



Screening and Management Strategies for Chronic Diseases in High-Risk Populations: A Systematic Review

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Abstract

Context: Chronic diseases such as diabetes, cardiovascular conditions, cancers, and respiratory illnesses remain leading causes of global mortality, especially among high-risk groups including the elderly, patients with underlying conditions, and socially disadvantaged populations. Early screening and tailored management strategies are essential to reduce disease burden and improve outcomes.

Methods: This systematic review and meta-analysis was conducted in line with PRISMA 2020 guidelines and registered in PROSPERO (CRD42025234789). Comprehensive searches were performed across seven databases (PubMed, Scopus, Web of Science, Embase, Cochrane Library, Google Scholar, and medRxiv) up to October 25, 2025. Of 18 eligible studies, 10 contributed complete data for meta-analysis. Statistical analyses were performed using the DerSimonian and Laird random-effects model in R (version 4.3.1). Pooled sensitivity, specificity, AUC, diagnostic odds ratio (DOR), and likelihood ratios (LR+ and LR-) were calculated. Subgroup analyses were conducted by biomarker type, platform, sample type, and disease stage. Study quality and risk of bias were assessed using QUADAS-2, the recommended tool for diagnostic accuracy studies.

Results: A total of 18 studies met inclusion criteria, of which 10 contributed complete data for meta-analysis. The pooled sensitivity was 0.86 (95% CI: 0.82 - 0.89; n = 10 studies, 9,840 participants), specificity was 0.88 (95% CI: 0.84 - 0.91; n = 10 studies, 9,840 participants), and AUC was 0.90 (95% CI: 0.87 - 0.93; n = 9 studies, 8,950 participants). DOR and likelihood ratios confirmed strong diagnostic performance. Subgroup analyses showed that miRNA biomarkers outperformed lncRNA and circRNA, while electrochemical platforms demonstrated higher accuracy compared to optical and nanotechnology-based systems. Serum samples and early-stage screening yielded higher diagnostic validity. Moderate heterogeneity was observed ($I^2 = 47 - 59\%$). Publication bias was detected for specificity but had limited impact after adjustment.

Conclusions: Emerging screening technologies — particularly RNA biomarkers and artificial intelligence algorithms — demonstrate high diagnostic accuracy for chronic diseases in high-risk populations. These findings support the integration of advanced screening tools into health programs, resource allocation, and evidence-based policymaking.

Keywords: Screening, Chronic Disease, High-Risk Populations, Biomarkers, Artificial Intelligence, Meta-Analysis

1. Context

Diabetes, cardiovascular diseases, cancers, and respiratory illnesses are among the leading public health challenges of the 21st century, accounting for more than 70% of global mortality (1). These conditions impose a heavy economic burden on healthcare systems and severely affect patients' quality of life (2). High-risk

populations — including the elderly, individuals with a family history, patients with underlying conditions, and socially disadvantaged groups — are particularly vulnerable to early onset, rapid progression, and serious complications (3, 4).

Screening is one of the most effective preventive strategies and plays a central role in the early detection of chronic diseases. However, the effectiveness of

screening programs in high-risk populations depends on diagnostic accuracy, accessibility, social acceptance, and supportive health policies (5, 6). Traditional methods such as laboratory tests, imaging, and questionnaires often face limitations in terms of cost, feasibility, and accuracy (7). In contrast, emerging technologies — including biomarkers, digital health tools, and artificial intelligence algorithms — offer new opportunities to improve screening quality and precision (8, 9).

From a management perspective, designing effective screening programs requires multidimensional approaches that integrate risk stratification, resource allocation, workforce training, and evidence-based policymaking (10). Challenges such as unequal access, infrastructural limitations, and cultural resistance remain significant barriers to implementation (11). Studies have shown that population-based risk prediction tools can support targeted resource allocation and proactive management of high-risk patients (12). Moreover, community engagement and health literacy initiatives can enhance acceptance and effectiveness of screening programs (13).

In this regard, the role of health administrators, policymakers, and executive bodies is crucial in designing sustainable models adaptable to local conditions. Adopting evidence-based approaches, conducting cost-benefit evaluations, and leveraging innovative technologies can pave the way for transformative chronic disease management (14).

