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Research paper

Use of machine learning approach to predict depression in the elderly in China: A longitudinal study

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ABSTRACT

Background: Early detection of potential depression among elderly people is conducive for timely preventive intervention and clinical care to improve quality of life. Therefore, depression prediction considering sequential progression patterns in elderly needs to be further explored.

Methods: We selected 1,538 elderly people from Chinese Longitudinal Healthy Longevity Study (CLHLS) wave 3–7 survey. Long short-term memory (LSTM) and six machine learning (ML) models were used to predict different depression risk factors and the depression risks in the elderly population in the next two years. Receiver operating curve (ROC) and decision curve analysis (DCA) were used to evaluate the prediction accuracy of the reference model and ML models.

Results: The area under the ROC curve (AUC) values of logistic regression with lasso regularisation (AUC=0.629, p-value=0.020) was the highest among ML models. DCA results showed that the net benefit of six ML models was similar (threshold: 0.00-0.10), the net benefit of lasso regression was the largest (threshold: 0.10-0.17 and 0.22-0.25), and the net benefit of DNN was the largest (threshold: 0.17–0.22 and 0.25–0.40). In two ML models, activities of daily living (ADL)/ instrumental ADL (IADL), self-rated health, marital status, arthritis, and number of cohabiting were the most important predictors for elderly with depression.

Limitations: The retrospective waves used in the LSTM model need to be further increased.

Conclusion: The decision support system based on the proposed LSTM+ML model may be very valuable for doctors, nurses and community medical providers for early diagnosis and intervention.

1. Introduction

Depression is a mental disorder manifested as persistent sadness, decreased interest in daily life activities, difficulty in concentrating, poor memory and lack of energy (Yeun et al., 2012). Depression is one of the most common mental illnesses, the third leading cause of disease burden worldwide and the number one cause of disability in middle-income and high-income countries (Guo et al., 2017). A total of 311 million people were diagnosed with depression worldwide, and this number increased by more than 18% between 2005 and 2015 (Vos et al., 2016). In addition, depression accounted for 3.0% of global disability adjusted life years and was the second cause of disability worldwide (Ferrari et al., 2013; Lie et al., 2017; Murray et al., 2013). The prevalence of depression among the elderly aged 55–74 is the highest in the world due to their special physiological characteristics and social relations. Therefore, the entire society needs to pay special attention to the potential risk of depression in the elderly population (Liao et al., 2020; Liu et al., 2018).

At present, China has the largest aging population and the fastest population growth in the world. The prevalence of depression in China is 4.2%, and the current patient population is conservatively estimated to exceed 54 million. In particular, the prevalence of depression among Chinese people over the age of 60 is as high as 22.7%, and more than 90% of them have not received timely and regular treatment (Zhang et al., 2012). Depression usually causes poor mental and physical health in elderly, affects the quality of life, significantly increases mortality and

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increases medical expenses (Alexapoulos, 2005; Cole and Dendukuri, 2003; Sutcliffe et al., 2007). Therefore, making early predictions of depression risk in elderly in the future can provide important information for timely and effective prevention and intervention of hospitals, nursing homes, communities and families to significantly improve the quality of life of the elderly and reduce medical costs (Ni et al., 2017; Suhara et al., 2017).

At present, most predictive studies on depression in the elderly population mainly focus on the following aspects. Firstly, biological indicators are used for a definite diagnosis of depression; however, they cannot predict the risk of depression in the future despite their extremely high accuracy (Gao et al., 2018; Jiang et al., 2016; Song et al., 2018; Xiao et al., 2018). Secondly, some studies have used cross-sectional data to explore the relationship between depression and its risk factors; however, these data cannot predict future risks of depression (Gan et al., 2015; Su et al., 2012; Yang et al., 2012). Thirdly, the prediction indicators of depression are more concentrated on a large sample level (such as morbidity and mortality), and no prediction of depression risk for different elderly people is available (Ben-Zeev et al., 2015; Hosny et al., 2013; Luo, 2017; Xie et al., 2018). The applicability of the three types of research results is still limited, especially affecting the early intervention and timely treatment of depression among nonmedical personnel in the community. Therefore, using demographic characteristics and general health information is important to predict depression in different elderly people.

In the current study, depression risk factors can be grouped into three main categories, as follows: (a) demographics, such as gender (Lee et al., 2006), age (Chan and Zeng, 2011), marital status (Chen et al., 2016), residence (Mansori et al., 2019) and number of cohabiting (Friberg et al., 2019); (b) health-related risk factors, including self-rated health (Bustos-Vazquez et al., 2017), physical activity (Wassink-Vossen et al., 2018), activities of daily living scale (ADL) (Ezema et al., 2019), instrumental ADL (IADL) (Wen et al., 2014), cognitive function (LaMonica et al., 2018) and smoking (Hu et al., 2019); (c) chronic disease risk factors, such as diabetes (Xiao et al., 2018), cerebrovascular disease (Shi et al., 2015), cataracts (Zhang et al., 2018a), glaucoma (Zhou et al., 2013), cancer (G?tze et al., 2020), gastric or duodenal ulcer (Piper et al., 1980) and arthritis (Matcham et al., 2013). Although most of these studies analyse the relationship between depression risk factors, some are limited to linear relationships, such as logistic models. However, machine learning (ML) and deep learning methods can iteratively and simultaneously analyse nonlinear, high-dimensional correlations between risk factors and capture the temporal relationships between risk factors (Lee et al., 2018; Orru et al., 2012; Zhang et al., 2019). Therefore, ML and deep learning methods can design data-driven models and algorithms with predictive capabilities in an unpredictable approach to achieve better output.

