



## Evaluation of the Effectiveness of Diabetic Foot Ulcer Recurrence Risk Prediction Models: A Systematic Review

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### Abstract

**Background:** We used the Predictive Model Bias Risk Assessment tool (PROBAST) tool to systematically evaluate the existing models worldwide, in order to provide a reference for clinical staff to select and optimize DFU recurrence risk prediction models.

**Methods:** Literature on DFU recurrence risk prediction model construction published in CNKI, China Biomedical Literature Database, Vipu China Knowledge, China Biomedical Literature Database, Vipu Chinese Journal Service Platform, Wanfang Data Knowledge Service Platform, Embase, PubMed, Web of Science, Cochrane Library and other databases were systematically searched. The search period was until January 29, 2024, encompassing all relevant studies published up to that date. Literature screening and data extraction were conducted by two researchers, and the PROBAST was used to evaluate the bias risk and applicability of the included literature.

**Results:** Finally, 9 literatures were included, 13 prediction models were established, and the area under the AUC or C-index ranged from 0.660 to 0.943. Nine models were validated internally and one model was validated externally. All the models constructed in the included literature are of high-risk bias, and the applicability of the models is reasonable. Common predictors in the prediction model were Wagner scale, glycosylated hemoglobin, and diabetic peripheral neuropathy.

**Conclusion:** Although most of the existing DFU risk prediction models have good prediction performance, they all have high risk of bias. It is suggested that researchers should update the existing models in the future, and future modeling studies should follow the reporting norms, so as to develop a scientific, effective and convenient risk prediction model that is more conducive to clinical practice.

**Keywords:** Predictive model bias risk assessment tool; Diabetic foot ulcer; Recurrence; Risk prediction model; Systematic review



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## Introduction

A diabetic foot ulcer (DFU) is a chronic wound that results from a combination of factors, including narrowing or occlusion of blood vessels in the lower limbs, infections, and neuropathy (1). It is one of the most serious and common chronic complications of diabetes mellitus, affecting approximately 18.6 million diabetic patients worldwide each year (2). The long duration of DFUs and their tendency to recur even after healing make them more difficult to treat and increase the risk of disability and death. Surveys have shown that the overall amputation rate of DFU patients is as high as 34% (68/200) (3), and meta-analysis has shown that the 5-year mortality rate of DFU patients worldwide is nearly 50% (4). Moreover, the one-year recurrence rate of DFU in mainland China is as high as 31.6%, with an annual morbidity and mortality rate of 14.4% (5).

These figures demonstrate that DFU and its high recurrence rate represent a significant public health concern, placing a considerable burden on society. It is therefore of great significance to construct a risk prediction model to identify the risk factors of DFU recurrence as early as possible and to take effective targeted interventions for high-risk groups in order to reduce the recurrence rate of DFU (6). In recent years, a variety of DFU recurrence risk prediction models have been developed by researchers worldwide. However, the risk of bias and clinical applicability of the relevant model development has not yet been clarified, and it is necessary to further evaluate their effectiveness. In light of the above, this study employed the PROBAST tool to conduct a comprehensive evaluation of existing DFU recurrence risk prediction models globally.

We aimed to provide a reference for clinical staff in selecting and optimizing the most suitable models for their clinical settings.

## Methods

### *Literature search strategy*

This study has been registered in the international prospective systematic review registry platform

(PROSPERO website) (registration number: CRD42023488958).

A computerized system was employed to search the literature on the construction of DFU recurrence risk prediction models published in the databases of China Knowledge, China Biomedical Literature Database, Vipu Chinese Journal Service Platform, Wanfang Data Knowledge Service Platform, Embase, PubMed, Web of Science, and Cochrane Library from the establishment of the database to January 29, 2024.

A search string was developed to identify prediction models for the recurrence of diabetic foot ulcers, using the following terms and specific search strategy examples as follows: (( (Diabetic foot ulcer (MeSH Terms)) OR (Foot ulcer (Title/Abstract))) OR (Diabetic foot (Title/Abstract))) OR (ulceration (Title/Abstract))) OR (Ulcer healing (Title/Abstract))) OR (DFU (Title/Abstract))) AND ( (recurrence (MeSH Terms)) OR (relapse (Title/Abstract))) AND ( ( ( ( (risk factor (Title/Abstract)) OR (influencing factor (Title/Abstract))) OR (predict\* (Title/Abstract))) OR (prediction model (Title/Abstract))) OR (risk prediction model (Title/Abstract))) OR (model construction (Title/Abstract))) OR (risk assessment model (Title/Abstract))) OR (prognostic model (Title/Abstract))) OR (nomogram (Title/Abstract))).

