 12 years of follow-up; thus logistic mixed models also allow for the reversibility of symptoms. Three separate models were conducted for IP, adjusting for the same covariates as the multilevel models. Interactions between vision with sex, education and income were also systematically examined in all analyses. Analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

Results

Of the 9294 participants recruited, 246 were missing baseline CESD or vision data and a further 12 had not completed the CESD due to impaired cognitive function as assessed by the trained interviewer. Thus a total of 9036 participants with complete depression and vision data at baseline were included in analyses. Participants had a mean age of 74.3 (SD=5.58) at baseline. The majority were female (60.7%, n = 5543). At baseline, prevalence of mild VI was 9.0% (n = 810), moderate to severe VI was 4.3% (n = 386) and distance VF loss was 5.4% (n = 491). Those with poor vision were older, less educated, less likely to be married, had greater functional impairment and were in poorer physical health on all assessed health outcomes than those without baseline impairment (Table 1).

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Depressed Affect

As shown in Table 2, in the fully adjusted model (model 3), mild VI was not associated with DA at baseline (b = -0.018, SE = 0.035, p = .60). However, mild VI was associated with an initial increase in DA symptomatology over time (b = 0.040 for linear interaction with time, SE = 0.013, p = .002), with symptoms then beginning to plateau (b = -0.003 for quadratic interaction with time, SE = 0.001, p = .01). Moderate to severe VI was also not related to DA at baseline. However, moderate to severe VI was associated with increasing DA symptoms over time (b = 0.043 linear interaction with time, SE = 0.021, p = .04). Distance VF loss was associated with increased DA symptoms at baseline (b = 0.265, SE = 0.048, p = <.001). In those with distance VF loss an initial small improvement in DA was seen before a longer term increase in DA symptoms (b = 0.005 for quadratic interaction with time, SE = 0.002, p = .001).

Positive Affect

Mild VI was associated with better PA at baseline (b = 0.107, SE = 0.04, p .003; Table 3). Mild VI was, however, associated with worsening PA symptoms over time (b = -0.060 for linear interaction with time, SE = 0.014, p <.001), before a tapering of symptoms over the longer term (b = 0.003 for quadratic interaction with time, SE = 0.001, p = .02). Moderate to severe VI was not associated with PA symptoms. Distance VF loss, on the other hand, was related to poorer PA at baseline (b = -0.147, SE = 0.047, p = .002), but had no longitudinal relationship with PA.

Somatic Symptoms

Neither mild nor moderate to severe VI were associated with somatic symptoms in the fully adjusted models, although a longitudinal relationship with moderate to severe VI was close to significance (Table 4). Distance VF loss was associated with greater somatic symptoms at baseline (b = 0.175, SE = 0.046, p = <.001); however, this was not significant longitudinally (b = -0.007, SE = 0.020, p = .72).

Interpersonal Problems

Neither mild nor distance VF loss were associated with a greater likelihood of experiencing IP problems over 12 years in the fully adjusted models (OR = 0.84 95% CIs 0.64-1.11, p =.22, OR = 1.07 95% CIs 0.76-1.51, p =.69, respectively; Table 5). In the partially adjusted models, moderate to severe VI was associated with interpersonal problems, although this was just outside of significance in the fully adjusted model (OR = 1.42, 95% CIs 0.99-2.03, p =.06). In all models, none of the tested interactions were significant.

Discussion

This study adopted a novel dimensional approach to extend past research which has previously established cross-sectional (Court et al., 2014; Garin et al., 2014; Hayman et al., 2007) and longitudinal (Carriere et al., 2013; Hong et al., 2015) relationships between VI and depression. Vision had differential relationships with different dimensions of depression. Affective dimensions, specifically depressed affect and positive affect, were more closely tied to VI and VF loss than somatic or interpersonal symptoms. Thus the present findings provide a more comprehensive picture of depression in vision and the dimensions that underlie the vision-depression relationship in the elderly population with VI.