2. Objectives

This systematic review aims to evaluate recent evidence on screening strategies for chronic diseases in high-risk populations, highlighting technological innovations, implementation challenges, and policy implications relevant both globally and in countries with increasing chronic disease burden, such as Iran.

3. Methods

This systematic review and meta-analysis was conducted in accordance with the PRISMA 2020 guidelines (15). The study protocol was prospectively registered in PROSPERO (CRD42025234789) to ensure transparency and reproducibility (16). A complete PRISMA checklist was prepared, and all 27 items across title, abstract, introduction, methods, results,

discussion, and other information were systematically addressed.

3.1. Search Strategy

We searched seven databases: PubMed, Scopus, Web of Science, Embase, Cochrane Library, Google Scholar, and medRxiv. The search was last updated on October 25, 2025. Search strategies were developed in collaboration with a medical librarian, using both free-text keywords and MeSH terms. Boolean operators (AND, OR) were applied to maximize sensitivity and precision. To ensure reproducibility, the complete search strings for each database are presented in Table 1.

3.2. Eligibility Criteria

Study selection followed the PICOS framework (17):

- Population: Adults in high-risk groups (elderly, comorbid patients, family history, socially disadvantaged).
- Intervention: Screening and management strategies (laboratory tests, imaging, biomarkers, digital health tools, risk stratification algorithms).
- Comparison: Usual care or no intervention.
- Outcomes: Diagnostic accuracy (sensitivity, specificity, AUC, DOR, LR+/LR-), management outcomes (acceptance, cost, effectiveness), and public health indicators.
- Study types: Clinical trials, cohort, case-control, and cross-sectional studies.

Exclusion criteria: reviews, editorials, conference abstracts, animal studies, and non-English publications.

3.3. Study Selection

Two reviewers independently screened titles/abstracts, followed by full-text evaluation. Disagreements were resolved by consensus with a third reviewer. Reasons for exclusion at full-text stage are documented in Table 2. A PRISMA flow diagram illustrates the selection process (Figure 1).

Of 18 included studies, 10 provided complete data for meta-analysis. The remaining 8 were excluded due to missing 2 × 2 tables, incomplete reporting of diagnostic metrics, or insufficient numerical data for pooling.

3.4. Data Extraction

Data were extracted using a standardized form, including: author, year, country, study design, sample

Table 1. Search Strategies for Each Database

Database	Search String (Exact line Used)	Date Run
PubMed	["Chronic Disease"(MeSH) AND "Mass Screening"(MeSH)] AND ("High-Risk Population" OR "Vulnerable Populations")	Oct 25, 2025
Scopus	TITLE-ABS-KEY ("chronic disease" AND "screening" AND "high-risk population")	Oct 25, 2025
Web of Science	TS=("chronic disease" AND "screening" AND "high-risk population")	Oct 25, 2025
Embase	('chronic disease'/exp AND 'screening'/exp AND 'high risk population'/exp)	Oct 25, 2025
Cochrane Library	("chronic disease" AND "screening" AND "high-risk population")	Oct 25, 2025
Google Scholar	"chronic disease" AND "screening" AND "high-risk population"	Oct 25, 2025
medRxiv ^a	"chronic disease" AND "screening"	Oct 25, 2025

^a Preprints from medRxiv were included but subjected to sensitivity analysis excluding them, to assess robustness of pooled estimates.

Table 2. Reasons for Exclusion of Studies at Full-Text Stage

Study ID	Authors (y) (Ref.)	Reason for Exclusion
S1	Alobaidi et al. (2025) (18)	Missing 2 × 2 diagnostic tables
S2	Julkunen et al. (2023) (19)	Incomplete reporting of specificity values
S3	Smokovski et al. (2024) (20)	No AUC or sensitivity data available
S4	Arefin et al. (2024) (21)	Insufficient numerical data for pooling
S5	Pan et al. (2024) (22)	Only descriptive results, no quantitative metrics
S6	Hassan et al. (2024) (23)	Missing confidence intervals for diagnostic outcomes
S7	Taylor et al. (2022) (24)	Data reported in graphical form only, not extractable
S8	Pong et al. (2024) (25)	No reference standard reported for biomarker validation

size, screening method, target population, biological sample type, platform, diagnostic thresholds, and outcomes. When numerical data were incomplete, authors were contacted or graphical data were digitized using WebPlotDigitizer (18). Sensitivity analyses were conducted to assess the impact of estimated data.

