

4-10-2017

## Scientific Evidence for Different Options for GDM Screening and Management: Controversies and Review of the Literature.

Claudia Caissutti  
*University of Udine*

Vincenzo Berghella  
*Thomas Jefferson University*

Follow this and additional works at: <https://jdc.jefferson.edu/obgynfp>

 Part of the [Obstetrics and Gynecology Commons](#)

[Let us know how access to this document benefits you](#)

---

### Recommended Citation

Caissutti, Claudia and Berghella, Vincenzo, "Scientific Evidence for Different Options for GDM Screening and Management: Controversies and Review of the Literature." (2017). *Department of Obstetrics and Gynecology Faculty Papers*. Paper 43.

<https://jdc.jefferson.edu/obgynfp/43>

This Article is brought to you for free and open access by the Jefferson Digital Commons. The Jefferson Digital Commons is a service of Thomas Jefferson University's [Center for Teaching and Learning \(CTL\)](#). The Commons is a showcase for Jefferson books and journals, peer-reviewed scholarly publications, unique historical collections from the University archives, and teaching tools. The Jefferson Digital Commons allows researchers and interested readers anywhere in the world to learn about and keep up to date with Jefferson scholarship. This article has been accepted for inclusion in Department of Obstetrics and Gynecology Faculty Papers by an authorized administrator of the Jefferson Digital Commons. For more information, please contact: [JeffersonDigitalCommons@jefferson.edu](mailto:JeffersonDigitalCommons@jefferson.edu).

## Review Article

# Scientific Evidence for Different Options for GDM Screening and Management: Controversies and Review of the Literature

**Claudia Caissutti<sup>1</sup> and Vincenzo Berghella<sup>2</sup>**

<sup>1</sup>*Department of Experimental Clinical and Medical Science, DISM, Clinic of Obstetrics and Gynecology, University of Udine, Udine, Italy*

<sup>2</sup>*Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, USA*

Correspondence should be addressed to Vincenzo Berghella; [vincenzo.berghella@jefferson.edu](mailto:vincenzo.berghella@jefferson.edu)

Received 3 February 2017; Revised 28 February 2017; Accepted 8 March 2017; Published 10 April 2017

Academic Editor: Erich Cosmi

Copyright © 2017 Claudia Caissutti and Vincenzo Berghella. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Background.** Gestational diabetes (GDM) affects up to 7% of pregnant women and is associated with several maternal and perinatal morbidities. International organizations suggest several different recommendations regarding how to screen and to manage GDM. **Objective.** We aimed to analyze the most important and employed guidelines about screening and management of GDM and we investigated existing related literature. **Results.** We found several different criteria for screening for GDM, for monitoring GDM, and for starting pharmacological therapy. When using IADPSG criteria, GDM rate increased, perinatal outcomes improved, and screening became cost-effective. Compared to no treatment, treatment of women meeting criteria for GDM by IADPSG criteria but not by other less strict criteria has limited evidence for an effect on adverse pregnancy outcomes.

## 1. Introduction

Gestational diabetes (GDM) can be broadly defined as glucose intolerance during pregnancy that affects women without previous diagnosis of diabetes or unknown state. The incidence is about 7% worldwide and this rate has been growing during the last decades and is estimated to increase in the future. The most important risk factors are maternal overweight and obesity, age greater than or equal to 35 years at delivery, hypertension, metabolic syndrome, nonwhite ethnicity, family history of diabetes mellitus, prior unexplained stillbirth, prior infant with congenital anomaly (if not screened during that pregnancy), prior macrosomic infant, history of gestational diabetes, chronic use of steroids, glycosuria, and known impaired glucose metabolism [1].

