

*In the name of God , the compassionate and the merciful*



# Thresholds in screening for gestational diabetes, a cluster field trial study with non-inferiority design

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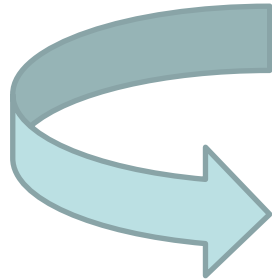
Shahid Beheshti University of Medical Sciences

November 2023

# Definition

## Previous definition

Gestational diabetes has been used to define women with onset or first recognition of abnormal glucose tolerance during pregnancy



## But

- Increasing prevalence of obesity and later age at pregnancy and lack of routine glucose screening/testing in this women.
- About 10 percent of women classified as having gestational diabetes have circulating islet-cell antibodies; these women may have a "latent" form of type 1 diabetes
- Gestational diabetes in lean pregnant women, need for insulin treatment of gestational diabetes, diabetic ketoacidosis during pregnancy, and postpartum hyperglycemia suggest preexisting unrecognized type 1 diabetes

International Association of Diabetes and Pregnancy Study Group  
(IADPSG) 2010

American Diabetes Association (ADA) 2011

Diabetes diagnosed during pregnancy is classified as overt or gestational

**Overt diabetes:**

Any of these criteria at initial prenatal visit:

- Fasting plasma glucose  $\geq 126$  mg/dL
- A1C  $\geq 6.5$  percent
- Random plasma glucose  $\geq 200$  mg/dL subsequently confirmed by elevated fasting plasma glucose or A1C
- GDM :
  - FBS  $\geq 92$  mg/dl and  $< 126$  mg/dl

*The* NEW ENGLAND  
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Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group\*

- The aim of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study was to clarify the risks of adverse outcomes associated with various degrees of maternal glucose intolerance less severe than that in overt diabetes mellitus.

# HAPO Study methods

25,505 pregnant women at 15 centers in nine countries  
underwent 75-g OGTT at 24 to 32 w of gestation

## Primary outcomes

- Macrosomia
- Primary C section
- Neonatal hypoglycemia
- Cord-blood c-peptide level above the 90th percentile

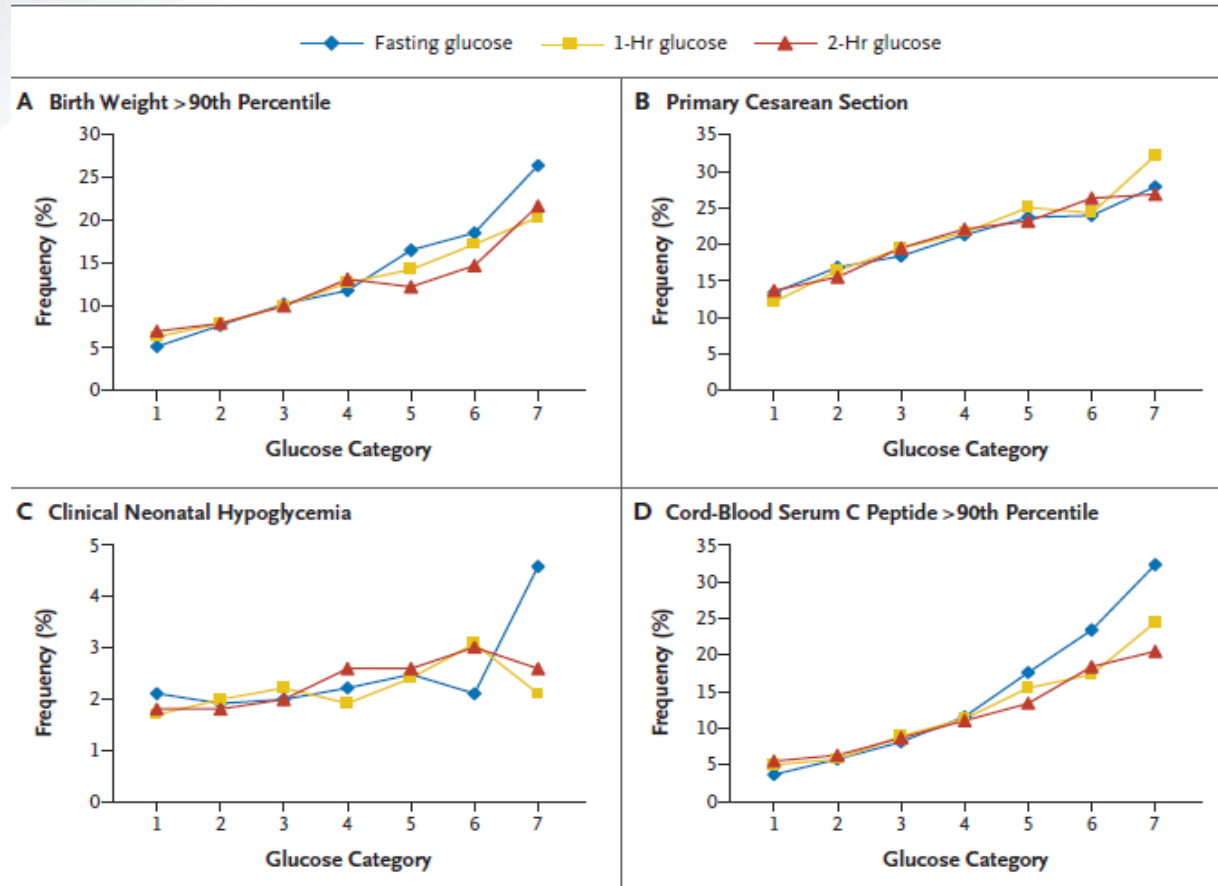
## Secondary outcomes

- preterm delivery
- Shoulder dystocia
- need for NICU
- hyperbilirubinemia
- preeclampsia

## Severe Adverse outcomes

- death
- birth injury
- major malformation

# Frequency of Primary Outcomes across the Glucose Categories



The results indicate strong, continuous associations of maternal glucose levels below those diagnostic of diabetes with increased birth weight even after adjustment for confounders

The results of HAPO study need to be translated to a practical guide line



## Adjusted Odds Ratios for Associations between Maternal Glycemia as a Continuous Variable and Primary and Secondary Perinatal Outcomes

Outcome	Plasma Glucose Level		
	Fasting	At 1 Hr	At 2 Hr
	<i>odds ratio (95% CI)</i>		
<b>Primary outcome</b>			
Birth weight >90th percentile	1.38 (1.32–1.44)	1.46 (1.39–1.53)	1.38 (1.32–1.44)
Primary cesarean section†	1.11 (1.06–1.15)	1.10 (1.06–1.15)	1.08 (1.03–1.12)
Clinical neonatal hypoglycemia	1.08 (0.98–1.19)‡	1.13 (1.03–1.26)	1.10 (1.00–1.12)
Cord-blood serum C peptide >90th percentile	1.55 (1.47–1.64)	1.46 (1.38–1.54)	1.37 (1.30–1.44)
<b>Secondary outcome</b>			
Premature delivery (before 37 wk)	1.05 (0.99–1.11)	1.18 (1.12–1.25)	1.16 (1.10–1.23)
Shoulder dystocia or birth injury	1.18 (1.04–1.33)	1.23 (1.09–1.38)	1.22 (1.09–1.37)
Intensive neonatal care	0.99 (0.94–1.05)	1.07 (1.02–1.13)	1.09 (1.03–1.14)
Hyperbilirubinemia	1.00 (0.95–1.05)	1.11 (1.05–1.17)	1.08 (1.02–1.13)
Preeclampsia	1.21 (1.13–1.29)	1.28 (1.20–1.37)	1.28 (1.20–1.37)

# First prenatal visit

- Measurement of FPG, A1C, or RPG

- Overt Diabetes:

- FPG  $\geq$  126 mg/dL (Fasting is defined as no caloric intake for at least 8 h)
- A1C  $\geq$  6.5%
- RPG  $\geq$  200 mg/dL

The value for GDM diagnosis at 1<sup>st</sup> trimester has not been resulted from their data, they extrapolated the results of FBS measured at 2<sup>nd</sup> trimester For providing this threshold.