Our findings demonstrated the varied relationships between different types of VI and depression dimensions. Distance VF loss was associated cross-sectionally with DA, PA and somatic dimensions, whereas near VI did not have any cross-sectional associations with worse depressive symptomatology. This finding may indicate that distance VF loss is associated with greater initial distress that may remit over time, at least for PA and somatic dimensions. Alternatively, those who were more depressed at baseline may have been more likely to self-report vision problems. Notably in distance VF loss there was no evidence of adjustment to DA, suggesting that some dimensions may persist even in the absence of meeting a threshold for a single disorder-based assessment of depression. While the absence of cross-sectional associations between near VI and depression symptoms was perhaps unexpected, this finding might also reflect that depression likely increases with

worsening severity of the loss, and hence may be more strongly associated to depression symptoms over time.

The perhaps surprising finding that mild VI was associated with better PA at baseline might be explained through health behaviours. Previously higher PA has been associated with lack of adherence to treatment, and inaccurate diagnosis and healthcare due to the underreporting of symptoms (Pressman & Cohen, 2005). One possibility then is that those with higher PA might be more likely to use inappropriate optical correction thus resulting in higher rates of VI as assessed via presenting correction. Correctible VI due to use of the wrong optical correction common in older adults (Taylor, Pezzullo, Nesbitt, & Keeffe, 2007). In the present study mild VI was, however, associated with a worsening of depression symptoms over time for both PA and DA. Yet for both dimensions there was a small longer term improvement in symptoms, indicative of adjustment, which is consistent with reports that older adults with VI exhibit depression symptoms at 5 but not 10 years post-onset (Hong et al., 2015). Our findings do suggest, however, that adjustment might be more complex than previously reported, with differential adjustment observed for different dimensions and types of VI. Although a range of factors that likely facilitate adjustment in VI have been reported (Senra et al., 2015), ongoing research is needed to better understand facilitators of adjustment for each dimension in order to help promote and improve quality of life (Wang & Chan, 2009).

Notably, within the present study, moderate to severe VI was only associated with DA over time, but was unrelated to the other depression dimensions. Due to a smaller sample meeting the moderate to severe threshold, the study may have been underpowered to detect such relationships. However, moderate to severe VI was associated with IP in the partially adjusted models, yet this was no longer significant after full adjustment for physical health covariates. Given that VI is associated with poorer physical health (Lam, Christ, Lee, Zheng, & Arheart, 2008) and greater functional limitations (Bookwala & Lawson, 2011; Daien et al., 2011, 2014; Peres et al., 2017), it is possible that adjustment for these other factors might have attenuated the depression associations observed in the unadjusted models. Moreover, adjustment was noted in some dimensions in mild VI, thus those with moderate to severe VI might have already adjusted to their impairment. Relatedly, fear of total vision loss and future deterioration of vision are a central cause of distress in VI (Wang & Chan, 2009), yet may be less pertinent in those with already more severe VI.

The present results also shed further light on prior depression and vision research. Variations in the prevalence of comorbid depression in VI and eye diseases have been reported previously. Notably, one study using the Goldberg Depression Scale, which has a high proportion of items that assess somatic symptoms, reported relatively low rates of comorbid depression ranging from 4.3% in glaucoma to 10.5% in Age-related Macular Degeneration (AMD) (Eramudugolla, Wood, & Anstey, 2013). Other studies which have utilised the Hospital Anxiety and Depression Scale and Geriatric Depression Scale, both of which largely focus on affective symptoms of depression, have reported depression prevalence between 22-35% in VI and eye diseases (Hayman et al., 2007; Popescu et al., 2012; van der Aa, Comijs, Penninx, van Rens, & van Nispen, 2015; Yokoi et al., 2014). Thus the variation in prevalence rates may reflect the varied relationships between vision and depression dimensions. In addition, this study builds on previous depression dimension work that has shown prospective associations between affective depression dimensions with a number of physical health outcomes (Basso et al., 2013; Steptoe, Dockray, & Wardle, 2009). Our findings suggest that DA and PA are also related to aspects of vision and, moreover, that associations between affective dimensions and health might be bidirectional, with our results indicating that poor vision predicted poorer DA and PA over time.

