Volume 4, Issue 5, 2026

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

DIAGNOSTIC ACCURACY OF GLYCOSYLATED HAEMOGLOBIN (HBA1C) FOR THE DETECTION OF GESTATIONAL DIABETES MELLITUS AMONG PREGNANT FEMALES ATTENDING A TERTIARY CARE OBSTETRIC OUTPATIENT DEPARTMENT

Hafiza Kashaf Qudsia[*1], Dr. Rabika Nargis[2], Madeeha Tahir[3], Naila Altaf Makhdoom[4], Warda Samad[5]

*[*1]SR gynecology Jinnah Hospital Lahore*
[2]Assistant Professor, Nishtar Medical university Multan
[3]Dr. Faisal Masood Teaching hospital Sargodha
[4]Senior Registrar
[4]Jinnah Hospital, Lahore
[5]Demonstrator, Nishtar Medical University, Multan

[*1]kashf.qudsia12@gmail.com, [2]drrabicanargis@gmail.com, [3]madeehatanveer4848@gmail.com, [4]drnailaaltafmakhdoom@gmail.com, [5]wardachohan60@gmail.com

DOI: https://doi.org/10.5281/zenodo.20391217

Keywords
Gestational diabetes mellitus; HbA1c; glycosylated haemoglobin; oral glucose tolerance test; diagnostic accuracy; South Asia; pregnancy screening

Article History
Received: 30 March 2026
Accepted: 08 May 2026
Published: 26 May 2026

Corresponding Author: *
Hafiza Kashaf Qudsia

Abstract

Background: *Gestational diabetes mellitus (GDM) is among the most common metabolic complications of pregnancy, affecting between 5% and 14% of pregnancies worldwide. Early and accurate diagnosis is essential to reduce adverse maternal and fetal outcomes. Although the 2-hour oral glucose tolerance test (OGTT) remains the diagnostic gold standard, it is cumbersome, time-consuming, and poorly tolerated by many pregnant women.*

Objective: *To determine the diagnostic accuracy of glycosylated haemoglobin (HbA1c) for detecting GDM among pregnant females at 18 to 24 weeks of gestation, using the OGTT as the reference standard.*

Methods: *A comparative cross-sectional study was conducted at Jinnah Hospital, Lahore, enrolling 168 consecutive pregnant women aged 18–40 years at 18–24 weeks of gestation. All participants underwent concurrent HbA1c measurement and a 2-hour 75 g OGTT. Receiver operating characteristic (ROC) curve analysis was performed to identify the optimal diagnostic threshold, and standard diagnostic accuracy metrics were computed.*

Results: *The true prevalence of GDM in this cohort was 31.5%. HbA1c demonstrated outstanding overall discriminatory capacity, with an area under the ROC curve (AUC) of 0.980 (95% CI: 0.962–0.997; $p < 0.001$). An HbA1c threshold of 5.3% was identified as the optimal cut-off, yielding a sensitivity of 94.3%, specificity of 96.5%, positive predictive value (PPV) of 92.6%, and negative predictive value (NPV) of 97.4%.*

Conclusion: *HbA1c at a threshold of 5.3% demonstrates excellent diagnostic accuracy for GDM screening in this South Asian obstetric population, offering a reliable, patient-friendly alternative to support primary metabolic triage and reduce over-reliance on the OGTT.*

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance that is first recognised during pregnancy.[1] It is one of the most common medical complications of pregnancy, affecting approximately 5% to 14% of all pregnancies globally, with considerable variation according to ethnic background, geographic region, and the diagnostic criteria employed.[2]

The clinical significance of GDM extends well beyond the index pregnancy. For the mother, GDM carries a substantially elevated risk of preeclampsia, operative delivery, and most importantly progression to overt type 2 diabetes mellitus (T2DM) in the years following delivery.[3] For the fetus, uncontrolled maternal hyperglycaemia during the second and third trimesters is associated with macrosomia, shoulder dystocia, neonatal hypoglycaemia, congenital anomalies, and in severe cases intrauterine death.[4] These risks underscore the imperative for accurate, early, and universally accessible GDM screening.