To the best of our knowledge, no previous studies have used longitudinal data to predict the risk of depression among different elderly people in China in the next few years. Therefore, the present study uses a large representative elderly database in China as a sample to investigate the following: 1) the use of the long short-term memory (LSTM) model to predict the level of different depression risk factors in the elderly population in the next two years by capturing time series information; 2) the use of six ML models to predict the risk of depression in the elderly population in two years.

2. Materials and methods

2.1. Description of Chinese longitudinal healthy longevity study (CLHLS) data

The data in this study were derived from CLHLS wave 3–7 (2002, 2005, 2008–2009, 2011–2012 and 2014) survey. CLHLS collected longitudinal data coordinated by the Centre for Healthy Aging and Development Studies of National School of Development at Peking University. The baseline survey was conducted in 1998 (wave 1), and the follow-up surveys (wave 2–8) were conducted in 2000, 2002, 2005, 2008-2009, 2011–2012, 2014 and 2017–2018 in approximately half of the counties and city districts in 23 Chinese provinces, which were randomly selected (Yin et al., 2020). The survey subjects include elderly aged 65 and above and their adult children aged 35–64. The questionnaire data collected provide information on family structure, living arrangements and proximity to children, ADL, physical performance, self-rated health, self-evaluation of life satisfaction, cognitive functioning, chronic disease prevalence, care needs and costs, social activities, diet, smoking and drinking behaviour, psychological characteristics, economic resources and care giving and family support among elderly respondents and their relatives. Information about the health status of the CLHLS participants, who were interviewed in the previous wave but died before the current survey, were collected by interviewing a close family member.

2.2. Definition of depression

The most widely used criteria for diagnosing depressive conditions are found in the International Classification of Diseases 10th Edition (ICD-10) published by the World Health Organisation and Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5) published by the American Psychiatric Association (APA). ICD-10 defines three typical depressive symptoms (depressed mood, anhedonia and reduced energy), two of which should be present for depressive disorder diagnosis. According to DSM-5, the two main depressive symptoms are depressed mood and loss of interest/pleasure in activities (anhedonia). These symptoms, as well as five out of the nine more specific symptoms listed, must frequently occur for more than two weeks (to the extent that functioning is impaired) for the diagnosis. In this study, depression is a mood disorder that is significant and lasts for at least two weeks, with depression and loss of pleasure as the core features, emphasising the representation of depression rather than the outbreak of depression.

2.3. Study variables

2.3.1. Outcome variables

Depression is measured using two levels of indicators, and the answer of “yes” to any question is considered a representation of depression. The two questions are as follows:

Question 1: Have you had a time in last 12 months when you felt sad, blue, or depressed for two weeks or more? (Yes = 1; No = 0)

Question 2: Have you had a time in last 12 months lasting two weeks or more when you lost interest in most things like hobbies, work, or activities that usually give you pleasure? (Yes = 1; No = 0)

2.3.2. Predictors

We chose the same predictors as in the wave 3–7 questionnaire due to the difference in the variable structure of the questionnaires under different waves. Specifically, the predictors mainly include the following three categories: (a) demographics, such as gender, age, marital status, residence and number of cohabiting; (b) health-related risk factors, including self-rated health, physical activity, ADL, IADL, cognitive function and smoking; (c) chronic disease risk factors, such as diabetes, cerebrovascular disease, cataracts, glaucoma, cancer, gastric or duodenal ulcer and arthritis.

2.3.3. Data pre-processing

The data of wave 1 and 8 are excluded because the interval between wave 1 and the other waves in the CLHLS survey is different (two years and three years), and the questions about depression in wave 8 are different from those in other waves. We use the data in waves 3–6 as the training set and the data in wave 7 as the test set. More specifically, we use the predictors in waves 3–6 to predict the risk factors of depression for the elderly in wave 7 (2014). Then, we use the predicted risk factors and the outcome variable (depression) in wave 7 and random selected 70% of the samples to train the parameters in the model, and then use the trained model and remaining 30% of the samples (actual predictors) to predict depression outcome in wave 7 (year of 2014). Eventually, we have identified the depressed individuals in the training sets (1077 elderly) and testing sets (461 elderly).

2.4. Statistical analysis

2.4.1. Processing of missing values

We use the k-nearest neighbour (k-NN) imputation algorithm to fill in the missing data in our study (Table 1), where each missing value on some records is replaced by a value obtained from related cases in the entire set of records (Beretta and Santaniello, 2016). The most notable features of k-NN imputation algorithm are as follows: a) the imputed value is the value that has actually appeared, and no secondary processing is performed; b) the distribution structure of the original data is retained in accordance with the variable information; c) k-NN imputation is completely nonparametric and does not depend on the relationship between y and x. We assume that k-NN method determines the closest k (k = 5) elderly with missing data in accordance with the Euclidean or L_2 distance.

2.4.2. Multivariate LSTM model

Traditional ML models cannot capture the interdependence of predictors in longitudinal data in different waves during the prediction process. We propose a recurrent neural network (RNN) for LSTM units to capture the interdependence of predictors in longitudinal data in different waves and estimate the future trends of predictors. The RNN model based on LSTM can capture the pattern of the entire data sequence; it has proven to be a powerful model to learn from sequential data (Whangbo et al., 2018). We use a 0–1 norm to normalise the value of inputs to address potential overfitting problems.

Table 1
The summary of missing values of different predictors for each wave.