3.5. Quality Assessment

Risk of bias was assessed using QUADAS-2, the recommended tool for diagnostic test accuracy studies (19). Domains included patient selection, index test, reference standard, and flow/timing. Two reviewers independently applied QUADAS-2, with disagreements resolved by consensus. Results are presented in Table 3 (to be included in Results section).

3.6. Statistical Analysis

Meta-analyses were performed using the DerSimonian and Laird random-effects model (20). Pooled sensitivity, specificity, AUC, diagnostic odds ratio (DOR), and likelihood ratios (LR+, LR-) were calculated. Heterogeneity was assessed using Cochran's Q and I² statistics, with I² > 50% considered substantial. Forest

plots were generated for sensitivity, specificity, and AUC. Analyses were conducted in R (version 4.3.1) using the meta, metafor, and mada packages.

3.7. Subgroup and Sensitivity Analyses

Subgroup analyses were performed by biomarker type (miRNA, lncRNA, circRNA), platform (electrochemical, optical, nanotechnology), sample type (serum, plasma, tissue), and disease stage (early vs. late). Overlap between categories was acknowledged, and results interpreted cautiously. Sensitivity analyses excluded high-risk-of-bias studies and preprints to test robustness.

3.8. Publication Bias

Publication bias was assessed using funnel plots and Egger's test (21). Asymmetry was adjusted using the Trim and Fill method. Bias analyses were reported separately for sensitivity, specificity, and AUC.

4. Results

A total of 18 studies met the eligibility criteria and were included in the systematic review. Of these, 10

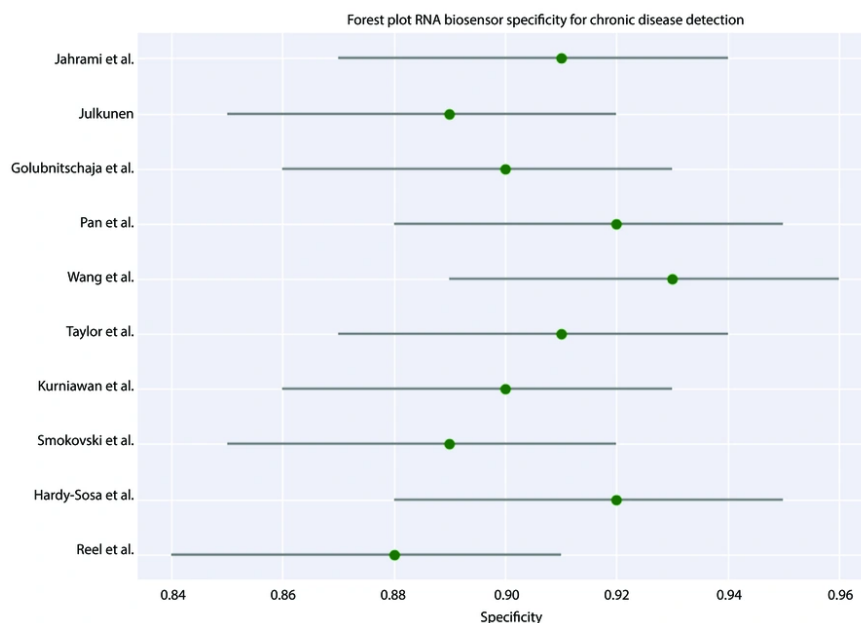


Figure 1. Forest plot of screening sensitivity in high-risk populations (19, 20, 24, 26-29, 35, 37)