The 2-hour, 75 g oral glucose tolerance test (OGTT), performed following an overnight fast of at least eight hours, remains the internationally endorsed gold standard for GDM diagnosis.[5] However, the OGTT carries well-recognised practical limitations: it is time-consuming, requires multiple venipunctures, demands prolonged fasting that is frequently difficult for pregnant women experiencing nausea or hyperemesis, and demonstrates suboptimal intra-individual reproducibility.[6] These barriers reduce patient compliance and impose a considerable logistical burden on already- stretched antenatal services.

Glycosylated haemoglobin (HbA1c) reflects average glycaemia over the preceding 8–12 weeks, requires no fasting, can be measured on a single blood sample at any time of day, and has excellent analytical reproducibility.[7] It has long served as the cornerstone of glycaemic monitoring in established diabetes and since 2010 has been accepted by several international bodies as a diagnostic tool for non-pregnant individuals.[5] Its potential role in GDM screening is therefore intuitive; however, its diagnostic validity during pregnancy remains contested, largely because physiological haemodilution, accelerated red cell turnover, and iron deficiency anaemia all common in pregnancy can lower HbA1c independently of glycaemia, potentially leading to underestimation of true glucose intolerance.

Global literature reports a wide spectrum of optimal HbA1c thresholds for GDM diagnosis, reflecting differences in population genetics, obesity prevalence, and the reference OGTT criteria used. Khalafallah and colleagues reported a sensitivity of 61% and specificity of 68% at a 5.1% cut-off, with a reassuring negative predictive value (NPV) of 93%.[6] Sevket et al. identified a 5.2% threshold using International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, achieving a sensitivity of 64.2% and specificity of 67.5%, and concluded that HbA1c alone could not replace the OGTT.[8] Conversely, Ødsæter et al. reported a sensitivity of 88% and specificity of 97.4% at their study-specific thresholds, suggesting that performance is highly context-dependent.

South Asian populations, including those in Pakistan, are known to exhibit insulin resistance at lower body mass index (BMI) thresholds than Western counterparts and carry a disproportionately high lifetime risk of T2DM.[9] Population-specific cut-offs are therefore necessary for meaningful clinical implementation. There is, however, a conspicuous paucity of locally validated data on the diagnostic performance of HbA1c in South Asian obstetric cohorts. This study was designed to address that gap.

The primary objective was to evaluate the diagnostic accuracy of HbA1c expressed as sensitivity, specificity, PPV, and NPV against the 2-hour OGTT gold standard, and to identify the optimal population-specific screening threshold among pregnant women at 18–24 weeks of gestation attending a tertiary care facility in Lahore, Pakistan.

Methods

A comparative cross-sectional diagnostic accuracy

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

study was conducted in the Department of Obstetrics and Gynaecology at Jinnah Hospital, Lahore — a major public tertiary referral centre in Punjab, Pakistan — over a six-month period following approval from the institutional ethics review board. The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants prior to enrolment.

Pregnant women aged 18–40 years presenting for routine antenatal care at gestational ages of 18–24 weeks (confirmed by last menstrual period and/or first-trimester ultrasound) were recruited using non-probability consecutive sampling. There was no restriction on parity. Exclusion criteria were: multiple-gestation pregnancy, active early pregnancy complications (threatened or inevitable miscarriage), and a pre-existing diagnosis of type 1 or type 2 diabetes mellitus. A sample size of 168 participants was determined to provide adequate statistical power for the planned ROC curve analysis.

After obtaining informed consent and recording standardised demographic and clinical variables on a structured proforma, a single 5 mL venous blood sample was drawn from each participant under strict aseptic conditions using an EDTA-containing vacutainer tube. Samples were transported immediately to the hospital pathology laboratory, where quantitative HbA1c analysis was performed using high-performance liquid chromatography (HPLC) the internationally accepted reference method.

