Chapter 3:

Validated prediction model of subthreshold depression in visually impaired older adults: based on a European and Australian sample

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Abstract

Objectives
To internally validate a prediction model for having subthreshold depression in visually impaired older adults in a European sample and externally validate this model in a comparable Australian sample.

Methods
An intercontinental cross-sectional study was performed. Included were 873 visually impaired patients (aged ≥50 years) from outpatient low vision rehabilitation organisations in the Netherlands and Belgium, and 124 patients (aged ≥50 years) from low vision rehabilitation organisations in Australia. Data on subthreshold depression, measured by the Centre for Epidemiologic Studies Depression scale (CES-D) and the Patient Health Questionnaire (PHQ)-9, and a broad spectrum of demographic, somatic, social and psychological factors were investigated. Multivariable logistic regression analysis was performed to determine the prediction model. Validation was conducted by bootstrapping and cross-validation methods. A nomogram was generated to give a visual representation of the risk of having subthreshold depression.

Results
Seven factors were found to predict subthreshold depression: lower age (β -0.03; 95% confidence interval (CI) -0.04 to -0.01), female gender (β 0.37; 95% CI 0.01 to 0.73), living alone (β 0.43; 95% CI 0.06 to 0.80), history of psychiatric disorder (β 0.69; 95% CI 0.38 to 1.10), received mental health services in the past (β 0.34; 95% CI 0.00 to 0.68), lower perceived health status (β -2.97; 95% CI -3.72 to -2.23), and lower acceptance of vision loss (β -0.66; 95% CI -0.87 to -0.45). The area under the curve (AUC) was 0.81, reflecting good discrimination and internal validation of the model. The model tested in the Australian sample yielded an AUC of 0.88, a calibration slope of 0.88 and a Hosmer-Lemeshow test of $\chi^2 = 66.37$; $P<0.001$. The generated regression coefficients were similar to the original values.

Conclusions
This study is the first to externally validate a prediction model for depression in a visually impaired sample. Good model validation indices suggest that the model is accurate enough to use in clinical practice to determine patients most at risk of having clinically significant depressive symptoms and to guide treatment decisions.

Introduction

About 3% of the European and Australian population are visually impairment and this percentage is expected to increase due to demographic ageing.[1] Recent studies show that about one third of visually impaired older adults experience subclinical symptoms of depression (called subthreshold depression) and about 5 to 7% meet the criteria of a major depressive disorder.[2] These numbers are at least twice as high as the prevalence in the general population.[3-4]

Evidence shows that subthreshold depression is associated with decreased health-related quality of life and functional decline,[3,5-7] and that it is the most important predictor of developing major depressive disorder.[8,9] For early diagnosis and treatment it is important to identify patients who are at high risk of having subthreshold depression.[10]

Former studies found inconsistent results on factors associated with depression in adults with visual impairment,[11-18] and prediction models were not externally validated. Therefore, it is still unclear which of these factors contribute to depression in visually impaired older adults and if findings are stable across different populations.

The aim of this study is to comprehensively assess potential predictor variables by internally validating a prediction model for subthreshold depression in a large sample of visually impaired older adults (aged ≥50 years) from the Netherlands and Belgium, and by externally validating this model in a comparable Australian sample. Based on previous research,[11-18] we hypothesize that demographic factors (gender, age, education, country of birth), somatic factors (vision-related factors, somatic comorbidity, perceived health status, history of psychiatric disorders), social factors (social support, work, living alone), psychological factors (acceptance of vision loss, perceived vision-specific quality of life), and received mental health services influence depression in visually impaired older adults.

Methods

Design
Cross-sectional data in 873 visually impaired patients from outpatient low vision rehabilitation organisations in the Netherlands and Belgium were collected between July 2012 and April 2013 as part of the baseline measurement of a randomised controlled trial (RCT, trial registration: http://www.trialregister.nl, identifier: NTR3296).[19] In addition, cross-sectional data of 124 patients from low vision rehabilitation organisations in Australia were collected between January 2013 and November 2014, which were also part of the baseline measurement of an RCT (trial registration: https://www.anzctr.org.au, identifier: ACTRN12612000318886).[20] Ethical approval was received from the Medical Ethics Committee of the VU University Medical Centre in Amsterdam, the University Hospital Leuven and the Human Research and Ethics Committee of the Royal Victorian Eye and Ear Hospital in Melbourne. It has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All participants provided written informed consent.

Participants
Eligibility criteria for the Dutch and Belgian participants were: a) being a client of a low vision rehabilitation organisation in the Netherlands or Belgium, b) being ≥50 years old, c) being able to adequately speak the Dutch language, and d) not being severely cognitively impaired (measured with the six-item screener, a short version of the Mini Mental State Examination).[21] Eligibility criteria for the Australian sample were: a) being a client of a low vision rehabilitation centre in Australia, b) being ≥50 years old, c) living independently in the community, d) English speaking, e)

having adequate hearing to respond to normal conversation, and e) not being cognitively impaired (assessed with the six-item cognitive impairment test).[22] In addition, patients in the Australian sample were only included if they had a score of ≥5 on the Patient Health Questionnaire (PHQ)-9, indicating minimal symptoms of depression.[23-25] There was no restriction on depression severity for eligibility in the Dutch/Belgian sample.