### *Literature inclusion and exclusion criteria*

Inclusion criteria: ① The subjects were patients with healed DFU; ② The study was to develop, construct and/or validate and evaluate a risk prediction model for DFU recurrence; ③ The outcome indicator was whether DFU recurred or not; ④ The types of study design included cohort study, cross-sectional study, nested case-control study, randomized controlled trial, and case-control study; ⑤ The language of the study was Chinese and English. Exclusion criteria: ① only risk factors were analyzed without risk prediction modeling. ② Review, conference abstracts; ③ Basic experiments, animal experi-

ments; ④ Predictive models constructed based on Meta-analysis/systematic evaluation; ⑤ incomplete data, unable to obtain valid data; ⑥ Unable to obtain the original text.

### *Literature screening and data extraction*

The process of data extraction was conducted by two researchers, both of whom were trained in evidence-based methods and were therefore able to screen the literature independently. They did so in strict accordance with the inclusion and exclusion criteria. In the event of disagreement, a third researcher (the corresponding author) was consulted in order to assist in judging and reaching agreement. The data were extracted in accordance with the CHARMS (Checklist for the Assessment of the Reporting of Meta-analyses and Systematic Reviews) (7) using Excel 2019. This included the first author, time of publication, country, study population and sample size, data source, follow-up time, modeling method, model presentation form, model performance, model validation method, predictors and their number, etc.

### *Quality evaluation of included studies*

The quality evaluation of the included studies, including risk of bias and applicability evaluation, was conducted independently by two investigators using the prediction model risk of bias assessment tool (PROBAST) (8), and the results were cross-checked. In the event of any disagreement, a third investigator was consulted to reach a consensus. The risk of bias assessment encompassed four domains (9): study population, predictors, outcomes, and statistical analysis. A total of 20 landmark questions were posed, each of which was categorized into three options. In the same domain, the risk of bias was rated as low if all questions were answered with "yes/probably yes," high if one question was answered with "no/probably not," and unclear if the answer was "no information." In the event that the response was "no information," the risk of bias for that domain was not discernible. If the risk of bias was rated as low in all four domains,

the overall risk of bias of the study was low. Conversely, if the risk of bias was rated as high in one domain, the overall risk of bias of the study was high. Finally, if the risk of bias was unclear in one domain but rated as low in the other domains, the overall risk of bias of the study was not clear. The applicability assessment encompassed three key elements: the study population, the predictors, and the outcome domains. Each domain was evaluated as either low risk of applicability, high risk of applicability, or unclear. In the event that all domains were deemed to present a low risk of applicability, the study was deemed to present a low risk of applicability. Conversely, if a high risk of applicability was identified in one domain, the overall applicability was deemed to be high. Finally, if an unclear risk of applicability was identified in one domain, accompanied by a low risk of applicability in the other domains, the overall applicability of the study was deemed to be unclear.

### *Data synthesis and statistical analysis*

In this study, fewer original studies met the nadir criteria, and there were significant differences in the effects of the same outcome indicators, making it impossible to combine the odds ratio (OR) values. Consequently, a qualitative descriptive analysis method was employed for a systematic appraisal. This approach facilitated the extraction of general information about the included studies, such as study type, target population, modeling methods, sample sizes, validation methodologies, and recurrence rates of diabetic foot ulcers. Additionally, we summarized the area under the receiver operating characteristic curve (AUROC) and the predictors, providing a categorical overview of the main findings.

## **Results**

### *Literature search results*

In this study, 3560 pieces of literature were initially searched through eight databases, screened step by step in strict accordance with the literature inclusion and exclusion criteria, and nine pieces of literature were finally included (10-18),

and the process of literature screening is shown in Fig. 1.