Subsequently, all participants underwent a standard 2-hour 75 g OGTT following an overnight fast of at least eight hours, in accordance with WHO and IADPSG diagnostic guidelines.[5,6] Venous plasma glucose concentrations at the 2-hour post-load time point were used to classify participants as OGTT-positive (GDM present) or OGTT-negative (no GDM), using the IADPSG threshold of ≥ 7.8 mmol/L (140 mg/dL) as the reference standard.

All data were entered and analysed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD); categorical variables as absolute frequencies and percentages. ROC curve analysis was performed to assess the overall discriminatory capacity of HbA1c and to identify the mathematically optimal diagnostic threshold, defined as the point on the ROC curve that maximised the Youden Index (sensitivity + specificity − 1).[9] A standard 2 × 2 contingency table was cross-tabulated to compute sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy against the OGTT reference standard. To examine the influence of potential confounders including maternal age, BMI category, and parity data were post- stratified and subgroup differences were tested using the chi-square test. A two-tailed p-value of ≤ 0.05 was considered statistically significant.

Results

A total of 168 participants were included in the final analysis. The mean age of the cohort was 29.47 ± 4.77 years (range: 21–39 years). The mean BMI was 25.87 ± 4.04 kg/m². On categorical BMI assessment, 44.6% (n = 75) had a normal BMI, 36.9% (n = 62) were overweight, and 18.5% (n = 31) were obese. Regarding obstetric history, 55.4% (n = 93) were multiparous and 44.6% (n = 75) were primigravida. The mean HbA1c value was 5.09% ± 0.38% (range: 4.5%–5.9%), and the mean 2-hour post-load plasma glucose concentration on OGTT was 127.20 ± 28.81 mg/dL. Baseline demographic and biochemical characteristics are summarised in Table 1.

Frontier in Medical & Health Research

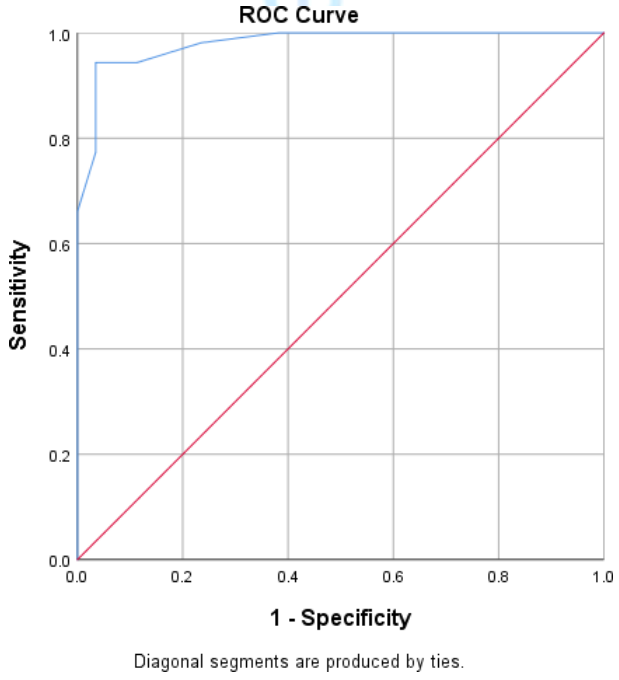
ISSN: (e) 3007-1607 (p) 3007-1593

Table 1. Baseline Demographic and Clinical Characteristics of the Study Cohort (n = 168)

Characteristic	Value (Mean ± SD or n [%])
Age (years)	29.47 ± 4.77
Body mass index (kg/m²)	25.87 ± 4.04
BMI category: Normal (< 25 kg/m²)	75 (44.6%)
BMI category: Overweight (25–29.9 kg/m²)	62 (36.9%)
BMI category: Obese (≥ 30 kg/m²)	31 (18.5%)
Parity: Multiparous	93 (55.4%)
Parity: Primigravida	75 (44.6%)
HbA1c (%)	5.09 ± 0.38
2-hour OGTT plasma glucose (mg/dL)	127.20 ± 28.81
GDM-positive (OGTT ≥ 140 mg/dL)	53 (31.5%)
GDM-negative (OGTT < 140 mg/dL)	115 (68.5%)

GDM = gestational diabetes mellitus; OGTT = oral glucose tolerance test; SD = standard deviation.

