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Risk prediction models for depression in community-dwelling older adults

Running title: Risk prediction models of late-life depression

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Abstract (246 w)

Objectives: to develop streamlined Risk Prediction Models (*Manto* RPMs) for late-life depression.

Design: Prospective study.

Setting: the Survey of Health, Ageing and Retirement in Europe (SHARE) study.

Participants: Participants were community residing adults aged 55 years or older.

Measurements: The outcome was presence of depression at a two-year follow up evaluation. Risk factors were identified after a literature review of longitudinal studies. Separate RPMs were developed in the 29,116 participants who were not depressed at baseline and in the combined sample of 39,439 of non-depressed and depressed subjects. Models derived from the combined sample were used to develop a web-based risk calculator.

Results: We identified 129 predictors of late-life depression after reviewing 227 studies. In non-depressed participants at baseline, the RPMs based on regression and LASSO penalty (34 and 58 predictors, respectively) and the RPM based on Artificial Neural Networks (124 predictors) had a similar performance (AUC: 0.730 – 0.743). In the combined depressed and non-depressed participants at baseline, the RPM based on neural networks (35 predictors; AUC: 0.807; 95% CI: 0.80 - 0.82) and the model based on linear regression and LASSO penalty (32 predictors; AUC: 0.81; 95% CI: 0.79 - 0.82) had satisfactory accuracy.

Conclusions: The *Manto* RPMs can identify community-dwelling older individuals at risk for developing depression over two years. A web-based calculator based on the streamlined *Manto* model is freely available for use by individuals, clinicians, and policy makers and may be used to target prevention interventions at the individual and the population levels.

Keywords: late-life depression; older adults; risk prediction; risk factor; physical illness

1. Introduction

Late-life depression remains largely under-recognized and undertreated, despite its negative impact on individuals and on society [1,2]. Knowledge of risk factors might improve recognition of depression and help the development and targeting of prevention strategies.

Risk factors for late-life depression are many and diverse. Late-life depression is caused by an interplay of heterogeneous dysfunctions affecting the individual's homeostasis across biological, psychological, and social domains [3–5]. One or more factors predisposing to depression may lead to a depressive episode when they cross a threshold or when a precipitating event occurs. Chronic medical illnesses [3,6,7], accumulation of micro-cerebrovascular damage [8], chronic subclinical inflammation impairing the brain's functional connectivity [9–11] and social isolation [12] confer vulnerability to depression. In predisposed individuals, a depressive episode may erupt after a major adverse event or when changes of the social milieu lead to changes in sleep or to social withdrawal [13–15]. Prospective studies have identified various risk factors for depression. [4,7,16] Some risk prediction models (RPMs) have been developed that estimate the probability that an individual will develop a clinical outcome in the future based on the presence of risk factors [17]. RPMs may help clinicians and policy makers to develop prevention strategies targeting individuals at risk [5,18–22] and to improve both patient outcomes and the cost-effectiveness of care.

Only few studies have attempted to develop prediction models for late-life depression all using small sets of risk factors, including demographic characteristics, health-related factors, disability and individual depressive symptoms [18,23,24]. Previous models were based on samples consisting of both depressed and non-depressed participants; this sample selection allows to assess risk prediction without requiring information on the presence of depression. However, it may overestimate the relevance of depressive symptoms as predictors of risk, since depressive symptoms may be indices of vulnerability to depression [25].

Extending our previous study [18] and others, [23,24] the present study uses an extensive set of literature-informed predictors, an information-rich, large database of community residing older

adults followed for 2 years, and multiple methods to develop and validate the *Manto*[*] RPMs for late-life depression. Our primary aim has been to obtain a model that estimates the risk of developing depression among older adults who are not depressed at the time of risk assessment. In addition, we developed streamlined models from a larger sample that included both depressed and non-depressed individuals so that they can be compared with models of earlier studies and used by both depressed and non-depressed individuals through an open-access web-based calculator.

2. Methods

This study followed the TRIPOD tool for transparent reporting of multivariable prediction models [26].

