

Comparison of diagnostic accuracy for diabetes diagnosis: A systematic review and network meta-analysis

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Background

- Oral Glucose Tolerance Test (2-hour post load glucose) (OGTT-2hr) ≥ 200 mg/dl is widely used as the gold standard to diabetes diagnosis, it has often been criticized to be time-consuming and inconvenient for patients.
- Given the increased convenience and relative ease of Fasting Plasma Glucose (FPG) ≥ 126 mg/dl and Hemoglobin A1c (HbA1c) $\geq 6.5\%$, they are potential alternatives of OGTT.
- The previous meta-analyses pooled sensitivity and specificity of FPG and HbA1c, however, it is still inconclusive which test has the best diagnostic accuracy.

Objectives

- To quantify the diagnostic accuracy (i.e., sensitivity, specificity, positive likelihood ratio (LR+), negative likelihood ratio (LR-), and diagnostic odds ratio (DOR)) of HbA1c, FPG, and a combination of both methods HbA1c or FPG relative to a standard OGTT for diabetic diagnosis
- To rank these index tests based pn their diagnostic performances

Conclusion

Our findings suggest that FPG ≥ 126 mg/dl should be recommended as the best diagnostic test for diabetes.

Method

- We performed a comprehensive literature search in PubMed, Embase, Cochrane Library, and Scopus from inception to September 24th, 2021.
- The process of study screening, study selection, data extraction, and risk of bias assessment were independently performed by two reviewers.
- The index tests of interest were HbA1c $\geq 6.5\%$ (48.0 mmol/L), FPG > 7.0 mmol/L (or ≥ 126 mg/dl), and the combination of HbA1c $\geq 6.5\%$ or FPG ≥ 126 mg/dl (HbA1c/FPG). The outcome of interest was diabetes diagnosed by the standard OGTT 2hr > 11.1 mmol/L (or ≥ 200 mg/dl).
- The diagnostic accuracy (i.e., sensitivity, specificity, LR+, LR-, DOR) of each of HbA1c, FPG, and combined HbA1c/FPG relative to OGTT were estimated for individual studies. The relative diagnostic performances among three index tests were then estimated using a bivariate random-effects network meta-analysis model using Bayesian framework. The relative ranking of interest indexed was also estimated from this model.

Results

- Out of 5,026 studies, 73 were included (Figure 1).
- The sensitivity of HbA1c $\geq 6.5\%$, FPG ≥ 126 mg/dl, and combination of HbA1c $\geq 6.5\%$ or FPG ≥ 126 mg/dl was 0.51 (95%Credible Interval (CrI): 0.43, 0.58), 0.49 (0.43, 0.55), and 0.64 (95%CrI: 0.51, 0.75) while the specificity was 0.96 (0.94, 0.97), 0.98 (0.97,0.98), and 0.95 (0.88, 0.98), respectively (Table 1).
- The diagnostic odds ratio (DOR) was also reported as 26.10 (15.75, 44.07), 41.86 (26.75, 64.62), 31.50 (12.24, 83.44), respectively Table 1).
- The corresponding positive likelihood ratio (LR+) was 13.36 (8.91, 20.72), 21.94 (15.04, 31.88), and 11.78 (5.48, 26.56).
- In terms of ranking, the combination of HbA1c $\geq 6.5\%$ or FPG ≥ 126 mg/dl is the best based on sensitivity whereas FPG ≥ 126 mg/dl is ranked the best based on specificity, LR+, and DOR (table 2)

Table 1: Performace of index tests versus OGTT

Index vs OGTT	Sensitivity (95%CrI)	Specificity (95%CrI)	LR+ (95%CrI)	LR- (95%CrI)	DOR (95%CrI)
HbA1c 6.5%	0.51 (0.43, 0.58)	0.96 (0.94, 0.97)	13.36 (8.91, 20.72)	0.51 (0.44, 0.60)	26.10 (15.75, 44.07)
FPG 126 mg/dl	0.49 (0.43, 0.55)	0.98 (0.97,0.98)	21.94 (15.04, 31.88)	0.52 (0.46, 0.59)	41.86 (26.75, 64.62)
HbA1c 6.5% or FPG 126 mg/dl	0.64 (0.51, 0.75)	0.95 (0.88, 0.98)	11.78 (5.48, 26.56)	0.38 (0.26, 0.52)	31.50 (12.24, 83.44)

