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A Prediction Model for Prevention and Management of Metabolic Syndrome Based on Machine Learning

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A Prediction Model for Prevention and Management of Metabolic Syndrome Based on Machine Learning

A Dissertation
Submitted to the Department of Medicine
and the Graduate School of Yonsei University
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requirements for the degree of
Doctor of Philosophy

Jung Hun Lee

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Abstract

A Prediction Model for Prevention and Management of Metabolic Syndrome Based on Machine Learning

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Digital health-based lifestyle interventions (e.g., mobile applications, short message services, wearable devices, social media, and interactive websites) are widely used to manage metabolic syndrome (MetS). This study aimed to confirm the usefulness of digital health-based lifestyle interventions using healthcare devices and propose a novel prediction model of prevention and management for MetS. Participants with one or more MetS risk factors were recruited from December 2019 to September 2020, and finally, 106 participants were analyzed. Participants were provided with five healthcare devices and applications. Characteristics were compared at baseline and follow-up, and lifelog data that were collected during the clinical trial were analyzed. With these results, the frequency of use of healthcare devices for continuous self-care was quantified, and a novel prediction model for the prevention and management of MetS was developed. The model predicts

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persistence in continuous engagement as well as abbreviated risk factors for self-care effects. Representative machine-learning classifiers were used and compared. In both models, the random forest classifier showed the best performance, and feature selection was optimized through random forest-recursive feature elimination. As a result, the prediction model for persistence showed recall of 83.0%, precision of 92.4%, an F1-score of 0.874, a Matthews correlation coefficient (MCC) of 0.844, and accuracy of 94.9%. The prediction model for abbreviated risk factors showed a recall of 79.8%, a precision of 87.2%, an F1-score of 0.834, and an MCC of 0.797 for increased abbreviated risk factors, and a recall of 75.1%, a precision of 85.5%, an F1-score of 0.800, and an MCC of 0.747 for decreased abbreviated risk factors. The prediction model proposed showed high performance. Based on self-care with digital health-based lifestyle interventions, prediction models could be helpful for the prevention and management of MetS.

Keywords: metabolic syndrome; digital health; lifestyle intervention; healthcare; machine learning

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Chapter 1.

Introduction

1.1. Objective

This study aimed to confirm the usefulness of digital health-based lifestyle interventions using healthcare devices and to propose a predictive model for prevention and management of MetS. Lifelog data were collected through healthcare devices, and features for prevention and management were extracted. With the features analyzed, a novel predictive model for the prevention and management of MetS was developed, consisting of persistence prediction for continued engagement and abbreviated risk factor prediction for self-care effects.

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1.2. Background

Metabolic syndrome (MetS) is a growing global public health challenge [1, 2]. Several population studies have highlighted the increased prevalence of MetS [3-6]. The National Health and Nutrition Examination Survey (2017–2018) has reported the prevalence of MetS as approximately 38.3% [5]. The corresponding values reported by the Korean National Health and Nutrition Survey in 2017 were 28.1% and 18.7% for men and women, respectively [6]. The increase in MetS was associated with several factors resulting from changing lifestyles, primarily aging, eating habits, physical inactivity, sedentary work, long working hours, and stress [7, 8]. MetS encompasses factors such as abdominal fat, hypertension, dyslipidemia, and glucose intolerance. In addition, it is a risk factor for type 2 diabetes, coronary heart disease, and other cardiovascular diseases [2, 9-13]. When diabetes is not yet present, the risk for progression to type 2 diabetes averages about a five-fold increase compared with those without the syndrome. Once diabetes develops, the cardiovascular risk increases even more [14].

Most individuals who develop the syndrome first acquire abdominal obesity without risk factors, but multiple risk factors begin to appear with time. In the beginning, they are usually only borderline elevated; later, in many individuals, they become categorically elevated [14]. In some, the syndrome culminates in type 2 diabetes (Figure 1.1). As the MetS advances, risk for cardiovascular disease and its complications increase. Those with diabetes can further acquire a host of complications, including renal failure, diabetic cardiomyopathy, and various neuropathies. When cardiovascular disease and diabetes exist concomitantly, the risk for subsequent cardiovascular morbidity is very high [9, 11-14]. Patients with MetS can manifest various other conditions that complicate their management. The presence of several or all of these outcomes commonly leads to the use of multiple medications (polypharmacy). Pharmacological interventions may help delay or manage complications associated with MetS. Polypharmacy carries the risk of adverse drug interactions and interferes with compliance, and for many patients, it imposes a prohibitive cost burden [14, 15]. The main aim of MetS management is to reduce modifiable risk factors (obesity, physical inactivity, and an atherogenic diet) through lifestyle changes [1, 12, 15-19]. Several studies have examined the impact of digital health technologies on lifestyle changes and health outcomes [12, 15-21].

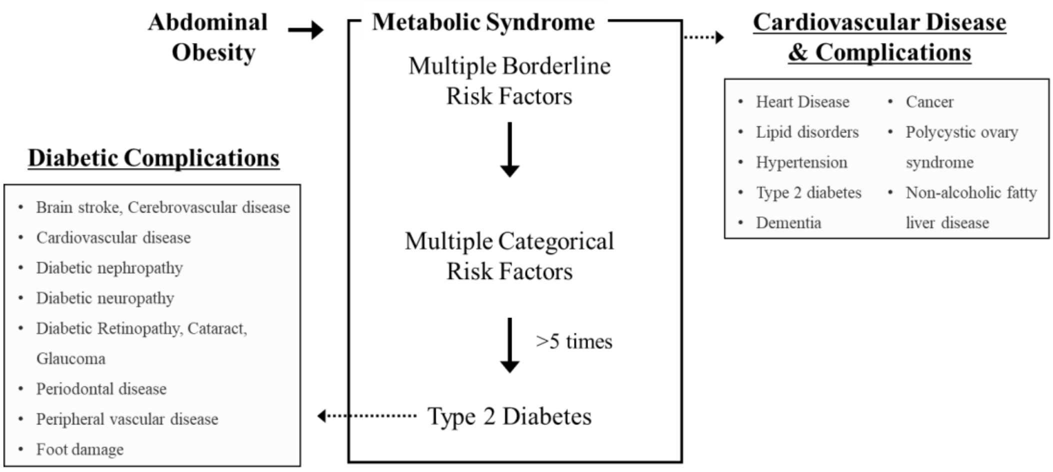

Figure 1.1. Clinical outcomes of the metabolic syndrome.

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1.3. Digital Health

Mobile technology has spread rapidly around the globe. Today, it is estimated that more than 5 billion people have mobile devices, and over half of these connections are smartphones [22]. Digital health is defined as an information and communication technology that supports health through electronic and mobile health solutions and uses big data, computational genomics, and artificial intelligence [23]. Across a patient's journey, digital health apps can be divided into two main categories: those focused on wellness management, which facilitates tracking and modification of fitness behaviors, lifestyle, stress, and diet, and those that specifically focus on health condition management, which supply information on diseases and conditions, enable access to care, and aid treatment, such as through medication reminders. Condition management apps account for 47% of all digital health apps, with a notable increase in disease-specific apps. For apps that provide disease-specific support and management, the top five therapy areas they focus on are all chronic conditions [24, 25]. Digital health-based lifestyle interventions may improve population health by increasing access to medical services and uptake of interventions [23-29]. Mobile applications, short message services (SMS), wearable devices, social media, and interactive websites have been used as intervention methods [16, 18, 19, 30-32].

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1.4. Metabolic Syndrome

Reaven developed the first concept of metabolic syndrome X [1, 2]. Based on the consultation, the World Health Organization (WHO) has defined a set of criteria. Many other international organizations or professional institutions, including the National Cholesterol Education Program's Adult Treatment Panel III (NCEP: ATP III), the European Group for the Study of Insulin Resistance (EGIR), the American Association of Clinical Endocrinology (AACE), the International Diabetes Federation (IDF), and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) have also proposed criteria for recording measurements [1, 2, 9]. In the present study, NCEP: ATP III and IDF criteria were used [2, 20]. Abdominal obesity was defined based on the Korean Society for the Study of Obesity's waist circumference (WC) cut-off values, which were used to determine MetS in this population [6]. MetS was defined as the presence of three or more of the following (Table 1.1): (1) WC of ≥ 90 cm in men or ≥ 85 cm in women; (2) fasting blood sugar (FBS) levels of ≥ 100 mg/dL; (3) systolic/diastolic blood pressure (SBP/DBP) of ≥ 130/85 mmHg; (4) high-density lipoprotein cholesterol (HDL-C) levels of < 40 mg/dL in men or <50 mg/dL in women; and (5) triglyceride (TG) levels of ≥150 mg/dL. In this study, participants with pre-MetS (defined as having 1 or 2 risk factors) were included for the prevention of MetS.

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Table 1.1. Definition of metabolic syndrome

Risk factors	Defining level	Criteria
Central obesity - Waist circumference	 ≥ 90 cm (males), ≥ 85 cm (females)	KSSO
Hyperglycemia - Fasting blood sugar	 ≥ 100 mg/dl	NECP ATP III, IDF
Dyslipidemia - Triglyceride - HDL-C	 ≥ 150 mg/dl < 40 mg/dl (males), < 50 mg/dl (females)	
Hypertension - Blood pressure	 ≥ 130 mmHg systolic or ≥ 85 mmHg diastolic	

HDL-C, high-density lipoprotein cholesterol; KSSO, Korean Society for the Study of Obesity; NACP: ATP III, National Cholesterol Education Program's Adult Treatment Panel III; IDF, International Diabetes Federation

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1.5. Related Work

Previous studies have reported weight loss in participants with MetS and obesity using remote monitoring and healthcare services combined with conventional treatment [16, 18, 19, 30, 31, 33]. Other studies examined the impact of lifestyle interventions delivered by health coaches alongside activity monitoring [32]. These studies showed activity changes among the participants based on feedback from the monitoring service. However, these studies only reported the effects of healthcare services based on digital health-based lifestyle interventions. In addition, no detailed study has been conducted to show that lifestyle interventions and self-care are required to improve MetS. Lifestyle interventions must be conducted according to the patient's characteristics, and self-care should be encouraged to prevent and manage MetS. Digital health-based lifestyle interventions may be key to achieving lifestyle changes and improving health [27, 28, 34]. People need to be able to adhere to lifestyle behaviors to make consistent and lasting changes. The importance of adherence in treating obesity or diabetes related to MetS has been widely described [35, 36]. The effectiveness of lifestyle interventions is dependent on timely confirmation of self-care. Digital health coordinators can provide personalized feedback and support in cases where it is not being maintained. Lifestyle changes can be assessed using both direct and indirect measures, including the levels of engagement, persistence, and physical activity, which all contribute to intervention uptake and help improve MetS outcomes.