Predictors	2002 N (%)	2005 N (%)	2008 N(%)	2011 N(%)	2014 N(%)	Total N(%)
Residence	0(0.00)	0(0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Age	0(0.00)	0(0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Gender	0(0.00)	0(0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Number of cohabiting	187 (12.16)	220 (14.30)	0 (0.00)	0 (0.00)	0 (0.00)	407 (5.29)
Self-rated health	4(0.26)	11 (0.72)	21 (1.37)	20 (1.30)	58 (3.77)	114 (1.48)
Cognitive function	39 (2.54)	38 (2.47)	57 (3.71)	118 (7.67)	34 (2.21)	286 (3.72)
Smoking	0(0.00)	0(0.00)	0 (0.00)	1 (0.07)	0 (0.00)	1 (0.01)
Regular exercise	0(0.00)	0(0.00)	0 (0.00)	2 (0.13)	2 (0.13)	4 (0.05)
Physical labor	2(0.13)	2(0.13)	2 (0.13)	2 (0.13)	0 (0.00)	8 (0.10)
ADL/IADL	2(0.13)	1(0.07)	0 (0.00)	47 (3.06)	68 (4.42)	118 (1.53)
Marital status	0(0.00)	0(0.00)	0 (0.00)	0 (0.00)	1 (0.07)	1 (0.01)
Diabetes	46 (2.99)	84 (5.46)	33 (2.15)	78 (5.07)	60 (3.9)	301 (3.91)
Cerebrovascular disease	43(2.8)	83 (5.40)	31 (2.02)	56 (3.64)	51 (3.32)	264 (3.43)
Cataracts	39 (2.54)	78 (5.07)	28 (1.82)	59 (3.84)	62 (4.03)	266 (3.46)
Glaucoma	42 (2.73)	87 (5.66)	30 (1.95)	65 (4.23)	66 (4.29)	290 (3.77)
Cancer	53 (3.45)	104 (6.76)	40 (2.60)	66 (4.29)	62 (4.03)	325 (4.23)
Gastric or duodenal ulcer	47 (3.06)	91 (5.92)	30 (1.95)	75 (4.88)	58 (3.77)	301 (3.91)
Arthritis	39 (2.54)	62 (4.03)	26 (1.69)	45 (2.93)	46 (2.99)	218 (2.83)

2.4.3. Logistic regression (LR)

LR is a member of the general linear model family. It has an underlying assumption that the output follows a Bernoulli distribution with parameter p, where p is the probability of success (in our case, the probability of depression for the elderly).

2.4.4. LR with lasso regularisation

Lasso regularisation is a penalised regression approach that estimates the regression coefficients by maximising the log-likelihood function (or the sum of squared residuals) with the constraint that the sum of the absolute values of the regression coefficients, $\sum_{j=1}^{k}|\beta_j|$, is less than or equal to a positive constant s. Lasso regularisation automatically deletes unnecessary covariates, and only the most significant variables are retained in the final model (Bielza et al., 2011). Some studies have shown that lasso regression has many ideal properties for logistic regression models with more covariates (Doerken et al., 2019; Wang et al., 2015). We selected a regularisation parameter (lambda) that resulted in the minimal misclassification error rate to penalise large coefficients that originated from small sample sizes. The minimal lambda was calculated by 10-fold cross-validation using the glmnet package.

2.4.5. RF

RF classifier is a set of decision trees from a randomly selected subset of a training set, which is an ensemble tree-based learning algorithm. The information content of the decision tree classifier is derived from each attribute in the dataset. Therefore, the decision tree classification algorithm initially selects the attribute with the most abundant information for classification (Payey et al., 2017). Sample training data sets are selected randomly and returned to ensure that the total size of each random sample is the same. For prediction, each decision tree is applied to the test set to evaluate the error, and the final classification decision is made by majority voting on all decision trees. We used out-of-bag (left-out samples after bagging) estimation to measure the prediction errors.

2.4.6. GBDT

GBDT is a flexible nonparametric statistical learning technique for classification and regression. GBDT improves the prediction appearance results by gradually improving the estimation (Xuan et al., 2019). In addition, GBDT uses a nonlinear regression procedure to improve the accuracy of trees. A series of decision trees was created; it produced a set of weak prediction models. We used 10-fold cross-validation to measure the prediction error.

2.4.7. SVM

SVM is a controlled classification algorithm based on statistical learning theory. The working principle of SVM is based on the concept of predicting the most appropriate decision function that separates the two classes on the basis of the definition of hyperplane, which can distinguish the two classes from each other in a most appropriate way (Suykens and Vandewalle, 1999; Vapnik, 2000). SVM has four widely used kernel functions, namely, the linear function, polynomial function, sigmoid function and radial basis function (RBF). RBF kernel SVM was used in this study.

2.4.8. DNN

DNN is an artificial neural network with multiple layers between the input and output layers (Bustos-Vazquez et al., 2017). The DNN searched for the correct mathematical manipulation to turn the input into output, whether it is a linear relationship or a nonlinear relationship. In the DNN, we constructed a five-layer feedforward model with adaptive moment estimation optimiser using the keras package. For the DNN, we developed the final models by randomly and manually tuning the hyperparameters, such as the number of layers and hidden units, learning rate, learning-rate decay, dropout rate, batch size and epochs, using the keras package. We used dropouts that randomly removed portions of units in the network, ridge regularisation that shrunk large coefficients and batch normalisation that normalised the means and variances of layer inputs to minimise potential overfitting.