Measures

Depression
The main outcome measure was subthreshold depression. In the Dutch/Belgian sample this was measured with the Centre for Epidemiologic Studies Depression scale (CES-D). The CES-D consists of 20-items, based on a 4-point Likert scale, ranging from 0 (rarely or none of the time) to 3 (most or almost all the time). The total score ranges from 0-60, with a cut-off score for subthreshold depression of ≥16.[26,27] In the Australian sample the PHQ-9 was used to measure subthreshold depression. The PHQ-9 is based on 9 questions on a 4-point Likert scale, ranging from 0 (not at all) to 3 (nearly every day). Total scores range from 0-27, with a cut-off score of ≥10 indicating subthreshold depression.[23-25] Both scales have been widely used and are considered valid and reliable instruments to measure depression in older adults with visual impairment. In several studies the CES-D and PHQ-9 have been compared; showing that both cut-off scores reliably measure the same underlying construct (i.e. subthreshold depression).[28,29]

Demographic, somatic and social variables
Gender, age, education, country of birth, work, living alone, somatic comorbidity, time of onset of the visual loss and the cause of vision loss were determined based on self-reports. Decimal visual acuity (Snellen) was retrieved from patient files at the low vision rehabilitation organisations and supplemented with answers that participants provided themselves (based on recent ophthalmic diagnostics). Social support was measured with one question in the Dutch/Belgian sample: 'Did family members or others offer support with tasks of everyday living that you needed because of your health problems?, and with one question in the Australian sample: 'If you needed some extra help with the tasks of everyday living would you say you have family members or friends you could count upon to help you?'

History of psychiatric disorders and received mental health services
In the Australian sample, history of psychiatric disorders and received mental health services in the past were based on self-report. In the Dutch/Belgian sample history of major depressive disorder, dysthymic disorder and/or panic disorder were diagnosed with the Mini International Neuropsychiatric Interview (MINI Plus 5.0.0. developed in clinician-rated format). The MINI is a brief diagnostic interview, which is considered a valid and reliable tool to define mental disorders according to the diagnostic and statistical manual of mental disorders (DSM)-IV based on telephone interviews in research and clinical practice.[30] Received mental health services were determined with the Perceived Need for Care Questionnaire (PNCQ), which showed acceptable reliability, validity and feasibility.[31]

Perceived health status
The Euroqol-5 Dimensions (EQ-5D) was used to determine perceived health status based on: mobility, self-care, activities of daily living, pain/discomfort and anxiety/depression. The health states defined by the EQ-5D responses were translated into EQ-5D utilities using Dutch[32] and New Zealand[33,34] value sets that have been derived from large population-based surveys, on a scale with 1 for full health and 0 for death (range -0.33 to 1, where negative values are valued as worse than death).

Acceptance of vision loss
The Adaptation to Vision Loss (AVL)-12 questionnaire was used in the Dutch/Belgian sample. This questionnaire measures psychological adaptation to vision loss, encompassing intrapersonal acceptance of vision loss and attitudes toward relationships with others (interpersonal acceptance).[35] It contains 12 questions on a 4-point Likert scale, ranging from 0 (strongly disagree) to 3 (strongly agree).[35,36] Higher scores relate to better acceptance. In the Australian sample the acceptance subscale of the Illness Cognition Questionnaire (ICQ) was used, containing 6 questions to measure acceptance of vision loss scored on a 4-point Likert scale, ranging from 1 (not at all) to 4 (completely agree).[37,38] Higher scores indicate greater use of acceptance (acknowledgement of one's visual impairment and perceived ability to manage its negative consequences) to cognitively assign meaning to one's vision loss e.g. "I have learned to live with my illness".

Vision-related quality of life
The Low Vision Quality of Life Questionnaire (LVQOL) was used in the Dutch/Belgian sample to measure vision-related quality of life.[39,40] The LVQOL comprises 21 items rated on a 6-point Likert scale, ranging from 1 (none) to 6 (great). Higher scores relate to better quality of life. The Vision and Quality of Life Index (VisQol) was used to measure vision-related quality of life in the Australian sample.[41,42] The VisQoL contains six items rated on either a 5- or 6-point Likert scale ranging from 'no effect' to 'unable to do', with some items having a non-applicable option which was treated as missing data. Scores for the LVQOL and the VisQoL were reversed so that higher scores relate to better vision-related quality of life.