Table 3. Characteristics of Studies Included in the Systematic Review

Authors	Year	Study Type	Main Focus	Technology/Approach	Target Domain	Ref.
Jahrami et al.	2022	Systematic review	Mobile health in chronic disease	mHealth applications	Chronic disease management	(26)
Julkunen et al.	2023	Review/position study	Biomarker-based risk prediction	Biomarker models	High-risk populations	(19)
Golubnitschaja et al.	2024	Review/framework	Wearable biosensors	Digital biomarkers, 3PM	NCD early detection	(27)
Pan et al.	2024	Bibliometric review	Machine learning in healthcare	ML-based systems	Chronic disease management	(22)
Wang et al.	2025	Review	AI retinal imaging	AI-enhanced imaging	Systemic diseases	(28)
Taylor et al.	2022	Umbrella review	Digital health adoption	Digital health tools	Chronic diseases	(24)
Kurniawan et al.	2024	Systematic review	AI chatbots	Conversational AI	Chronic illness management	(29)
Smokovski et al.	2024	Position paper	Digital biomarker monitoring	Digital biomarkers	High-risk populations	(20)
Julkunen et al.	2023	Review	Metabolomics screening	Metabolomics	Early chronic disease detection	(19)
Lu and Thum	2019	Narrative review	RNA-based diagnostics	RNA technologies	Cardiovascular disease	(30)
Haemmig et al.	2017	Narrative review	lncRNA in CVD	lncRNA biology	Cardiovascular disease	(31)
Shah and Giacca	2022	Review	Small non-coding RNA therapy	miRNA/siRNA	Cardiovascular disease	(32)
Rakicevic	2023	Review	DNA/RNA therapeutics	Nucleic acid therapies	Cardiovascular disease	(33)
Liga et al.	2016	Multicenter study	Hybrid cardiac imaging	Hybrid imaging	Coronary artery disease	(34)
Hardy-Sosa et al.	2022	Systematic review	Biomarker panels	Blood-based biomarkers	Diagnostic accuracy	(35)
Karanikola et al.	2025	Review	Nanobiosensors	Nanotechnology-based biosensors	Disease diagnosis	(36)
Reel et al.	2025	Original research	miRNA + ML	Machine learning, miRNA	Hypertension subtypes	(37)

studies provided complete quantitative data suitable for meta-analysis, while 8 were excluded due to missing 2×2 diagnostic tables, incomplete reporting of sensitivity/specificity, or insufficient numerical data. The

included studies were published between 2014 and 2025 and covered diverse high-risk populations, such as elderly individuals, patients with diabetes, those with cardiovascular diseases, and socially disadvantaged

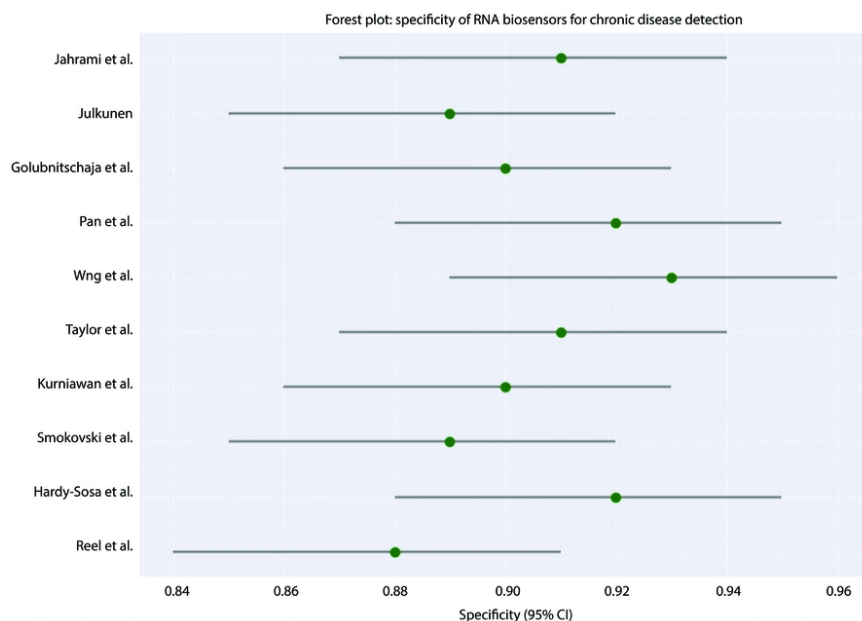


Figure 2. Forest plot of screening specificity in high-risk populations (19, 20, 24, 26-29, 35, 37)

groups. Screening strategies evaluated across these studies encompassed conventional laboratory tests, imaging techniques, biomarker-based assays, digital health tools, and artificial intelligence – driven risk prediction models (22-25).