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Chapter 2.

Materials and Methods

2.1. Study Design

The study participants were enrolled between December 2019 and September 2020 using participants from the Wonju Cohort Study. The Wonju Cohort Study included a community-based cohort in Wonju, Korea, and medical examinations and epidemiological investigations were performed to identify cardiovascular and chronic diseases [37]. In the Wonju Cohort Study, participants with one or more MetS risk factors were invited to confirm the study’s explanation and their intention to participate. The inclusion criteria were as follows: 40–80 years of age, one or more MetS risk factors, and no difficulty using healthcare devices. Exclusion criteria were as follows: participants were excluded if they were taking medication, had difficulty using healthcare devices, or could not follow instructions related to the intervention. The participants were evaluated at two time points. The first assessment examined risk factors for MetS. Selected participants received five healthcare devices. Lifelog data were collected by an application installed on the

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participants' smartphones. A lifestyle intervention was introduced after 6 weeks to induce lifestyle changes and continuous engagement with the healthcare devices. At 26 weeks, the risk factors for MetS were assessed again (Figure 2.1). The Institutional Review Board of the Wonju College of Medicine, Yonsei University (CR319089), approved the study. The study protocol was registered at the Clinical Research Information Service (KCT0005783).

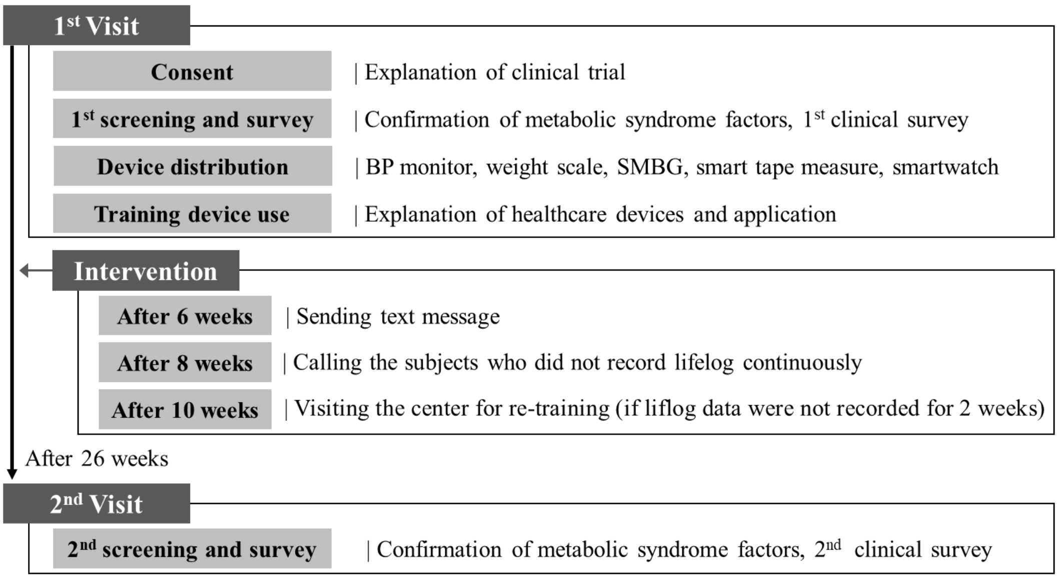

Figure 2.1. Study design. BP, blood pressure; SMBG, self-monitoring blood glucose

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2.2. Participants

The Wonju cohort study included 1,519 participants, of whom 867 had one or more MetS risk factors. Participants were recruited for the clinical trial via phone, and 355 participants confirmed their participation. The participants were assessed during a hospital visit, and the study aims were explained. Among them, 136 participants presented with more than one risk factor and agreed to participate in the clinical trial. Each participant received five healthcare devices. Finally, the analysis included data from 106 participants who were examined at the 26-week follow-up assessment. One participant received diabetes mellitus medication, 22 participants withdrew their consent (due to difficulties participating in the study or unavailability, among others), and seven participants who did not use the provided devices for more than half the study period were excluded from the analysis (Figure 2.2).

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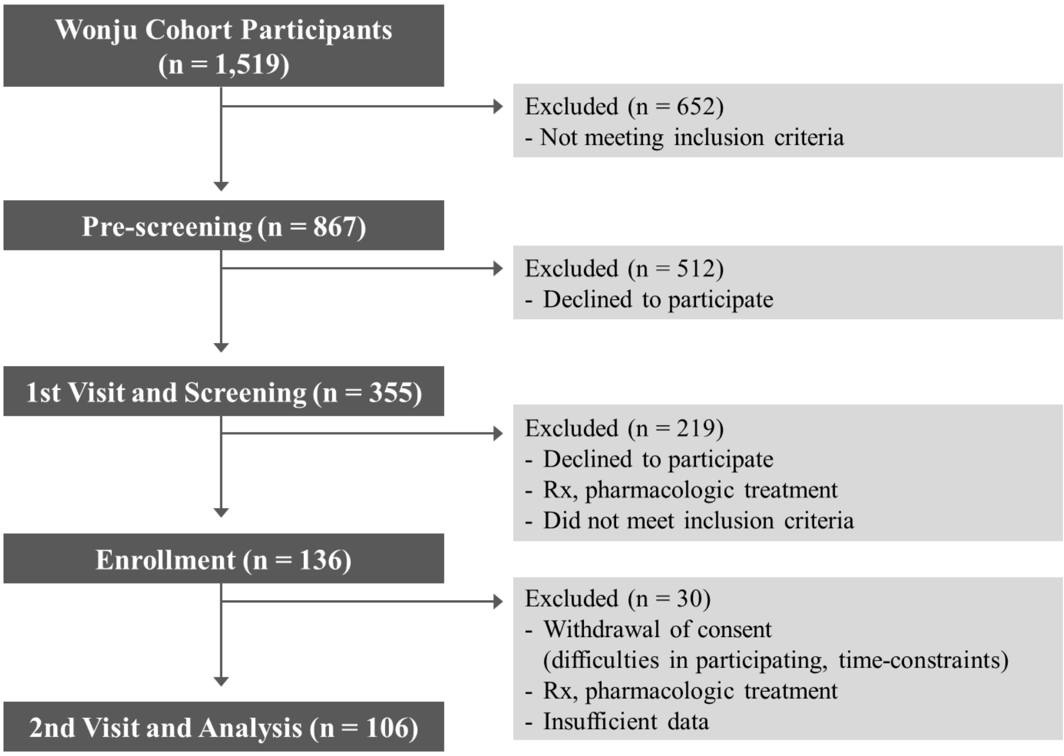

Figure 2.2. Flow chart of the study design.

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2.3. Lifelog Data Using Healthcare Devices

Lifelog data are the personal health data gathered daily and automatically by the provided application and healthcare devices. The provided healthcare devices were a blood pressure (BP) monitor (Omron HEM-9200T, Omron Healthcare, Japan); a self-monitoring blood glucose (SMBG) device (CareSens N Premier, I-SENS, Korea); a weight scale (Efilscale, LifeSemantics, Korea); a smart tape measure (PIE, Bagel Labs, Korea); and a smartwatch (Galaxy Watch Active 1, Samsung Electronics, Korea). For lifelog data, SBP, DBP, and heart rate (HR) were collected from the BP monitor, FBS from the SMBG device, step counter from the smartwatch, weight from the weight scale, and WC from the smart tape measure. These devices were connected to an application that recorded all the relevant measurements and automatically transferred the participants' lifelog data from their smartphones to a web-based server. It was recommended that the devices be used three or more times per week. Medical staff had real-time access to the lifelog data through a designated website.

2.4. Group Classification

Participants who received lifestyle interventions were included in the analysis. The participants with pre-MetS or MetS were divided into two groups according to the baseline and follow-up (26-week) assessment findings. The participants with pre-MetS were divided into two groups based on changes in their risk factors: the prevention group, with reduced

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and consistent risk factors, and the non-prevention group, with increased risk factors. The participants in the MetS with the aim of management were divided into two groups: the improvement group, with reduced risk factors, and the non-improvement group, with consistent and increased risk factors.

2.5. Engagement, Persistence, and Physical Activity

The engagement was defined as the frequency of device use per week, based on pre-specified criteria that involved two rules: (1) All five healthcare devices were used more than the minimum frequency required; (2) The total weekly frequency of device use was greater than the minimum frequency required. “Persistence” refers to the continuous number of satisfied engagements. The maximum persistence during the study period was analyzed. Physical activity was measured with a step counter embedded in the provided smartwatch. In this study, the prevention and improvement groups were used as a reference for lifestyle changes. Digital health-based lifestyle interventions were implemented during weeks 6, 8, and 10. Text messages were delivered from week 6; phone calls were made from week 8, and face-to-face re-training was conducted from week 10. Any questions from the participants were resolved by the medical staff via phone calls or visits.

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2.6. Prediction Model Based on Machine Learning

2.6.1. Machine-learning classifiers

In this study, eight types of classifiers were adopted: decision trees (fine, medium, coarse), discriminant analysis (linear, quadratic), logistic regression, naïve Bayes, support vector machines (linear, quadratic cubic fine gaussian, medium gaussian, coarse gaussian), nearest neighbor classifiers (fine, medium, coarse, cosine, cubic, weighted), ensemble classifiers (boosted trees, bagged trees, subspace discriminant, RUSBoost trees), and neural network (narrow, medium, wide, bi-layered, tri-layered). Details regarding different machine-learning classifiers are listed in Table 2.1. The prediction performance was compared for each classifier that was trained and evaluated on five-fold cross-validation.

(1) Decision tree: The decision tree is non-parametric and can efficiently deal with large, complicated datasets without imposing a complicated parametric structure. This classifier works by examining the discriminatory ability of the extracted features one at a time to create a set of rules that ultimately leads to a complete classification system. This method classifies a population into branch-like segments that construct an inverted tree with a root node, internal nodes, and leaf nodes. A root node, called a “decision node,” represents a choice that divides all records into two or more mutually exclusive subsets. Internal nodes, called chance nodes, represent one of the possible choices available in the tree structure; the top edge of the node is connected to its parent node, and the bottom edge is connected to its child nodes or leaf nodes. Leaf nodes, called end nodes, represent the final result of a combination of decisions or events [38, 39].

(2) Discriminant Analysis: This classification algorithm is based on the assumption that the data of different classes obey different Gaussian distributions. The main process is first training a classifier to fit a function that can estimate the parameters of the distribution of each class, and then using the classifier to predict new samples. The linear discriminant analysis (LDA) is the most widely used discrimination analysis. In LDA, the key step is to find a projection hyperplane in k-dimensional space, then project different classes of samples onto the hyperplane, maximizing the between-class distances and minimizing the within-class distances.