Psychometric assessment of the outcome measures
Rasch analyses on the AVL-12, ICQ, the LVQOL and the VisQoL questionnaires were performed to ensure that these scales had satisfactory psychometric properties and to convert ordinal ratings of the questionnaires to estimates of interval measures (expressed in logits). Rasch analysis was performed with Winsteps software (version 3.81; Chicago, IL, USA)[43] using the Andrich single rating scale model.[44] The Acceptance subscale of the ICQ demonstrated excellent fit to the Rasch model, with good scale precision (2.96) and targeting (0.90), and no evidence of multidimensionality, misfit or differential item functioning (DIF). To optimize the AVL, we deleted items 8 'although the circumstances of my life have been changed, I am still the same person I was before my visual impairment' and 12 'it is better for persons with vision problems to let other people do things for them' due to misfit. Following this, most fit statistics were satisfactory, although scale precision remained just under the 2.0 cut-off (1.86). We collapsed categories for items 2, 4 and 6 to resolve disordered thresholds in the VisQoL and, while all other fit statistics were adequate, the VisQoL's precision (1.70) also remained under the optimal cut-off. For the LVQOL, we collapsed categories from 6 to 4 to resolve disordered thresholds. There was evidence of multidimensionality, with the reading/writing items loading substantively (i.e. items 18-21, 23, 24) and these six items were therefore removed. This also made the content of the LVQOL more comparable to the VisQol. Following this, items 11 'Understanding your visual impairment' and 22 'Finding out the time for yourself' were deleted due to misfit. Most fit parameters were satisfactory following these amendments; however, the variance explained by the measures was low (<50%), suggesting potential 'noise' in the measurement. Person measures derived from Rasch analysis ranged from negative to positive logits, with high person measures indicating higher levels of the construct (e.g. quality of life/acceptance).

Sample size estimation
At least 10 events per candidate variable for the derivation of a model and at least 100 events for validation studies have been recommended.[45,46] Our sample and the number of events far exceeds all approaches for determining samples sizes and, therefore, is expected to provide robust estimates. Because there were few missing values in the predictor variables (n=26) and the outcome (n=5), analyses were performed in patients with complete data (96.6% of the study patients).

Statistical analysis

Model development and validation
First, the abovementioned 15 candidate predictor variables were selected to be tested in the model. To build the final prediction model, we used the Stata module "Global Search Regression" (GSREG) to automatically select the best-fitting model. Clinically meaningful interactions were examined and included in the model if necessary. Regression coefficients were estimated with standard logistic regression analysis, which maximizes the log-likelihood of the fit of the model to the data. Interactions between age or gender and other predictors were tested. We conducted a further test of the specification of the model using Stata's linktest command, which adds the predicted value (_hat) and the predicted value squared (_hatsq) to the model.

Assessment of model performance
Nagelkerke R^2 was used to characterize the degree of variation in risk explained by the model. The Brier score was used as an overall performance measure to calculate the disagreement between expected rates and the binary variable. A Brier score of 0 indicates a perfect model, while 0.25 indicates a non-informative model. The Brier score is easier to interpret with the "scaled version" which compensates for the difference in maximum Brier scores between the two samples (Brierscaled = 1 – Brier / Briermax, where Briermax = mean(p)*(1 – mean(p)), to allow a range between 0% and 100%). The scaled Brier score is comparable to Pearson's R^2 statistic. In addition, we assessed the predictive performance of the model by examining measures of calibration and discrimination. Performance measures included the average area under the ROC curve (AUC), sensitivity and specificity for depression. We constructed a calibration plot to examine the agreement between the predicted probabilities of the prediction model with the observed depression. The Hosmer-Lemeshow test was used to indicate the difference between predicted and measured outcomes in the derived model.

For the internal validation of the model bootstrapping (1000 replications) and a 10-fold cross-validation method was used, which involves randomly splitting the data into 10 equally sized groups (Dutch/Belgian sample). The model is developed in 9 of the 10 groups, and its performance evaluated in the remaining group; this entire process is repeated 10 times so that each of the 10 groups is used to test the model. The performance of the model is taken as the average over the 10 iterations. For internal validation of the final model, also bootstrapping was used: the difference in predictive abilities of a model fitted to each bootstrap sample and the original model was calculated to determine an estimate of optimism. Subsequently, this estimate was subtracted off the naive estimate of predictive ability in the original dataset, leading to optimism corrected R^2, Brier score, AUC, calibration plot and Hosmer-Lemeshow test. After the process of internal validation, the regression coefficients in the model were corrected for optimism with the heuristic shrinkage estimator γ of van Houwelingen and le Cessie. This way it is expected that the model would best withhold in future studies with similar settings and patients. In addition, we conducted the external validation for our modified original model in the Australian cohort. We assessed the predictive performance by examining the same measures of calibration and discrimination used for the internal validation of our model. All tests were two-sided, with P<0.05 considered to indicate statistical significance. Statistical analyses were performed with Stata/SE software, version 13.1 (StataCorp LP). Finally, a nomogram of the risk factors was constructed to provide a user-friendly graphical representation of the results, in which the prediction model would be reduced to a single numerical estimate of the probability of having subthreshold depression tailored to the profile of an individual patient.