2.4.9. Model evaluation

We constructed the following six ML prediction models using these predictors: (1) LR, (2) LR with lasso regularisation (lasso regression), (3) RF, (4) gradient-boosted decision tree (GBDT), (5) support vector machines (SVM) and (6) deep neural network (DNN). Then, we used the value of area under the receiver operating curve (ROC) (AUC), prospective prediction results (sensitivity (Eq. (1)), specificity (Eq. (2)), accuracy (Eq. (3)), positive predictive value (PPV) (Eq. (4)), negative predictive value (NPV) (Eq. (5))) and decision curve analysis (DCA) to evaluate the performance of each ML model. We selected the threshold value of expected prediction results on the basis of the ROC (i.e., the value with the shortest distance to the perfect model). Delong test was used to compare the differences between the ROC curves of different statistical models. Delong test compares the AUC by calculating the standard error of different AUC or the difference in AUC. Decision curve analysis is a novel method for evaluating diagnostic tests and prediction models. In summary, the method is based on the principle that the relative disadvantages of false positives (e.g., error diagnosed as depression) and false negatives (e.g., missed depression) can be expressed in terms of a probability threshold (Vickers and Elkin, 2006; Zachariasse et al., 2018). A decision analytic measure called net benefit is then calculated for each possible threshold probability, which places benefits and disadvantages on the same scale (Zhang et al., 2018b). To gain an in-depth understanding of the contribution of each predictor to the ML model, we also calculated the importance of variables in the GBDT and RF models for each result.

$$Sensitivity = \frac{TP}{TP + FN} \tag{1}$$

$$Specificity = \frac{TN}{TN + FP} \tag{2}$$

$$Accuracy = \frac{TN + TP}{TN + TP + FN + FP} \tag{3}$$

$$Positivepredictivevalue = \frac{TP}{TP + FP} \tag{4}$$

$$Negativepredictivevalue = \frac{TN}{TN + FN} \tag{5}$$

Here, true negatives (TN) and true positives (TP) indicate the elderly that were accurately identified as not suffering depression and suffering depression, respectively; false negatives (FN) and false positives (FP) indicate the elderly that were inaccurately identified as not suffering depression and suffering depression, respectively. Fig. 1 shows the architecture of our model.

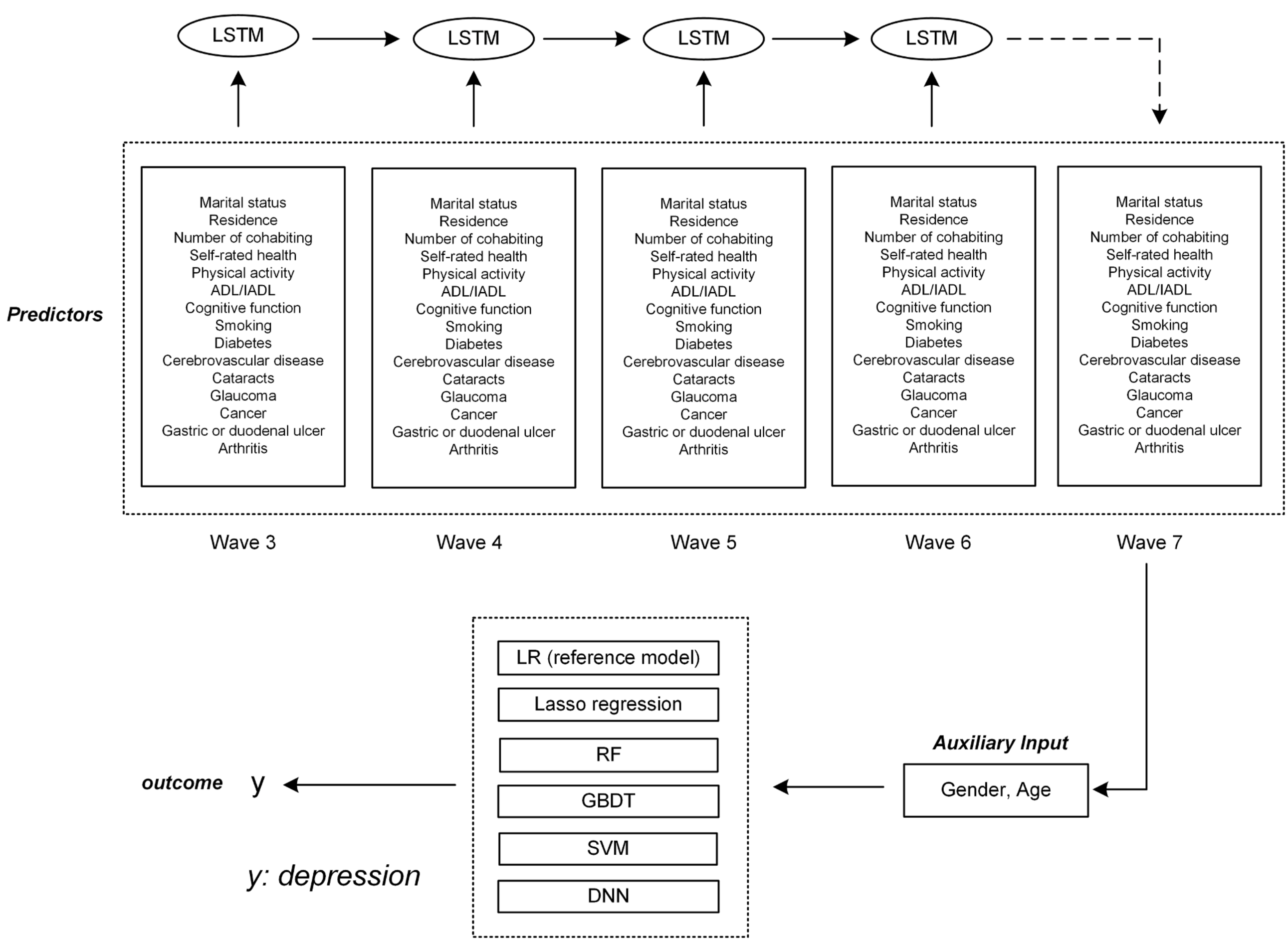

Fig. 1. The architecture of the prediction model for the elderly with depression.