(3) Logistic Regression: Logistic regression is a generalized linear model. Generalized linear models are composed of two parts: a linear part and a link function. The linear part of the classification model is calculated, and the output of this calculation is conveyed through the link function. In the case of logistic regression, the linear result is run through a logistic function. The logistic function only returns values between 0.0 and 1.0 [40].

(4) Naïve Bayes (NB): An NB classifier is a classification system based on Bayes' theorem that assumes all the attributes are fully independent given the output class, called the conditional independence assumption. The main advantage of the NB classifier is that it is easy to construct without needing complicated iterative parameter estimation schemes. In addition, the NB classifier is robust to noise and irrelevant attributes [41, 42].

(5) Support Vector Machine (SVM): The SVM is a popular classifier based on finding optimal separating decision hyperplanes between classes with the maximum

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margin between patterns of each class. It can benefit from a maximum margin hyperplane in a transformed feature space using a kernel function to map the dataset into an inner product space to create a non-linear structure. Common kernel functions include Gaussian, linear, quadratic, and cubic kernels [43, 44].

(6) Nearest Neighbor Classifiers: K-Nearest Neighbor (KNN) is one of the simplest classification algorithms. Its main idea is to find the K-nearest samples of new data in the feature space and then classify it into a specific class according to the k neighbors. The KNN classifier is simple but requires no training time. The training dataset is identified by an unknown window of class labels spread over the feature space. A new dataset is assigned a class label based on the single closest neighbor or K-nearest examples considering the Euclidean distance [44-46].

(7) Ensemble Classifiers: Different from other classification algorithms that only contain one classifier, Ensemble Classifiers are proposed to use multiple classifiers to improve the final performance. Its strategy is to aggregate multiple weak learners into strong learners. The weak learners can be decision trees, KNNs, or other single classifiers. The main aggregation strategies include bagging, boosting, and the random subspace method. In bagging, the training set is randomly sampled k times with replacement, producing k training sets with sizes equal to the original training set. Boosting induces an ensemble of learners by adaptively changing the distribution of the training set based on the performance of the previously created regressors. In the random subspace method, the regressor consists of multiple learners constructed systematically by pseudo-randomly

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selecting subsets of the feature vector, that is, learners constructed in randomly chosen subspaces [47-51].

(8) Neural network (NN): Artificial neural networks (ANN) or simply neural networks (NN) are generalized mathematical models that exhibit biological nervous systems, which inspire the learning process of the human brain. ANN is a widely used approach. These methods typically have good predictive accuracy; however, they are not easy to interpret. Model flexibility increases with the neural network's size and the number of fully connected layers. The model is a feed-forward, fully connected NN for classification. The first fully connected layer of the neural network has a connection with the network input, and each subsequent layer has a connection with the previous layer. Each fully connected layer multiplies the input by a weight matrix and then adds a bias vector. An activation function follows each fully connected layer. The final fully connected layer and the subsequent activation function produce the network's output classification scores and predicted labels [52, 53].

2.6.2. Feature selection

Feature selection is one of the techniques used for dimensionality reduction; in this technique, relevant features are selected, and irrelevant and redundant features are discarded. A reduction in input dimensionality can improve performance either by decreasing the learning speed and model complexity or by increasing generalization capacity and classification accuracy. The selection of suitable features can also reduce the measurement cost and improve understanding of the problem. The Recursive Feature

Elimination (RFE) selection method is a recursive process that ranks features according to some measure of their importance. At each iteration, the importance of each feature is determined, and the least important one is removed. The (inverse) order in which features are eliminated is used to construct a final ranking. The feature ranking method of random forest-recursive feature elimination (RF-FFE) is based on a measure of variable importance given by random forest. For any given tree in a random forest, there is a subset of the learning set not used by it during training because each tree was grown only on a bootstrap sample. These subsets, called “out-of-bag” (OOB), can give unbiased measures of prediction error. Intuitively, irrelevant features will not change the prediction error when altered in this way, in contrast to the relevant ones. The relative loss in performance between the “original” and “shuffled” data sets is therefore related to the relevance of the shuffled feature. In RF-RFE, this feature importance measure is coupled with the RFE [54-57].

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Table 2.1. List of machine-learning classifiers and description

Classifier	Description
Decision Tree	
Fine Tree	Maximum number of splits: 100, Split criterion: Gini's diversity index, Surrogate decision splits: Off
Medium Tree	Maximum number of splits: 20, Split criterion: Gini's diversity index, Surrogate decision splits: Off
Coarse tree	Maximum number of splits: 4, Split criterion: Gini's diversity index, Surrogate decision splits: Off
Discriminant Analysis	
Linear Discriminant	Covariance structure: Full
Quadratic Discriminant	Covariance structure: Full
Logistic Regression	
Logistic Regression	-
Naïve Bayes Classifiers	
Gaussian Naïve Bayes	Distribution name for numeric predictors: Gaussian, Distribution name for categorical predictors: Not Applicable
Kernel Naïve Bayes	Distribution name for numeric predictors: Kernel, Distribution name for categorical predictors: Not Applicable, Kernel type: Gaussian, Support: Unbounded
Support Vector Machine	
Linear SVM	Kernel function: Linear, Kernel scale: Automatic, Box constraint level: 1, Multiclass method: One-vs-One, Standardize data: true
Quadratic SVM	Kernel function: Quadratic, Kernel scale: Automatic, Box constraint level: 1, Multiclass method: One-vs-One, Standardize data: true
Cubic SVM	Kernel function: Cubic, Kernel scale: Automatic, Box constraint level: 1, Multiclass method: One-vs-One, Standardize data: true
Fine Gaussian SVM	Kernel function: Gaussian, Kernel scale: sqrt(the number of predictors)/4, Box constraint level: 1, Multiclass method: One-vs-One, Standardize data: true
Medium Gaussian SVM	Kernel function: Gaussian, Kernel scale: sqrt(the number of predictors), Box constraint level: 1, Multiclass method: One-vs-One, Standardize data: true
Coarse Gaussian SVM	Kernel function: Gaussian, Kernel scale: sqrt(the number of predictors)*4, Box constraint level: 1, Multiclass method: One-vs-One, Standardize data: true

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Table 2.1. List of machine-learning classifiers and description (*continued*)

Classifier	Description
Nearest Neighbor Classifiers	
Fine KNN	Number of neighbors: 1, Distance metric: Euclidean, Distance weight: Equal, Standardize data: true
Medium KNN	Number of neighbors: 10, Distance metric: Euclidean, Distance weight: Equal, Standardize data: true
Coarse KNN	Number of neighbors: 100, Distance metric: Euclidean, Distance weight: Equal, Standardize data: true
Cosine KNN	Number of neighbors: 10, Distance metric: Cosine, Distance weight: Equal, Standardize data: true
Cubic KNN	Number of neighbors: 10, Distance metric: Minkowski (cubic), Distance weight: Equal, Standardize data: true
Weighted KNN	Number of neighbors: 10, Distance metric: Euclidean, Distance weight: Squared inverse, Standardize data: true
Ensemble	
Boosted Trees (AdaBoost)	Ensemble method: AdaBoost, Learner type: Decision tree, Maximum number of splits: 20, Number of learners: 30, Learning rate: 0.1
Bagged Trees (Random Forest)	Ensemble method: Bag, Learner type: Decision tree, Maximum number of splits: sample size-1, Number of learners: 30
Subspace Discriminant	Ensemble method: Subspace, Learner type: Discriminant, Number of learners: 30, Subspace dimension: 6
Subspace KNN	Ensemble method: Subspace, Learner type: Nearest neighbors, Number of learners: 30, Subspace dimension: 6
RUSBoost Trees	Ensemble method: RUSBoost, Learner type: Decision tree, Maximum number of splits: 20, Number of learners: 30, Learning rate: 0.1
Neural Network	
Narrow NN	Number of fully connected layers: 1, First layer size: 10, Activation: Rectified linear units (ReLU), Iteration limit: 1,000, Regularization strength (Lambda): 0, Standardize data: Yes
Medium NN	Number of fully connected layers: 1, First layer size: 25, Activation: ReLU, Iteration limit: 1,000, Regularization strength (Lambda): 0, Standardize data: Yes
Wide NN	Number of fully connected layers: 1, First layer size: 100, Activation: ReLU, Iteration limit: 1,000, Regularization strength (Lambda): 0, Standardize data: Yes

Bi-layered NN	Number of fully connected layers: 2, First layer size: 10, Second layer size: 10, Activation: ReLU, Iteration limit: 1,000, Regularization strength (Lambda): 0, Standardize data: Yes
Tri-layered NN	Number of fully connected layers: 3, First layer size: 10, Second layer size: 10, Third layer size: 10, Activation: ReLU, Iteration limit: 1,000, Regularization strength (Lambda): 0, Standardize data: Yes

2.6.3. Performance evaluation

The participants' characteristics at baseline were compared with those at follow-up using the paired *t*-test or Wilcoxon signed-rank test. An independent-samples *t*-test or Mann–Whitney *U* test was used to compare the differences between the two groups. The accuracy (Equation 2.1), recall (Equation 2.2), precision (Equation 2.3), F1-score (Equation 2.4), and Matthews correlation coefficient (MCC) (Equation 2.5) were used to evaluate the performance of the proposed prediction model. The percentage of correctly classified values in each class is calculated using accuracy. Precision is defined as the percentage of true positive predictions, whereas recall is defined as the percentage of correct positive predictions that are predicted to be positive. Precision and recall are both equal to 1. When the dataset is unbalanced (the number of samples in one class is much larger than the number of samples in the other classes), accuracy cannot be considered a reliable measure anymore because it provides an overly optimistic estimation of the classifier's ability for the majority class. The F1-score is the harmonic mean of precision and sensitivity, which is extensively used to deal with such unbalanced data. MCC accounts for true positives and negatives as well as false positives and negatives and is a balanced measure even when the classes are of varying sizes. The MCC is, in essence, a correlation coefficient between -1 and +1. The *AUC* (area under the curve) is the closed graph area surrounded by the receiver operating characteristic (ROC) curve and the right ordinate and abscissa. The *AUC* is used to evaluate the algorithm's performance and generalization ability in the classification problem. The better the model's performance, the closer the *AUC* value is to 1, which is good when *AUC* >0.85 [40, 47, 58, 59]. Analyses were performed using IBM SPSS Statistics 25 (SAS Institute, Cary, NC, USA) and MATLAB 2021b (MathWorks, USA). *P*-values of <0.05 were considered statistically significant.

$$Accuracy = \frac{TP + TN}{TP + FP + FN + TN} \qquad \text{(Equation 2.1)}$$

$$Recall = \frac{TP}{TP + FN} \qquad \text{(Equation 2.2)}$$

$$Precision = \frac{TP}{TP + FP} \qquad \text{(Equation 2.3)}$$

$$F1\text{-}score = 2 \times \frac{Precision \times Recall}{Precision + Recall} \qquad \text{(Equation 2.4)}$$

$$MCC = \frac{(TP \times FN) - (FP \times FN)}{\sqrt{(TP + FP) \times (TN + FP) \times (TP + FP) \times (TN + FN)}} \qquad \text{(Equation 2.5)}$$

, where TP means true positive, i.e., the number of positive samples predicted as positive samples, FP is false positive, i.e., the number of negative samples predicted as positive samples, TN is a true negative, and FN is a false negative.