Results

Patient characteristics
Female gender was dominant in both samples (60.6% in Dutch/Belgian and 65.3% in Australian sample) and mean age was slightly higher in the Dutch/Belgian sample (73.4 years vs. 69.6 years). Participants in the Australian sample were less often born in the country that they now live in and more often had diabetic retinopathy than the Dutch/Belgian sample in which cataract was more prevalent. Due to differences in inclusion criteria, participants in the Australian sample were significantly more likely to have experienced subthreshold depression. In addition, they had a lower perceived health status, lower acceptance of vision loss and lower vision-specific quality of life (Table 1).

TABLE 1. Patient characteristics in the European (***n***=899) and Australian sample (***n***=124)

Patient characteristics	**European**	**Australian**	
Categorical variables	n (%)	n (%)	P
Subthreshold depression	317 (35)	83 (67)	<0.001
Female gender	545 (61)	81 (65)	0.314
Education			
None or primary school	155 (19)	12 (10)	
Secondary school	506 (60)	81 (65)	0.050
Higher education or University	178 (21)	31 (25)	
Born in country that participants now live in	859 (96)	81 (65)	<0.001
Somatic comorbidity	549 (61)	104 (84)	<0.001
History of psychiatric disorder(s)	172 (19)	48 (39)	<0.001
Received mental health services in the past	381 (42)	51 (41)	0.791
Cause of visual impairment (multiple options possible)			
Macular degeneration	410 (46)	46 (37)	0.074
Glaucoma	139 (16)	19 (15)	0.968
Cataract	129 (14)	4 (3)	<0.001
Diabetic retinopathy	36 (4)	23 (19)	0.001
Other	371 (41)	57 (46)	<0.001
Having work	87 (10)	8 (6)	0.212
Live alone	418 (47)	47 (38)	0.072
Social support	252 (28)	109 (88)	<0.001
Continuous variables	Mean (SD)	Mean (SD)	P
Age in years	73.4 (12.1)	69.6 (11.5)	0.001
Perceived health status	0.73 (0.25)	0.59 (0.19)	<0.001
Time of onset of visual loss in years§	8.0 [3.0 - 20.0]	10.0 [4.0 - 25.0]	0.092
Person measures of acceptance of vision loss *	0.37 (1.16)	-0.12 (3.07)	0.001
Person measures of vision-specific quality of life†	1.04 (1.21)	0.34 (1.51)	<0.001

Means, standard deviation (*SD*) and range are reported for continuous variables, median and 25-75% percentiles are provided when the variable has an asymmetric distribution (§).

* Measured with the Adaptation to Vision Loss (AVL) questionnaire in the Dutch/Belgian sample and the Illness cognition Questionnaire (ICQ) in the Australian sample.

† Measured with the Low Vision Quality Of Life (LVQOL) questionnaire in the Dutch/Belgian sample and with the Vision and Quality of Life Index (VisQol) questionnaire in the Australian sample.

Derived prediction model in the Dutch and Belgian sample

Our derived model contained seven predictors: age, gender, living alone, history of psychiatric disorder, received mental health services in the past, perceived health status, and acceptance of vision loss (Table 2). The linktest output showed an insignificant value for _hatsq (*P*=0.856), so the hypothesis was rejected that variables were omitted, indicating that the model is not misspecified. The derived multivariable prediction model explained 35.2% of total variance of depression (Nagelkerke's R^2). The Brier score was 0.164 and the Hosmer-Lemeshow test indicated no statistically significant difference between predicted and measured outcomes (*P*=0.974) in the derived model. The AUC was 0.805 (95 CI: 0.775, 0.835, Table 3, Figure 1A).

After internal validation (based on bootstrapping) the model more accurately detected depression. Model validation resulted from the 10 cross-validation samples for depression was similar to the AUC calculated using the whole sample (AUC, 0.798, 95% CI: 0.767, 0.828). The calibration plot showed good agreement between observed and predicted probabilities (Figure 2A-2B). According to the le Cessie–van Houwelingen test, the model displayed adequate fit. The shrinkage estimator γ, where p is the number of regression parameters and the model χ^2 is the total likelihood ratio statistic computed using the full set of p parameters, was (199.27-11)/199.27) ≈0.9727. This indicates that 2.73% was fit due to noise. We used this shrinkage factor to correct the regression coefficients for over-optimism (Table 2). Model performance in the external test cohort was good, with 54% of total variance of depression explained by the model (Nagelkerke's R^2), a Brier score of 0.17, a Hosmer-Lemeshow test indicating a statistically significant difference between predicted and measured outcomes (*P*<0.001) and an AUC of 0.882 (95% CI: 0.822, 0.941, Table 3, Figure 1B).