2.1 Identification and selection of predictors for model development

We conducted a literature review to narrow the number of SHARE variables introduced in our prediction models (Supplementary Methods, par. 1.2). The review included longitudinal studies of community-dwelling participants older than 50 years, examining the association between predictors and depression over a follow-up of at least six months. To include a predictor in the RPM, it had to be: (i) prospectively associated with depression; (ii) assessed with simple questions that respondents could answer and not requiring instrumental or laboratory measures, as judged by consensus between M.B.M. and F.T.; and (iii) included in the Survey of Health, Ageing and Retirement in Europe (SHARE) database.

2.2 Study design, setting, and study population

[*] The name *Manto* of our RPMs is derived from Greek mythology. Manto (Greek: Μαντώ) was a sibyl oracle, daughter of the Theban blind oracle Tiresias. After the sack of Thebes, she fled, founded the Italian city of Mantua, and created the Mantua lake with her tears. Most of her prophesies were about misfortunes.

In constructing the Manto RPMs, we used a large number of demographic, health, and psychosocial risk variables from the SHARE Study. The selection of SHARE variables was guided by a review of risk factors of depression [27]. SHARE collected information on a wide range of factors from community-dwelling Europeans aged 50 years or older [27]. Our study used predictor data from wave 5 (collected in 2013), consisting of baseline and retrospective information, and outcome data from wave 6 (collected in 2015). Eligibility criteria for this study were age older than 55 years at wave 5 and availability of data on depression at wave 6, obtained 2 years after wave 5. We included individuals in midlife (55+) because it is the time in which some adults experience stress by the nearing transition to retirement and also the time in which health problems begin to emerge.

The SHARE study had been approved by the Ethics Council of the Max Planck Society and by each country's ethics committees. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, revised in 2008.

2.3 Outcome definition

Depression was assessed with the EURO-D, [28] which rates the presence or absence of 12 depressive symptoms (depressed mood, pessimism, death wishes, guilt, sleep problems, loss of interest, irritability, loss of appetite, fatigue, concentration difficulties, lack of enjoyment, and tearfulness). The EURO-D has sound psychometric properties documented in previous studies [28,29]. The total score ranges from 0 to 12; a score of 4 or higher indicates the presence of major depression. This criterion has been validated with interview-based assessments [28].

2.4 Data analysis

First, analyses were conducted in participants without a diagnosis of depression at baseline (EURO-D score < 4) to identify risk factors unrelated to depressive symptoms. Then, analyses

were repeated on the combined sample of depressed and non-depressed subjects to build a streamlined web-based depression risk calculator for use by the public. Analyses on the combined sample were based on the assumption that users of the risk calculator may not know their depression status. For each population, we developed one model employing the Artificial Neural Network (ANN) and two models employing Logistic Regression (LR). ANN are prediction algorithms that allow complex nonlinear relationships between the response variable and its predictors. These ANN models were based on multilayer perceptrons with fully connected layers of neurons. The ANN of the non-depressed sample aimed to maximize the accuracy of prediction by using all available information on risk factors. The ANN of the combined sample was used to develop the web risk calculator, which is intended for use by the public. For this reason, we limited the questions to a number likely to be answered by users and achieve an optimal trade-off between accuracy and number of predictor variables.

LR models employed the Least Absolute Shrinkage and Selection Operator (LASSO) penalty [30], a variable selection method that removes variables with a weak association with the model's outcome. In each set of analyses, we developed two LR models by varying the level of required information. The first logistic models (full-LR) select predictors by choosing the penalty parameter that minimizes the Mean Squared Error (MSE). The second logistic model (lean-LR) imposed an additional restriction on the maximum number of predictors. This optimal trade-off was established based on the examination of validation curves which display the relationship between the number of predictors and model performance. In the LR models, missing data on continuous variables were imputed by the median value because some variables had skewed distributions, while on categorical predictors a "missing data" additional category was used.

All models were validated with a k-fold cross-validation (CV). The models' predictive accuracy was evaluated with the Area Under the Receiver Operating Characteristic curve (AUC-ROC for model discriminative accuracy) and with the Mean Squared Error (MSE, equivalent to the Brier score). We report the optimal values of Sensitivity, Specificity, Positive Predictive Value

(PPV) Negative Predictive Value (NPV) , as well as calibration data and curves to describe the agreement between the estimated and observed number of events *at each threshold of risk* [31]. Calibration is particularly relevant to examining whether a model under- or overestimates risk among specific ranges of risk scores.