ROC curve analysis revealed that continuous HbA1c values possessed outstanding overall discriminatory power for differentiating GDM-positive from GDM-negative women. The area under the ROC curve (AUC) was 0.980 (95% CI: 0.962–0.997; p < 0.001), indicating near-perfect class separation and confirming the strong biomarker potential of HbA1c in this population (Figure 1).



Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Interrogation of the ROC curve coordinates using the Youden Index identified an HbA1c threshold of 5.3% as the optimal cut-off. Elevating the threshold to 5.35% resulted in an unacceptable reduction in sensitivity to 77.4%, while lowering it to 5.15% compromised specificity to 88.7%. The 5.3% threshold therefore represented the superior clinical trade-off between minimising missed diagnoses (false negatives) and minimising unnecessary secondary investigations (false positive)

At the 5.3% cut-off, the HbA1c test classified 54 participants (32.1%) as screen-positive and 114 (67.9%) as screen-negative. Cross-tabulation against the OGTT reference standard yielded 50 true positives, 111 true negatives, 4 false positives, and 3 false negatives. The resulting diagnostic accuracy metrics are displayed in Table 2.

Table 2. 2 × 2 Diagnostic Cross-Tabulation of HbA1c (≥ 5.3% Threshold) Against the OGTT Gold Standard

HbA1c Result	OGTT Positive	OGTT Negative	Row Total	PPV / NPV
Screen-positive (≥ 5.3%)	50 (True Positive)	4 (False Positive)	54	**PPV: 92.6%**
Screen-negative (< 5.3%)	3 (False Negative)	111 (True Negative)	114	**NPV: 97.4%**
Column total	**53**	**115**	**168**	
Diagnostic accuracy	**Sensitivity: 94.3%**	**Specificity: 96.5%**	**Overall accuracy: 95.8%**	

NPV = negative predictive value; OGTT = oral glucose tolerance test; PPV = positive predictive value.

At this threshold, the overall diagnostic accuracy of the HbA1c test was 95.8% (161/168 correctly classified). The high NPV of 97.4% indicates that a screen-negative result on HbA1c can, with
considerable clinical confidence, preclude the need for a confirmatory OGTT in the vast majority of women — a finding with important resource-allocation implications for antenatal services in low- and middle-income settings.

Discussion

This study investigated the diagnostic accuracy of HbA1c as a primary screening tool for GDM in a South Asian obstetric population, using the 2-hour OGTT as the reference standard. The principal finding is that HbA1c demonstrates outstanding discriminatory capacity in this context, as reflected by an AUC of 0.980 — one of the highest values reported in the published literature on this topic. At the population-specific optimal threshold of 5.3%, the test achieved a sensitivity of 94.3% and a specificity of 96.5%, with a PPV of 92.6% and an NPV of 97.4%.

These figures compare favourably with — and in most cases substantially exceed — those reported in comparable studies. Khalafallah et al., using a 5.1% threshold in an Australian cohort of mixed ethnicity, reported a sensitivity of only 61% and a specificity of 68%.[6] Sevket et al., applying the IADPSG diagnostic framework in Turkey, found that a 5.2% threshold yielded a sensitivity of 64.2% and a specificity of 67.5%, leading those authors to conclude that HbA1c alone was insufficient to replace the OGTT.[8] The considerably higher performance observed in the present cohort may reflect the higher background prevalence of GDM in South Asian women (31.5% in our sample), the narrower range of comorbidities in our relatively young cohort, and the greater signal-to-noise ratio that accompanies a higher-prevalence population in diagnostic accuracy studies.