The nomogram presented in Figure 3 maps the predicted probabilities into points on a scale from 0 to 10 in a graphical interface. The predicted probability for a patient to have subthreshold depression is accumulated by the total points that the various covariates correspond to. For example: a women (+1.1 points) of 60 years old (+7.2 points), who lives alone (+1.3 points), has a history of depression (+2.1 points), a perceived health status of 0.4 (+4 points) and a person measure of acceptance of vision loss of 1 (+ 2 points), will have a total score of 17.7, corresponding to a probability of 45% of having subthreshold depression.

TABLE 2. Final model estimates for subthreshold depression in European sample (*n*=873)

	Multivariable logistic regression*		Multivariable logistic regression§		Recalibration of the linear predictor**
	β (95% CI)	*p*	$\beta_{bootstrapping}$ *(95% CI)*	*P*	$\beta_{recalibration}$ *(95% CI)*
Age	-0.0271 (-0.0426, -0.0116)	0.001	-0.0271 (-0.0423, -0.0119)	<0.001	-0.02636 (-0.0415, -0.01157)
Gender (female)	0.3378 (0.0234, 0.7322)	0.037	0.3778 (0.0079, 0.7477)	0.045	0.3675 (0.0077, 0.7273)
Live alone	0.4437 (0.0845, 0.8030)	0.015	0.4437 (0.0604, 0.8271)	0.023	0.4316 (0.05875, 0.8045)
History of psychiatric disorder	0.7131 (0.2958, 1.1304)	0.001	0.7131 (0.3908, 1.1354)	0.001	0.6936 (0.3801, 1.1044)
Received mental health services in the past	0.3500 (0.0147, 0.6854)	0.041	0.3500 (0.0029, 0.6972)	0.048	0.3404 (0.0028, 0.6782)
Perceived health status	-3.7899 (-4.4741, -3.1056)	<0.001	-3.0557 (-3.8220, -2.2895)	<0.001	-2.9723 (-3.7177, -2.2270)
Acceptance of vision loss	-0.6810 (-0.8703, -0.4917)	<0.001	-0.6810 (-0.8985, -0.4634)	<0.001	-0.6624 (-0.8740, -0.4507)

*: Model adjusted for age, gender, live alone, history of psychiatric disorder, received mental health services in the past, perceived health status, and acceptance of vision loss.
§: Internal validation of performance was estimated with bootstrapping (1000 replications).
**: The heuristic shrinkage estimator γ of van Houwelingen and le Cessie: where p is the number of regression parameters and the model χ^2 is the total likelihood ratio statistic computed using the full set of p parameters. In our model, γ was equal to γ= (199.27-11)/199.27) ≈0.9727. $\beta_{recalibration}$=0.9727× $\beta_{bootstrapping}$. 2.73% of fit due to noise.

TABLE 3. Performance of the prediction model for depression

Performance measure	Internal validation	External validation
R^2 (Nagelkerke)	35%	54%
Brier	0.16	0.17
Brierscaled	0.27	0.24
AUC	0.81	0.88
Calibration intercept	-0.001	1.570
Calibration slope	1.007	0.880
Hosmer Lemeshow test	χ^2=2.21 *P*=0.974	χ^2=66.37 *P*<0.001

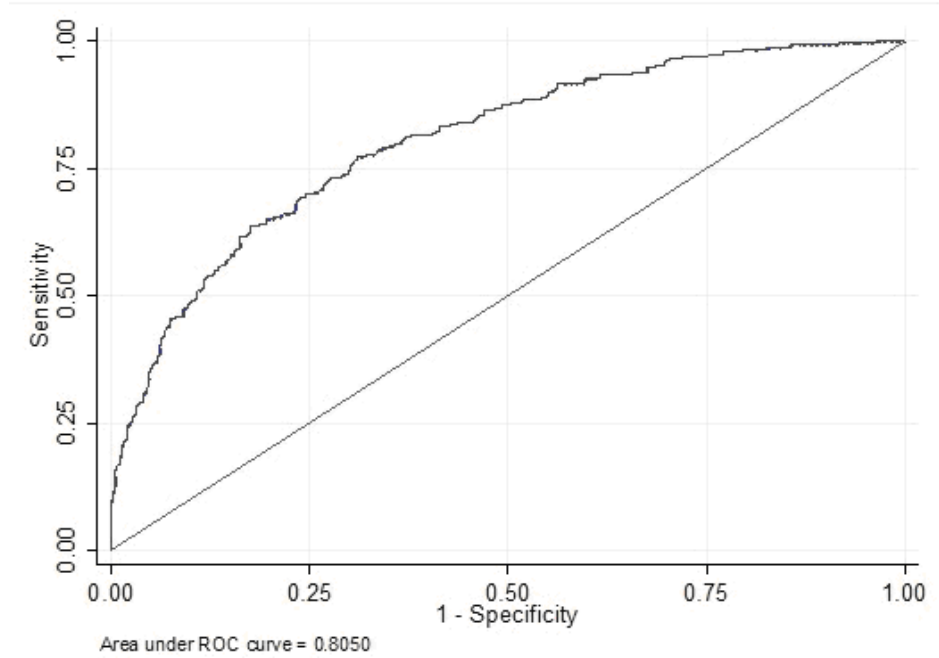

FIGURE 1A. Receiver operating characteristic (ROC) curve for the subthreshold depression prediction model in the European dataset (*n*=873)