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Chapter 3.

Effect of Digital Health-based Lifestyle Intervention

3.1. Participant's Characteristics

The participants' characteristics at baseline and follow-up assessments are presented in Table 3.1. Significant differences in WC, SBP, DBP, and HDL-C were observed in the pre-MetS participants ($P < 0.05$). The average number of risk factors decreased from 1.7 (0.5) to 1.6 (1.1) ($P > 0.05$). Significant differences in MetS were observed in weight, BMI, risk factors, WC, SBP, DBP, and FBS. The average number of risk factors decreased from 3.6 (0.6) to 2.4 (1.1) ($P < 0.05$). There were 42 participants in the pre-MetS prevention group with reduced and consistent risk factors and 14 in the non-prevention group with increased risk factors. MetS was present in 43 participants in the improvement group with reduced risk factors and in 17 participants in the non-improvement group with consistent and increased risk factors.

Table 3.1. Participant characteristics at baseline and follow-up assessments

Characteristics	Pre-MetS (n = 46)			MetS (n = 60)		
	Baseline	Follow-up	*P*-value	Baseline	Follow-up	*P*-value
General Characteristics						
Sex (male/female)	17/29	-	-	25/35	-	-
Age (years)	63.9 (6.8)	-	-	65.2 (5.9)	-	-
Height (cm)	160.1 (8.0)	-	-	160.0 (9.3)	-	-
Weight (kg)	62.1 (9.1)	61.8 (8.9)	0.29	67.9 (11.4)	67.1 (11.3)	<0.001
BMI (kg/m^2)	24.2 (2.9)	24.2 (2.9)	0.75	26.4 (2.7)	26.0 (2.7)	<0.001
Risk factors	1.7 (0.5)	1.6 (1.1)	0.58	3.6 (0.6)	2.4 (1.1)	<0.001
Risk factors of MetS						
WC	87.9 (7.5)	84.4 (7.2)	<0.001	93.3 (7.1)	88.7 (8.4)	<0.001
SBP	138.0 (15.7)	125.5 (15.2)	<0.001	140.1 (15.7)	127.0 (13.0)	<0.001
DBP	90.1 (9.1)	79.9 (9.2)	<0.001	89.6 (8.1)	80.3 (9.0)	<0.001
FBS	92.4 (9.2)	91.5 (10.9)	0.56	101.7 (10.8)	96.9 (9.1)	<0.001
HDL-C	55.1 (9.0)	52.9 (10.0)	<0.05	46.6 (9.1)	46.5 (10.0)	0.98
TG	118.6 (55.2)	136.1(73.2)	0.05	166.7 (103.1)	170.7 (114.0)	0.63
Group Classification						
Reduced risk factors	-	18	-	-	43	-
Consistent risk factors	-	14	-	-	16	-
Increased risk factors	-	14	-	-	1	-

Values were presented as mean (standard deviation); MetS, metabolic syndrome; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.

3.2. Effectiveness of Prevention and Management of MetS

Changes in the number of risk factors between baseline and follow-up are presented (Table 3.2). For the pre-MetS participants, while the prevention and non-prevention groups did not differ statistically significantly at baseline, significant differences were observed at the follow-up ($P < 0.001$). Furthermore, these two groups had the highest WC and BP values at baseline. Both prevention and non-prevention groups showed significant within-group differences between baseline and follow-up ($P < 0.001$). The prevention group showed significant decreases in WC (19%) and BP (53%), while the non-prevention group showed significant increases in HDL-C (50%) and TG (43%). The baseline and follow-up data for MetS participants revealed statistical differences between the improvement and non-improvement groups. In the improvement group, the number of MetS risk factors was greater at baseline ($P < 0.05$) but smaller at the follow-up ($P < 0.001$). The improvement group showed a significant difference between baseline and follow-up ($P < 0.001$). The improvement group showed a significant reduction in the WC (44%), BP (49%), FBS (40%), HDL-C (19%), and TG (19%), whereas the non-improvement group showed no significant changes.

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Table 3.2. Change in the number of risk factors

Characteristics	Pre-MetS (n = 46)			MetS (n = 60)		
	Prevention (n = 32)	Non-Prevention (n = 14)	*P*-value	Improvement (n = 43)	Non-Improvement (n = 17)	*P*-value
Baseline	1.6 (0.5)	1.7 (0.5)	0.56	3.7 (0.7)	3.3 (0.5)	<0.05
WC	14 (43.8)	6 (42.9)		41 (95.3)	13 (76.5)	
Blood pressure	30 (93.8)	10 (71.4)		38 (88.4)	15 (88.2)	
FBS	3 (9.4)	2 (14.3)		26 (60.5)	12 (70.6)	
HDL-C	2 (6.3)	3 (21.4)		27 (62.8)	7 (41.2)	
TG	3 (9.4)	3 (21.4)		25 (58.1)	9 (52.9)	
Follow-up	1.0 (0.8) †	2.9 (0.3) †	<0.001	2.0 (1.0) †	3.4 (0.5)	<0.001
WC	8 (25.0)	8 (57.1)		22 (51.2)	13 (76.5)	
Blood pressure	13 (40.6)	10 (71.4)		17 (39.5)	16 (94.1)	
FBS	2 (6.3)	4 (28.6)		9 (20.9)	9 (52.9)	
HDL-C	3 (9.4)	10 (71.4)		19 (44.2)	9 (52.9)	
TG	5 (15.6)	9 (64.3)		17 (39.5)	10 (58.8)	

Values are presented as mean (standard deviation); † represents statistically significant difference between baseline and follow-up (*P*-value < 0.001); MetS, metabolic syndrome; WC, waist circumference; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.

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3.3. Effectiveness of Digital Health-based Lifestyle Interventions

The frequency of device use is presented in Figures 3.1 and 3.2. The frequency of healthcare device use increased when lifestyle interventions were implemented; specifically, during week 10, when re-training was provided, the frequency of device use was higher than that in weeks 6 and 8, when text messages and phone calls were introduced, respectively. In the pre-MetS and MetS groups, the level of engagement with BP monitors, weight scales, and smart tape measures gradually increased and stabilized from week 14 onward.

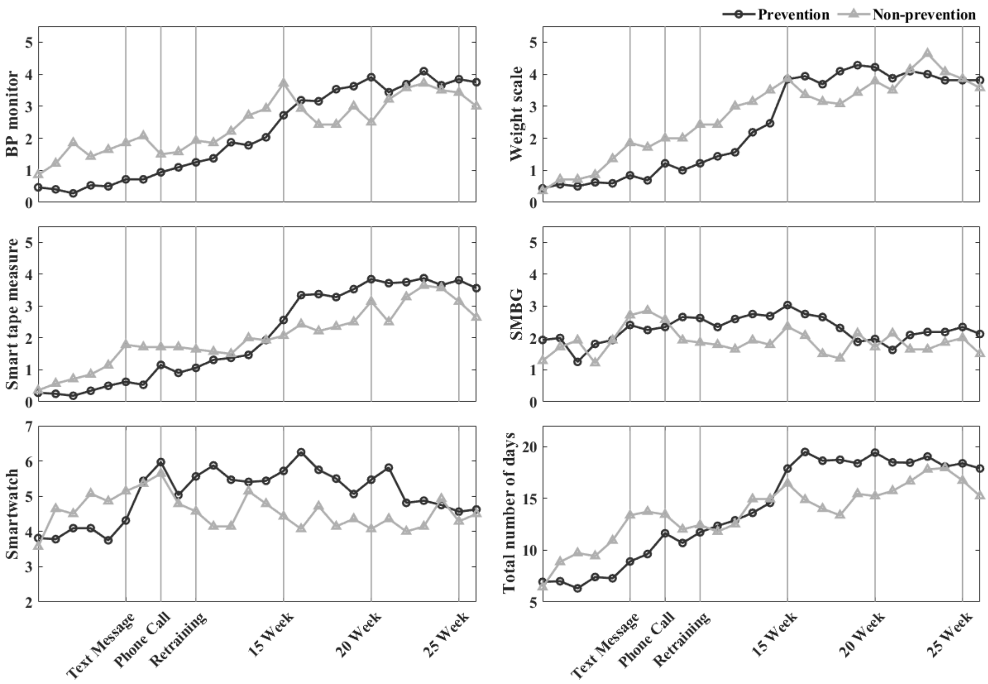

Figure 3.1. The number of days healthcare device use in the pre-MetS group.
BP, blood pressure; SMBG, self-monitoring blood glucose

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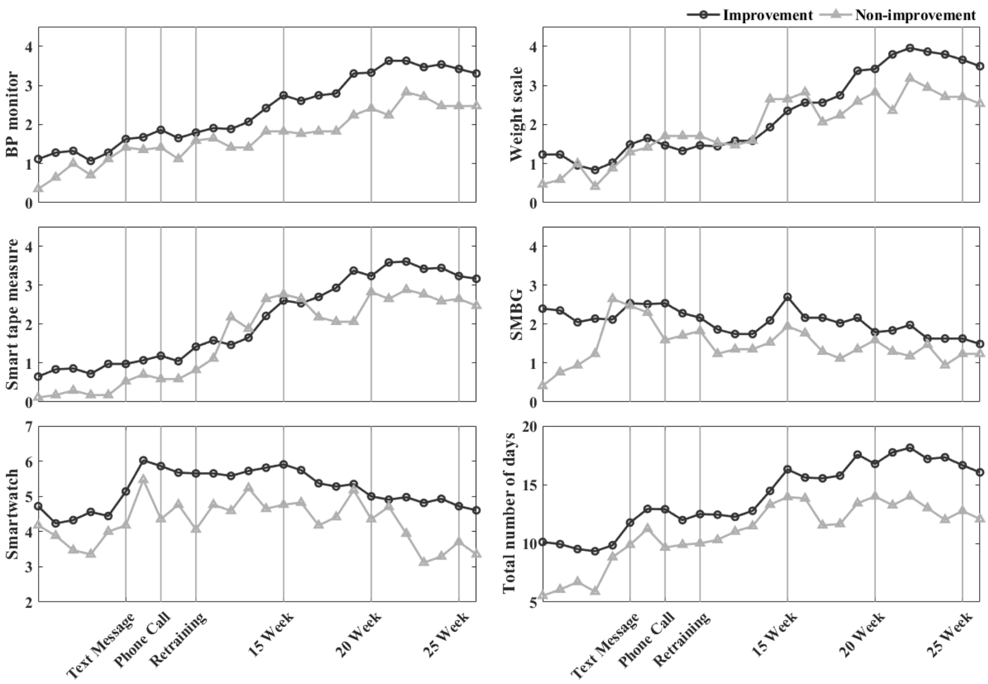

Figure 3.2. The number of days healthcare device use in the MetS group.
BP, blood pressure; SMBG, self-monitoring blood glucose

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3.4. Characteristic of Self-care Using Healthcare Devices

3.4.1. The frequency of healthcare device use

The frequency of use of healthcare device after 14 weeks in shown in Table 3.3. For those with pre-MetS, there were significant differences in the use of a smart tape measure, SMBG, or smartwatch and the total number of use days between the prevention and non-prevention groups ($P < 0.05$). For those with the MetS, there were significant differences between the improvement and non-improvement groups ($P < 0.05$) using the five healthcare devices and the total number of use days.