3. Results

3.1. Characteristics and odds ratio of elderly with depression

As shown in Table 2, among the 1,538 elderly in CLHLS 2014, 289 elderly (18.8%) had depression. Female elderly (21.2%) present higher proportion than male elderly (16.1%). The high proportions of self-rated health of elderly were poor and very poor (36.6% and 38.9%, respectively). The elderly with regular exercise (15.2%) had lower proportion than the elderly without regular exercise (20.7%). The ADL/IADL score of the elderly with depression (21.36±8.04) was higher than that of elderly without depression (19.25±7.34). Divorced and elderly who never married had high proportions (50.0% and 33.3%, respectively). The elderly with gastric or duodenal ulcer (31.6%) had higher

Table 2
Characteristics and odds ratio of elderly with depression presenting to the CLHLS 2014.

Predictors		All elderly N (%)	Elderly depression N (%)	Elderly non-depression N(%)	p-value	crude OR (95% CI)	adjusted OR (95%CI)
Residence	city	292(19.0)	53(18.2)	239(81.8)	0.404	reference	reference
	town	602(39.1)	105(17.4)	497(82.6)		0.953(0.662-1.372)	0.798(0.532-1.196)
	rural	644(41.9)	131(20.3)	513(79.7)		1.152(0.808-1.641)	0.963(0.642-1.444)
Age		83.73±5.71	83.92±5.89	83.69±5.67	0.534	1.007(0.985-1.029)	0.998(0.972-1.024)
Gender	male	728(47.3)	117(16.1)	611(83.9)	0.010	reference	reference
	female	810(52.7)	172(21.2)	638(78.8)		1.408(1.086-1.825)	1.230(0.899-1.683)
Number of cohabiting		2.56±1.88	2.41±1.59	2.6±1.94	0.129	0.946(0.880-1.016)	0.938(0.866-1.017)
Self-rated health	very good	145(9.4)	19(13.1)	126(86.9)	<0.001	reference	reference
	good	469(30.5)	42(9.0)	427(91.0)		0.652(0.366-1.162)	0.645(0.358-1.160)
	so so	596(38.8)	107(18.0)	489(82.0)		1.451(0.858-2.455)	1.447(0.838-2.496)
	bad	292(19.0)	107(36.6)	185(63.4)		3.836(2.240-6.568)	3.683(2.040-6.651)
	very bad	36(2.3)	14(38.9)	22(61.1)		4.220(1.848-9.636)	4.217(1.728-10.293)
Cognitive function		4.77±0.63	4.72±0.7	4.78±0.62	0.175	0.879(0.729-1.060)	0.999(0.814-1.228)
Smoking	Yes	278(18.1)	51(18.3)	227(81.7)	0.113	reference	reference
	No	1259(81.9)	238(18.8)	1022(81.2)		1.032(0.738-1.443)	0.831(0.566-1.220)
Regular exercise	Yes	534(34.7)	81(15.2)	453(84.8)	0.008	reference	reference
	No	1004(65.3)	208(20.7)	796(79.3)		1.461(1.103-1.936)	1.039(0.744-1.450)
Physical labor	Yes	1231(80.0)	234(19.0)	997(81.0)	0.661	reference	reference
	No	307(20.0)	55(17.9)	252(82.1)		0.930(0.672-1.286)	0.989(0.694-1.412)
ADL/IADL		19.64±7.52	21.36±8.04	19.25±7.34	<0.001	1.035(1.019-1.051)	1.005(0.983-1.027)
Marital status	married and living with spouse	603(39.2)	86(14.3)	517(85.7)	0.001	reference	reference
	married but not living with spouse	25(1.6)	4(16.0)	21(84.0)		1.145(0.384-3.417)	1.070(0.336-3.407)
	divorced	8(0.5)	4(50.0)	4(50.0)		6.012(1.476-24.490)	7.888(1.670-37.255)
	widowed	887(57.7)	190(21.4)	697(78.6)		1.639(1.240-2.166)	1.475(1.070-2.034)
	never married	15(1.0)	5(33.3)	10(66.7)		3.006(1.003-9.008)	2.553(0.790-8.248)
Diabetes	Yes	102(6.6)	25(24.5)	77(75.5)	0.126	reference	reference
	No	1436(93.4)	264(18.4)	1172(81.6)		0.694(0.433-1.111)	0.818(0.487-1.373)
Cerebrovascular disease	Yes	240(15.6)	47(19.6)	193(80.4)	0.732	reference	reference
	No	1298(84.4)	242(18.6)	1056(81.4)		0.941(0.664-1.333)	1.614(1.069-2.436)
Cataracts	Yes	280(18.2)	58(20.7)	222(79.3)	0.362	reference	reference
	No	1258(81.8)	231(18.4)	1027(81.6)		0.861(0.624-1.188)	0.994(0.697-1.419)
Glaucoma	Yes	32(2.1)	9(28.1)	23(71.9)	0.172	reference	reference
	No	1506(97.9)	280(18.6)	1226(81.4)		0.584(0.267-1.275)	0.757(0.321-1.785)
Cancer	Yes	19(1.2)	3(15.8)	16(84.2)	0.736	reference	reference
	No	1519(98.8)	286(18.8)	1233(81.2)		1.237(0.358-4.274)	2.179(0.546-8.691)
Gastric or duodenal ulcer	Yes	76(4.9)	24(31.6)	52(68.4)	0.003	reference	reference
	No	1462(95.1)	265(18.1)	1197(81.9)		0.480(0.290-0.792)	0.709(0.404-1.245)
Arthritis	Yes	225(14.6)	73(32.4)	152(67.6)	<0.001	reference	reference
	No	1313(85.4)	216(16.5)	1097(83.5)		0.410(0.299-0.562)	0.516(0.367-0.726)