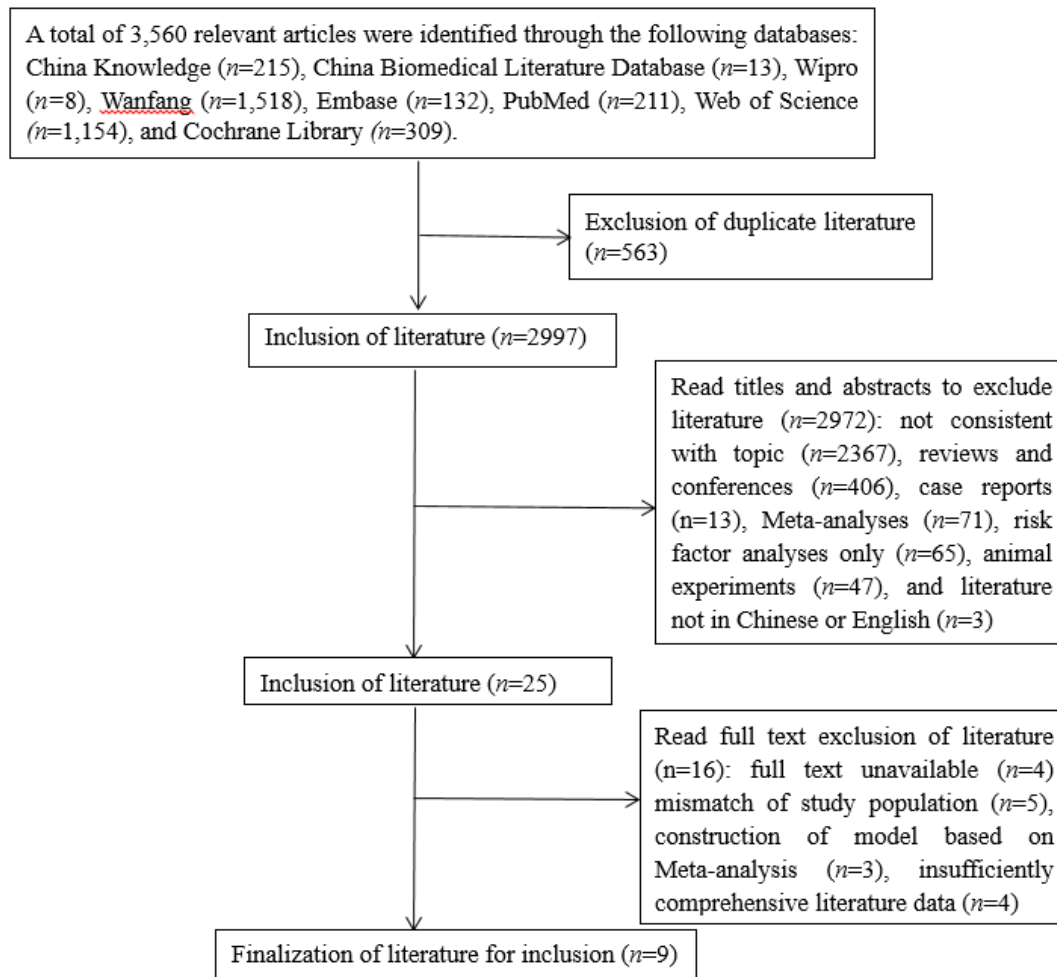


Fig. 1: Literature screening flowchart

### Basic characteristics and modeling of the included literature

A total of nine papers were included in this study. All were published within the last five years, with seven originating from China (10-12,14-15,17-18) and two from the Netherlands (13,16). The data for the studies were obtained primarily through a combination of medical record data and follow-up visits. The total number of modeling samples included in the nine papers ranged from 70 to 456 cases, and the number of outcome events

ranged from 22 to 126 cases. Six studies (11-13, 16-18) employed logistic regression as a modeling method, with one study (12) additionally utilizing support vector machine and BP neural network. Three studies (10, 14, 15) employed Cox proportional regression. The form of model presentation was as follows: risk assessment formula in four studies, column line graph in four studies, and not mentioned in one study. The fundamental characteristics and model construction of the included literature are presented in Table 1.

**Table 1:** Basic characteristics of the included literature and the prediction model construction

Note: DFU, diabetic foot ulcer, "-" means not mentioned.

| Included literature                 | The year of publication | country | Study subjects and sample size<br>(Outcome event / participant: m / n)  | data sources   | fl.up time                    | Modeling method  | Model presentation      |
|-------------------------------------|-------------------------|---------|---|--|-------------------------------|--|-------------------------|
| Wei Lei et al (2023) (10)           | 2023                    | China   | DFU patient (47 / 226)  | Clinical data; telephone or outpatient follow-up   | In 1 year (January / times)   | And Cox proportional regression                                    | ABAS                    |
| Wang Hong and Li Liang (2023) (11)  | 2023                    | China   | DFU healing patients admitted to the Central Hospital of Jiaozuo Coal Industry (Group) Co., Ltd. (22 / 70)  | Clinical data; Outpatient follow-up and telephone follow-up  | In 1 year                     | Logistic regression  | Risk assessment formula |
| Zhang Juan et al (2023) (12)        | 2023                    | China   | DFU patients healed after hospitalization / wound clinic of Ningxia Medical University General Hospital (116 / 390)   | Electronic medical record; telephone follow-up, outpatient follow-up and out-of-hospital follow-up management system | In 1 year                     | Logistic Regression, support vector machine, and BP neural network | -                       |
| AAND S W et al (2021) (13)          | 2021                    | Holland | DFU patients who had foot ulcers within 48 months of multidisciplinary diabetic foot clinics in 3 university medical centers and 4 community hospitals (126 / 304)  | Electronic medical record; telephone follow-up   | 18 Months                     | Logistic regression  |                         |
| Lai Jianjun and Sun Yan (2024) (14) | 2024                    | China   | DFU patients with ulcer healing in Affiliated Provincial Hospital of Shandong First Medical University (51 / 172)   | Clinical data; follow up by telephone or outpatient service  | 3~12 Months (January / times) | And Cox proportional regression                                    |                         |
| Wang Yinrong et al (2023) (15)      | 2023                    | China   | DFU patients healed after hospitalization of Hainan Provincial Hospital of Traditional Chinese Medicine (69 / 263)  | Medical records, electronic medical records and nursing records; wechat, telephone and outpatient follow-up          | In 2 years (April /)          | And Cox proportional regression                                    | ABAS                    |
| AAND S W et al (2020) (16)          | 2020                    | Holland | DFU patients who had had foot ulcers in the 18 months prior to the study (71 / 171) recruited from multidisciplinary diabetic foot clinics from 2 university hospitals and 8 large public general hospitals | Electronic medical record; outpatient follow-up  | 18 Months                     | Logistic regression  | Risk assessment formula |
| Lv Jing et al (2023) (17)           | 2022                    | China   | DFU patient in a hospital in Chengdu (125 / 465)  | Hospital information system; telephone follow-up, outpatient follow-up and out-of-hospital management system         | In 1 year                     | Logistic regression  | Risk assessment formula |
| Xia Lei(2023) (18)                  | 2023                    | China   | A tertiary A hospital in Nanjing and a tertiary A hospital in Zhenjiang were diagnosed with DFU healing and discharged patients for the first time (98 / 375)   | Hospital electronic medical record system; outpatient service, recurrent hospitalization, or telephone follow-up     | In 1 year                     | Logistic regression  | ABAS                    |