- Gestational Diabetes

- If results not diagnostic of overt diabetes and FPG are 92–126 mg/dL , diagnose as GDM



## At 24-28 weeks of Gestation

- The OGTT-75 g glucose should be performed in the morning after an overnight fast of at least 8 h.
- The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:
  - Fasting: 92 mg/dL (5.1 mmol/L)
  - 1 h: 180 mg/dL (10.0 mmol/L)
  - 2 h: 153 mg/dL (8.5 mmol/L)



Several studies revealed that applying these thresholds increased the prevalence of GDM by 2-3 times with no specific advantage in terms of pregnancy outcomes.

# Effects of Implementing International Association of Diabetes and Pregnancy Study Groups Gestational Diabetes Screening on Pregnancy Outcomes at a Small Community Teaching Hospital

Jody M. Gerome,<sup>1</sup> Lucy K.M. Bucher,<sup>2</sup> and Godwin Dogbey<sup>1</sup>

Can J Diabetes 39 (2015) 128–132



Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage:

www.canadianjournalofdiabetes.com

Canadian Diabetes Association



Original Research

Evaluation of the International Association of the Diabetes in Pregnancy Study Group New Criteria: Gestational Diabetes Project



Jason M. Kong MD<sup>a,\*</sup>, Ken Lim MD<sup>b</sup>, David M. Thompson MD<sup>a</sup>



Journal of  
*Clinical Medicine*



Review  
**The Impact of Diagnostic Criteria for Gestational Diabetes Mellitus on Adverse Maternal Outcomes: A Systematic Review and Meta-Analysis**

Fahimeh Ramezani Tehrani<sup>1</sup>, Marzieh Saei Ghare Naz<sup>1</sup>, Razieh Bidhendi Yarandi<sup>1</sup> and Samira Behboudi-Gandevani<sup>2,\*</sup>

# Assessing the incidence of gestational diabetes and neonatal outcomes using the IADPSG guidelines in comparison with the Carpenter and Coustan criteria in a Belgian general hospital

P. Oriot<sup>1</sup>, P. Selvais<sup>1</sup>, J. Radikov<sup>2</sup>, J. L. Jacobs<sup>2</sup>, U. Gilleman<sup>2</sup>, R. Loumaye<sup>2</sup>, C. Fernandez<sup>2</sup>

## Gestational diabetes screening with the new IADPSG guidelines: a cost-effectiveness analysis

Costa et al. *BMC Pregnancy and Childbirth* (2019) 19:249  
<https://doi.org/10.1186/s12884-019-2406-4>

BMC Pregnancy and Childbirth

RESEARCH ARTICLE

Open Access

Change in prevalence of gestational diabetes and obstetric complications when applying IADPSG screening criteria in a Belgian French speaking University



# Screening for Gestational Diabetes Mellitus: Are the Criteria Proposed by the International Association of the Diabetes and Pregnancy Study Groups Cost-Effective?

# BMJ Open Implications of the introduction of new criteria for the diagnosis of gestational diabetes: a health outcome and cost of care analysis

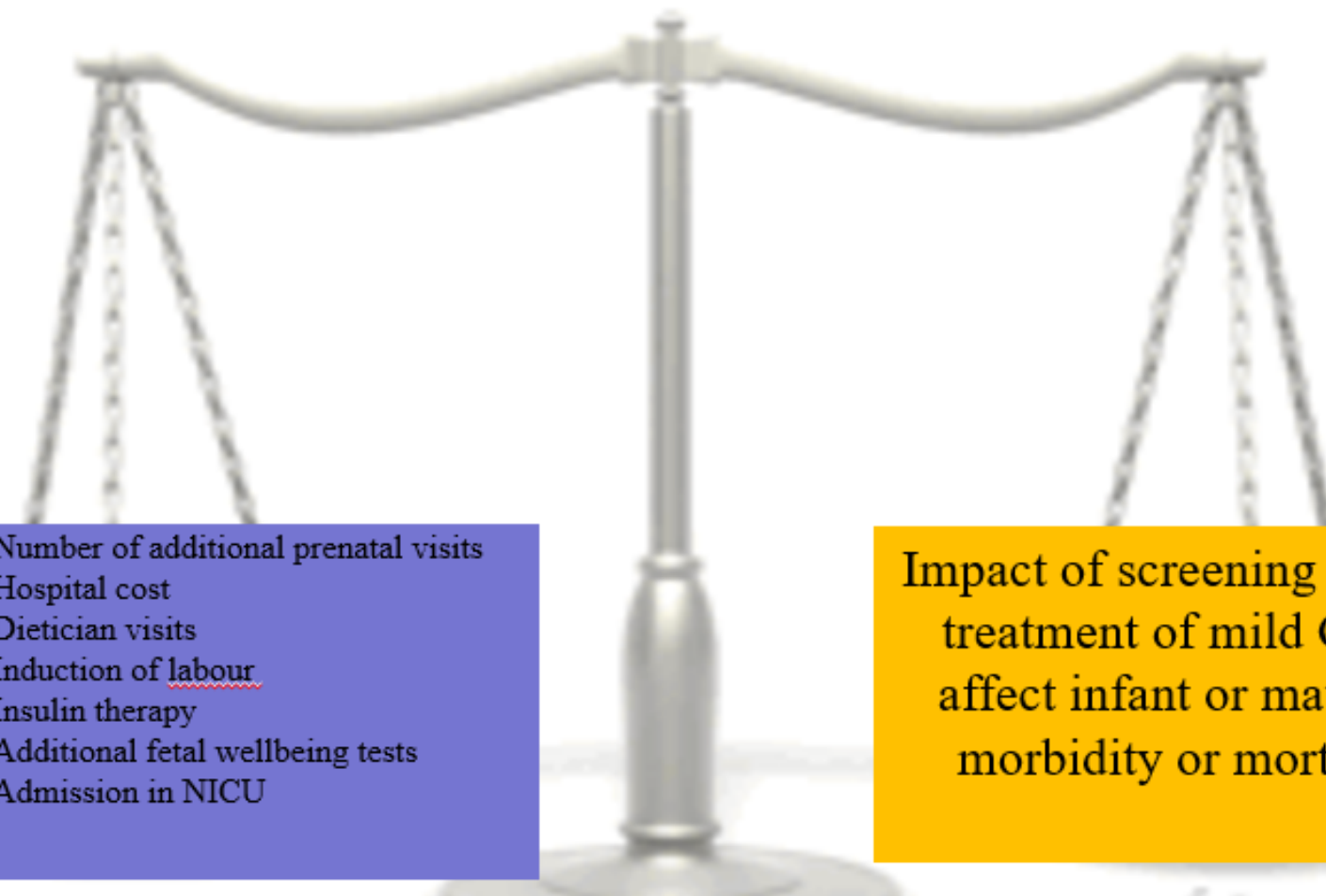
Thomas J Cade,<sup>1,2,3</sup> Alexander Polyakov,<sup>3,4</sup> Shaun P Brennecke<sup>2,3</sup>

Cade TJ, *et al. BMJ Open* 2019;**9**:e023293. doi:10.1136/bmjopen-2018-023293

**Conclusion** New criteria for the diagnosis of GDM have increased the incidence of GDM and the overall cost of GDM care. Without obvious changes in short-term outcomes, validation over other systems of diagnosis may require longer term studies in cohorts using universal screening and treatment under these criteria.