Finally, the performance of models built on the total sample were compared with that of previous RPMs on late-life depression, [18,23,24] conducted on samples consisting of depressed and non-depressed individuals.

3. Results

3.1 Identification and selection of predictors

Literature review was conducted on June the 1st, 2019 and identified 209 prospective studies and 18 meta-analyses assessing the prospective association of sociodemographic and clinical risk factors with late-life depression (Figure S1). This review enabled us to identify 71 distinct types of risk factors, 19 within the sociodemographic domain, 21 within the psychological domain, and 31 within the physical domain (Table S2). We matched risk factors identified from literature with available data on individual variables from the SHARE study (Table S3), excluding risk factors that could not be translated into questions (n=2), predictors that were not measured by the SHARE study (n=21), and variables with many missing data (n=3). Ten predictors with missing data above the pre-defined threshold were retained because of their clinical relevance. In the end, 129 variables remained available for model development, of which 107 had less than 3% of missing data.

3.2 Sample characteristics

There were 66,188 eligible participants in wave 5 of the SHARE study. Of these, 57,444 participants were aged 55 years or older and 39,439 participants had depression data at wave 6. A EURO-D score of 4 or higher was identified in 9,848 participants, indicating the presence of

major depression. Of the 29,116 participants without major depression (EURO-D < 4) at baseline (Figure S2), 51.5% were female, with a mean age of 67 years (Table 1, Figure S3 and Table S4).

In the combined sample at wave 5, 24.6% (9,688/39,439) of participants had depression. Those with depression symptoms at baseline were more likely to have depression during follow up (Figure S4). Among those who had depression at follow-up (wave 6), 54.9% (5,433/9,904) had been already depressed at baseline, 45.1% (4,471/9,904) had not been depressed.

3.3 RPMs among non-depressed participants at baseline

In non-depressed participants (N=29,116), the three RPM models had similar predictive accuracy (all values of AUC-ROC above 0.73, Table 2) despite large differences in the number of retained predictors. Specifically, the ANN model selected 124 predictors and the full-LR model selected 58. We plotted validation curves of the relationship between regression model complexity and performance (Figure S5). The performance of complex models with over 100 predictors was only slightly worse than its peak value. Overall, retaining 20 to 40 predictors was associated with steep improvement in model performance. Thus, we limited the number of predictors of the lean-LR model to 35, and 34 were retained. All models yielded satisfactory specificity. Despite similar discrimination profiles, however, the ANN and the full-LR model had a marginally better calibration than the lean-LR model (Table 2 and Figure 1, right panel). Thus, the full-LR model may be considered the best trade-off between the level of required information and prediction performance (Tables S5 – S7).

All models included the following predictors (Table 3, Tables S8 and S9): Age, sex, low participation in activities, depressive symptoms, use of medications for anxiety or depression, loneliness, low quality of life, negative views on aging, lack of vitality, low optimism, poor perceived physical health, many medical consultations, and use of painkillers and hypnotics. The full-LR model included additional information on socioeconomic variables, a broad range of

depressive symptoms and views on aging, predictors related to medical health and unhealthy lifestyle.

3.4 RPMs in the combined sample of depressed and non-depressed participants at baseline

We repeated analyses in the combined sample (N=39,439) to develop RPMs for use by the public. We imposed a maximum number of 35 predictors in the ANN model, while the full-LR model retained 70 predictors. Based on validation curves, the number of predictors in the lean-LR model was limited to 35, of which 32 were retained (Table S10). The three models yielded similar levels of accuracy despite different RPM methodology and number of predictors. Performance was better in the combined sample of depressed and non-depressed participants at baseline than in non-depressed participants at baseline (all values of AUC-ROC above 0.80, Table 2). All models had satisfactory calibration profiles; the ANN and the full-LR models had only a slight advantage over the lean-LR at high values of observed risk (Figure S6; Tables S11 – S13). Nonetheless, the lean-LR model was chosen because of its brevity and the ease of interpretation lend it best for clinical use. Applying a risk threshold of 20%, the lean-LR model maintained a high level of sensitivity (84%) and NPV (91.5%) but a lower PPV (41.3%) and is suitable for depression screening by clinicians who can ascertain the presence of depression through clinical examination. In contrast, a high-risk threshold of 55% would yield a more balanced trade-off between positive predictive value (74%) and negative predictive value (79.4%) and may be informative to individual users.