3.4.2. Engagement and persistence

Changes in the prevention and improvement groups after week 14 are considered, and the criteria for the achievement of engagement and persistence are determined. The rules of engagement were defined as follows: Rule 1: Weight scale, smart tape measure, and BP monitor were used on more than 3 days per week; the SMBG was used on more than 2 days per week, with the pre-and post-meal use counted as a single event. Smartwatch was used for more than 5 days per week. Rule 2: The number of days when devices were used was more than 16. Weekly engagement criteria were satisfied when either of the rules were met. The overall engagement levels in the prevention and non-prevention groups of the pre-MetS participants, during the 26 weeks were 10.6 (6.1) and 9.9 (6.3), respectively ($P > 0.05$), and in the improvement and non-improvement groups of the pre-MetS participants 10.2 (5.8) and 7.1 (6.1), respectively ($P < 0.05$). The maximum levels of persistence in the

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prevention, non-prevention, improvement, and non-improvement groups were 8.9 (5.7), 6.8 (4.7), 7.5 (4.8), and 5.4 (4.9), respectively. Although the engagement and persistence levels in the prevention and improvement groups were relatively high, the differences were not significant ($P > 0.05$).

3.4.3. Physical activity

Changes in physical activity levels were statistically significant after 14 weeks ($P < 0.001$). Physical activity was 7,171.7 (4,735.3), 5,699.3 (4,937.6), 7,323.6 (5,310.9), and 4,843.5 (4,589.4) steps in the prevention, non-prevention, improvement, and non-improvement groups, respectively (Table 3.3). There were relatively large decreases in the WC and BP in the prevention and improvement groups with high physical activity.

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Table 3.3. Engagement differences between the groups

Characteristics	Pre-MetS (n = 46)			MetS (n = 60)		
	Prevention (n = 32)	Non-Prevention (n = 14)	*P*-value	Improvement (n = 43)	Non-Improvement (n = 17)	*P*-value
Frequency of healthcare device use per week after 14 weeks						
Weight scale	4.0 (2.7)	3.7 (2.3)	0.13	3.3 (2.7)	2.6 (2.5)	<0.01
Smart tape measure	3.5 (2.8)	2.8 (2.5)	<0.01	3.2 (2.7)	2.5 (2.7)	<0.01
BP monitor	3.5 (2.8)	3.1 (2.4)	0.12	3.2 (2.6)	2.3 (2.5)	<0.001
SMBG	2.3 (2.1)	1.8 (1.7)	<0.05	1.9 (1.9)	1.4 (1.6)	<0.001
Smartwatch	5.3 (2.9)	4.3 (3.3)	<0.01	5.1 (2.9)	4.2 (3.1)	<0.001
Total number of use days	18.6 (10.2)	15.8 (9.4)	<0.01	16.7 (9.8)	13.0 (9.7)	<0.001
Physical activity	7,171.7 (4,735.3)	5,699.3 (4,937.6)	<0.001	7,323.6 (5,310.9)	4,843.5 (4,589.4)	<0.001
Criteria for achievement per 26 weeks						
Engagement	10.6 (6.1)	9.9 (6.3)	0.57	10.2 (5.8)	7.1 (6.1)	0.06
Persistence	8.9 (5.7)	6.8 (4.7)	0.23	7.5 (4.8)	5.4 (4.9)	0.11

Values were presented as mean (standard deviation); MetS, metabolic syndrome; BP, blood pressure; SMBG, self-monitoring blood glucose

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Chapter 4.

Prediction Model for Prevention and Management of MetS

4.1. Feature Extraction and Preprocessing

A novel predictive model for the prevention and management of MetS was proposed, consisting of persistence prediction for continued engagement and abbreviated risk factor prediction for self-care effects. Lifelog data measured from five healthcare devices (BP monitor, weight scale, SMBG, smart tape measure, smartwatch) were used for feature extraction (Figure 4.1). Each feature was calculated by moving one day through a window of 7 days with an overlap of 6 days. The extracted features used seven clinical data points and five frequency-of-use data points. Clinical data used SBP, DBP, HR, weight, WC, FBS, and the number of steps parameters. The median filter was used for data, and if there was a difference of more than 20% from the previous value, it was replaced with the previous data. FBS was used as the minimum data value measured before and after meals. The

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frequency-of-use days were calculated as the number of days of using healthcare devices in the window.

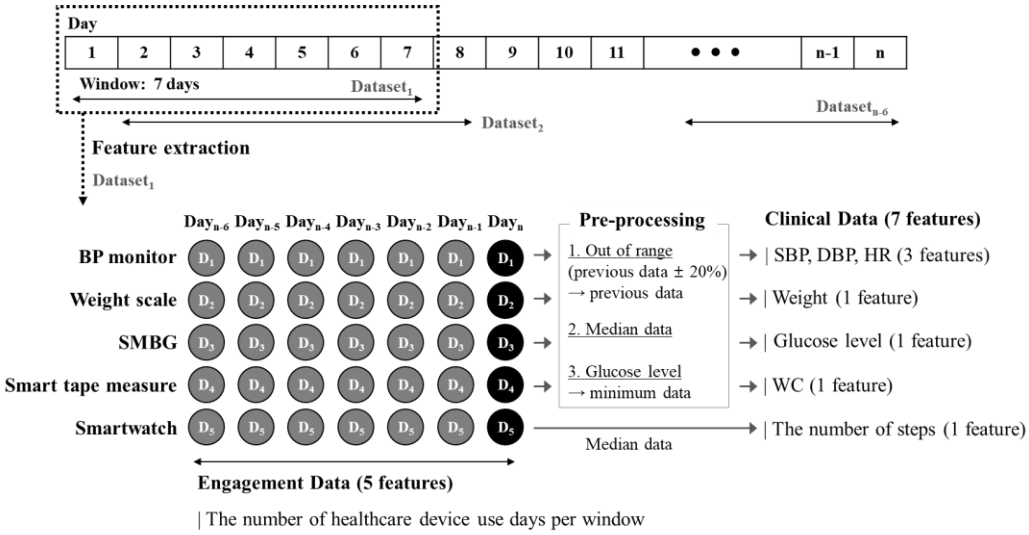

Figure 4.1. Feature extraction and preprocessing.
BP, blood pressure; SMBG, self-monitoring blood glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; WC, waist circumference

4.2. Data Labeling

Data were labeled for model to predict persistence and abbreviated risk factors. The model was developed based on 4 weeks, considering the results of engagement and persistence in the prevention group and improvement group, as well as the size of the window and overlap. The labeling of continued engagement was determined to have been achieved when the datasets of 7–28 days from the current time point were satisfied with engagement, to avoid overlapping data (Figure 4.2 (left)). To label abbreviated risk factors, the number of risk factors was calculated with the data of SBP, DBP, WC, and FBS measured at present and 4 weeks later, and whether the risk factors maintained, increased, or decreased was confirmed (Figure 4.2 (right)).

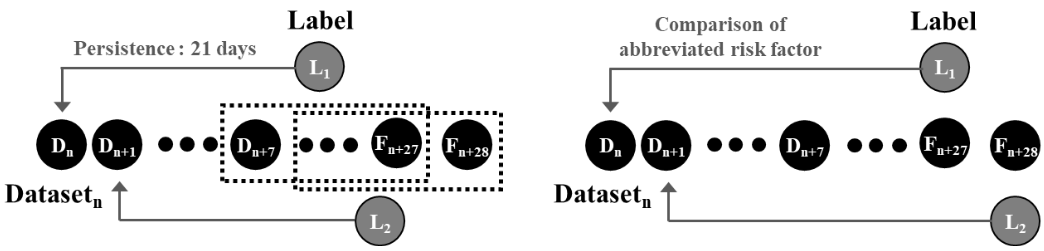

Figure 4.2. Data Labeling for prediction model: persistence (left), abbreviated risk factors (right)

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4.3. Prediction Model for Persistence

4.3.1. Comparison of machine-learning models

In the persistence prediction model, seven clinical data points and six frequency-of-use data points were used. Performance was compared through decision trees, discriminant analysis, logistic regression, naïve Bayes, support vector machines, nearest neighbor classifiers, ensemble classifiers, and a neural network (Table 4.1). The ensemble classifier using bagged trees showed the best performance, with a recall of 87.0%, precision of 94.8%, F1-score of 0.907, MCC of 0.885, accuracy of 96.2%, and *AUC* of 0.98. In terms of feature importance, FBS, the number of steps, the number of use days (SMBG), weight, and the number of use days (smartwatch) ranked highly (Figure 4.3).