## Cost

## Benefit

- 
- Number of additional prenatal visits
  - Hospital cost
  - Dietician visits
  - Induction of labour
  - Insulin therapy
  - Additional fetal wellbeing tests
  - Admission in NICU

Impact of screening for and treatment of mild GDM affect infant or maternal morbidity or mortality

# Conclusion

- ❖ For every 100,000 pregnancies screened using the IADPSG recommendations, 27 QALYs are gained compared with the current standard of care at an additional cost of \$15,265,992.
- ❖ The incremental cost-effectiveness ratio(ICER) is \$565,407 per QALY gained.
- ❖ When post delivery care was not accomplished, the IADPSG strategy was no longer cost-effective.



- 
- The average cost of each additional case of GDM recognized using new criteria is \$1971

*American Journal of Obstetrics & Gynecology*

- The average estimated cost of each additional case of GDM be recognized using new criteria in **Iran** is \$500
- If the prevalence of GDM in Iran is increased from 10% to 20% using new criteria, considering 1,520,000 birth annually, the average annual cost of GDM will be \$800,000,000

## WHO recommendation 2016

To conduct research at national or regional level addressing GDM screening from a health economic perspective before implementation of any GDM screening programs

Ramezani Tehrani and Gulf Study Cooperative Research Group  
*Diabetol Metab Syndr* \_#####\_  
<https://doi.org/10.1186/s13098-019-0493-z>

Diabetology &  
Metabolic Syndrome

**STUDY PROTOCOL**

**Open Access**

# Cost effectiveness of different screening strategies for gestational diabetes mellitus screening: study protocol of a randomized community non-inferiority trial

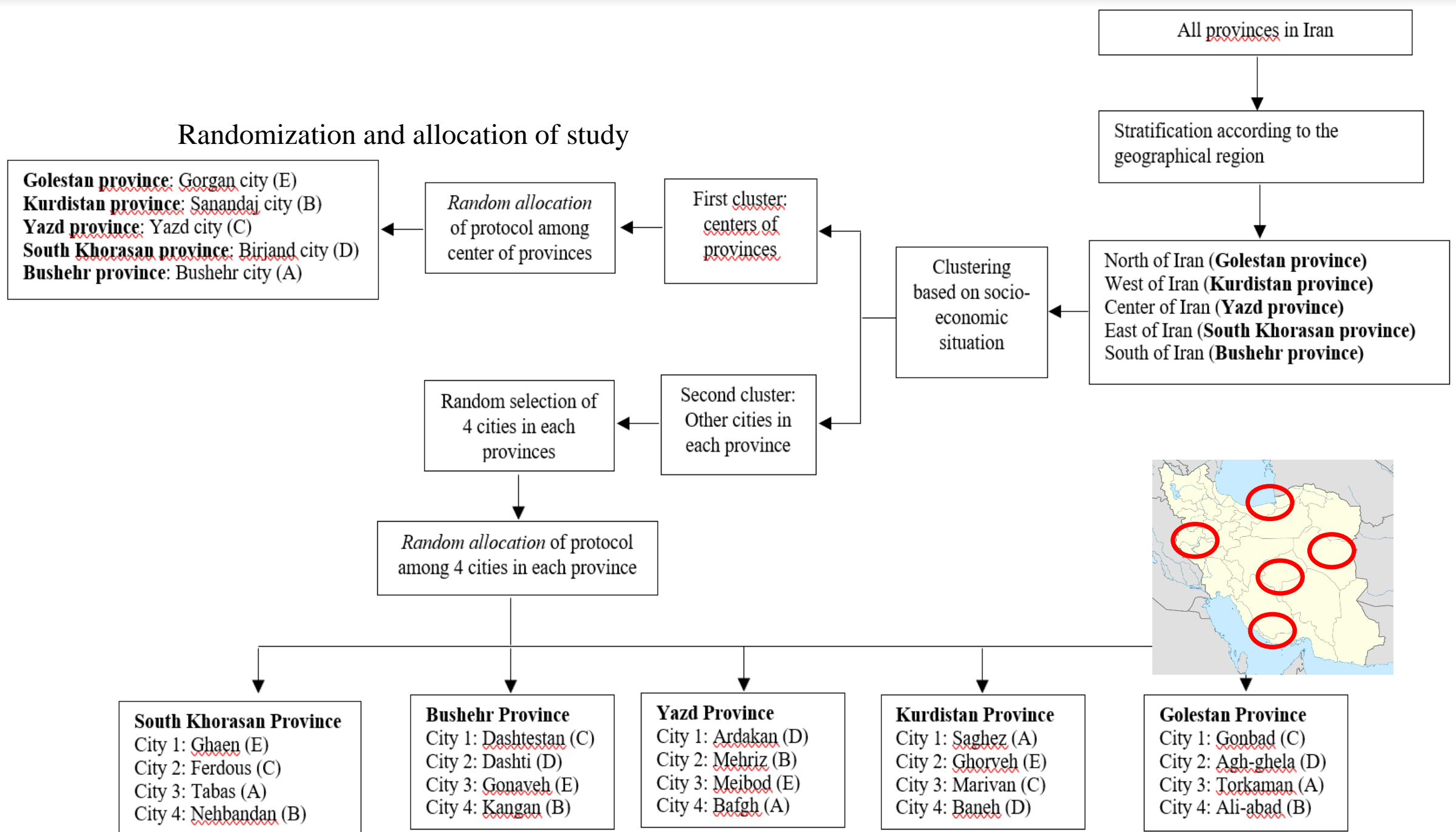


Fahimeh Ramezani Tehrani\* and Gulf Study Cooperative Research Group

- **Type of study**
  - Randomized population based community-field trials
- **Sample size**
  - 38,000
- **Sampling method:**
  - multi stage, stratified probability sampling procedure
- **Place of the study**
  - Five provinces located in various geographic regions of Iran (north, south, east, west, center); 5 cities in each provinces