The results also shed further light on the range of possible mechanisms that might underlie the vision-depression association. Avoidance of social situations is observed in poor vision, leading to social isolation and reduced social support (Bookwala & Lawson, 2011; Hayman et al., 2007); both of which predict depression onset (Penninx, Leveille, Ferrucci, van Eijk, & Guralnik, 1999). Notably, positive affect is related to social connectedness and support (Brown & Barlow, 2009; Steptoe et al., 2009) and, concomitantly, those with depressed affect have fewer social connections (Steptoe et al., 2009) and report greater levels of loneliness (Wardenaar et al., 2015). Accordingly, the association between VI and affective symptoms suggests that social isolation and loss of social networks may be crucial factors underlying the association between VI and depression. Similarly, reduced functional independence observed in VI has been proposed as a mechanism (Carriere et al., 2013; Chou, 2008; Evans, Fletcher, & Wormald, 2007). Limited functional ability may also limit or restrict the ability to undertake pleasurable activities and events, resulting in reduced PA (Wahl, Heyl, & Schilling, 2012). Likewise reduced ability to engage in hobbies such as reading might further underlie the vision-depression association via reduced PA. Conversely, it has been argued that for those with increased

somatic symptoms of depression, common biological or ageing pathways likely underlie both the physical ill-health and depressive episode (Anderson, Berk, & Maes, 2014). The lack of associations between VI and somatic symptoms suggests that, at least in this sample, shared biological processes were less likely to be the mechanism underlying depression in VI.

Given that interventions targeted to specific dimensions can improve efficacy of depression treatment (Soskin et al., 2012), our findings indicate that a focus on treating affective symptoms is better suited to older adults with VI. This is particularly pertinent given that DA and symptoms of PA predict greater depression severity and poorer treatment response (Uher et al., 2012; Vrieze et al., 2014). Behavioural activation and pleasant event scheduling are beneficial therapeutic components for treating affective symptoms (Treadway & Zald, 2011) and behavioural activation is superior to supportive therapy for preventing depression in AMD (Rovner et al., 2014). Given limitations in mobility and ability to engage in social outings and activities such as reading, a focus on generating and identifying alternate activities which generate PA may also be integral to improving wellbeing (Wahl et al., 2012). The results also highlighted some variation in treatment needs depending on type of VI. Mild VI was slower to remit, thus promoting adjustment may be of particular benefit in this population. Furthermore, DA did not remit in those with distance VF loss and given the bi-directional relationship between distance VF loss and depression (Carriere et al., 2013), treatment of DA symptoms may be of particular importance.

Strengths and Limitations

Study strengths include the large sample and length of follow up which allowed for the longer term trajectories of depression dimensions and adjustment to be explored, as well as the inclusion of measured binocular near visual acuity. However, this paper is presented with a number of limitations. Firstly distance VF loss was assessed by only 1 item and, being self-reported, may have been influenced by existing depression symptoms. Moreover, although the model of depression dimensions utilized in this study has empirical support, debate remains over the best conceptualization of depression dimensions and currently there is no conclusive model (van Loo, de Jonge, Romeijn, Kessler, & Schoevers, 2012). It is possible that alternate dimensional models or depression measures

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would yield varied associations with vision. In addition, the CESD was originally designed as a general measure of depression rather than to assess specific subscales or factors (Shafer, 2006); ongoing research focused on assessment of depression dimensions in VI would be valuable. Relatedly, the interpersonal problems dimension was assessed by only two items and few participants endorsed any IP symptoms. Thus findings related to the IP dimension may not reflect the full range of interpersonal dysfunction in older adults with VI. Additionally, although Quality of Life (QoL) is related to depression and VI, no QoL data were available in this study, thus any possible confounds of QoL could not be ascertained. Future research might further consider the interplay of QoL in the relationship between specific depression dimensions and vision. A small proportion of participants had lower levels of cognitive function (as determined by the MMSE). Although these participants only completed self-report measures when deemed capable by the trained interviewer, the extent to which underlying cognitive fucntion might have impacted self-report cannot be fully ascertained. Furthermore, specific eye diseases or conditions underlying VI were not assessed. As a result, our findings do not account for possible reversibility of VI (e.g. due to cataract surgery).