Table 4.1. Performance evaluation of the classifier in persistence prediction model

Classifier	Recall (%)	Precision (%)	F1-score	MCC	Accuracy (%)	*AUC*
Decision Tree						
Fine Tree	71.6	79.9	0.755	0.694	90.0	0.92
Medium Tree	67.2	77.4	0.720	0.652	88.7	0.90
Coarse Tree	56.9	76.4	0.652	0.583	86.9	0.77
Discriminant Analysis						
Linear Discriminant	64.8	72.5	0.684	0.605	87.1	0.91
Quadratic Discriminant	78.9	64.4	0.710	0.625	86.1	0.91
Logistic Regression						
Logistic Regression	62.0	75.7	0.681	0.609	87.5	0.92
Naïve Bayes						
Gaussian Naïve Bayes	81.4	51.8	0.633	0.527	79.7	0.89
Kernel Naïve Bayes	95.9	31.8	0.477	0.340	54.8	0.89
Support Vector Machine						
Linear SVM	61.8	76.4	0.683	0.613	87.7	0.91
Quadratic SVM	66.6	80.7	0.730	0.669	89.4	0.92
Cubic SVM	77.3	84.6	0.808	0.760	92.1	0.93
Fine Gaussian SVM	80.0	90.2	0.848	0.812	93.8	0.95
Medium Gaussian SVM	69.8	81.5	0.752	0.694	90.1	0.91
Coarse Gaussian SVM	61.1	77.5	0.684	0.616	87.8	0.91

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Table 4.1. Performance evaluation of the classifier in persistence prediction model (*continued*)

Classifier	Recall (%)	Precision (%)	F1-score	MCC	Accuracy (%)	*AUC*
Nearest Neighbor						
Fine KNN	86.7	88.3	0.875	0.841	94.7	0.92
Medium KNN	74.7	84.2	0.792	0.741	91.5	0.95
Coarse KNN	64.4	79.0	0.709	0.645	88.7	0.93
Cosine KNN	75.4	83.2	0.791	0.739	91.4	0.95
Cubic KNN	73.7	83.5	0.783	0.730	91.2	0.95
Weighted KNN	83.1	89.8	0.863	0.829	94.3	0.96
Ensemble						
Boosted Trees	70.2	83.9	0.765	0.712	90.7	0.94
Bagged Trees	**87.0**	**94.8**	**0.907**	**0.885**	**96.2**	**0.98**
Subspace Discriminant	61.4	73.6	0.669	0.592	86.9	0.91
Subspace KNN	85.3	96.2	0.904	0.882	96.1	0.98
RUSBoost Trees	83.4	65.4	0.733	0.656	86.9	0.93
Neural Network						
Narrow NN	72.0	78.9	0.753	0.690	89.8	0.94
Medium NN	76.9	82.2	0.794	0.741	91.4	0.95
Wide NN	81.8	85.9	0.838	0.795	93.2	0.95
Bi-layered NN	73.7	80.6	0.770	0.712	90.5	0.94
Tri-layered NN	73.1	79.3	0.761	0.700	90.1	0.94

Highest performance for evaluation metrics is in bold font; SVM, support vector machine; KNN, k-nearest neighbor; NN, neural network; MCC, Matthews correlation coefficient; AUC, area under the receiver operating characteristic curve

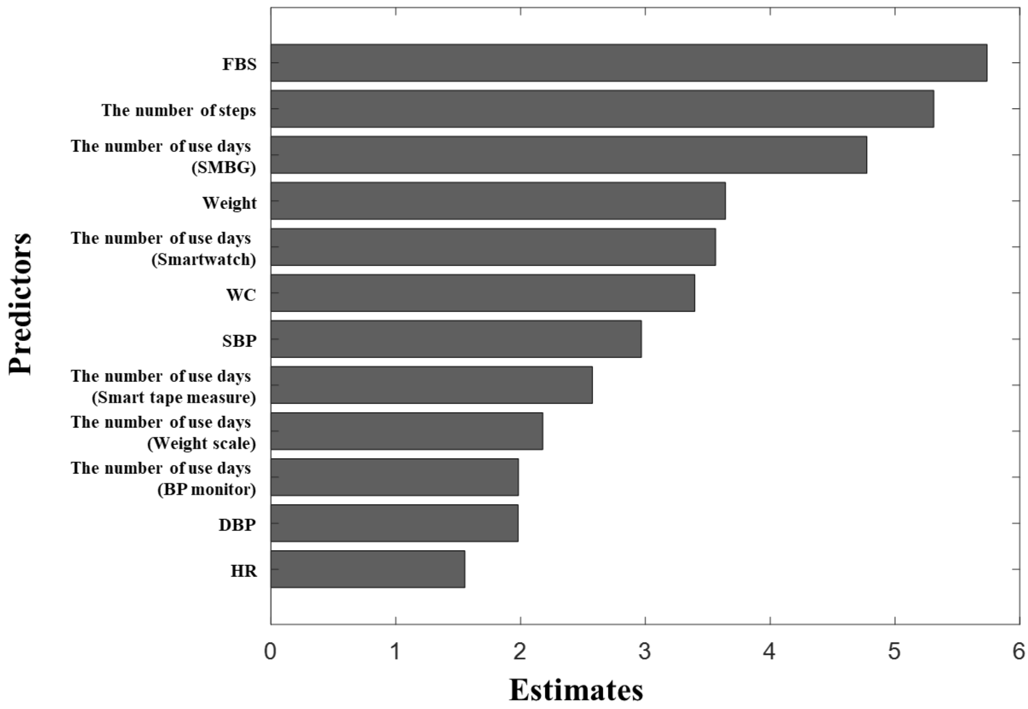

Figure 4.3. Feature importance in persistence prediction model. FBS, fasting blood sugar; SMBG, self-monitoring blood glucose; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate

4.3.2. Feature selection and performance evaluation

The RF-RFE algorithm was used for feature optimization. The recall process according to the RF-RFE process is presented in Figure 4.4. Feature optimization selected the minimum feature that stabilized the prediction result. In this study, the top five features (the number of use days (WC), weight, the number of steps, SBP, and FBS) for stabilizing prediction results were finally determined. As a result, the optimized feature showed a recall of 83.0%, precision of 92.4%, F1-score of 0.874, MCC of 0.844, and accuracy of 94.9% (Table 4.2).

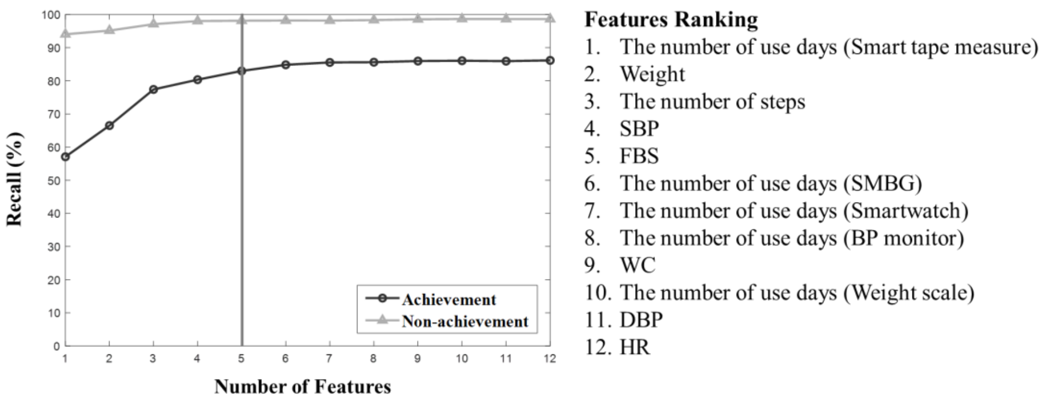

Figure 4.4. Feature selection and performance evaluation in the persistence prediction model. SBP, systolic blood pressure; FBS, fasting blood sugar; SMBG, self-monitoring blood glucose; BP, blood pressure; WC, waist circumference; DBP, diastolic blood pressure; HR, heart rate.

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Table 4.2. Ensemble (bagged trees) model performance evaluation in the persistence prediction model

	Precision (%)	Recall (%)	F1-score	MCC	Accuracy (%)
Achievement	83.0	92.4	0.874	0.844	94.9
Non-achievement	98.1	95.5	0.968		

MCC, Matthews correlation coefficient

4.4. Prediction Model for Abbreviated Risk Factors

4.4.1. Comparison of machine-learning model

In the abbreviated risk factor prediction model, seven clinical data points and six frequency-of-use data points were used. Performance was compared through decision trees, discriminant analysis, naïve Bayes, support vector machines, nearest neighbor classifiers, ensemble classifiers, and neural networks (Table 4.3). Therefore, the best performance was shown when the ensemble classifier's bagged tree (random forest) was used. Increased risk factors showed a recall of 78.4%, precision of 85.0%, F1-score of 0.816, and MCC of 0.774 and reduced risk factors showed a recall of 76.3%, precision of 85.0%, F1-score of 0.804, and MCC of 0.751. In terms of feature importance, FBS, DBP, SBP, and the number of steps ranked highly (Figure 4.5).

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Table 4.3. Performance evaluation of the classifiers in the abbreviated risk factors prediction model

Classifier	Increased risk factors				Decreased risk factors				*A* (%)	*AUC*
	R **(%)**	***P*** **(%)**	***F1***	***M***	***R*** **(%)**	***P*** **(%)**	***F1***	***M***		
Decision Tree										
Fine Tree	51.5	71.2	0.598	0.529	53.2	69.4	0.602	0.504	72.0	0.76
Medium Tree	38.2	64.1	0.479	0.408	36.9	62.8	0.465	0.363	66.1	0.69
Coarse Tree	33.7	57.2	0.424	0.343	43.3	51.7	0.471	0.317	62.0	0.62
Discriminant Analysis										
Linear Discriminant	8.7	45.3	0.147	0.129	9.6	46.2	0.159	0.107	58.8	0.65
Quadratic Discriminant	26.5	48.6	0.343	0.253	37.8	38.1	0.379	0.177	57.7	0.66
Naïve Bayes										
Gaussian Naïve Bayes	21.7	48.4	0.300	0.226	41.1	33.4	0.369	0.136	55.2	0.64
Kernel Naïve Bayes	40.5	54.4	0.464	0.363	24.9	52.0	0.337	0.233	62.6	0.70
Support Vector Machine										
Linear SVM	0.0	-	-	-	0.0	-	-	-	58.5	0.49
Quadratic SVM	25.4	67.8	0.370	0.343	21.6	62.6	0.321	0.264	64.0	0.67
Cubic SVM	61.4	69.9	0.654	0.578	59.6	70.6	0.646	0.552	74.5	0.81
Fine Gaussian SVM	59.0	88.6	0.708	0.674	54.1	86.7	0.666	0.617	79.1	0.90
Medium Gaussian SVM	27.9	78.1	0.411	0.404	23.7	75.9	0.362	0.341	66.7	0.75
Coarse Gaussian SVM	0.0	-	-	-	0.0	-	-	-	58.5	0.51

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Table 4.3. Performance evaluation of the classifiers in the abbreviated risk factors prediction model (*continued*)