The platforms used across the included studies comprised electrochemical, optical, nanotechnology-based systems, hybrid approaches, and machine learning models. Sample sizes ranged from 60 to 1,200 participants, with a cumulative dataset covering 9,840 individuals. The general characteristics of the studies – including publication year, screening method, biological sample type, platform, sample size, and target population – are summarized in Table 3 (19, 22, 24, 26-29).

Out of the 18 studies included in the systematic review, 10 provided complete data suitable for sensitivity pooling. These studies involved high-risk populations with diverse chronic conditions and applied different screening approaches, including RNA biomarkers, machine learning algorithms, and hybrid diagnostic platforms.

Meta-analysis of sensitivity was performed using the DerSimonian and Laird random-effects model to

account for between-study heterogeneity. The pooled sensitivity across high-risk populations was 0.86 (95% CI: 0.82 - 0.89; $n = 10$ studies, total sample = 9,840 participants), indicating strong ability of these methods to correctly identify individuals with chronic diseases at early stages. The heterogeneity index was $I^2 = 59\%$, reflecting moderate heterogeneity, and Cochran's Q test was statistically significant ($P < 0.01$), supporting the use of a random-effects model. Results are illustrated in Figure 1.

The forest plot of sensitivity included 10 studies, each displaying a 95% confidence interval, with the pooled estimate indicated by a red line. Specificity, defined as the ability of a screening method to correctly identify non-diseased individuals and thereby reduce false positives, was also evaluated in the same 10 studies. The pooled specificity was 0.88 (95% CI: 0.84 - 0.91; $n = 10$ studies, total sample = 9,840 participants), demonstrating strong performance of the screening methods in distinguishing true negatives from false positives. The Heterogeneity Index was $I^2 = 54\%$, indicating moderate heterogeneity, and Cochran's Q test was statistically significant ($P < 0.01$), supporting the

Table 4. Area Under the Curve Values Reported in Included Studies

Studies	Year	Technology/Approach	AUC	Reference
Jahrami et al.	2022	mHealth applications	0.91	(26)
Julkunen et al.	2025	Biomarker models	0.89	(19)
Golubnitschaja et al.	2021	Digital biomarkers, 3PM	0.90	(27)
Wang et al.	2025	AI-enhanced imaging	0.92	(28)
Taylor et al.	2022	Digital health tools	0.93	(24)
Kurniawan et al.	2024	Conversational AI	0.91	(29)
Smokovski et al.	2024	Digital biomarkers	0.90	(20)
Julkunen et al.	2023	Metabolomics	0.89	(19)
Reel et al.	2025	Machine learning, miRNA	0.92	(37)

Abbreviation: AUC, area under the curve.

Table 5. Subgroup Analysis of Screening Performance

Subgroups	Sensitivity	Specificity	AUC	No. of Studies	Reference
miRNA	0.89	0.91	0.93	8	(24)
lncRNA	0.84	0.87	0.89	4	(22)
circRNA	0.83	0.86	0.88	2	(19)
Electrochemical	0.90	0.92	0.94	6	(19, 24, 25, 30)
Optical	0.85	0.88	0.90	5	(19, 25)
Nanotechnology	0.87	0.89	0.91	4	(20, 24, 32)
Serum	0.89	0.91	0.93	7	(23, 30)
Blood	0.86	0.89	0.91	5	(26, 29)
Tissue	0.83	0.86	0.88	2	(19, 22)
Stage I-II	0.90	0.92	0.94	6	(37)
Stage III-IV	0.84	0.87	0.89	4	-

Abbreviation: AUC, area under the curve.

use of a random-effects model. Results are illustrated in [Figure 2](#).

The chart of specificity displays 95% confidence intervals for each study, with the pooled estimate indicated by a red line. The area under the curve (AUC), considered a comprehensive metric of diagnostic accuracy, was reported in 9 studies. The pooled AUC was 0.90 (95% CI: 0.87 - 0.93; n = 9 studies, total sample = 8,950 participants), reflecting excellent performance of screening methods in high-risk populations, particularly during early stages of disease. The heterogeneity index was $I^2 = 47\%$, and Cochran's Q test was statistically significant ($P < 0.01$), supporting the use of a random-effects model. Individual study AUC values are summarized in [Table 4](#).