Predictors in the lean-LR model included sex, age, not reading books or newspapers, absence of activities in the previous year, depressive symptoms, loneliness, poor quality of life, negative views on aging, lack of vitality and optimism, difficulty in activities of daily living, dizziness, pain, and fatigue (Table S10, S14, S15).

3.5 Comparison with previous models

The newly developed models had better discrimination and calibration profiles (AUC 0.66) than the DRAT-up (AUC 0.74) [18] and the Okamoto-Harasawa (AUC: 0.657) models [24]. DRAT-up significantly underestimated the risk of depression in the high-risk strata (Figure S6, Table S16 – S17). The models of Xu et al. could not be reproduced due to lack of data on network parameters [23]. Our models used information on individual depressive symptoms. Our symptom-based models were superior to a model, in which prediction was based on information on categorical information on depression (present/absent) at baseline, which resulted in a sensitivity of 55% and specificity of 85% (AUC 0.701, Table S16).

4. Discussion

We developed *Manto,* a set of risk prediction models (RPMs), and showed that they have satisfactory accuracy in predicting the development of major depression in non-depressed, community residing older adults over a period of two years. The prediction performance of *Manto* RPMs is even stronger in the combined sample of both depressed and non-depressed individuals at baseline. Manto is available as a web-based risk calculator for clinicians and individuals.

The *Manto* RPMs and the online calculator we developed (https://manto.unife.it/) may be used by individuals, clinicians, and policy makers to identify older persons at risk for depression. Our web-based risk calculator is freely available and is based on information that can be obtained during the time frame of a routine medical visit (about 15 minutes) [32]. It uses predictors from the lean-LR model of the combined sample to estimate the probability of being at high risk for depression in the next two years, expressed as a percentage. Depression is best managed by shared decision-making [33]. The risk calculator may contribute to this process by offering to users a continuous estimate of risk that may aid individuals and their health care provider in clinical decision making. We did not study the relationship of Manto prediction scores to treatment and prevention interventions and, thus, cannot provide risk cut-off points for clinical decisions. The relationship of risk scores to clinical action depends on the healthcare context and on the availability of cost-

effective preventive interventions [33–35]. For instance, a high-risk score (e.g. above 50 - 60%) may yield the best trade-off between positive and negative predictive values and aid individual users in the decision to seek clinical evaluation. In contrast, a low risk score (e.g. 20%) may guide large scale screening initiatives that require higher sensitivity. The role of Manto needs to be further studied in specific clinical and community contexts.

Many of the identified predictors of late-life depression are modifiable and may inform the selection and targeting of prevention interventions. Among non-depressed individuals at baseline, the full-LR model identified paucity of leisure and intellectual activities, scarcity of social activities, poor physical health, unhealthy lifestyle, depressive symptoms, and negative views on aging as significant predictors of development of depression. A subset of variables from these domains were also part of the streamlined lean-LR model, with only a small loss in accuracy, i.e. a tendency to overestimate the risk of depression at higher risk values, and to underestimate the risk at lower risk values [31]. Loss of purpose, demoralization, pessimism [15,36], perceived poor health and life satisfaction were predictors of depression, but may also be symptoms of depression or indices of vulnerability related to depression [5]. Consistent with a dynamic symptom network theory of late-life depression [4,14,37], risk factors for depression or symptoms of depression can initiate a cascade of interactions among them that may evolve into a self-sustained depressive syndrome [15]. Interventions targeting modifiable risk factors may prevent the development of a full-blown depression, but empirical studies need to examine whether and to what extent such interventions are successful.