Classifier	Increased risk factors				Decreased risk factors				*A* (%)	*AUC*
	R **(%)**	***P*** **(%)**	***F1***	***M***	***R*** **(%)**	***P*** **(%)**	***F1***	***M***		
Nearest Neighbor										
Fine KNN	77.0	77.5	0.772	0.717	73.9	77.2	0.755	0.685	81.9	0.82
Medium KNN	47.2	60.0	0.528	0.435	44.2	64.1	0.523	0.418	69.2	0.81
Coarse KNN	5.8	59.2	0.105	0.140	3.7	40.0	0.067	0.047	59.0	0.67
Cosine KNN	47.9	61.0	0.537	0.446	45.9	63.9	0.534	0.426	69.7	0.81
Cubic KNN	46.5	58.6	0.519	0.422	44.1	62.9	0.518	0.409	68.6	0.8
Weighted KNN	71.2	79.4	0.751	0.696	68.7	78.0	0.731	0.659	81.0	0.89
Ensemble										
Boosted Trees	41.3	68.2	0.514	0.449	38.2	69.6	0.494	0.413	68.1	0.75
Bagged Trees	**78.4**	**85.0**	**0.816**	**0.774**	**76.3**	**85.0**	**0.804**	**0.751**	**85.3**	**0.93**
Subspace Discriminant	0.1	100.0	0.030	0.032	1.6	53.8	0.031	0.054	58.6	0.64
Subspace KNN	68.5	78.5	0.732	0.674	66.7	78.1	0.719	0.646	79.9	0.89
RUSBoost Trees	69.4	53.1	0.602	0.496	68.3	50.1	0.578	0.435	62.1	0.73
Neural Network										
Narrow NN	40.0	59.4	0.478	0.391	34.5	54.7	0.423	0.300	64.6	0.71
Medium NN	53.1	61.5	0.570	0.477	53.7	64.0	0.584	0.471	70.1	0.79
Wide NN	71.7	72.1	0.719	0.651	68.4	69.7	0.690	0.599	77.2	0.84
Bi-layered NN	49.7	66.4	0.569	0.489	41.6	55.3	0.475	0.344	67.1	0.75
Tri-layered NN	48.7	65.3	0.558	0.477	46.2	57.1	0.511	0.381	67.9	0.76

R, Recall; *P*, Precision; *F1*, F1-score; *M*, Matthews correlation coefficient; *A*, Accuracy; *AUC*, area under the receiver operating characteristic curve; Highest performance for evaluation metrics is in bold font; SVM, support vector machine; KNN, k-nearest neighbor; NN, neural network;

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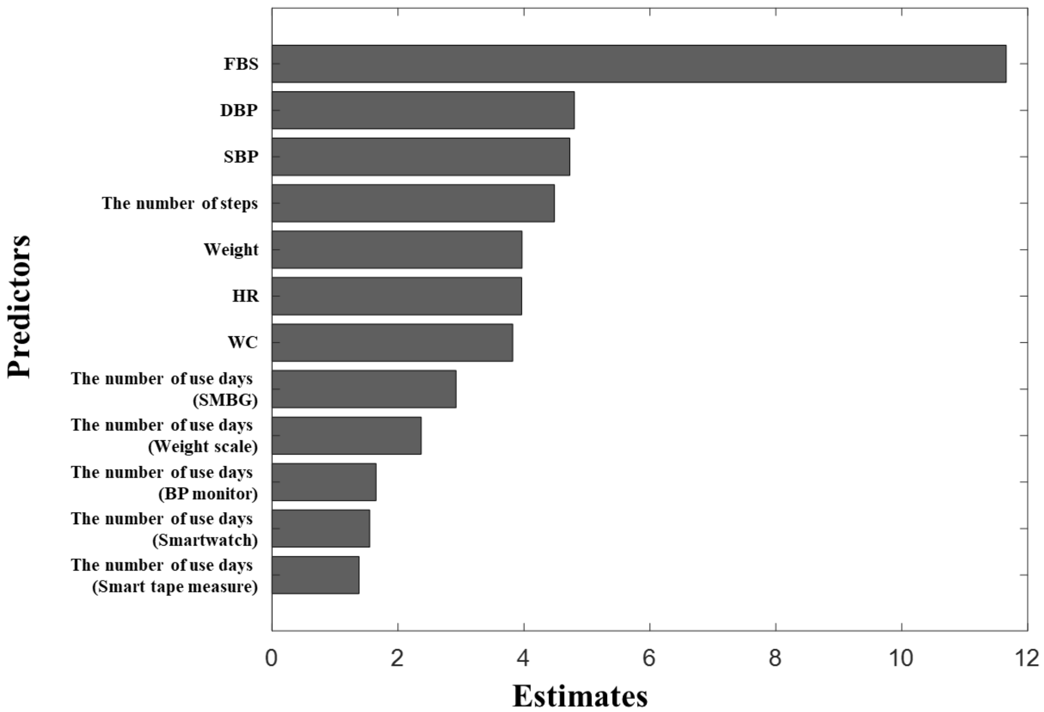

Figure 4.5. Feature importance in the abbreviated risk factors prediction model.
FBS, fasting blood sugar; DBP, diastolic blood pressure; SBP, systolic blood pressure; SMBG, self-monitoring blood glucose; HR, heart rate; WC, waist circumference

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4.4.2. Feature selection and performance evaluation

The RF-RFE algorithm was used for feature optimization. The recall process according to the RF-RFE process is presented in Figure 4.6. Feature optimization selected the minimum feature that stabilized the prediction result. In this study, the top seven features (FBS, DBP, SBP, the number of steps, HR, the number of use days (weight scale), and WC) for stabilizing prediction results were finally determined. Therefore, the optimized characteristics showed a recall of 79.8%, a precision of 87.2%, an F1-score of 0.834, and an MCC of 0.797 in increased abbreviated risk factors, and a recall of 75.1%, a precision of 85.5%, an F1 score of 0.800, and an MCC of 0.747 in decreased abbreviated risk factors. (Table 4.4).

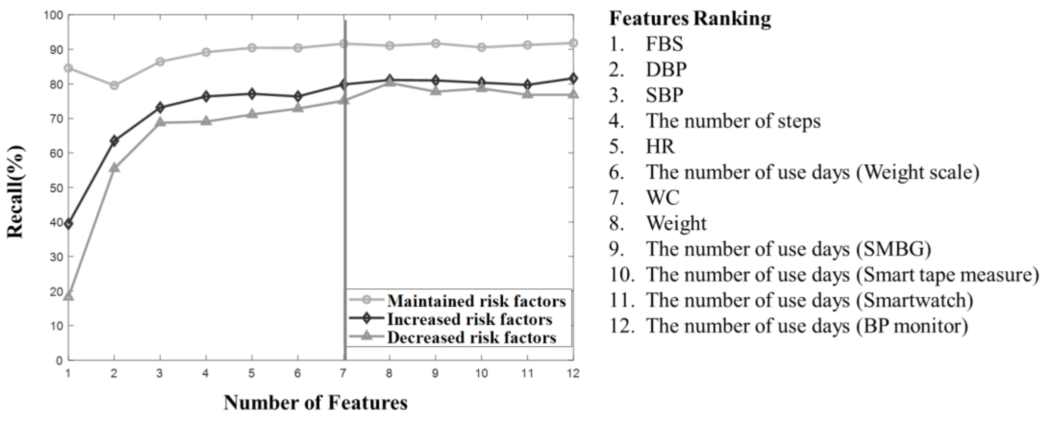

Figure 4.6. Feature selection and performance evaluation in the abbreviated risk factors prediction model. FBS, fasting blood sugar; DBP, diastolic blood pressure; SBP, systolic blood pressure; SMBG, self-monitoring blood glucose; HR, heart rate; WC, waist circumference

Table 4.4. Ensemble (bagged trees) model performance evaluation in the abbreviated risk factors prediction

	Recall (%)	Precision (%)	F1-score	MCC	Accuracy (%)
Maintained risk factors	91.6	85.3	0.884	0.708	85.7
Increased risk factors	79.8	87.2	0.834	0.797	
Decreased risk factors	75.1	85.5	0.800	0.747	

MCC, Matthews correlation coefficient

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Chapter 5.

Discussion and Conclusion

Digital health-based lifestyle interventions were presented for MetS prevention and management, which included using healthcare devices to support lifestyle changes and sustained long-term self-care. Previous studies compared the outcomes of participants who received and did not receive lifestyle interventions [16, 18, 19, 30-33]. There is some evidence that lifestyle interventions may be effective. However, this study examined the participants' characteristics based on changes in MetS risk factors and proposed prediction models to prevent and manage MetS by using healthcare devices. The use of healthcare devices for promoting continued interest in lifestyle interventions and self-care was confirmed and the appropriate frequency of use was recommended. Although all participants used the same lifestyle interventions, group differences were observed. These findings suggest that some modifications to lifestyle interventions may be required based on the participant's characteristics. to increase the likelihood of lifestyle changes.

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A prediction model for the prevention and management of MetS was proposed in this study. The model predicts persistence in continuous engagement as well as abbreviated risk factors for self-care effects. The model constructed using random forest performed best among representative machine-learning classifiers. RF-RFE was used to optimize feature selection. As a result, the persistence prediction model showed a recall of 83.0%, a precision of 92.4%, an F1-score of 0.874, an MCC of 0.844, and an accuracy of 94.9%. In increased abbreviated risk factors, the prediction model showed a recall of 79.8%, a precision of 87.2%, an F1 score of 0.834, and an MCC of 0.797, while decreased abbreviated risk factors showed a recall of 75.1%, a precision of 85.5%, an F1 score of 0.800, and an MCC of 0.747.

5.1. Digital Health-Based Lifestyle Intervention

5.1.1. Comparison of studies

Previous findings have suggested that digital health-based lifestyle interventions effectively improve health. MetS management research is changing from the classic intervention methods such as web-based education programs, e-mail feedback, telephone, and SMS toward an intervention method using an application, wearable devices, and coaching through health monitoring [16, 18, 19, 30-33]. In this study, phone calls, text messages, and re-training were used from week 6 to help increase engagement with lifestyle interventions. Text messages and phone calls had little impact; re-training in person helped increase engagement. The re-training focused on problems with smartphone use, connectivity with healthcare devices, and device use. The user's ability to interact with a device may limit self-care adoption in this context; these limitations should be addressed as soon as possible.

Oh et al. provided a body composition monitor (including weight measurement) and a pedometer to the intervention group (n = 212) and conducted health counseling through the recorded data. The control group (n = 210) was given a weight scale and a step counter for 24 weeks. Participants were recommended to measure at least three times a week. In the test group and control group, weight decreased by 2.2 (3.6) kg and 0.8 (2.8) kg, respectively, and the decrease was higher in the intervention group that received healthcare [31]. Park et al. provided smartwatches for participants with and without MetS. Participants (n = 43) with MetS had statistically significant decreases in BMI, WC, TG, and BP. Participants (n = 68) without MetS showed statistically significant differences in BMI, WC, and HDL-C [19]. Mao et al. provided participants (n = 763) with a scale, pedometer, and BP monitor and performed health coaching through live video, phone calls, and text messages through an application. During the 4-month study, an average of 3.2% of total weight was lost, and 28.6% of participants decreased their weight by more than 5% [32]. Huh et al. provided wearable devices to participants (n = 20) and asked them to walk regularly for 12 weeks. Participants were provided with self-feedback on their exercise volume through a mobile application. After 12 weeks, risk factors decreased from 3.4 to

2.9. There was a decrease in 11 (55%) participants and no change in 7 (35%). Physical activity was 7,510.04 (3,525) steps [30].