**Predictive model performance and predictors**

In the included literature, a total of 13 prediction models were established. Out of these, 12 models (10-14, 16-18) were evaluated for differentiation using the area under the ROC curve (AUC), with AUC values ranging from 0.660 to 0.943. Among these, 9 prediction models (10-12, 14, 16-18) had AUC values greater than 0.7, indicating moderate or better prediction performance. Conversely, 3 prediction models (13, 16) had AUC values below 0.7, reflecting poor model performance. Additionally, 1 prediction model (15) was evaluated using the C-index for differentiation, achieving a value of 0.796, which indicates good prediction performance. The calibration methods employed included the Hosmer-Lemeshow test, calibration

curves, decision curve analysis, and Brier scores. The models constructed in five studies (12, 13, 15, 16, 18) were internally validated using 10-fold cross-validation, bootstrap sampling, and random splitting, respectively. One of the studies (18) also underwent external validation via time period validation. The external validation AUC was 0.732, indicating fair prediction performance. The final model included three to eight predictors. The Wagner classification, glycosylated hemoglobin, and peripheral neuropathy were observed with a frequency of at least three, and thus were categorized as common predictors of DFU recurrence. For a detailed examination of the predictive performance and predictors of the specific model, please refer to Table 2.

**Table 2:** Predictive model performance and predictors

| Inclusion of literature               | Model Performance   |  | model validation   | Predictors and their quantities  |
|---------------------------------------|---|--|--|--|
|                                       | AUC/C-index   | Calibration methods                        |  |  |
| Wei Lei et al (2023) (10)             | AUC of 0.906  | -  | -  | 8: sex, age (older), BMI, ulcer location, W classification, I classification, fl classification, hs-CRP  |
| WANG Hong, LI Liang (2023) (11)       | AUC of 0.812  | Hosmer-Lemeshow goodness-of-fit test       | -  | 4: Wagner classification (3 to 5), glycosylated hemoglobin $\geq 7.0\%$ , peripheral neuropathy, and moderate to severe infections   |
| Zhang Juan et al (2023) (12)          | The AUC of the logistic regression model is 0.855, the AUC of the SVM model is 0.937, and the AUC of the BPNN model is 0.837. | Hosmer-Lemeshow goodness-of-fit test       | Internal validation (Randomized splitting method and 10-fold cross validation) | 8: BMI, duration of diabetes, smoking history, foot ulcer grading, glycosylated hemoglobin, ulcer location on the sole of the foot, foot self-management behaviors, and perceived level of risk for DFUs   |
| AAND S W et al (2021) (13)            | Model 1 AUC was 0.690 (2SD 0.040), model 2 AUC was 0.660 (2SD 0.023)  | Brier scores, calibration curves           | Internal Verification (10 fold cross validation)                               | Model 1 (6): age (younger), severity of peripheral neuropathy, shorter time to healing from previous ulcers, mild lesions, use of walking aids, no foot temperature monitoring at home; Model 2 (7): age (younger), plantar ulcers, shorter time to healing from previous ulcers, minor lesions, alcohol consumption, use of walking aids, foot care received at a university medical center |
| Lai, Jianjun and Sun, Yan (2024) (14) | AUC of 0.832  | calibration curves                         | -  | 4: ABI (protective factors), coronary heart disease, ulcer depth score, subcutaneous sinus tract or submerged wound score  |
| Wang Yinrong et al (2023) (15)        | C-index of 0.796  | Calibration curve, decision curve analysis | Internal validation (Bootstrap sampling method)                                | 6: age ( $>63$ years), duration of diabetes ( $>10$ years), glycosylated hemoglobin ( $>9.07\%$ ), albumin ( $\leq 39.57$ g/L), C-reactive protein ( $>4.14$ mg/L), and white blood cell count ( $>7.09 \times 10^9/L$ )   |
| AANDSW et al (2020) (16)              | Model 1 AUC was 0.680, Model 2 AUC was 0.760  | Brier scores                               | Internal Verification (10 fold cross validation)                               | Model 1 (5): increased peak plantar pressure (in kPa) in the forefoot, presence of minor lesions, long duration of previous  |