Self-help interventions [38], vigilant follow-up, treatment of subclinical depression symptoms [14,37,39], and streamlined psychosocial interventions aimed to increase meaningful, rewarding activities [19,40–42] may be used to prevent development of depression in older adults at risk. Policy makers may use the Manto RPMs to target older populations at risk for depression and develop appropriate interventions or consider some of the available community-based interventions [43],

e.g. promotion of illness awareness, help-seeking, and self-management [1], or comprehensive interventions including the Program to Encourage Active, Rewarding Lives for Seniors (PEARLS) [44], Healthy IDEAS (Identifying Depression, Empowering Activities for Seniors) [45], SAMHSA's Promoting Emotional Health and Preventing Suicide, Tool Kit [46], and others. Providing information on depression risk in an accessible way may raise awareness among clinicians and individuals [47]. Depressed older adults often hold stigmatizing beliefs and do not recognize the need for help, or have negative views about treatment and avoid mental health care [48]. The performance of *Manto* RPMs is superior to that of DRAT-up, our earlier model for prediction of late-life depression. By relying on five selected predictors, DRAT-up had reached a fair level of accuracy (AUC: 0.74 to 0.77) but its positive and negative predictive values were low [18]. The superior performance of *Manto* RPMs is likely due to the inclusion of a larger number of prediction variables and the use of advanced methodology. Our findings are not directly comparable to the Xu et al RPM study on late-life depression, which used machine-learning but lacked cross-validation [23]. The model of Xu et al was based on twelve risk factors collected from a prospective study spanning 22 years. When it included "look-back" data that had been *collected* 12 years prior to baseline, its accuracy was somewhat higher than that of *Manto* RPM (AUC: 0.87, compared to *Manto*'s 0.80). Our study did not use information that extends back to such a long period because recall bias might limit the reliability of such information.

Our study has limitations. We were unable to find a dataset with a large number large number of predictors similar to that of SHARE that could be used for an external validation of our findings. Our model is relevant to populations of the countries participating in the SHARE Study and needs to be further tested in samples with greater social and ethnic heterogeneity. In addition, cognitive dysfunction, anxiety and neuroticism are risk factors for late-life depression [5,49]. Introducing streamlined assessments in RPMs might improve their performance. Further studies need to explore the model's clinical utility and its potential for widespread implementation. Considering the low rate of missing data, we used a simple imputation technique. It is doubtful

that the results would have changed substantially had we used multiple imputation. The RPM focused on the prediction of depression over a 2-year period. Therefore, it is unclear whether the same variables can predict the occurrence of depression over a shorter or a longer period. Finally, the data were collected prior to the COVID pandemic, which might have shifted the importance of some risk factors for late-life depression.

The study has several strengths. The selection of predictors for its RPMs was based on a review of 227 studies on the association of sociodemographic and clinical variables with late-life depression. The RPMs were tested on a database of 39,439 community residing older adults with information on 129 potential predictors of depression and a 2 year follow-up. Unlike previous investigations, [18,50] the current study employed multiple advanced methods of analyses, including Artificial Neural Networks and Regularized Regression algorithms to reach an optimal trade-off between the number of predictors and the performance of risk prediction models.

In conclusion, the *Manto* RPMs can be used to identify community-dwelling older adults at risk for developing depression over a period of two years. The risk calculator based on the *Manto* RPM may be used by older adults and by clinicians during routine medical visits to assess the risk of depression development. The Manto RPMs and the risk calculator may aid policy makers in developing and targeting prevention strategies.

Author contributions

MBM conceived the study, contributed to data analysis and wrote the manuscript. LC, FC, PP conceived the study, conducted data analysis and wrote the manuscript. FT and GA contributed to the study design and wrote the manuscript.

Conflict of interest

Prof. Alexopoulos has served on advisory boards of Janssen and Eisai and has been on the speakers' bureaus of Lundbeck, Otsuka, and Allergan. No other authors report conflicts of interest.

Data statement

The data has not been previously presented orally or by poster at scientific meetings. The data that support the findings of this study are openly available at the SHARE study website (http://www.share-project.org/), specifically at http://doi.org/10.6103/SHARE.w5.710 and http://doi.org/10.6103/SHARE.w6.710.