Note: CrI: Credible Interval

Table 2: The relative ranking of index tests

Index vs OGTT	Rank sensitivity (95%CrI)	P(Best) sensitivity	Rank specificity (95%CrI)	P(Best) specificity	Rank LR+ (95%CrI)	P(Best) LR+	Rank LR- (95%CrI)	P(Best) LR-	Rank DOR (95%CrI)	P(Best) DOR
HbA1c 6.5%	2 (2,3)	0.017	2 (2,3)	0.019	2 (1,3)	0.026	2 (1,2)	0.394	3 (1,3)	0.034
FPG 126 mg/dl	3 (2,3)	0.006	1 (1,2)	0.964	1 (1,3)	0.905	1 (1,1)	0.595	1 (1,3)	0.689
HbA1c 6.5% or FPG 126 mg/dl	1 (1,1)	0.977	3 (2,3)	0.017	3 (1,3)	0.069	3 (2,3)	0.011	2 (1,3)	0.277

Note: CrI: Credible Interval, DOR: Diagnostic Odds Ratio, LR+: Positive Likelihood Ratio, LR-: Negative Likelihood Ratio

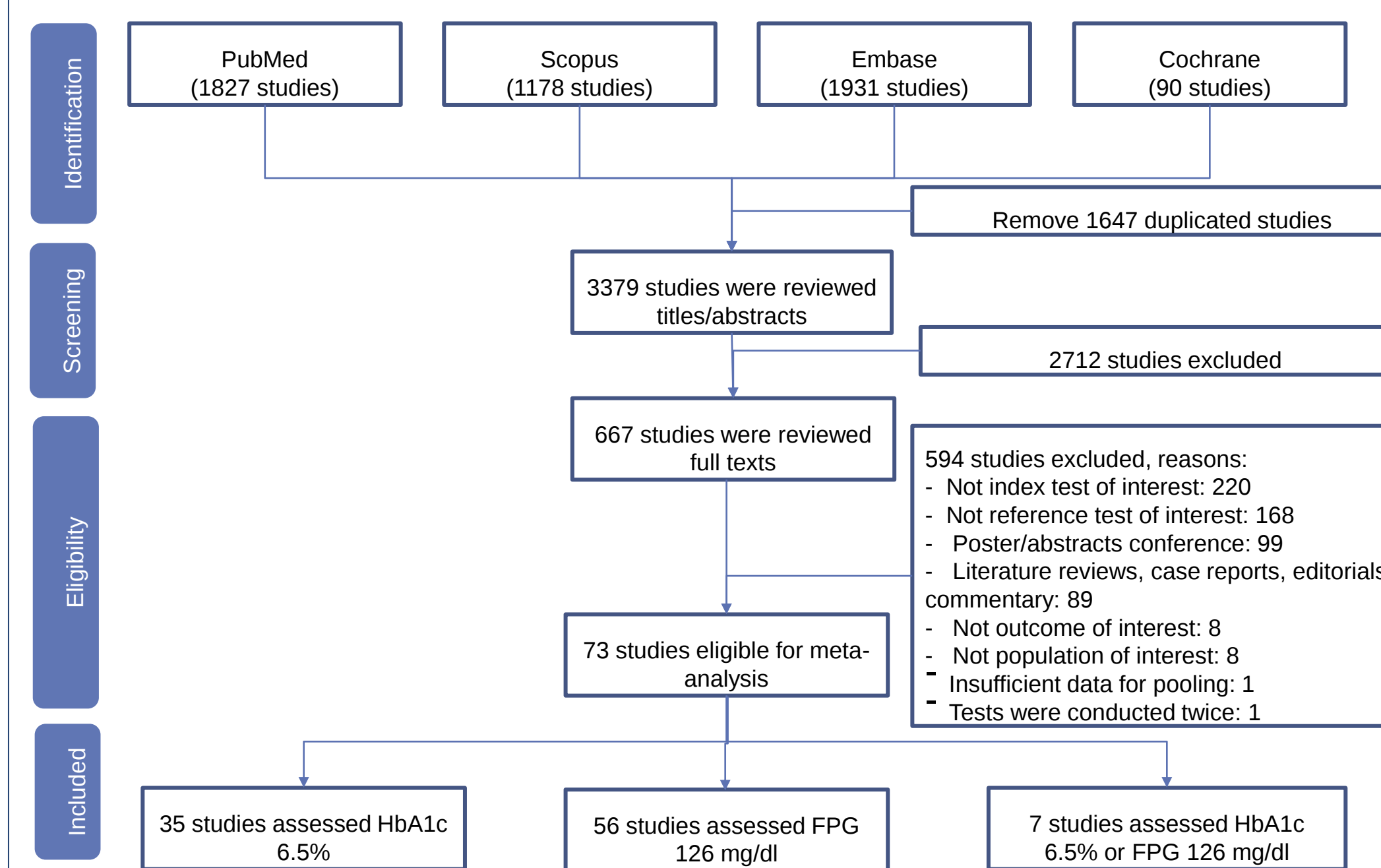


Figure 1: PRISMA Flow chart of study selection

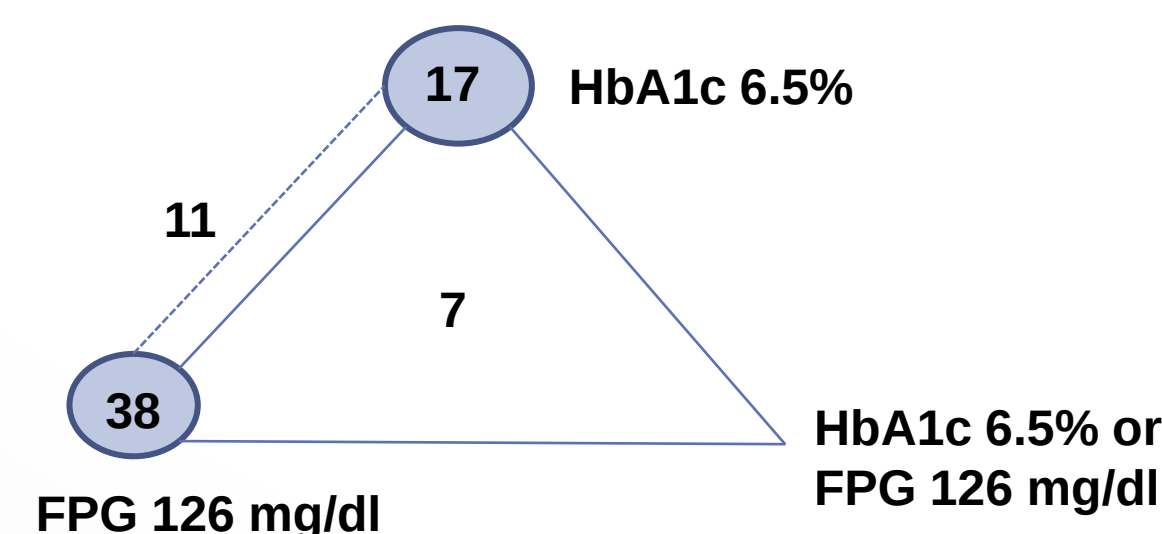


Figure 2: Network plot

7 studies investigated all three index tests (HbA1c $\geq 6.5\%$, FPG ≥ 126 mg/dl, and HbA1c/ FPG); 11 studies investigated two index tests HbA1c $\geq 6.5\%$, FPG ≥ 126 mg/dl; 17 studies investigated only HbA1c $\geq 6.5\%$, 38 studies investigated only FPG ≥ 126 mg/dl