Table 2: Continued ...

|                           |   |  |  |   |
|---------------------------|---|--|--|---|
|                           |   |  |  | foot ulcers, living alone, and less change in the number of steps per day (SDs); Model 2 (3): presence of minor lesions, longer duration of previous foot ulcers, location of previous foot ulcers. |
| Ly Jing et al (2023) (17) | AUC of 0.855  | Hosmer-Lemeshow goodness-of-fit test                     | -  | 5: Smoking, abnormal foot skin color, callus, diabetic peripheral neuropathy, coronary heart disease  |
| Xia Lei (2023) (18)       | The AUC was 0.890, External validation AUC of 0.723 | Hosmer-Lemeshow goodness-of-fit test, calibration curves | Internal validation (Bootstrap sampling method) and external validation (time period validation) | 6: Wagner classification, peripheral vascular lesions, osteomyelitis, multidrug-resistant bacterial infection, callus, history of amputation  |

Note: BMI, body mass index; W classification, wound classification; I classification, ischemia classification; fl classification, foot infection classification; hs-CRP, high-sensitivity C-reactive protein; DFUs, diabetic foot ulcers; ABI, ankle-brachial index; and "-" indicates not mentioned

### ***Evaluation of risk of bias and applicability of prediction models***

#### ***Risk of prediction model bias***

In the domain of research subjects, all included literatures were considered to have a low risk of bias, two literatures (13, 16) had data from randomized controlled trials and seven literatures (10-12, 14, 15, 17, 18) were from nested case-control studies with appropriate data sources and the inclusion and exclusion criteria were reasonable and consistent. In the predictor domain, all papers had detailed descriptions of the study population and the predictors were valid, whereas two papers (12, 14) included scales for the assessment of the predictors but did not describe the process and criteria for the assessment in detail, so the risk of bias was assessed as unclear. In the outcome domain, the risk of bias was assessed as unclear in 3 papers (10, 11, 14) because information on the method of outcome classification was not reported. In the area

of statistical analysis, all 9 publications were rated as having a high risk of bias for the following reasons: First, 8 literatures (10-16, 18) had events per variable (EPV) <20 for the independent variables, which is an insufficient sample size and may result in lower model stability and reliability; Second, 1 literature (18) transformed continuous variables into  $\geq 2$  categories; Third, 1 paper (12) did not use multiple interpolation to deal with missing data; Fourth, five papers (11, 13, 16-18) screened predictors by one-way analysis of variance; and fifth, in terms of evaluating the performance of the predictive model, three papers (11, 12, 17) used only the Hosmer-Lemeshow goodness-of-fit test for calibration, and one paper (10) did not report the calibration information of the predictive model. Sixth, four papers (10, 11, 14, 17) did not use internal validation methods for subsequent adjustment of model performance (Table 3).

**Table 3:** Risk of bias and applicability of the included literature

| Included in the literature           | Risk of bias         |           |              |           | Risk of applicability |           |              | Ensemble     |           |
|--------------------------------------|----------------------|-----------|--------------|-----------|-----------------------|-----------|--------------|--------------|-----------|
|                                      | Subject investigated | Predictor | Final result | Analyse   | Subject investigated  | Predictor | Final result | Risk of bias | Usability |
| Wei Lei et al (2023) (10)            | Low risk             | Low risk  | NK           | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| Wang Hong and Li Liang (2023) (11)   | Low risk             | Low risk  | NK           | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| Zhang Juan et al (2023) (12)         | Low risk             | NK        | Low risk     | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| AANDS W et al (2021) (13)            | Low risk             | Low risk  | Low risk     | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| Lai Jian-jun and Sun Yan (2024) (14) | Low risk             | NK        | NK           | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| Wang Yinrong et al (2023) (15)       | Low risk             | Low risk  | Low risk     | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| AANDS W ey al (2020) (16)            | Low risk             | Low risk  | Low risk     | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| Lv Jing et al (2023) (17)            | Low risk             | Low risk  | Low risk     | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |
| Xia Lei(2023) (18)                   | Low risk             | Low risk  | Low risk     | High Risk | Low risk              | Low risk  | Low risk     | High Risk    | Low risk  |



### ***Evaluation of predictive model applicability***

The models from the nine studies were rated as having low applicability risk, with each model demonstrating good applicability. The reason for this is that the subjects and study design, the definition and assessment of predictors (including the time of assessment), and the definition and analysis method of the results (including the time interval) of the included literature are all consistent with this systematic evaluation question (Table 3).