## Randomization and allocation of study



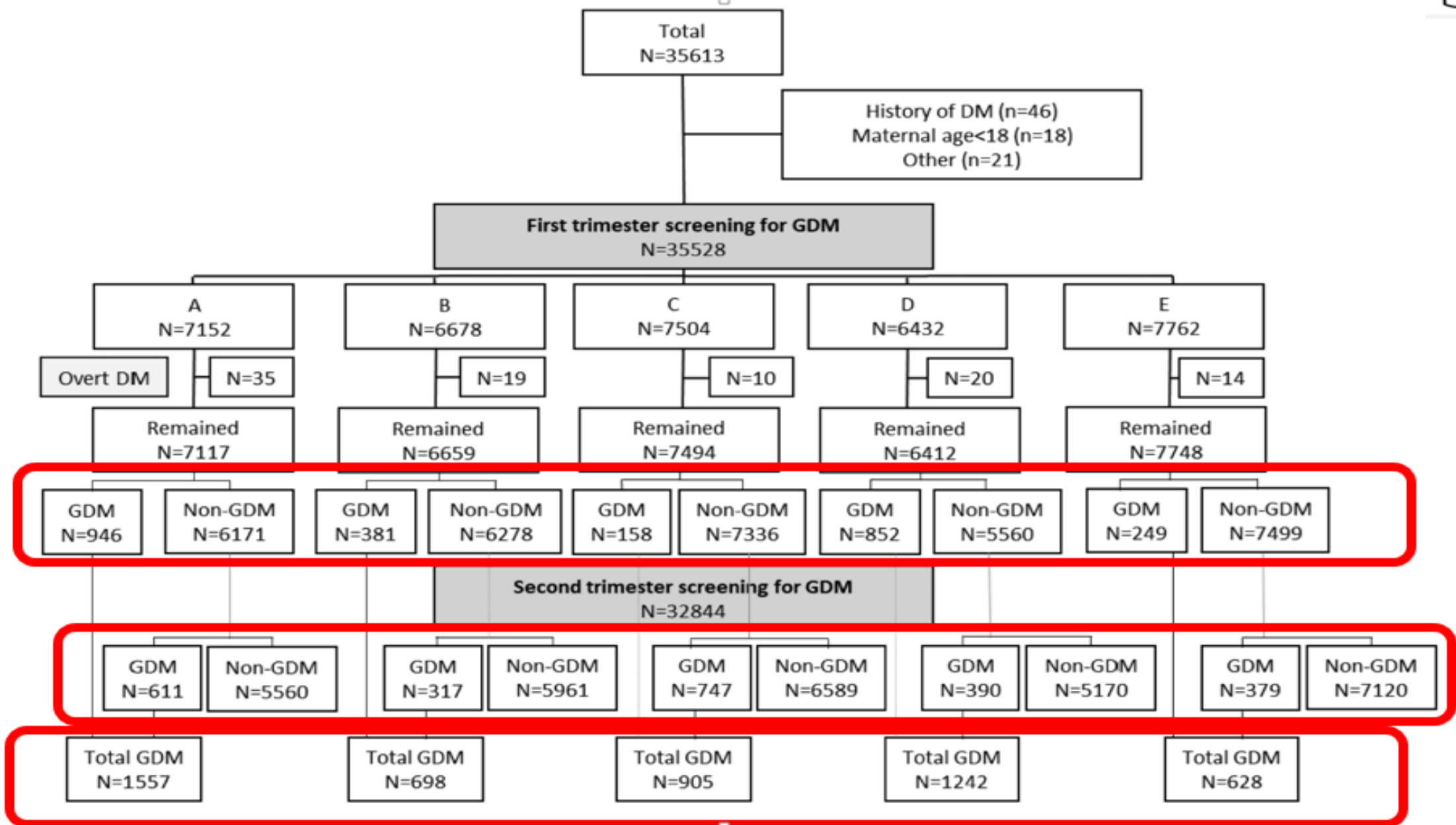
# Endpoint Outcomes



- Primary outcomes:
  - Macrosomia and primary cesarean section (CS).
- Secondary outcomes:
  - preeclampsia, preterm birth, low birth weight (LBW), birth trauma including fracture of clavicle and brachial plexus injury, neonatal hypoglycemia, hypocalcemia and hyperbilirubinemia, admission to the neonatal intensive care unit (NICU), and still birth.



	First trimester	Second trimester		
Protocol	Diagnostic criteria for GDM	Method for GDM screening	Diagnostic threshold of test	Diagnostic criteria
A	92 mg/dL < FPG > 126 mg/dL	One step with 2-h 75g OGTT	Fasting $\geq$ 92 mg/dL 1 h $\geq$ 180 mg/dL 2 h $\geq$ 153 mg/dL	GDM is defined as any of the given plasma glucose values met or exceeded
B	100 mg/dL < FPG > 126 mg/dL	One step with 2-h 75g OGTT	Fasting $\geq$ 92 mg/dL 1 h $\geq$ 180 mg/dL 2 h $\geq$ 153 mg/dL	GDM is defined as two or more of the given plasma glucose values are met or exceeded
C	100 mg/dL < FPG > 126 mg/dL	One step with 2-h 75g OGTT	Fasting $\geq$ 92 mg/dL 1 h $\geq$ 180 mg/dL 2 h $\geq$ 153 mg/dL	GDM is defined as any of the given plasma glucose values met or exceeded
D	92 mg/dL < FPG > 126 mg/dL	Two steps with 50g GCT- 1 h following 3-h 100g OGTT	50 g GCT: BS-1 h: $\geq$ 140 mg 100 g OGTT: Fasting $\geq$ 95 mg/dL 1 h $\geq$ 180 mg/dL 2 h $\geq$ 155 mg/dL 3 h $\geq$ 140 mg/dL	GDM is defined as if two or more of the given plasma glucose values in 100g OGTT are met or exceeded
E	100 mg/dL < FPG > 126 mg/dL	Two steps with 50g GCT- 1 h following 3-h 100g OGTT	50 g GCT: BS-1 h: $\geq$ 140 mg 100 g OGTT: Fasting $\geq$ 95 mg/dL 1 h $\geq$ 180 mg/dL 2 h $\geq$ 155 mg/dL 3 h $\geq$ 140 mg/dL	GDM is defined as if two or more of the given plasma glucose values in 100g OGTT are met or exceeded



Randomized Controlled Trial

> J Clin Endocrinol Metab. 2022 Jun 16;107(7):e2906-e2920.

doi: 10.1210/clinem/dgac181.

# A Cluster Randomized Noninferiority Field Trial of Gestational Diabetes Mellitus Screening

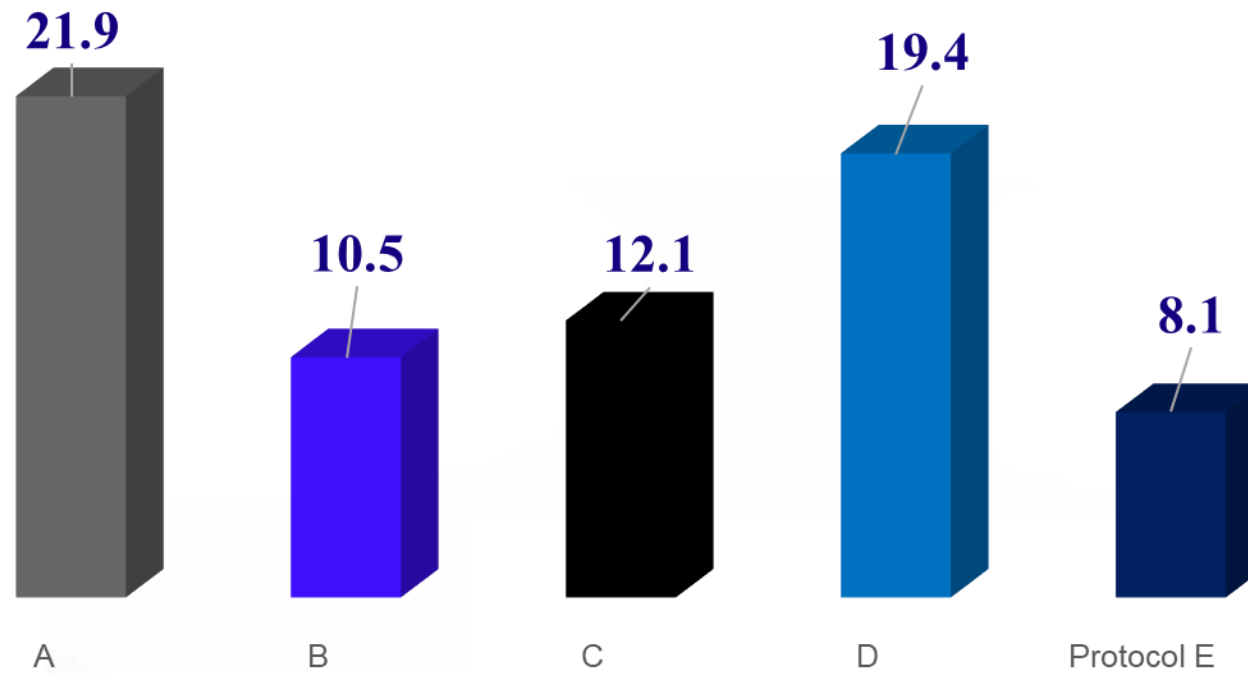
Fahimeh Ramezani Tehrani <sup>1</sup>, Samira Behboudi-Gandevani <sup>2</sup>, Farshad Farzadfar <sup>3 4</sup>,  
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Majid Valizadeh <sup>5</sup>, Mehrandokht Abedini <sup>8</sup>, Maryam Rahmati <sup>1</sup>, Razieh Bidhendi Yarandi <sup>9</sup>,  
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Mina Amiri <sup>1</sup>, Farzam Bidarpour <sup>14</sup>, Mehdi Javanbakht <sup>15</sup>, Iraj Nabipour <sup>16</sup>, Ensieh Nasli Esfahani <sup>17</sup>,  
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Affiliations + expand

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# Prevalence of GDM per screening protocol



ITT analyses showed that the upper boundary of the 95% CI for both primary CS and macrosomia were lower than the noninferiority margin of 1.7, satisfying the noninferiority of less strict protocols B, C, D, and E compared with protocol A. However, noninferiority was not shown in comparing primary CS in protocol E vs A.