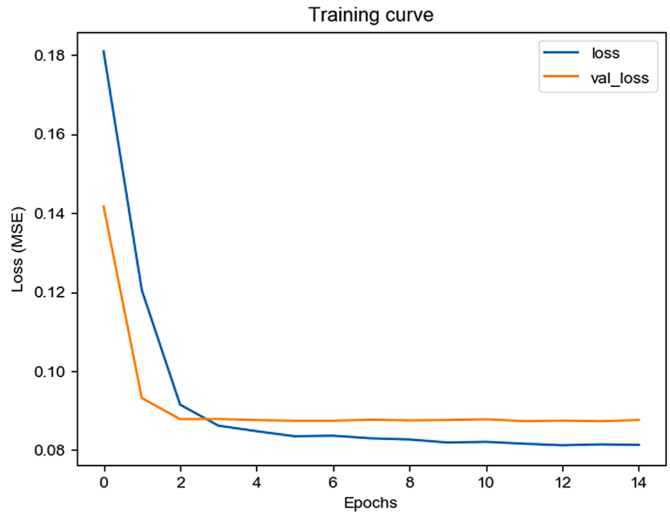

Fig. 2. The training curve of LSTM (MSE, Mean squared error; LSTM, long short-term curve).

proportion than the elderly without gastric or duodenal ulcer (18.1%). The elderly with arthritis (32.4%) had higher proportion than the elderly without arthritis (16.5%).

Then, we analysed the crude and adjusted odds ratio for the elderly with depression (vs. non-depression) for each predictor using binary logistic regression. The analysis showed that the elderly with poor (adjusted OR=3.683; 95%CI: 2.040–6.651) and very poor (adjusted OR =4.217; 95% CI: 1.728–10.293) self-rated health status had higher risk of depression than those with good self-rated health status. The elderly with marital status of divorced and widowed had greater odds of depression than the elderly with other marital statuses (adjusted OR = 7.888; 95% CI: 1.670–37.255 and adjusted OR = 1.475; 95% CI: 1.070–2.034). The elderly without cerebrovascular disease was more likely to be diagnosed with depression (adjusted OR =1.614; 95% CI: 1.069–2.436). The elderly without arthritis had low risk of depression (adjusted OR =0.516; 95% CI: 0.367–0.726).

3.2. *Prediction appearance for elderly with depression using ML models*

The prediction performance of LSTM is shown in Fig. 2. The mean squared error (MSE) of the training curve is basically the same in the training set and the validation set (around 0.08), indicating that the prediction performance of LSTM is good. Fig. 3A shows the comparison of the ROC curves of different ML models for elderly with depression. The SVM had the lowest AUC value among the six ML models (AUC=0.578) (Table 3), and the AUC values of logistic regression with lasso regularisation (AUC=0.629, p-value=0.020) was significantly higher than those of the logistic regression model. The threshold values of the logistic regression, lasso regression, RF, GBDT, SVM and DNN were 0.329, 0.252, 0.223, 0.323, 0.201 and 0.173, respectively. The GBDT had the highest accuracy (0.759, 95% CI: [0.718–0.798]), and the accuracy of logistic regression (0.659, 95% CI: [0.614–0.703]), lasso regression (0.670, 95% CI: [0.625–0.713]), SVM (0.564, 95% CI: [0.517–0.610]) and DNN (0.571, 95% CI: [0.524–0.616]) was relatively low. The accuracy of RF (0.482, 95% CI: [0.435–0.528]) was the lowest. The GBDT had the lowest sensitivity (0.429), whereas RF had the highest sensitivity (0.753). The specificity of the GBDT was the highest (0.826), and the specificity of the RF was the lowest (0.427). GBDT had the highest PPV (0.330), whereas the SVM had the lowest PPV (0.208). Lasso regression had the highest NPV (0.900), whereas the SVM had the lowest NPV (0.867). DCA results (Fig. 3B) showed that within the threshold ranges of 0.00-0.10, the net benefit of six ML models was