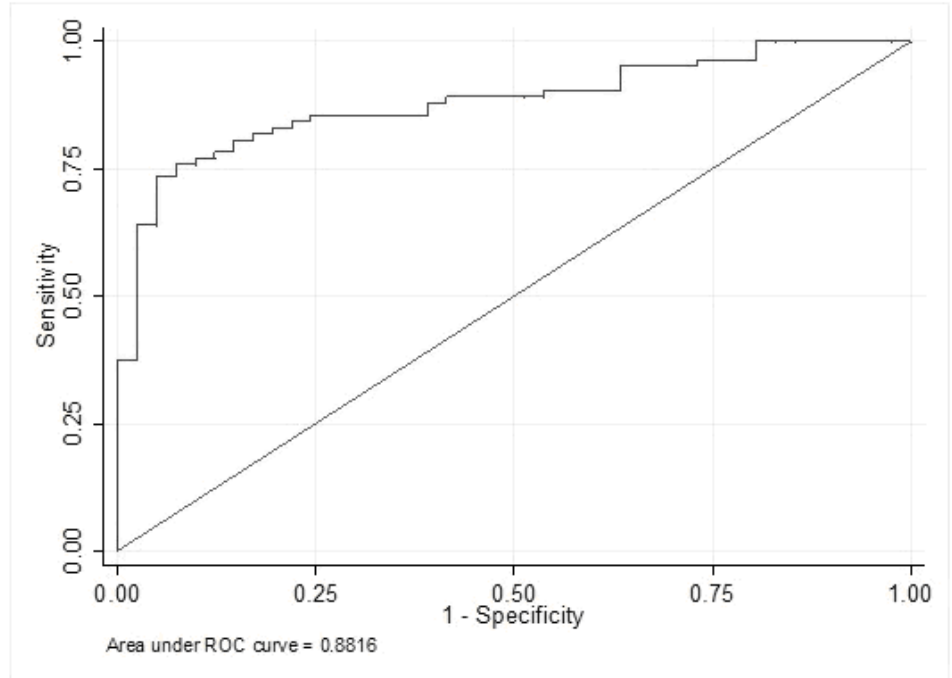

FIGURE 1B. Receiver operating characteristic (ROC) curve for the subthreshold depression prediction model in the Australian dataset (*n*=124)

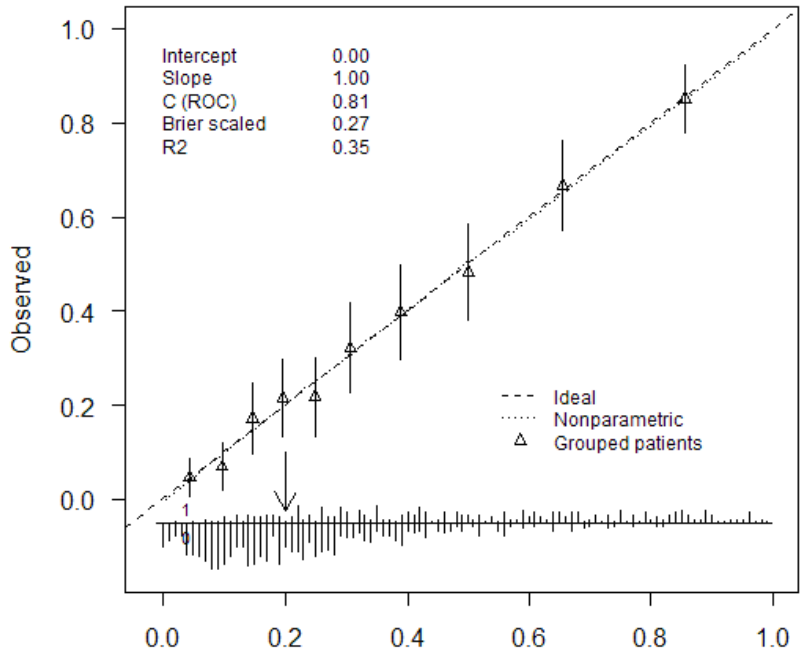

FIGURE 2A. Calibration plot for the subthreshold depression prediction model in the European dataset (*n*=873) at internal validation