The choice of diagnostic threshold profoundly influences clinical decision-making, and the rationale for selecting 5.3% over adjacent values warrants explicit justification. Raising the cut-off to 5.4% caused sensitivity to collapse to 77.4%, translating into a false-negative rate of approximately 22.6%. In the context of GDM screening, false negatives are clinically consequential: women with unrecognised GDM

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

are denied dietary modification, glycaemic monitoring, and — where indicated — pharmacological intervention, exposing them and their fetuses to the full spectrum of GDM-related complications, including macrosomia, shoulder dystocia, and neonatal hypoglycaemia.[4] Conversely, lowering the threshold to 5.2% preserved sensitivity at the cost of reducing specificity to 88.7%, generating a materially higher false-positive rate. False positives in this setting impose unnecessary psychological burden on healthy pregnant women, trigger unjustified dietary restrictions, and consume finite OGTT slots that could be more appropriately directed at genuinely high-risk individuals.[6] The 5.3% threshold therefore represents a well-justified clinical equilibrium.

From a clinical workflow perspective, the NPV of 97.4% is perhaps the most practically significant metric derived from this study. It implies that approximately 97–98% of women screening below the 5.3% threshold can be reliably excluded from GDM diagnosis without a confirmatory OGTT. In a publicly funded obstetric service managing high patient volumes, this capacity to safely triage the majority of the antenatal population away from the resource-intensive OGTT pathway would translate into substantial savings in laboratory costs, phlebotomy chair time, and patient-facing appointment burden.

The observed performance is also consistent with the broader biological rationale for HbA1c screening in South Asian populations. South Asian women exhibit accelerated progression to insulin resistance at lower BMI thresholds than European counterparts, partly attributable to higher visceral fat content relative to total body weight.[9] This phenotypic predisposition means that glycaemic dysregulation in South Asian pregnancy is often more pronounced, rendering HbA1c a marker of chronic average glycaemia a more sensitive detector of early GDM in this demographic than in populations with lower baseline metabolic risk.

The fact that 55.4% of our participants were multiparous and more than half fell into elevated BMI categories (overweight or obese) further contextualises our findings. Both multiparity and elevated BMI are independently associated with accelerated pancreatic beta-cell exhaustion during gestation and heightened peripheral insulin resistance,[2] factors that increase the probability that HbA1c will rise to detectable levels by 18–24 weeks. The post-stratification analyses performed in this study controlling for age, BMI, and parity are therefore essential to determine whether the 5.3% threshold retains homogeneous performance across all demographic subgroups, or whether more aggressive screening thresholds may be warranted in obese or multiparous women specifically.

Several limitations of this study should be acknowledged. First, HbA1c reflects the integrated average of glycaemia over the preceding 8–12 weeks and does not capture postprandial glucose excursions

— the principal pathological mechanism in GDM — in the way that a 2-hour post-load glucose measurement does. A woman with postprandial hyperglycaemia that developed only recently may have a normal or near-normal HbA1c, leading to an underestimated risk of a false-negative result at gestational ages towards the lower end of the 18–24 week window.[6]

Second, physiological haemodilution and the shortened erythrocyte lifespan that characterise healthy pregnancy compounded by the high prevalence of iron deficiency anaemia in our patient population can spuriously lower HbA1c values, independently of actual glycaemic control.[3] In women with concurrent anaemia, a compensatory downward adjustment to the screening threshold may be clinically appropriate, but this was beyond the scope of the current analysis. Future studies should formally assess HbA1c diagnostic performance stratified by haemoglobin concentration and ferritin status.

Third, this was a single-centre study conducted at a tertiary urban hospital, and the findings may not be fully generalisable to rural or primary care obstetric populations in Pakistan, where nutritional profiles, healthcare-seeking behaviour, and referral patterns differ. Multi-centre replication studies are therefore recommended before the 5.3% threshold is adopted as a

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

universal national standard.