## **Discussion**

### ***Existing DFU Recurrence Risk Prediction Models: Performance and Bias***

This systematic evaluation identified 13 prediction models across nine studies, with 10 models (10-12, 14-18) achieving an AUC or C-index greater than 0.7, which accounts for 76.92%. This indicates acceptable predictive performance with some clinical value in distinguishing high-risk DFU recurrence populations. However, twelve models (10-17) lacked external validation, raising concerns about their generalizability. The overall risk of bias among existing models was high, primarily due to statistical issues such as inadequate sample sizes ( $EPV < 20$ ), inappropriate transformation of continuous variables into multicategorical forms, inadequate handling of missing data without multiple imputation, reliance on univariate analysis for predictor screening, and insufficient calibration assessments, often limited to the Hosmer-Lemeshow goodness-of-fit test. Future model development should ensure adequate sample sizes ( $\geq 100$  and  $EPV \geq 20$ ) to reduce bias in regression coefficients and enhance predictive reliability and stability (19). To prevent overfitting, transformation of continuous variables into multicategorical forms should be minimized (20), and appropriate methods like multiple imputation should be employed to handle missing data effectively (21). Univariate analysis neglects variable interactions and potential covariate issues, risking important multivariate relationships. LASSO regression can mitigate multi-

collinearity and enhance model simplicity and stability (23); however, none of the studies in this evaluation utilized LASSO, increasing bias risk. Future studies should consider LASSO regression and implement both internal and external validations, employing methods beyond random splits, such as cross-validation and bootstrap sampling. Comprehensive calibration assessments, including large-scale calibration, calibration curves, and a combination of Hosmer-Lemeshow tests, are recommended (22).

### ***Predictive Value of Key Indicators for DFU Recurrence***

Our systematic evaluation indicated that Wagner classification, glycosylated hemoglobin (HbA1c), and diabetic peripheral neuropathy (DPN) are significant predictors of DFU recurrence. Higher Wagner classifications correlate with an increased risk of recurrence, likely due to deeper ulcers and worsening infections, which elevate inflammatory factors like calcitonin (PCT), interleukin-6 (IL-6), and C-reactive protein (CRP). These inflammatory markers can inhibit the expression of the anti-vascular growth factor Omentin-1 and the regulation of neovascularization factor VEGF, complicating the maintenance of tissue oxygenation post-healing and contributing to DFU recurrence (24-27). HbA1c serves as a standard for assessing glycemic control; poor control results in a high-glycemic microenvironment, lowering antioxidant enzyme levels and heightening oxidative stress, hindering complete DFU healing and increasing recurrence likelihood (28, 29). DPN is an independent risk factor for DFU recurrence, aligning with findings by Xie Ji-Xuan et al (30). DPN leads to sensory, motor, and autonomic dysfunction, resulting in foot muscle atrophy, dry and cracked skin, abnormal temperatures, and increased mechanical stress, all of which elevate recurrence risk (31, 32). To reduce DFU recurrence rates, clinical staff should implement targeted treatment and nursing strategies based on Wagner classification; patients should be encouraged to actively manage their blood glucose by regularly monitoring HbA1c and adhering to medical advice. Additionally, healthcare profes-

sionals can assess DFU recurrence risk using the Michigan Neurological Screening Inventory (MNSI), the Nociceptive Touch and Temperature Test (NTT), and the Vibratory Sensory Threshold (VPT) (31, 32). DPN can also be monitored through the MNSI and sensory testing (VPT) (33), allowing for tailored preventive and therapeutic measures to improve foot muscle and skin condition, alleviate mechanical pressure, and reduce DPN-related damage.