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Table 1. Total sample characteristics

	Not depressed at baseline (N = 29,116)	Depressed and Non-Depressed at baseline (N= 39,439)
Age, mean (SD), y	67.0 (8.3)	67.9 (8.6)
Female sex, No. (%)	14,897 (51.2)	22,028 (55.9)
Education, median (IQR), y	12 (9 – 14)	12 (8 - 14)
Current job situation, No. (%)		
Retired	18,799 (64.4)	25,290 (64.1)
Employed or self-employed	6,890 (23.7)	8,463 (21.5)
Unemployed	620 (2.1)	921 (2.3)
Permanently sick or disabled	493 (1.7)	1 082 (2.7)
Homemaker	1,889 (6.5)	2,989 (7.6)
Other	272 (0.9)	405 (1.0)
Marital status, (%)		
Married and living together with spouse	7,111 (73.7)	9,001 (70.4)
Married, living separated from spouse	103 (1.1)	40 (0.4
Never married	408 (4.2)	538 (4.2)
Divorced	736 (7.6)	1,017 (8.0)
Widowed	1,205 (12.5)	1,975 (15.4)
Poor physical performance/ disability (any), (%)	11,928 (41.0)	18,991 (49.1)
Functional limitations (any), No. (%)	3,588 (12.3)	7,175 (18.5)

BMI 30 and above - obese, No. (%)	5,828 (20.0)	8,349 (21.5)
Use of drugs for anxiety or depression, No. (%)	934 (3.2)	2,356 (6.2)
Depression at baseline (EURO-D ⩾ 4), No. (%)	-	9,688 (24.6)
Depression at follow-up (EURO-D ⩾4), No. (%)	4,471 (15.4)	9,904 (25.8)
Depressive symptoms at baseline, %		
Depression	22.9	38.5
Pessimism	9.2	15.5
Suicidality	1.4	6.5
Guilt	3.2	7.9
Sleep	23.0	35.0
Interest	2.3	8.3
Irritability	16.6	27.9
Appetite	2.5	7.4
Fatigue	21.8	35.3
Concentration	7.9	15.6
Enjoyment	6.0	10.9
Tearfulness	11.7	22.7

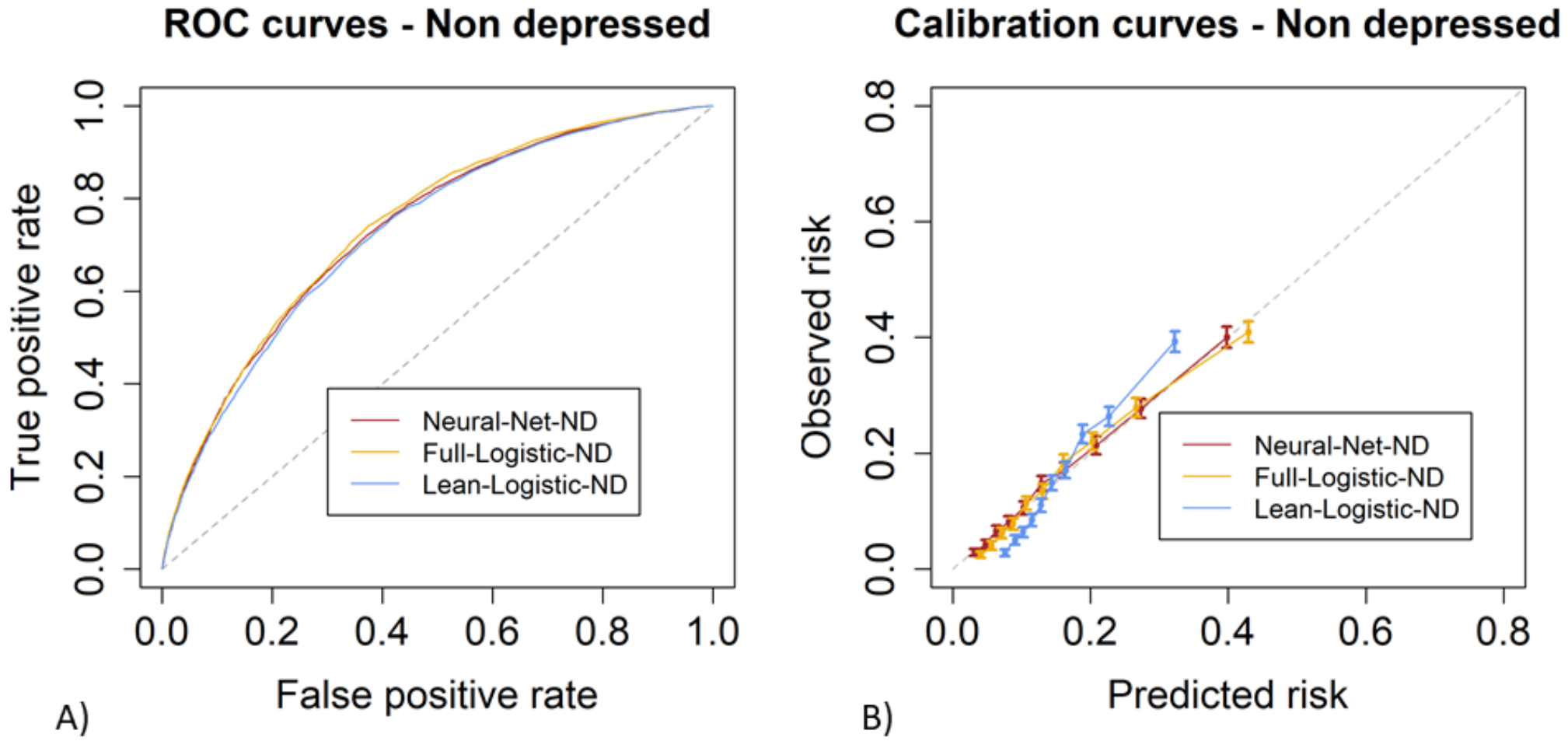
Table 2. Performance of Risk Prediction Models