Conclusion

This study demonstrates that HbA1c possesses outstanding diagnostic accuracy for gestational diabetes mellitus screening in a South Asian tertiary care population, achieving an AUC of 0.980. An HbA1c threshold of 5.3% provides the optimal balance between sensitivity (94.3%) and specificity (96.5%), with strong positive (92.6%) and negative (97.4%) predictive values. These findings support the role of a single-point, non-fasting HbA1c measurement as a primary triage tool in antenatal metabolic screening, with the capacity to substantially reduce the burden of universal OGTT testing on patients and healthcare systems alike. Adoption of this threshold in routine obstetric practice — pending multi-centre validation — could meaningfully improve the efficiency, equity, and accessibility of GDM diagnosis in resource-constrained clinical environments.

Declarations

Conflict of Interest: The authors declare no conflict of interest. Funding: This research received no external funding.

Ethical Approval: Institutional ethical approval was obtained prior to study commencement. Written informed consent was secured from all participants.

Data Availability: The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

REFERENCES

Khalafallah A, Phuah E, Al-Barazan AM, Nikakis I, Radford A, Clarkson W, et al. Glycosylated haemoglobin for screening and diagnosis of gestational diabetes mellitus. BMJ Open. 2016;6(4):e011059. https://doi.org/10.1136/bmjopen-2016-011059

Kopylov AT, Kaysheva AL, Papysheva O, Gribova I, Kotaysch G, Kharitonova L, et al. Association of proteins modulating immune response and insulin clearance during gestation with antenatal complications in patients with gestational or type 2 diabetes mellitus. Cells. 2020;9(4):1032. https://doi.org/10.3390/cells9041032

Renz PB, Cavagnolli G, Weinert LS, Silveiro SP, Camargo JL. HbA1c test as a tool in the diagnosis of gestational

Sevket O, Sevket A, Ozel A, Dansuk R, Kelekci S. The use of HbA1c as an aid in the diagnosis of gestational diabetes mellitus. J Obstet Gynaecol. 2014;34(8):690–692. https://doi.org/10.3109/01443615.2014.925855

American Diabetes Association Professional Practice Committee. Diagnosis and classification of diabetes: Standards of Care in Diabetes — 2024. Diabetes Care. 2024;47(Suppl 1):S20–S42. https://doi.org/10.2337/dc24-S002

International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676–682. https://doi.org/10.2337/dc09-1848

Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al; HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358(19):1991–2002. https://doi.org/10.1056/NEJMoa0707943

Agarwal MM. Gestational diabetes mellitus: An update on the worldwide prevalence, diagnostics, and regional grievances. World J Diabetes. 2018;9(11):204–216. https://doi.org/10.4239/wjd.v9.i11.204

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Youden WJ. Index for rating diagnostic tests. Cancer. 1950;3(1):32–35. https://doi.org/10.1002/1097-0142(1950)3:1<32::aid-cncr2820030106>3.0.co;2-3

Zhu WW, Yang HX, Wei YM, Yan J, Wang Z, Li XL, et al. Evaluation of the value of fasting plasma glucose and HbA1c for early screening of gestational diabetes mellitus in a Chinese population. Diabetes Care. 2013;36(3):586–590. https://doi.org/10.2337/dc12-1157

Rajput R, Yadav Y, Rajput S, Nanda S. Utility of HbA1c in diagnosis of gestational diabetes mellitus in Asian Indians. Diabetes Res Clin Pract. 2012;98(2):267–270. https://doi.org/10.1016/j.diabres.2012.09.005

Bhavadharini B, Mahalakshmi MM, Deepa M, Harish R, Malanda B, Kayal A, et al. Elevated glycated hemoglobin (HbA1c) levels in early pregnancy predict gestational diabetes mellitus and adverse pregnancy outcomes in southern Indian women. J Diabetes Complications. 2016;30(8):1460–1466. https://doi.org/10.1016/j.jdiacomp.2016.07.016

Chiefari E, Arcidiacono B, Foti D, Brunetti A. Gestational diabetes mellitus: an updated overview of immune-mediated mechanisms, macro- and micro-nutrients, and predispositions. Front Endocrinol. 2017;8:191. https://doi.org/10.3389/fendo.2017.00191

Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529–536. https://doi.org/10.7326/0003-4819-155-8-201110180-00009