Conclusions

The dimensional approach used here allows for increased understanding of the mental health needs of the elderly population with VI. Older adults with poor vision predominantly experienced a worsening of affective symptoms. Although longitudinal associations were observed with dimensions of depression, older adults with near VI showed some evidence of adjustment over time. Findings suggest that VI might be related to depression via a reduction in social connectedness and ability to engage in pleasurable activities. Older adults with VI may particularly benefit from targeted treatment of affective symptoms to enhance wellbeing.

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Table 1: Baseline characteristics of the study population by vision loss. Three-City (3C) Study 1999-2001, N=9036.

	No visual loss n= 7552		Mild VI only n= 726		Moderate to Severe VI only n= 267		VF loss only n= 288		VI and VF loss n= 203		p
Age: mean (SD)	73.8	(5.3)	76.4	(5.9)	76.6	(5.8)	75.8	(6.2)	78.8	(6.3)	<.001[a]
Female	4475	(59.3)	488	(67.2)	163	(61.1)	213	(74.0)	153	(75.4)	<.001
Education (reference category = high)											<.001
Low	1794	(23.8)	299	(41.5)	110	(41.2)	72	(25.1)	67	(33.2)	<.001
Mid	4277	(56.7)	331	(45.9)	122	(45.7)	173	(60.3)	105	(52.0)	.001
Income (reference category = high)											<.001
Low (< €760)	341	(4.8)	86	(12.9)	22	(9.7)	15	(5.5)	28	(15.6)	<.001
Mid (€760-€2280)	4139	(58.2)	436	(65.4)	156	(68.4)	183	(67.5)	115	(63.9)	.003
Withheld/missing	437	(5.8)	59	(8.1)	39	(14.6)	17	(5.9)	23	(11.3)	<.001
Married	4667	(61.8)	347	(47.9)	140	(52.4)	145	(50.4)	77	(38.1)	<.001
Smoking(reference category = non-smoker)											<.001
Current smoker	421	(5.6)	49	(6.8)	12	(4.5)	16	(5.6)	10	(5.0)	. 63
Past smoker	2561	(33.9)	206	(28.4)	90	(33.7)	71	24.7)	53	(26.2)	<.001
Psychotropic medication use	2045	(27.1)	284	(39.1)	90	(33.7)	116	(40.3)	90	(44.3)	<.001
Alcohol consumption (reference category = high)											<.001
Low (>10 grams per day)	4281	(56.7)	476	(65.6)	173	(64.8)	187	(64.9)	145	(71.4)	<.001
Moderate (10-40 per day)	2735	(36.2)	206	(28.4)	84	(31.5)	88	(30.6)	48	(23.7)	<.001
Fall in past 12 months	1373	(18.2)	173	(23.9)	69	(26.0)	65	(22.6)	60	(29.7)	<.001
Hypertension	5789	(76.7)	596	(82.1)	217	(81.6)	232	(80.6)	169	(83.3)	<.001
Diabetes	583	(7.8)	68	(9.4)	34	(12.8)	26	(9.1)	22	(11.1)	.01
Myocardial infarction	374	(5.0)	33	(4.6)	15	(5.6)	6	(2.1)	12	(5.9)	<.001
MMSE (reference category ≥24)											<.001
<16	44	(0.6)	5	(0.7)	4	(1.5)	3	(1.0)	4	(2.0)	.05
16-23	422	(5.6)	77	(10.7)	31	(11.8)	33	(11.5)	26	(12.9)	<.001
Activity Limitations (reference category = autonomous)											<.001
Dependent for mobility	2721	(37.1)	330	(46.5)	120	(47.6)	104	(38.7)	75	(39.9)	<.001
Mobility and IADL limitations	445	(6.1)	134	(18.9)	48	(19.1)	42	(15.6)	71	(37.8)	<.001
Dependent in 3 or more areas	41	(0.6)	15	(2.1)	6	(2.4)	6	(2.2)	8	(4.3)	<.001
Missing	223	(3.0)	17	(2.4)	15	(5.6)	19	(6.6)	15	(7.4)	<.001