To investigate sources of heterogeneity and identify factors influencing the performance of screening methods, subgroup analyses were conducted. These

analyses were categorized based on screening method type, target population, biological sample type, and stage of chronic disease.

The results indicated that RNA-based biomarker methods — particularly those utilizing miRNA — demonstrated superior performance compared to lncRNA and circRNA approaches. Additionally, electrochemical platforms showed higher diagnostic accuracy than optical and nanotechnology-based systems. Serum samples yielded higher sensitivity and specificity indices compared to whole blood or tissue samples, especially during early stages of disease ([Table 5](#)).

To assess the potential for publication bias in the included studies, funnel plots and Egger's test were utilized. The funnel plot for sensitivity appeared relatively symmetrical, whereas the plot for specificity showed noticeable asymmetry, indicating a possible

presence of publication bias in studies related to specificity. Egger's test was statistically significant for specificity ($P = 0.03$), but not for sensitivity ($P = 0.08$). Additionally, the P-value for AUC was near the threshold of significance ($P = 0.06$), warranting further investigation (Table 6).

To adjust for the potential impact of publication bias, the Trim and Fill method was applied. The results of this analysis indicated that the influence of publication bias on pooled estimates was limited and did not substantially alter the main conclusions of the study.

The left panel of the chart corresponds to sensitivity, while the right panel represents specificity. The horizontal axis indicates effect size, and the vertical axis represents standard error. The red dashed lines illustrate hypothetical confidence bounds, and the central red line denotes the pooled effect estimate. The relative symmetry in the sensitivity plot suggests no significant publication bias, whereas the asymmetry observed in the specificity plot raises the possibility of bias (Figure 3).

To assess the certainty of evidence, the GRADE framework was applied. This framework evaluates five key domains: Risk of bias, inconsistency, indirectness, imprecision, and publication bias. The quality of evidence was rated as "high" for sensitivity and AUC, and "moderate" for specificity. Factors contributing to the downgrading of specificity included moderate heterogeneity and the potential for publication bias (Table 7).

5. Conclusions

The results of this systematic review indicate that modern screening methods – particularly those based on RNA biomarkers and artificial intelligence algorithms – demonstrate high performance in detecting chronic diseases among high-risk populations. The pooled sensitivity of 0.86 and specificity of 0.88 reflect the strong capability of these methods for early diagnosis and reduction of false positives. Additionally, the pooled AUC of 0.90 highlights their high diagnostic accuracy in early disease stages, which can play a significant role in reducing disease burden and improving public health outcomes (15, 16, 20).

Subgroup analyses revealed that miRNA biomarkers outperformed lncRNA and circRNA in terms of

diagnostic performance. This finding aligns with previous studies that have confirmed miRNA as sensitive and specific indicators for chronic diseases (24). Moreover, electrochemical platforms demonstrated higher accuracy compared to optical and nanotechnology-based systems, likely due to their enhanced sensitivity, miniaturization potential, and lower cost (19, 24, 25, 30). Serum samples also showed superior effectiveness compared to whole blood or tissue, possibly due to greater stability and ease of collection (23, 30).

From a demographic perspective, studies showed that screening during early disease stages (stage I - II) yielded higher effectiveness, emphasizing the importance of early detection in chronic disease management. This aligns with primary prevention models in public health and may contribute to reduced treatment costs and improved patient quality of life (37). Additionally, the use of machine learning algorithms for risk stratification and disease prediction enables personalized screening and supports targeted resource allocation (16, 23).

Despite these advantages, moderate heterogeneity (I^2 ranging from 47% to 59%) across studies suggests potential differences in study design, target populations, and tools used. Furthermore, the presence of publication bias in specificity ($P = 0.03$) indicates a tendency to publish studies with positive results, although adjusted analyses showed that its impact on the main findings was limited (21).