In the present study, the number of risk factors in participants with pre-MetS decreased from 1.7 (0.5) to 1.6 (1.1) at baseline and follow-up ($P > 0.05$). Weight was reduced by 0.25 (1.62) kg. The risk factors of participants with MetS decreased from 3.6 (0.6) to 2.4 (1.1) ($P < 0.01$). Weight was reduced by 0.89 (2.13) kg. In the prevention and improvement groups, physical activity was 7,171.7 (4,735.3), and 7,323.6 (5,310.9) steps, and in the non-prevention and non-improvement groups, it was as low as 5,699.3 (4,937.6), and 4,843.5 (4,589.4) steps. Risk factors improved significantly when compared to the previous study [30-32]. Although weight loss and physical activity were low, a large number of participants did lose weight. This is thought to be the result of the intervention provided to the participants, which focused more on self-care than weight management.

5.1.2. Engagement, persistence, and physical activity

The prime emphasis in the management of MetS is the mitigation of the modifiable, underlying risk factors (obesity, physical inactivity, and atherogenic diet) through lifestyle changes. Increased levels of physical activity help reduce weight and body mass index, improving the overall risk factor profile. Engagement levels were assessed using those in prevention and improvement groups as references, as these groups effectively managed the risk factors for pre- and post-MetS. Two rules define engagement criteria: the number of device use days per week (rule 1) and the total number of device use days (rule 2). These rules helped prevent engagement failures due to problems with healthcare devices. Based on existing studies, persistence was measured as devices used at least three times a week. [31]. However, it was considered that there would be differences depending on the convenience of the participants in using the equipment [60], so the criteria were referred to the prevention and improvement groups. The smartwatch that can be worn on the wrist had the highest use, five times a week, and the scale, smart tape measure, and BP monitor were measured more than three times a week. However, in the case of an SMBG, which requires blood to be obtained by using a lancet, the frequency of use (twice a week) was low. Engagement was defined by these characteristics, and persistence was reflected in the amount of continuously satisfactory engagement. In addition, it was hypothesized that lifestyle changes might be associated with increased persistence. In this study, engagement and persistence levels in the prevention and improvement groups were relatively high, but not significant. Therefore, the period remaining after 14 weeks of regular use of the healthcare devices was relatively short.

5.1.3. Change in risk factors

The prevention and improvement groups used more of the provided healthcare devices than the other groups. The levels of satisfied engagement and maximum persistence were high. The prevention group showed a significant decrease in the WC (19%) and BP (53%), whereas the non-prevention group showed a significant increase in HDL-C (50%) and TG (43%). The improvement group showed significant reductions in the WC (44%), BP (49%), FBS (40%), HDL-C (19%), and TG (19%), whereas the non-improvement group showed no significant changes. The prevention and improvement groups had the highest levels of

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engagement, persistence, and physical activity, with a significant decrease in risk factors. The number of risk factors observed in the non-prevention group of pre-MetS participants increased. Despite moderate physical activity levels, the WC and BP increased slightly, and the HDL-C and TG levels increased significantly, suggesting challenges related to dietary habits. Dietary habits are associated with hyperglycemia, hypertriglyceridemia, hypertension, low HDL cholesterol levels, and abdominal obesity [61, 62]. In the non-improvement group of the MetS participants, the five risk factors did not change or changed slightly. This group had lower engagement, persistence, and physical activity levels than the other groups. Continuous self-care monitoring using lifestyle interventions is recommended.

5.1.4. Drop-Out

In a previous study, the drop-out rate was approximately 48% in the first 4 weeks [30] and 20% during the observation period [31]. Drop-out risk is associated with participant age, lack of familiarity with smartphones or wearable devices, and mobile application use. However, 23 (16%) of the 138 participants dropped out of this study. Reasons for dropping out included difficulties associated with study participation, time-constraints, and an unwillingness to continue. All participants had experience with long-term cohort studies and understood clinical trials and healthcare service protocols, which may account for the lower drop-out rate in this study than that in previous studies. However, seven (6%) participants failed to use the provided devices for >13 weeks.

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5.2. Prediction Model for Prevention and Management of MetS

5.2.1. Lifelog data and data labeling

Participants were given five healthcare devices: a BP monitor, weight scale, SMBG, smart tape measure, and smartwatch. Lifelog data were used to evaluate engagement, persistence, and physical activity levels. The level of engagement was represented by the number of times a device was used during the window by the participants to maintain self-care easily. Data were labeled to evaluate engagement and persistence. This was determined based on 4 weeks, which represents half of the analysis results, considering the limitations of the data measurement period, time-window, and overlap.

5.2.2. Feature extraction

Self-care utilizes values measured through healthcare devices, but it can take a long time to confirm meaningful changes in the measured values. In the short term, it may be difficult to recognize the amount of change because the value measured by the healthcare device is a small or the values are similar. This makes it difficult to motivate participants, as it is difficult for them to identify health improvements. In addition, the values may have been affected by the participants' body positions, measurement sites, and device measurement errors [63]. Therefore, in this study, preprocessing of the data was performed. If the value is more than 20% of the previous value, it is replaced with the previous data. In addition, a median filter was used in consideration of outliers. For FBS, the minimum data value measured before and after meals was used. This accounted for the concentration of data on one side due to the difficulty of selecting pre- and post-meal options for applications in FBS measurement. Finally, seven clinical data points and five weekly usage days were used as features for the development of the predictive model.

5.2.3. Feature selection and performance evaluation

A novel predictive model for the prevention and management of MetS was developed, consisting of persistence prediction for continued engagement and abbreviated risk factor prediction for self-care effects. Representative machine-learning classifiers were compared. In both models, the random forest showed the best performance. RF-RFE was used for optimal feature selection. The random forest grows hundreds of diverse classification trees and uses them together as a composite classifier. The final classification of a given sample is decided by applying the majority rule over the votes of the individual classifiers. To produce uncorrelated and dissimilar predictions, each tree is grown using only a reduced sample (a bootstrap) of the training set. As random forest uses OOB subsets to estimate the importance, computational efforts are not increased. Moreover, the random forest was developed as a multiclass algorithm, which suggests that it could provide a better measure of importance for this kind of problem than the combination of binary problems used, for example, by support vector machine [54-56].

Five features of the participation prediction model and seven features of the abbreviated risk factor prediction model were finally selected. These characteristics included weight-related indicators such as the number of steps, WC, and weight. These goals and recommendations for the clinical management of MetS aim for a 10% reduction

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in abdominal obesity and require 30–60 min of moderate-intensity exercise daily as an activity level [2]. SBP and DBP were associated and had characteristics that showed significant differences before and after clinical trials. In the persistence prediction model, recall, precision, F1-score, and MCC all showed values of 80% or higher. In the abbreviated risk factor prediction model, the performance of the increased abbreviated risk factors was about 80% or higher, and the decreased abbreviated risk factors were 74% or higher.

5.3. Limitations

There are several limitations to this study. The digital health-based intervention was performed in a single group. Additionally, in some studies, even if equipment for self-care management is provided, the improvement effect of MetS may be insufficient if motivation is not achieved through appropriate intervention [64, 65]. For self-care through the proposed level of engagement, persistence, and physical activity, it is important to inform participants about steady health management by using the application and phone consistently [35, 36]. The participants' experience using wearable devices was not considered; device familiarity may affect engagement levels. The age of the participants in this study is high, which might make it difficult to use healthcare devices, and participants may require help [65]. If you are unfamiliar with the connection between the healthcare devices and the application or the use of the devices, data omissions or errors may occur. Improper data collection may affect analysis results. Additionally, the number of participants in this study was insufficient. For this reason, some group analyses used

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parametric and non-parametric methods. In future, additional lifelog data collection may improve the performance of the artificial intelligence-based model. The proposed predictive model for prevention and management of MetS should be validated in clinical trials. This study accounted only for the presence of a risk factor, rather than when it occurred. Future studies should examine the impact of risk factor timing on disease onset.

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Abstract in Korean

기계학습 기반의 대사증후군 예방 및 관리를 위한 예측 모델

디지털 헬스 기반 생활습관 중재 (모바일 애플리케이션, 단문 메시지 서비스, 웨어러블 장치, 소셜 미디어 및 대화형 웹사이트 등)는 대사증후군 관리에 사용되고 있다. 본 연구는 헬스케어 기기를 활용하여 디지털 헬스 기반 생활습관 중재의 유용성을 확인하고 대사증후군 예방 및 관리를 위한 예측 모델을 제안하였다. 2019 년 12 월부터 2020 년 9 월까지 하나 이상의 대사증후군 위험 요인을 가진 참여자를 모집하였고 최종 106 명이 선정되었다. 참여자는 5 개의 헬스케어 기기와 애플리케이션이 제공되었다. 임상시험 전후 특성을 비교하였으며, 참여 기간 동안 수집된 라이프로그 데이터를 분석하였다. 이러한 결과를 기반으로 지속적인 자가관리를 위한 헬스케어 기기의 사용 빈도를 정량화 하였으며, 대사증후군 예방 및 관리를 위한 예측 모델을 개발하였다. 예측 모델은 연속적인 참여를 위한 지속성과 자가 관리 효과를 위한 간소화된 위험 요소 예측으로 구성된다. 대표적인 기계 학습 분류기를 사용하여 성능을 평가하였고 결과를 비교하였다. 두 모델은 랜덤 포레스트 분류기가 가장 좋은 성능을 보였으며, 랜덤 포레스트-재귀적 특징

제거를 통해 특징 선택을 최적화하였다. 그 결과 지속성 예측모델은 재현율 83.0%, 정밀도 92.4%, F1-score 0.874, Matthews 상관계수(Matthews correlation coefficient, MCC) 0.844, 그리고 정확도 94.9%를 보였다. 간소화된 위험인자 예측모형에서 위험인자 증가 예측은 재현율 79.8%, 정밀도 87.2%, F1-score 0.834, 그리고 MCC 0.797 이였으며, 위험인자 감소 예측은 재현율 75.1%, 정밀도 85.5%, F1-score 0.800, 그리고 MCC 0.747 이였다. 제안된 예측 모델은 높은 성능을 확인하였다. 디지털 헬스 기반 생활습관 중재를 통한 자가관리를 기반으로 제안된 예측 모델은 대사증후군 예방 및 관리에 유용한 도움이 될 것이다.

Keywords: 대사증후군; 디지털 헬스; 생활습관중재; 헬스케어; 기계학습