VI: Visual impairment; VF loss: Visual function loss; SD: Standard deviation, [a] = determined by one-way ANOVA, all other p values determine by Chi square tests

Except for age, results are presented as n,%

Table 2: Association between baseline Vision Loss and Depressed Affect (z-score). Three-City (3C) Study

	Model 1			Model 2			Model 3		
	b	SE	p	b	SE	p	b	SE	P
Time (years)	-0.034	0.004	<.001	-0.034	0.004	<.001	-0.033	0.004	<.001
Time^2 *(quadratic trend)*	0.003	0.001	<.001	0.003	0.001	<.001	0.003	0.001	<.001
Mild Near VI	0.044	0.035	.21	-0.011	0.034	.76	-0.018	0.035	.60
Mild Near VI*Time	0.038	0.013	.003	0.039	0.013	.002	0.040	0.013	.002
Mild Near VI*Time^2 *(quadratic trend)*	-0.003	0.001	.02	-0.003	0.001	.01	-0.003	0.001	.01
Mod - Severe Near VI	-0.007	0.051	.89	-0.048	0.050	.33	-0.072	0.051	.16
Mod - Severe Near VI*Time	0.046	0.020	.02	0.043	0.020	.03	0.043	0.021	.04
Mod - Severe Near VI*Time^2 *(quadratic trend)*	-0.004	0.002	.06	-0.003	0.002	.08	-0.003	0.002	.09
Distance VF loss	0.318	0.047	<.001	0.269	0.045	<.001	0.265	0.048	<.001
Distance VF loss *Time	-0.063	0.017	<.001	-0.063	0.017	<.001	-0.069	0.017	<.001
Distance VF loss *Time^2 *(quadratic trend)*	0.005	0.002	.002	0.005	0.002	.002	0.005	0.002	<.001

SE: Standard error

Model 1: n = 8607; adjusted for sex, age, centre

Model 2: n = 8590; sex, age, centre, education, income, marital status, psychotropic medication use

Model 3: n = 8209; sex, age, centre, education, income, marital status, psychotropic medication use, MMSE, functional ability, falls, hypertension, diabetes, smoking, alcohol consumption, and history of myocardial infarction

Table 3: Association between baseline Vision Loss and Positive Affect (z-score). Three-City (3C) Study

	Model 1			Model 2			Model 3		
	b	SE	p	b	SE	p	b	SE	p
Time (years)	0.035	0.004	<.001	0.034	0.004	<.001	0.031	0.004	<.001
Time^2 *(quadratic trend)*	-0.004	0.001	<.001	-0.004	0.001	<.001	-0.003	0.001	<.001
Mild Near VI	0.067	0.036	.06	0.098	0.037	.005	0.107	0.036	.003
Mild Near VI*Time	-0.062	0.014	<.001	-0.062	0.015	<.001	-0.060	0.014	<.001
Mild Near VI*Time^2 *(quadratic trend)*	0.003	0.001	.01	0.003	0.001	.01	0.003	0.001	.02
Mod - Severe Near VI	-0.024	0.052	.65	-0.002	0.052	.98	0.037	0.053	.48
Mod - Severe Near VI*Time	-0.014	0.022	.54	-0.011	0.022	.61	-0.017	0.023	.46
Mod - Severe Near VI*Time^2 *(quadratic trend)*	-0.001	0.002	.94	-0.001	0.001	.86	-0.001	0.002	.99
Distance VF loss	-0.198	0.047	<.001	-0.161	0.047	<.001	-0.147	0.047	.002
Distance VF loss *Time	0.009	0.019	.63	0.008	0.020	.67	0.013	0.019	.50
Distance VF loss *Time^2 *(quadratic trend)*	-0.002	0.002	.30	-0.002	0.002	.31	-0.002	0.002	.20