#### Protocol B vs A

- macrosomia, 6% vs 5.9%, OR = 1.01, 95% CI, 0.95- 1.08
- primary CS, 14.1% vs 15.4%, OR = 0.85, 95% CI, 0.56-1.28,

#### protocol C vs A

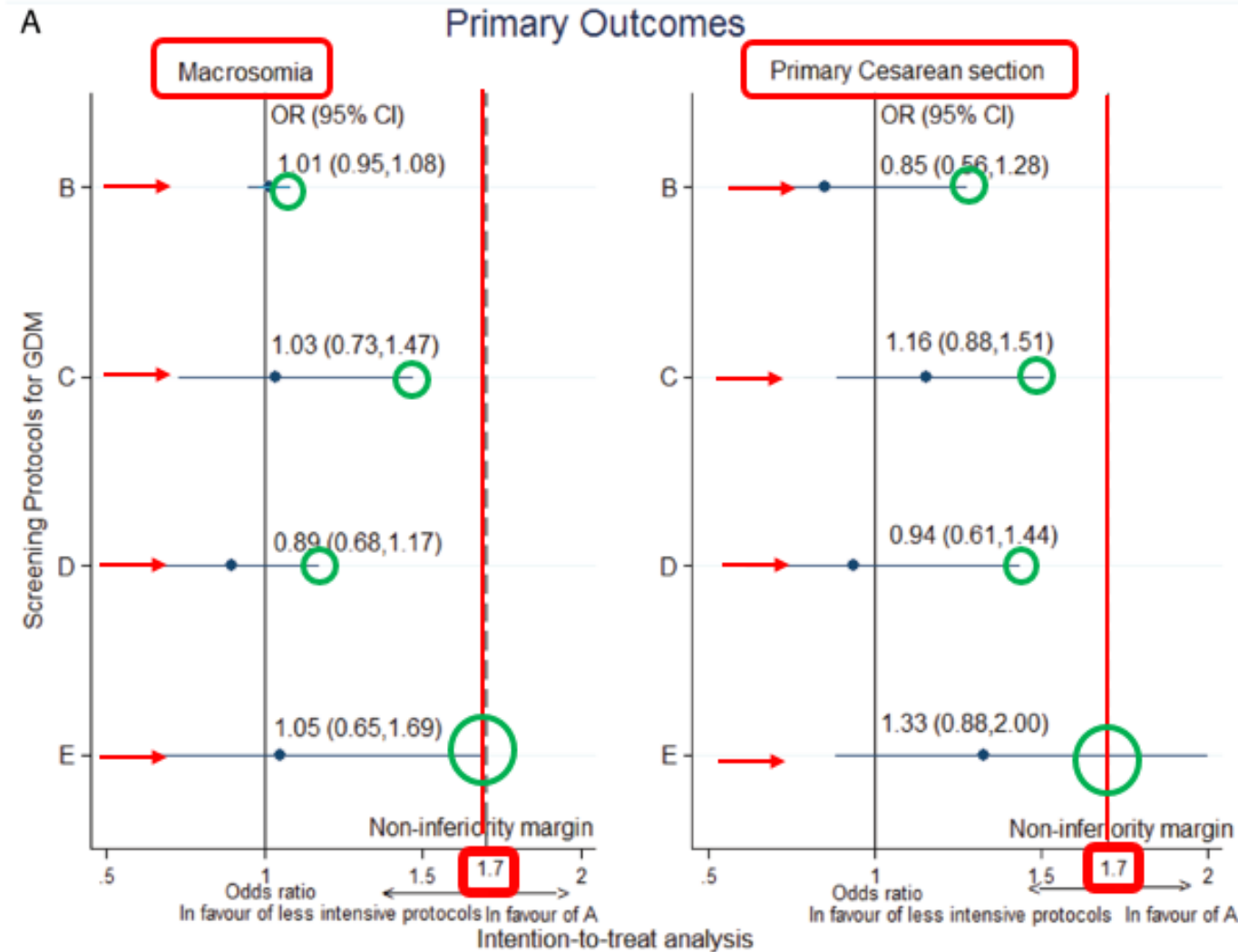
- macrosomia, 6.1% vs 5.9%, OR = 1.03, 95% CI, 0.73-1.47
- primary CS, 16.8% vs 15.4%, OR = 1.16, 95% CI, 0.88-1.51,