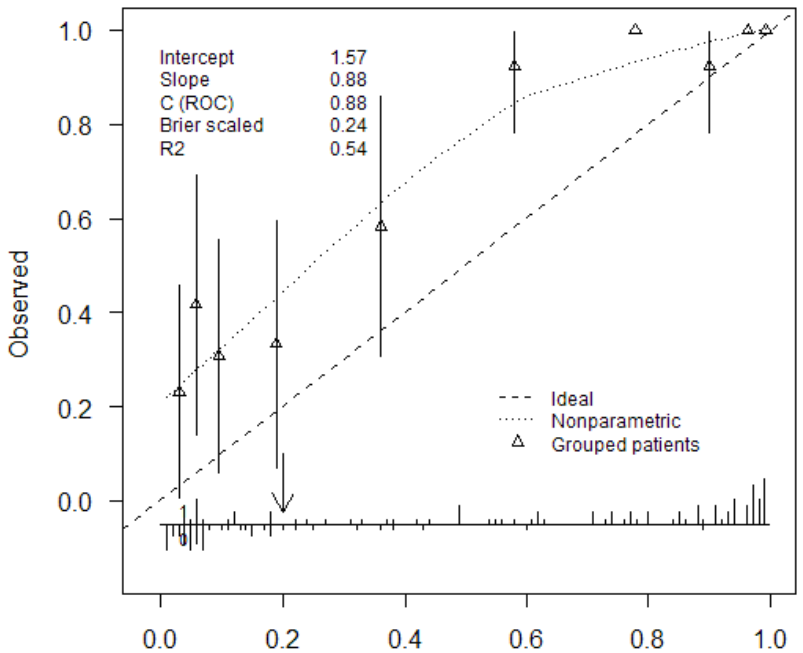

FIGURE 2B. Calibration plot for the subthreshold depression prediction model in the Australian dataset (n=124) at external validation