	Not depressed at baseline (N=29 591) [a]		
	ANN	**Full-LR**	**Lean-LR**
N. risk factors	124	58	34
AUC (95% CI)	0.737 (0.730-0.745)	0.743 (0.718-0.766)	0.730 (0.706-0.754)
MSE (95% CI)	0.117 (0.115-0.120)	0.118 (0.110-0.126)	0.121 (0.113-0.129)
Population below the selected risk threshold (20%)	73.6%	74.4%	78.8%
Sensitivity	53.3%	53.0%	44.6%
Specificity	78.4%	79.5%	83.0%
PPV	31.1%	32.1%	32.5%
NPV	90.3%	90.2%	89.1%
Accuracy	74.6%	75.4%	77.1%

	Total sample (N=39,439)		
	ANN	**Full-LR**	**Lean-LR**
N. risk factors	35	70	32
AUC (95% CI)	0.807 (0.799 - 0.815)	0.809 (0.794 - 0.824)	0.805 (0.790 - 0.821)
MSE (95% CI)	0.144 (0.140 - 0.147)	0.143 (0.137 - 0.149)	0.146 (0.139 - 0.152)
Population below the selected risk threshold (20%)	53.3%	53.2%	47.4%
Sensitivity	80.3%	80.2%	84.3%
Specificity	65.0%	64.7%	58.4%
PPV	44.3%	44.1%	41.3%
NPV	90.5%	90.4%	91.5%
Accuracy	69.0%	68.7%	65.1%

AUC, Area Under the Curve; MSE, Mean Square Error; PPV, Positive Predictive Value; NPV, Negative Predictive Value. Reported values of Sensitivity, Specificity, PPV and NPV are based on a risk threshold of 20%, which optimizes sensitivity (⩾80%). The full set of values at each risk threshold are reported in the supplement. a. Participants with EURO-D total score < 4.

Figure 1. Receiver operation curves and calibration curves



Red: Artificial Neural Network model (ANN); Yellow: full Logistic Regression model (full-LR); Blue: lean Logistic Regression model (lean-LR)

Table 3. Predictors retained in the risk prediction models (participants without baseline depression)