#### protocol D vs A

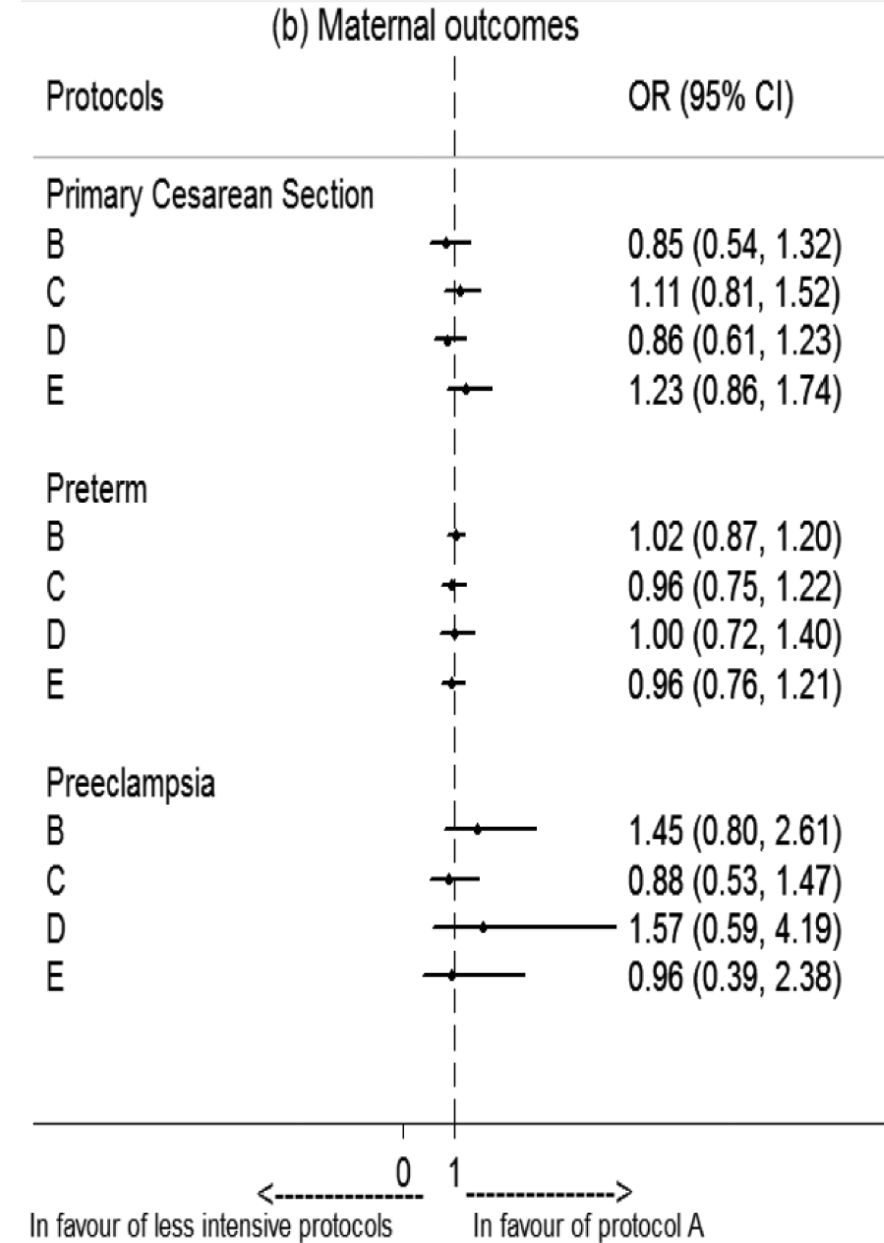
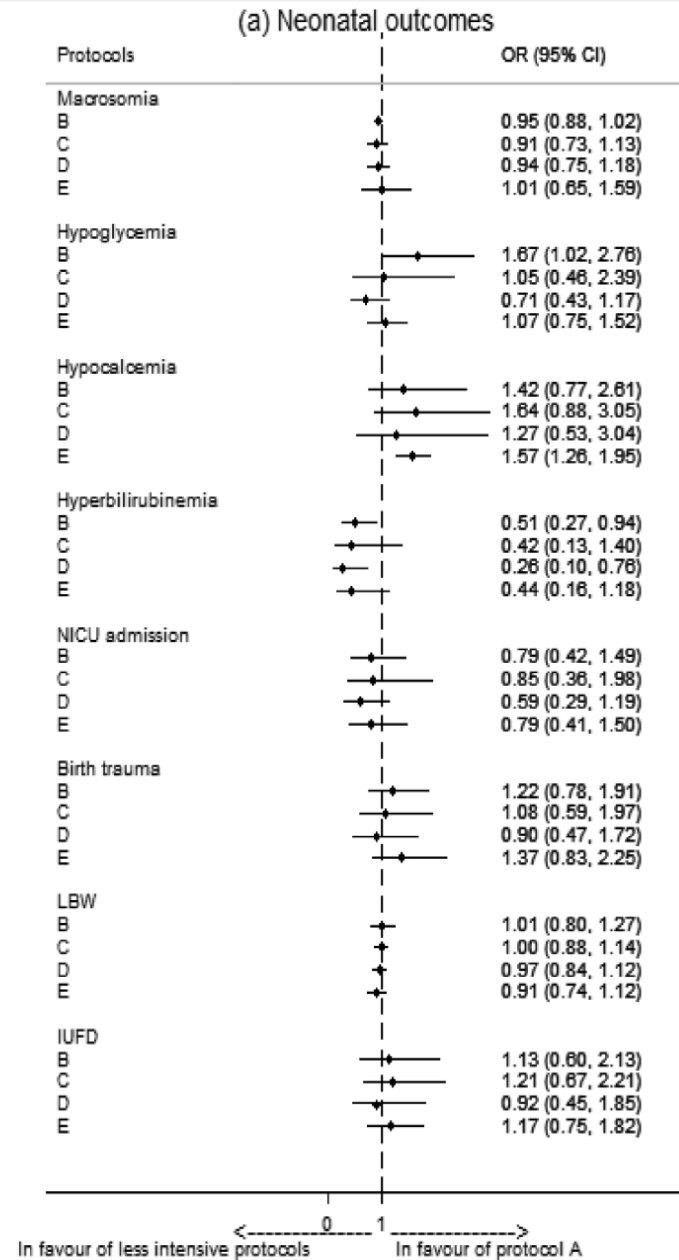
- (macrosomia, 5.3% vs 5.9%, OR = 0.89, 95% CI, 0.68-1.17
- primary CS, 14.5% vs 15.4%, OR = 0.94, 95% CI, 0.61-1.44,

#### protocol E vs A

- macrosomia 6.2% vs 5.9%, OR = 1.05, 95% CI, 0.65-1.69),
- primary CS, 17.1% vs 15.4%, OR = 1.33, 95% CI, 0.88- 2.00.



The IADPSG GDM definition significantly increased the prevalence of GDM diagnosis. However, the less strict approaches were not inferior to other criteria in terms of adverse maternal and neonatal outcomes.







#### OPEN ACCESS

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SPECIALTY SECTION  
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# One-step versus two-step screening for diagnosis of gestational diabetes mellitus in Iranian population: A randomized community trial

Fahimeh Ramezani Tehrani<sup>1</sup>, Maryam Rahmati<sup>1</sup>,  
Farshad Farzadfar<sup>2</sup>, Mehrandokht Abedini<sup>3</sup>,  
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Fereidoun Azizi<sup>7</sup> and Samira Behboudi-Gandevani<sup>8\*</sup>

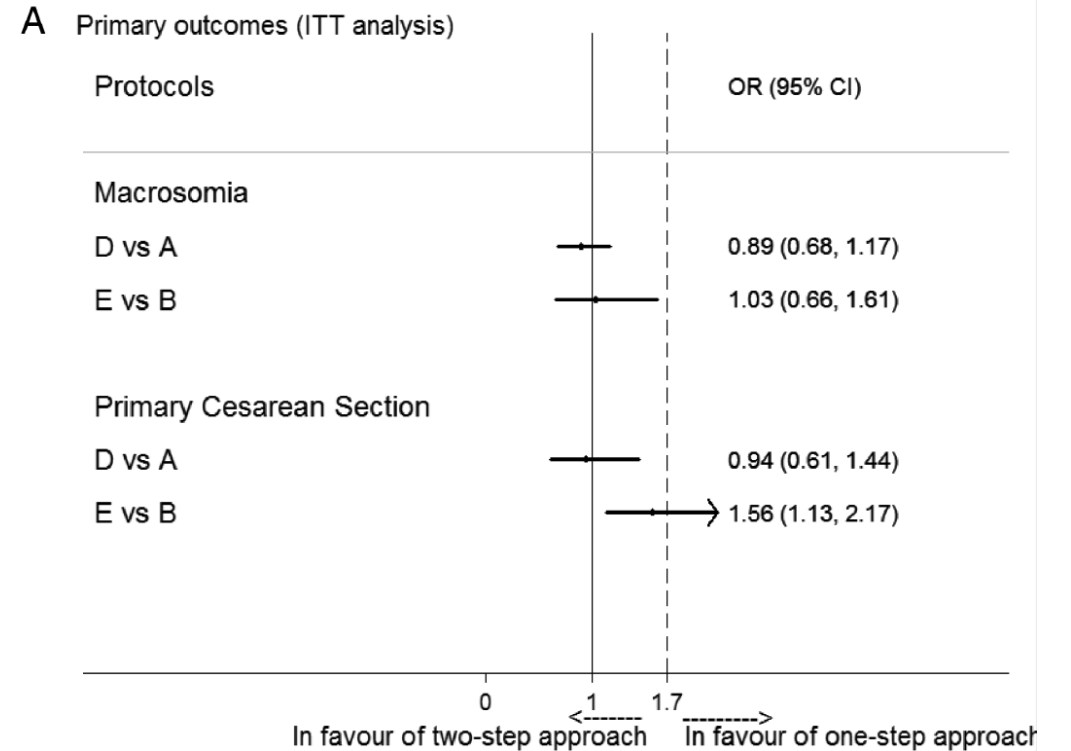
## 2-step test vs 1-step test method of screening

### Primary Outcomes

Intention to treat analysis showed that the upper boundary of the 95% CI for the OR of both macrosomia and primary CS were below the margin 1.7, satisfying the noninferiority of the 2-step compared to the 1-step screening approach. However, primary CS comparing protocol E vs B noninferiority is not shown.