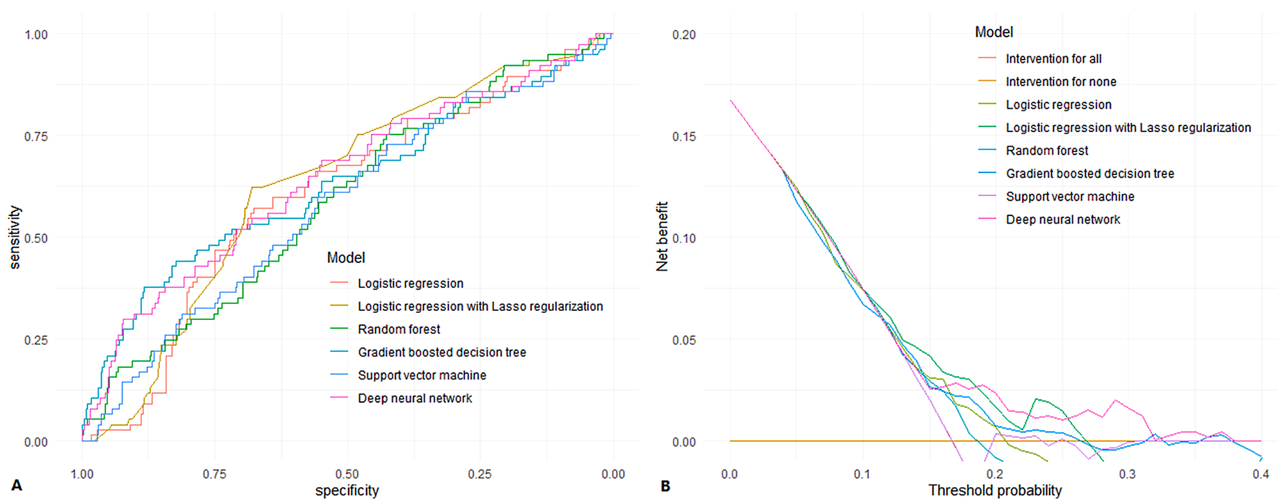

Fig. 3. Predictive performance of six machine learning models for elderly with depression (A, ROC curve. The x-axis represents specificity (probability of negative test given that the elderly did not have the depression), and the y-axis represents sensitivity (probability of a positive test given that the elderly had the depression). B, decision curve analysis. The x-axis represents the threshold probability of the depression. The y-axis represents net benefit.).

Table 3
Prediction performance of elderly with depression using 6 machine learning models.

Model	AUC	p-value*	Threshold	Accuracy	Sensitivity	Specificity	PPV	NPV
Logistic regression	0.605	Reference	0.329	0.659(0.614-0.703)	0.571	0.677	0.262	0.887
Logistic regression with Lasso regularization	0.629	0.020	0.252	0.670(0.625-0.713)	0.623	0.680	0.281	0.900
Random forest	0.589	0.624	0.223	0.482(0.435-0.528)	0.753	0.427	0.209	0.896
Gradient boosted decision tree	0.630	0.454	0.323	0.759(0.718-0.798)	0.429	0.826	0.330	0.878
Support vector machine	0.578	0.545	0.201	0.564(0.517-0.610)	0.571	0.563	0.208	0.867
Deep neural network	0.644	0.427	0.173	0.571(0.524-0.616)	0.688	0.547	0.234	0.897

AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value.
*p-value is the result of Delong test of AUC curve based on the comparison of each machine learning model.

similar, within the threshold ranges of approximately 0.10-0.17 and 0.22-0.25, the net benefit of lasso regression was the largest, and within the threshold ranges of approximately 0.17–0.22 and 0.25–0.40, the net benefit of DNN was the largest.

3.3. Importance of predictive variables

Fig. 4 shows the importance of the predictors in the RF and GBDT models. In RF, Age,ADL/IADL, self-rated health, marital status, arthritis, number of cohabiting are the most important predictors for elderly with depression (Fig. 4A). The variable importance is similar to that in the GBDT model (Fig. 4B).

4. Discussion

This study is based on CLHLS wave 3–7 (2002, 2005, 2008, 2011 and 2014) panel data of 1,538 elderly people, where population information, social economy, health and other variables are obtained. We use the LSTM model to obtain the predicted values of different variables in the next two years and apply the predicted values and six ML methods (logistic regression, lasso regression, RF, GBDT, SVM and DNN) to diagnose depression in the elderly population. The results show that the analysis framework combined with the LSTM model and other ML models shows excellent performance in the prediction of depression in the elderly population. Specifically, the LSTM+ML framework can characterise and merge complex high-order interactions between time patterns and variables for model prediction and successfully capture the correlation information between static data and dynamic data. This correlation information are integrated with temporal information extracted from dynamic data to improve depression prediction of the elderly population. In addition, the DCA results show that there are differences in the net benefit of the six ML models within different thresholds.

Thus far, the LSTM model has been successfully applied to many studies involving time series prediction, such as traffic flow prediction (Li et al., 2020; Wei et al., 2019), infectious disease prediction (Gu et al., 2019; Xu et al., 2020; Zhu et al., 2019) and human trajectory prediction (Shi et al., 2019; Zaroug et al., 2020). However, no research has analysed the prediction of LSTM model in the risk factors of depression in Chinese elderly. Most studies have also shown that, compared with traditional shallow models and autoregressive integrated moving average models, LSTM-based deep learning prediction models can capture time correlation more effectively, and using auxiliary data can significantly improve prediction performance (Chae et al., 2018; Wang et al., 2019a; Wang et al., 2019b; Zhang and Nawata, 2017). This approach also provides possibilities for the study to predict the future depression tendency of the elderly by using nonclinical data. At the same time, this research provides potential for future clinical application of this field.