Predictor	ANN (n=124)	Full-LR (n=58)	Lean-LR (n=34)	Predictor	ANN (n=124)	Full-LR (n=58)	Lean-LR (n=34)
SOCIODEMOGRAFIC				History of Parkinson's disease	■	■	
Age	■	■	■	History of hip or femoral fracture	■		
Sex	■	■	■	Recent diagnosis of cancer	■		
Ethnicity	■			Recent diagnosis of hip fracture	■		
Education	■	■		Use of glucocorticoids or steroids	■		
Marital status	■			Perceived Health	■	■	■
LIVING CONDITIONS				**BIOLOGICAL PARAMETERS**			
Rural/Urban residence				History of hypercholesterolemia	■		
Household size	■	■		**HEALTHCARE RELATED**			
Relocation	■			Seeing a medical doctor	■	■	■
Widowhood	■			Previous hospitalization	■		
Recent bereavement				Entering a nursing home		■	
SOCIAL CONTACTS				Unable to afford medical visit	■	■	
Help from outside household	■			Unable to see doctor due to waiting times	■		
Given help	■			Satisfaction with the health system	■	■	
Number of children	■	■		Use of drugs for hypercholesterolemia	■		
Number of grandchildren	■			Use of drugs for osteoporosis	■		
Presence of siblings	■			Use of drugs for stomach burns	■		
EMPLOYMENT/ ECONOMIC				Use of drugs for chronic bronchitis	■		
Current occupation status	■	■		Use of antihypertensives	■		
Financial stability	■	■		Use of drugs for coronary diseases	■		
Able to regularly buy groceries	■			Use of drugs for heart diseases	■	■	
ACTIVITIES				Use of drugs for diabetes	■		
Participation in voluntary or charity work	■			Use of drugs for joint pain	■	■	■
Playing cards or games	■			Use of analgesics	■	■	■
Educational or training course	■			Use of hypnotics	■	■	■
Sport or a social or other kind of club	■	■		No use of Drugs	■		
activities in religious organizations	■	■	■	Use of Drugs for other conditions	■	■	
activities in political organizations				**PHYSICAL CONDITION**			
Reading books or newspapers	■	■		Visual function	■	■	
Playing word or number games	■	■	■	Reading ability	■	■	
No activities in last year [a]	■	■	■	Hearing function	■		

Computer skills				Dental problems			
MENTAL HEALTH				BMI			
Depression				Weight loss			
Concentration				Difficulties in walking 100m			
Enjoyment				Difficulties in picking up a small coin from table			
Tearfulness				Difficulties in sitting for two hours			
Pessimism				Difficulties in getting up from a chair			
Suicidality				Difficulties several flights of stairs			
Guilt				Difficulties one flight of stairs			
Sleep				Difficulties stooping, kneeling, crouching			
Interest				Difficulties extending arms above shoulder			
Irritability				Difficulties pulling or pushing large objects			
Appetite				Difficulties carrying weights over 5kg			
Fatigue				No difficulties [b]			
Age of onset of affective disorders				Difficulties dressing			
Use of drugs for anxiety or depression				Difficulties using the telephone			
COGNITIVE				Difficulties taking medications			
History of Alzheimer's disease or other dementia				Difficulties doing work in house			
PSYCHOLOGICAL DIMENSIONS				Difficulties in managing money			
Life's satisfaction/Quality of life				Difficulties walking across a room			
Loneliness				Difficulties bathing or showering			
Age prevents from doing things				Difficulties eating, cutting up food			
Out of control				Difficulties getting in or out of bed			
Feel left out of things				Difficulties using toilet			
Do the things you want to do				Difficulties using a map in a strange place			
Family responsibilities prevent from doing things				Difficulties preparing hot meal			
Shortage of money stops				Difficulties shopping for groceries			
Look forward to each day				No difficulties [c]			
Life has meaning				Experience of falls			
Look back on life with happiness				Fear of falling			
Feel full of energy				Dizziness, faints or blackouts			
Full of opportunities				**PHYSICAL SYMPTOMS**			
Future looks good				Presence of pain			
PHYSICAL ILLNESSES				Fatigue			

History of heart attack				**HABITS / LIFESTYLE**			
Recent diagnosis of heart attack				Smoking			
History of stroke				Vigorous physical activity			
Recent diagnosis of stroke or cerebral vascular disease				Moderate physical activity			
History of diabetes or hyperglycaemia				Alcohol consumption			
History of chronic lung disease				Physical inactivity			

a. from a list of 10 activities; b. from a list of 10 ADLs; c. from a list of 13 ALDs