The respective results were as follows:

- macrosomia
  - D vs A: OR= 0.89, 95% CI, 0.68-1.17
  - E vs B: OR= 1.03, 95% CI, 0.66-1.61
- primary CS
  - D vs A: OR = 0.94, 95% CI, 0.61-1.44
  - E vs B: OR = 1.56, 95% CI, 1.13-2.17

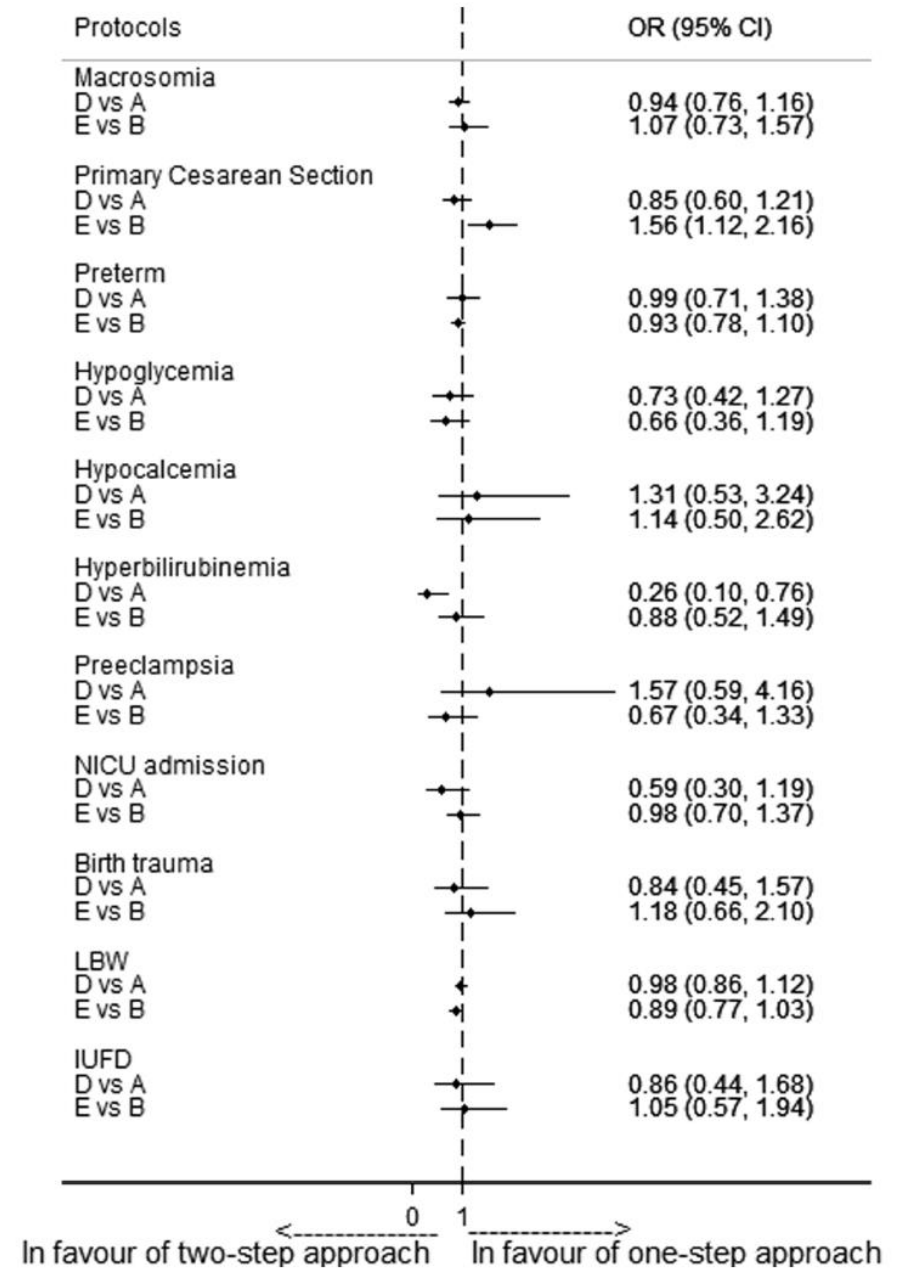


OR and 95% CI for primary and secondary outcomes comparing 2-step test vs 1-step test (D vs A and E vs B).

## 2-step test vs 1-step test method of screening

### Secondary Outcomes

There were no statistically significant differences in the adjusted odds of adverse pregnancy outcomes in the 2-step compared with the 1-step screening approaches, considering multiplicity adjustment.



Randomized Controlled Trial > Front Endocrinol (Lausanne). 2023 Jun 2;14:1155007.

doi: 10.3389/fendo.2023.1155007. eCollection 2023.

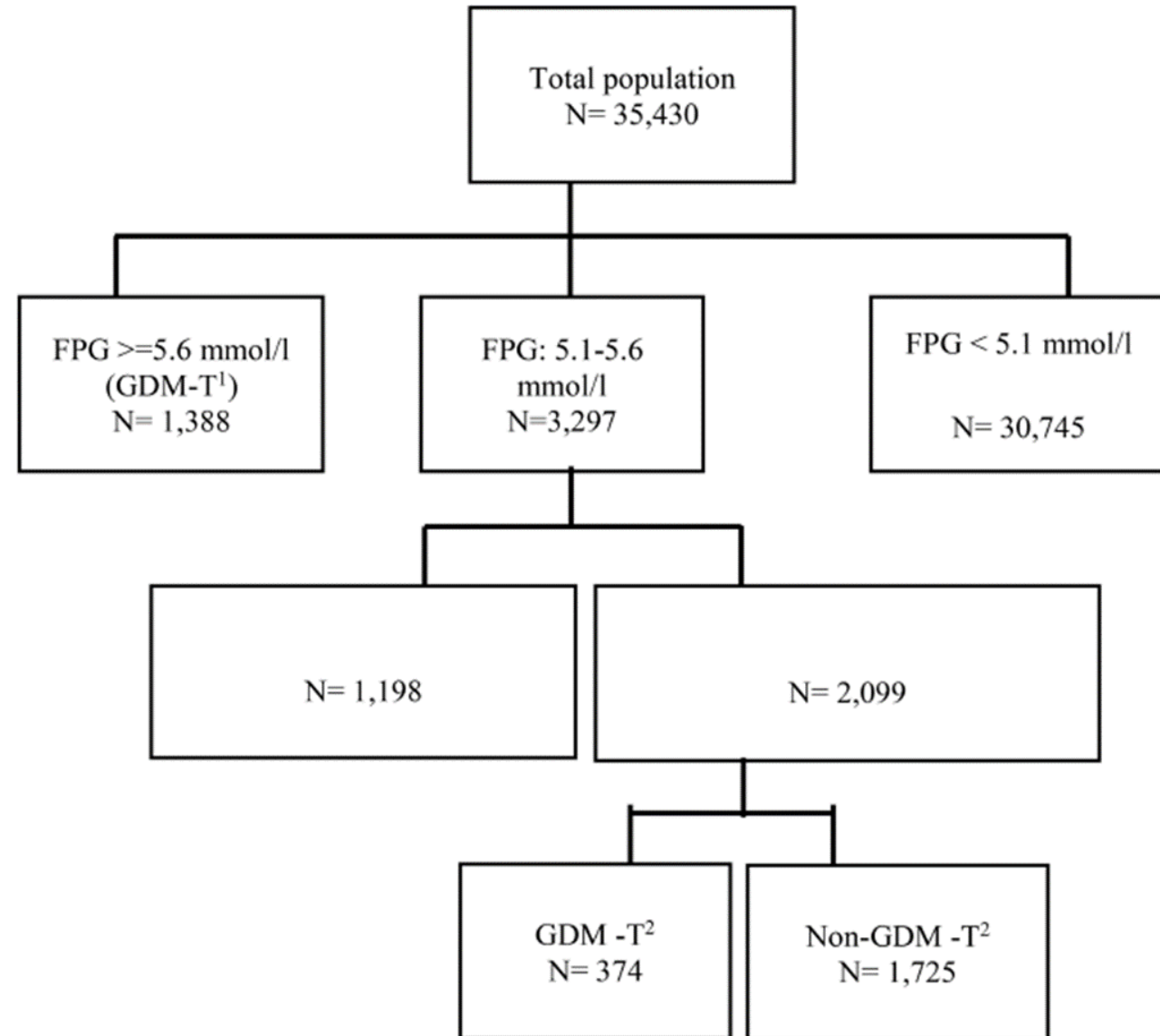
## Does fasting plasma glucose values 5.1-5.6 mmol the first trimester of gestation a matter?