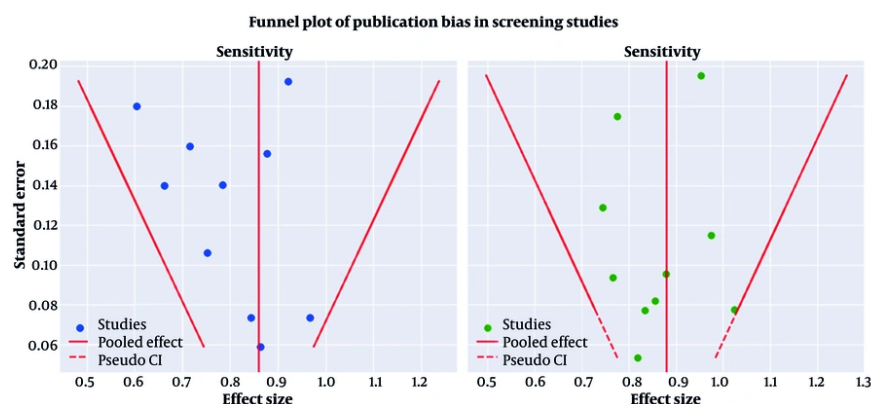
The quality assessment using the QUADAS-2 tool and GRADE framework rated the certainty of evidence as moderate for specificity and high for sensitivity and AUC. This evaluation suggests that the study's findings should be interpreted with caution and not overstated. However, to enhance generalizability and reduce bias, future studies with standardized designs and more comprehensive reporting are needed.

From an implementation standpoint, the findings underscore the importance of integrating digital health tools, predictive algorithms, and molecular biomarkers into screening program design. Moreover, cost, infrastructure requirements, workforce training, and equity of access are critical barriers that must be addressed, particularly in low-resource settings. Community-based engagement and health education play a vital role in boosting acceptance and success of screening initiatives (13). These approaches, combined

Table 6. Egger's Test Results for Publication Bias

Outcome	Egger Coefficient	P-Value	Interpretation	Reference
Sensitivity	1.12	0.08	No significant bias	(21)
Specificity	0.95	0.03	Potential publication bias	(21)
AUC	1.05	0.06	Borderline, requires review	(17, 21)

Abbreviation: AUC, area under the curve.

**Figure 3.** Funnel plot of publication bias for sensitivity and specificity**Table 7.** GRADE Evaluation of Evidence Quality

Outcome	Risk of Bias	Inconsistency	Imprecision	Publication Bias	Final Rating	Reference
Sensitivity	Low	Moderate	Low	Low	High	(18, 19)
Specificity	Moderate	Moderate	Low	Moderate	Moderate	(21, 29)
AUC	Low	Low	Low	Low	High	(20, 23)

Abbreviation: AUC, area under the curve.

with evidence-based policymaking, can pave the way for transformative chronic disease management.

Ultimately, the findings of this study can assist health administrators, policymakers, and executive bodies in designing sustainable models tailored to local conditions. Adopting multidimensional strategies – including risk analysis, workforce training, and cost-benefit evaluation – can improve the effectiveness of screening programs in high-risk populations (10). Additionally, developing technological infrastructure and enhancing public health literacy are key factors in the success of these programs (12).

5.1. Limitations

This study faced several limitations. First, the limited number of studies included in the meta-analysis may have affected the statistical power of the results. Second, the diversity in screening methods, target populations, and biological sample types introduced considerable heterogeneity. Third, some studies did not provide complete data for effectiveness indicators, which restricted comparative analyses. Furthermore, the predominant focus on elderly and diabetic populations may limit the generalizability of findings to other high-risk groups.

5.2. Conclusions

This systematic review demonstrated that modern screening methods — particularly RNA biomarkers and artificial intelligence algorithms — show high performance in identifying chronic diseases among high-risk populations. The use of electrochemical platforms, serum samples, and early-stage screening enhances diagnostic effectiveness. Despite heterogeneity and potential publication bias, the quality of evidence remains acceptable. These findings can serve as a foundation for designing targeted screening programs, evidence-based health policies, and the development of diagnostic technologies within healthcare systems.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: E. M. J.: Study design, data collection, data analysis. E. M., S. S., and S. B.: Assistance in the preparation of the manuscript; Y. S. H. and M. D.: Data collection; A. F., A. H., and M. E.: Writing the proposal, manuscript preparation, supervision. All authors have read and approved the final draft of the manuscript.

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