ML models based on LSTM technology can perform high-precision prediction tasks, and the AUC value of some models is close to 0.7. This result shows the feasibility of predicting the depression of the elderly based on the LSTM+ML technical framework. It also proves the accuracy and predictive ability of screening the risk factors of depression in the elderly in other research. Among all ML models, the performance of the lasso regression and DNN models is comparable to the reference model, and the performance of the SVM is significantly lower than the reference model. However, some ML models (lasso regression and DNN) show high AUC value and net benefit. This result may have the following reasons. Firstly, if a significant nonlinearity exists between the predictors and the outcome of depression in the elderly and the data between different categories of predicted results are unbalanced, then most ML models have better ability to deal with the nonlinear relationship between variables, probably becoming more suitable as classifiers (Kuhn et al., 2013). Secondly, the Euclidean distance, from which SVM relies, is not the best approach to deal with the classification of depression in the elderly. In addition, SVM is not robust in identifying outliers in the input variable space or feature space, and may be more affected by the imbalance of data classification (Hastie et al., 2009; Weston et al., 2001). Thirdly, considering the limited sample size of the

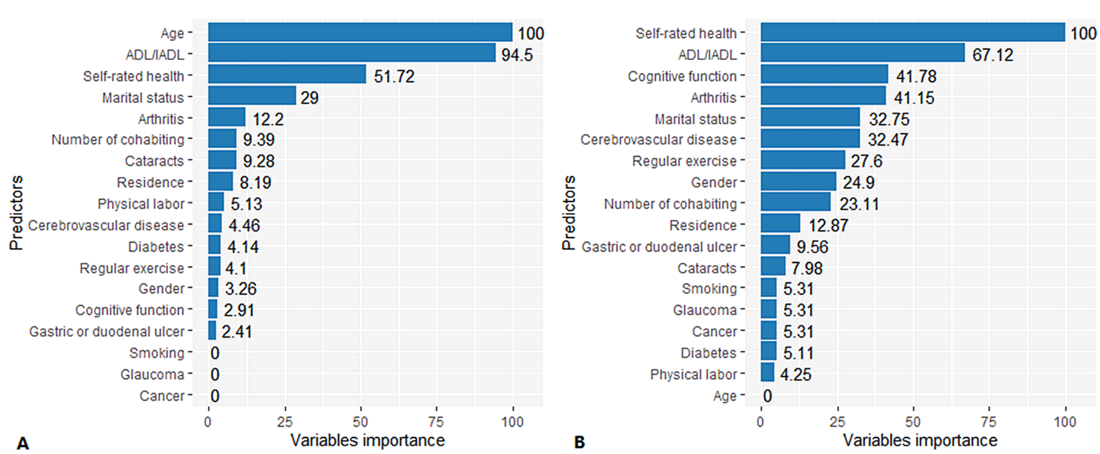

Fig. 4. Variable importance of random forest (A) and gradient-boosted decision tree (B) prediction model for elderly with depression.

unbalanced CLHLS longitudinal data between different waves, regularisation, cross-validation and dropout methods are used to minimise overfitting of the model; however, the reference model does not have an advantage in adjusting model parameters (Tibshirani, 2011).

When predicting depression in the elderly population, we should determine a threshold for identifying depressed and nondepressed elderly. Ideally, the model should have high PPV and NPV prediction accuracy. However, a trade-off is found between PPV and NPV. In identifying depression, the top priority is high PPV; Meanwhile, we also need to consider that elderly people at high risk of depression can be identified as much as possible, so we also need to consider sensitivity to identify more high-risk groups of depression. Therefore, a truly high-efficiency model needs to be better in the two indicators of PPV and sensitivity. Finally, we conducted a decision curve analysis that provides different service providers with more flexible choices. Service providers (such as doctors, nurses and community workers) can choose appropriate thresholds based on their domain knowledge. Specifically, it can be dynamically adjusted according to the prevalence level of depression in the elderly in the area or the ability of hospitals to recognize depression. If the prevalence in the area is high, the threshold of the machine learning model can be appropriately increased to obtain the highest net benefit. Meanwhile, high-level/psychiatric professional hospitals have a higher medical technology to identify depression than low-level hospitals, so the threshold level can also be appropriately increased to obtain the best net benefit.

In addition, we identify the importance of the predictors using the RF and GBDT models to minimise the dimensions of the predictors. We found that in the two ML models, the top important predictors are ADL/IADL, self-rated health, marital status, and arthritis. Meanwhile, some variables (such as smoking and cancer) are less important in both prediction models. The results show that when considering many factors to predict depression in elderly, establishing a low-dimensional decision support model, which can reduce the difficulty of collecting information for some medical personnel (especially community medical providers), is efficient.

5. Limitations

This research has several limitations. Firstly, because these models are derived from nationally representative survey data, the clinical use of such modelling strategies may benefit from data at specific locations and other calibrations of models for specific areas in counties or patient population. Secondly, CLHLS data do not include medical utilisation and clinical indicators of the elderly. These data have been found to predict depression in the elderly. Thirdly, due to the limitations of the questionnaire structure and the number of CLHLS waves, the LSTM model cannot use more wave data to predict the risk factors of depression for elderly, thereby affecting the predictive performance of the risk factors. Finally, the ability to diagnose depression of the elderly depends on local medical resources, and indications and clinical thresholds may vary between emergency departments and clinicians.

6. Conclusions

This study revealed the method of using LSTM+ML analysis framework to predict the risk of depression in the elderly population through CLHLS data (five waves). The LSTM+ML model can successfully capture high-dimensional and time-series information of risk factors for depression in elderly. The decision support system based on the predictive model of this research may be very valuable for doctors, nurses and community medical providers for early discovery and intervention. Further research is needed to test the effect of using the system in a clinical environment.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Dataset are distributable only by CLHLS team and are available in public registrations on CLHLS website: https://opendata.pku.edu.cn/dataverse/CHADS and are also available on request from the corresponding author on reasonable request.

Contributors

Dai Su and Yingchun Chen contributed to the conception and design of the project; Dai Su, Kevin He, and Xingyu Zhang contributed to the analysis and interpretation of the data; Dai Su and Xingyu Zhang contributed to the data acquisition and provided statistical analysis support; Dai Su drafted the article. Dai Su, Yingchun Chen and Xingyu Zhang are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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