### ***Future Exploration of DFU Risk Prediction Models***

DFU risk prediction models can identify high-risk groups early and predict recurrence likelihood, aiding healthcare workers in developing effective prevention strategies to reduce DFU recurrence, enhance patient quality of life, and decrease morbidity and mortality rates. However, research on clinical risk prediction models for DFU recurrence using real-world data only commenced in 2020, necessitating further exploration for widespread clinical application. Our evaluation revealed that all prediction models from the nine included studies were at high risk of bias. Future researchers should consult PROBAST (8) and TRIPOD (34) guidelines to avoid bias and enhance transparency in model development. Most existing DFU recurrence models are based on logistic regression; incorporating machine learning (ML) algorithms is vital for promoting early interventions and improving patient outcomes (35). For instance, a model developed by Juan Zhang et al (12) using support vector machine (SVM) and BP neural networks showed an AUC of 0.943, demonstrating stable diagnostic efficacy, yet it requires validation across multiple centers to confirm its accuracy and predictive capacity. Future work should explore various ML algorithms and validate them with larger samples to identify the most effective models for clinical practice. Additionally, visualizing prediction models through applets and web calculators could enhance usability and improve screening efficiency.

### **Limitations and conclusions**

This systematic review has several limitations. First, it included only published literature in Chinese and English, omitting gray literature, which may result in missing significant studies. Second, the heterogeneity among the prediction models prevented a quantitative meta-analysis, leading to reliance solely on descriptive qualitative analysis. Third, none of the studies adhered to TRIPOD guidelines, compromising transparency in the model construction process and potentially affecting the quality assessment of the literature.

### **Conclusion**

Nine risk prediction models for DFU recurrence were analyzed, most showing good predictive performance, though with a high risk of bias. Common predictors included Wagner classification, glycosylated hemoglobin, and diabetic peripheral neuropathy. Current models are not yet suitable for widespread clinical use and require further exploration. Future research should focus on external validation of these models using large, multi-center samples to enhance quality and generalizability. Researchers are also encouraged to follow PROBAST and TRIPOD guidelines to develop scientifically sound and effective DFU recurrence risk prediction models conducive to clinical practice.

### **Journalism Ethics Considerations**

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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## Conflict of interest

The authors declare that there is no conflict of interests.

## References

1. An N, Liu CQ, Yang X, et al (2023). Analysis of risk factors for recurrence of diabetic foot ulcers after healing. *Journal of Vascular and Endovascular Surgery*,9 (11): 1219-1223.
2. Armstrong D G, Tan T W, Boulton A, et al (2023). Diabetic Foot Ulcers: a Review. *JAMA*, 330 (1): 62-75.
3. Zhang X, LI Q, Zhou X, et al (2024). Risk factors for amputation in diabetic foot ulcers: a retrospective analysis. *Int Wound J*, 21 (4): e14832.
4. Chen L, Sun S, Gao Y, et al (2023). Global mortality of diabetic foot ulcer: a systematic review and meta-analysis of observational studies. *Diabetes Obes Metab*, 25 (1): 36-45.
5. Guo Q, Ying G, Jing O, et al (2023). Influencing factors for the recurrence of diabetic foot ulcers: a meta-analysis. *Int Wound J*, 20 (5): 1762-1775.
6. Hsu CR (2019). The key to diabetic foot disease prevention and treatment - Interpretation of 2019 domestic and international guidelines for diabetic foot prevention and treatment. *China Clinical New Medicine*,12 (12): 1259-1262.
7. Palazón-bru A, Martín-pérez F, Mares-garcía E, et al (2020). A general presentation on how to carry out a CHARMS analysis for prognostic multivariate models. *Stat Med*, 39 (23): 3207-3225.
8. Moons K, Wolff R F, Riley R D, et al (2019). PROBAST: A Tool to Assess Risk of Bias and Applicability of Prediction Model Studies: Explanation and Elaboration. *Ann Intern Med*, 170 (1): W1-W33.
9. Chen XP, Zhang Y, Zhuang YY, et al (2020). PROBAST: an assessment tool for risk of bias in diagnostic or prognostic multifactorial prediction modeling studies. *Chinese Journal of Evidence-Based Medicine*, 20 (06): 737-744.
10. Wei L, Wang YT, Sun Y (2023). Predictive value of wound, ischemia and foot infection grading for recurrence of diabetic foot ulcers within 1 year and construction of prediction model. *Journal of Vascular and Endoluminal Vascular Surgery*, 9 (12): 1454-1459.
11. Wang H, Li L (2023). Influencing factors and risk modeling of recurrence after ulcer healing in diabetic foot patients. *China Journal of Practical Medicine*, 23 (01): 54-58.
12. Zhang J, Li HF, Li XM, et al (2023). Construction of a diabetic foot ulcer recurrence risk prediction model: based on logistic regression and support vector machine and BP neural network model. *Chinese Family Medicine*,26 (32): 4013-4019.
13. Aan D S W, Schut M C, Abu-hanna A, et al (2021). Development of a prediction model for foot ulcer recurrence in people with diabetes using easy-to-obtain clinical variables. *BMJ Open Diabetes Res Care*, 9 (1): e002257.
14. Lai JJ, Sun Y (2024). The value of the DMIST scale in predicting recurrence of diabetic foot ulcers within 1 year after healing and the construction of a prediction model. *Journal of Vascular and Endovascular Surgery*, 10 (01): 6-11.
15. Wang YR Qiu XT, Pan L (2023). Analysis of factors influencing the recurrence of diabetic foot ulcers after healing and construction of risk prediction model. *Military Nursing*, 40 (5): 62-65.
16. Aan D S W, Abu-hanna A, Bus S A (2020). Development of a multivariable prediction model for plantar foot ulcer recurrence in high-risk people with diabetes. *BMJ Open Diabetes Res Care*, 8 (1): e001207.
17. Lv J, Yuan L, Li R, et al (2022). Construction of a predictive model for diabetic foot ulcer recurrence risk. *Nursing Research*,36 (06): 993-998.
18. Xia L (2023). Construction and validation of a 1-year recurrence risk prediction column chart model for diabetic foot ulcer patients. *Jiangsu University*, 2023.
19. Ogundimu E O, Altman D G, Collins G S (2016). Adequate sample size for developing prediction models is not simply related to events per variable. *J Clin Epidemiol*, 76: 175-182.
20. Wynants L, Collins G S, Van Calster B (2017). Key steps and common pitfalls in developing and validating risk models. *BJOG*, 124 (3): 423-432.
21. Mühlenbruch K, Kuxhaus O, di Giuseppe R, et al (2017). Multiple imputation was a valid approach to estimate absolute risk from a pre-