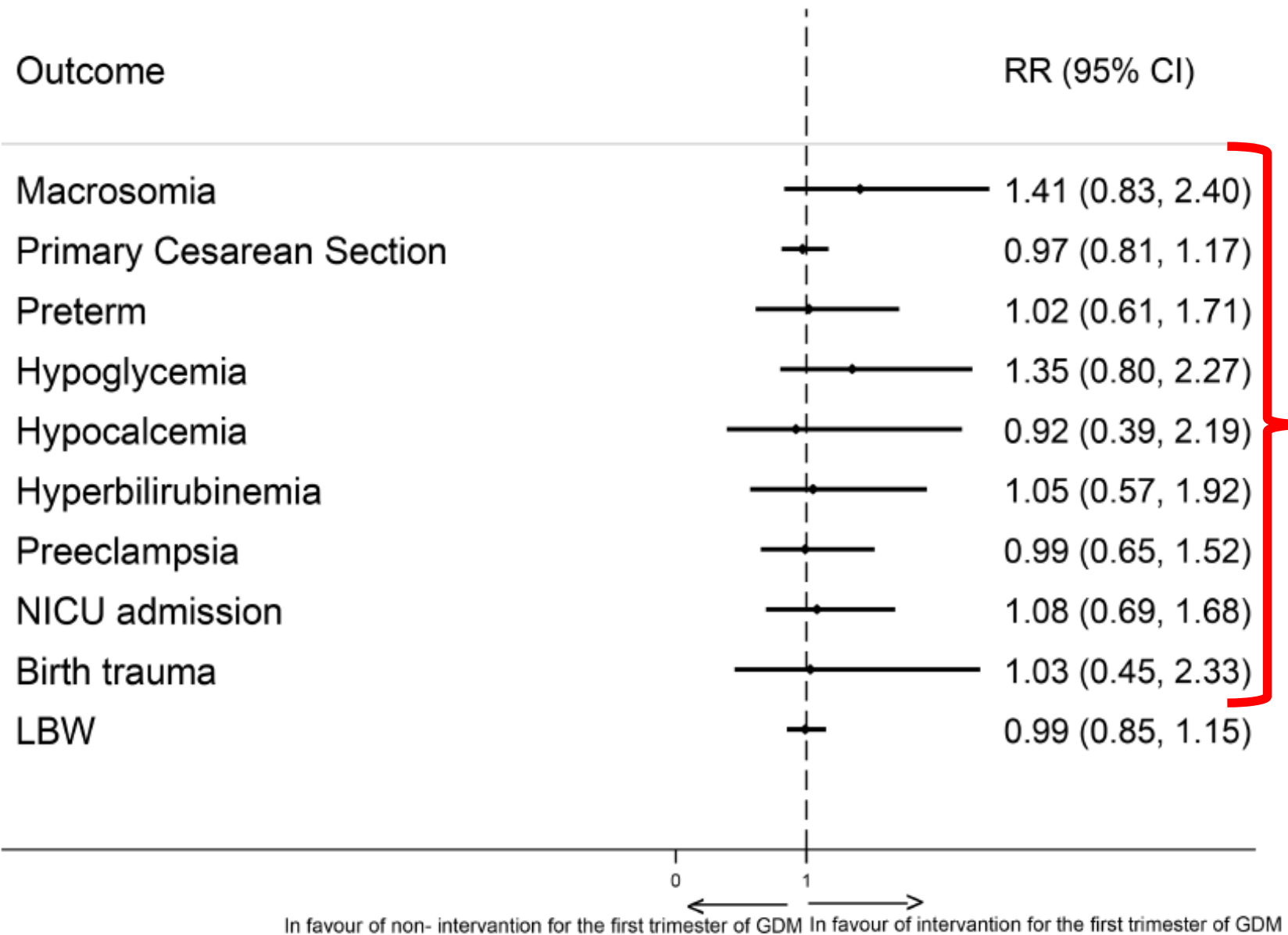
Fahimeh Ramezani Tehrani<sup>1</sup>, Farshad Farzadfar<sup>2</sup>, Farhad Hosseinpanah<sup>3</sup>, Maryam Rahmati Faegheh Firouzi<sup>1</sup>, Mehrandokht Abedini<sup>4</sup>, Farzad Hadaegh<sup>5</sup>, Majid Valizadeh<sup>3</sup>, Farahnaz Torkestani<sup>6</sup>, Davood Khalili<sup>5</sup>, Masoud Solaymani-Dodaran<sup>7</sup>, Razieh Bidhendi-Yara Marzieh Bakhshandeh<sup>9</sup>, Afshin Ostovar<sup>10</sup>, Marzieh Rostami Dovom<sup>1</sup>, Mina Amiri<sup>1</sup>, Fereidoun Azizi<sup>11</sup>, Samira Behboudi-Gandevani<sup>12</sup>

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# Various screening and diagnosis approaches for gestational diabetes mellitus and adverse pregnancy outcomes: a secondary analysis of a randomized non-inferiority field trial

- **Aim of study:** We evaluate which screening and diagnostic approach resulted in the greatest reduction in adverse pregnancy outcomes due to increased treatment
- **Conclusion:** We conclude that screening approaches for GDM reduced the risk of adverse pregnancy outcomes to the same or near the same risk level of healthy pregnant women, except for the risk of NICU admission that increased significantly in groups diagnosed with GDM compared with healthy pregnant women. Individuals with slight increase in FPG (92–100 mg/dL) at first trimester, who were diagnosed as GDM, had an even increased risk of macrosomia in comparison to those group of women with FPG 92–100 mg/ dL in the first trimester, who were not diagnosed with GDM, and developed GDM in second trimester

## Take home Message and Future Considerations



- Gestational diabetes and controversies are old friends!
- There remains strong consensus that establishing a uniform approach to diagnosing GDM will benefit patients, caregivers, and policymakers. Longer-term outcome studies are currently underway.
- The conflicting recommendations from expert groups underscore the fact that there are data to support each strategy.
- The IADPSG criteria (“one-step strategy”) have been adopted internationally as the preferred approach. Data comparing population-wide outcomes with one-step versus two-step approaches have been inconsistent and mainly showed no differences between two groups in terms of maternal and neonatal outcomes.
- The results of our study could be a large step forward in developing guidelines



Thank you for your attention