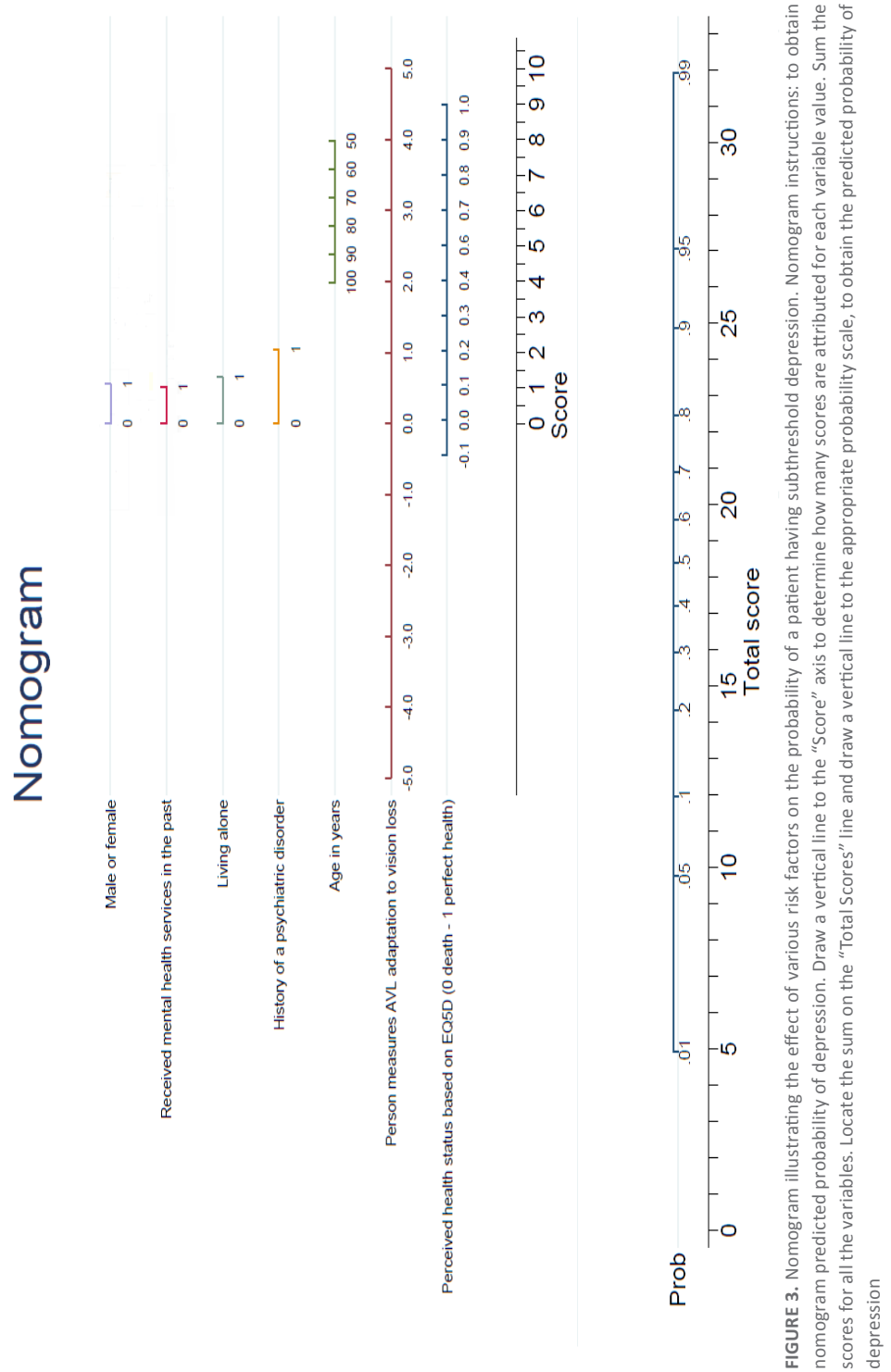

FIGURE 3. Nomogram illustrating the effect of various risk factors on the probability of a patient having subthreshold depression. Nomogram instructions: to obtain nomogram predicted probability of depression. Draw a vertical line to the "Score" axis to determine how many scores are attributed for each variable value. Sum the scores for all the variables. Locate the sum on the "Total Scores" line and draw a vertical line to the appropriate probability scale, to obtain the predicted probability of depression

Discussion

This study determined a prediction model of subthreshold depression in visually impaired older adults living on two different continents by using a variety of demographic, somatic, social and psychological factors. Younger age, female gender, living alone, history of a psychiatric disorder, use of mental health services in the past, lower perceived health status and lower acceptance of vision loss were associated with a higher risk of having subthreshold depression in this population. The explained variance of the prediction model was 35%, demonstrating that the prognostic factors explain a reasonable fraction of the variance between individual patients. This is comparable to the explained variances found in other studies that investigated factors related to depression in people with visual impairment (range 20 to 41%).[11-15] With respect to calibration, the AUC was satisfactory: above 0.80 in both samples. This means that the predicted and observed probabilities are well in agreement, suggesting that the prediction model is accurate enough to use in clinical practice.

Most of the predictors are comparable to those found in community subjects[4,47] and subjects with other chronic disabilities.[48-50] Female gender, living alone, history of a psychiatric disorder and previous use of mental health services (in line with the recurrent nature of depression) have been found as predictors of depression in various populations.[47-50] Only the predictor younger age was not comparable to other studies, which may be caused by the disruptive influence of visual impairment at a relatively younger age when people are still engaged in work or other activities or responsibilities such as parenting. In addition, we found that it is not the severity of the disability which is critical for mental health in visually impaired people, but rather the individual's psychological response to this situation. Acceptance of vision loss explained a large part of the variance of having subthreshold depression in older adults with visual impairment. Interventions, therefore, need to focus on acceptance of vision loss as an initial strategy to address depression.

Strengths and limitations

This study included a comprehensive assessment of a range of potential predictor variables highlighted in previous research. Outcomes were internally validated by means of bootstrap-corrected indices of discrimination and 10-fold cross-validation, which has not been performed in previous studies on depression in people with visual impairment. There are good indications that this procedure results in estimates that can also be expected in future patients. Furthermore, the current study is the first to externally validate a prediction model of depression in a similar visually impaired population from a different continent, which we believe increases generalisability. Together with the relatively high explained variance, this suggests that the prediction model could be confidently used in practice to guide treatment decisions. Another strength of our study was the use of Rasch analysis to ensure psychometric properties of outcome measures prior to analysis.

A limitation of our study is, firstly, the use of different questionnaires for similar (latent) constructs, which may have confounded our results and complicates the use of our nomogram. Secondly, to increase clinical relevance, a threshold was used to determine depression instead of a continuous scale, which may have led to loss of information and reduction of power. Thirdly, questions on visual functioning, adjustment and social and emotional well-being were combined in an overall vision-related quality of life score, which may have caused us to overlook the specific influence of visual functioning on depression, which has been reported by others.[15,17,18] Finally, outcomes may not be generalizable to less industrialized nations and causality cannot be inferred based on the cross-sectional data. Future studies are necessary to determine if these factors actually lead to change in depression over time.

In addition, people in the Australian sample were only included if they had minimal symptoms of depression while there was no restriction on depression severity for eligibility in the European sample. Therefore, people in the Australian sample were significantly more likely to have subthreshold depression, somatic comorbidity and a history of psychiatric disorders. This lead to more homogeneity and less variability in the outcomes in the Australian sample, which may have increased difficulty to confirm our (internally validated) model in the Australian sample. Still, the quality of the model was maintained based on the external validation, which only adds to the quality of the prediction model that we found in the current study.

Implications for practice

Prediction tools are as generalizable as the sample from which they are derived. In this way, we believe that our model is unique, because we validated our model in a European and Australian sample, which may well be closer to real world practice than previous studies limited to single-region populations. As such, we believe that professionals will find greater confidence in its applicability. Our model could provide clinical practice with a tool to predict subthreshold depression in older adults with visual impairment. However, the use of different questionnaires to measure perceived health status and acceptance of vision loss (for which we used Rasched person measures) complicates the use of our nomogram. The model indicates that patients who are (relatively) younger, women, have a history of mental health problems, live alone, have poorer health and lower acceptance of their vision loss should be more carefully watched and screened for depression. Moreover, early intervention programmes could target acceptance of visual impairment as an initial strategy to prevent or reduce depression in older adults with visual impairment.

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