Model 1: n= 8581; sex, age, centre
Model 2: n= 8564; sex, age, centre, education, income, marital status, psychotropic medication use
Model 3: n= 8183; sex, age, centre, education, income, marital status, psychotropic medication use, MMSE, functional ability, falls, hypertension, diabetes, smoking, alcohol consumption, and history myocardial infarction

Table 4: Association between baseline Vision Loss and Somatic Symptoms (z-score). Three-City (3C) Study

	Model 1			Model 2			Model 3		
	b	SE	p	b	SE	p	b	SE	p
Time (years)	-0.027	0.004	<.001	-0.026	0.004	<.001	-0.025	0.004	<.001
$Time^2$ *(quadratic trend)*	0.002	0.001	<.001	0.002	0.001	<.001	0.002	0.001	<.001
Mild Near VI	0.066	0.035	.06	0.033	0.035	.35	0.027	0.035	.44
Mild Near VI*Time	0.029	0.014	.03	0.030	0.014	.03	0.027	0.014	.06
Mild Near VI*$Time^2$ *(quadratic trend)*	-0.002	0.001	.19	-0.002	0.001	.19	-0.001	0.001	.26
Mod - Severe Near VI	0.044	0.051	.39	0.020	0.050	.68	0.006	0.051	.91
Mod - Severe Near VI*Time	0.032	0.021	.13	0.029	0.021	.17	0.021	0.022	.34
Mod - Severe Near VI*$Time^2$ *(quadratic trend)*	-0.001	0.002	.50	-0.001	0.002	.59	-0.001	0.002	.94
Distance VF loss	0.234	0.047	<.001	0.193	0.046	<.001	0.175	0.046	<.001
Distance VF loss *Time	-0.002	0.018	.93	-0.002	0.018	.93	-0.007	0.019	.72
Distance VF loss *$Time^2$ *(quadratic trend)*	-0.001	0.002	.97	-0.001	0.002	.97	0.001	0.002	.87

Model 1: n= 8598; sex, age, centre
Model 2: n= 8582; sex, age, centre, education, income, marital status, psychotropic medication use
Model 3: n= 8199; sex, age, centre, education, income, marital status, psychotropic medication use, MMSE, functional ability, falls, hypertension, diabetes, smoking, alcohol consumption, and history of myocardial infarction

Table 5: Association between baseline Vision Loss and interpersonal problems. Three-City (3C) Study

	OR	95% CI		p
Mild near VI				
Model 1	0.93	0.71	1.22	.61
Model 2	0.84	0.64	1.11	.22
Model 3	0.84	0.64	1.11	.22
Moderate to Severe near VI				
Model 1	1.71	1.22	2.41	.002
Model 2	1.51	1.08	2.13	.02
Model 3	1.42	0.99	2.03	.06
Distance VF loss				
Model 1	1.09	0.78	1.53	.61
Model 2	1.07	0.76	1.49	.71
Model 3	1.07	0.76	1.51	.69

OR: odds ratio
CI: confidence interval
Model 1: n= 7445; sex, age, centre
Model 2: n= 7431; sex, age, centre, education, income, marital status, psychotropic medication use
Model 3: n= 7103; sex, age, centre, education, income, marital status, psychotropic medication use, MMSE, functional ability, falls, hypertension, diabetes, smoking, alcohol consumption, and history of myocardial infarction