- diction model based on case-cohort data. *J Clin Epidemiol*, 84: 130-141.
22. Mok HF, Chen YP, Han H, et al (2024). Methods and steps of clinical prediction modeling research. *Chinese Journal of Evidence-Based Medicine*, 24 (02): 228-236.
23. Xi LJ, Guo ZY, Yang XK, et al (2023). Application of LASSO and its extension methods in variable screening for regression analysis. *Zhonghua Yu Fang Yi Xue Za Zhi*, 57(1): 107-111.
24. Oley M H, Oley M C, Kepel B J, et al (2024). Hyperbaric Oxygen Therapy for Diabetic Foot Ulcers Based on Wagner Grading: a Systematic Review and Meta-analysis. *Plast Reconstr Surg Glob Open*, 12 (3): e5692.
25. Zhou Shujie, Zhao Ling, Ke Tingyu (2024). Correlation analysis between common clinical indicators and diabetic foot ulcers. *Journal of Kunming Medical University*, 45 (01): 61-66.
26. Wang Y, Xue F, Lin SN, et al (2023). Correlation between serum reticulin-1 and vascular endothelial growth factor levels and Wagner's grading in patients with diabetic foot. *Chinese Journal of Practical Diagnosis and Therapy*, 37 (06): 565-569.
27. Wu J, Bista Raju, CHA PP, et al (2023). Characterization of inflammatory markers in diabetic foot patients and their relationship with foot ulcer prognosis. *Journal of Sichuan University (Medical Edition)*, 54 (06): 1233-1238.
28. Huang Z H, Li S Q, Kou Y, et al (2019). Risk factors for the recurrence of diabetic foot ulcers among diabetic patients: a meta-analysis. *Int Wound J*, 16 (6): 1373-1382.
29. Zhu XL, Liao WQ, Zhang C, et al (2023). Pathogenesis and treatment of diabetic foot ulcers. *Chinese Journal of Dermatology and Venereology*, 37 (04): 367-372.
30. Xie JX, Dai X, Huang SH, et al (2023). A prospective study of risk factors for diabetic foot ulcers in the Zhuang population. *Chinese Journal of Gerontology*, 43 (01): 55-59.
31. Xia L, Zhuang R, Wu L, et al (2022). Meta-analysis of risk factors associated with recurrent diabetic foot ulcers. *Chinese Journal of Modern Nursing*, (09): 1143-1148.
32. Sen C K, Roy S, Khanna S (2023). Diabetic Peripheral Neuropathy Associated with Foot Ulcer: One of a Kind. *Antioxidant Redox Signal*, 10.1089/ars.2022.0093.
33. Yang J, Xing Y, Shi Q (2023). The Michigan Neurologic Screening Scale. The Value of Michigan Nerve Screening Scale, Nociceptive Tactile Warming Test and Vibratory Sensory Threshold in Diagnosing Diabetic Peripheral Neuropathy. *Chinese Journal of Continuing Medical Education*, (08): 727-730.
34. Moons K G, Altman D G, Reitsma J B, et al (2015). Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD). Explanation and elaboration. *Ann Intern Med*, 162 (1): W1-73.
35. Liu YA, Yang SW, Li LZ (2021). Research progress on the application of machine learning in disease prediction. *Journal of Nursing*, 28 (07): 30-34.