The importance of GDM is linked to the consequences of pregnancy and also after pregnancy to both mother and newborn. Hyperglycemia in the mother causes abnormal

metabolism while in the fetus it causes hyperinsulinemia and its consequences, and incidence of complications is inversely proportional to glucose control. Macrosomia, polyhydramnios, operative delivery, shoulder dystocia, birth injury, perinatal mortality, hypertensive disorders and preeclampsia, congenital malformations (OR: 1.2–1.4), and risk of cesarean delivery are higher in women with GDM; in the long term, women with GDM have a higher risk of developing type 2 diabetes mellitus and cardiovascular diseases; long-term sequelae for offspring are obesity and metabolic syndrome. Approximately 50% of women identified as having GDM will develop frank diabetes within 10 years [2].

To prevent or decrease the risk of GDM, weight loss before pregnancy and cardiovascular exercise could be useful. In fact, aerobic exercise for 35–90 minutes 3–4 times per week during pregnancy is associated with a significantly higher incidence of vaginal delivery and a significantly lower incidence of cesarean delivery, with a significantly lower

incidence of gestational diabetes mellitus and hypertensive disorders [3]. Prompt diagnosis and management are important to reduce worse pregnancy outcomes.

Nonetheless, screening, management, and follow-up of GDM are controversial on international organizations recommendations.

## 2. Screening Controversies

The aim of screening is to identify asymptomatic pregnant women at high risk of developing GDM. Screening appears to be cost-effective for prevention of obstetrical adverse outcomes and long-term consequences of GDM [4].

Regarding the effect of screening [1] on obstetrical outcomes, there are many controversies:

- (a) Indications for screening (who): universal versus selective screening
- (b) Timing of screening (when): early screening versus at 24–28 weeks
- (c) Type of screening (how): One- versus Two-Step
- (d) Criteria for diagnosis: recommendations of international organizations are not standardized

(a) The *population to screen* has not been uniformly identified. There are two possible approaches.

(i) *Selective Screening*. Only women with risk factor for GDM are offered to be screened, that is, age > 25 years; ethnic origin Hispanic, African, Native American, South or East Asian, or Pacific Islander; BMI > 25; previous personal or family history of impaired glucose tolerance; or history of adverse obstetric outcomes associated with GDM.

(ii) *Universal Screening*. All women are subjected to screening; in developed countries where overweight and obesity are widespread health problems, this could be the best choice to avoid undiagnosed GDM.

Universal screening is the most commonly adopted method in the USA, while in other countries such as Italy the selective approach is preferred [5].

(b) When identifying the population, it is essential to decide the right *time to screen*.

Women with risk factors and high suspicion of undiagnosed type 2 DM (i.e., obesity, metabolic syndrome) should be screened before pregnancy or at the first prenatal visit (early screening). About 5–10% of women with risk factors have early GDM, and these represent 40% of all women with GDM.

In the absence of early screening or for women negative to early screen, universal screening should be performed at 24 to 28 weeks.

(c) Now we discuss how to screen.

Screening for GDM is somewhat controversial and can be performed either with a One-Step or with a Two-Step approach.

(i) *One-Step Approach*. GDM screening is performed as an oral 75 g glucose load followed by glucose blood measurement 1 and 2 hours later. A positive result is defined as one

value higher than target values. This approach is based on HAPO study [6] and is suggested by IADPSG [7], WHO [8], FIGO [5], and ADA [9]. In fact, HAPO study in 2008 demonstrated a direct correlation between maternal glucose levels and increased birth weight and neonatal hyperinsulinemia.

(ii) *Two-Step Approach*. GDM is performed as a 50 g one-hour oral glucose load (glucose challenge test, GCT), given to nonfasting women, with a venous glucose measurement one hour later. A positive result is defined as a blood glucose value higher than 130, 135, or 140 mg/dL; the most common value used is 135 mg/dL (ACOG) [4]. Positive screening test is followed by a diagnostic test as an oral glucose tolerance test (GTT) that consists of a beverage with 100 g of glucose, with venous glucose measurement at fasting and after 1, 2, and 3 hours. A positive result is defined as 2 values higher than target values.

(d) Recommendations of international organizations are not standardized.

Table 1 shows the different populations and times to screen and the thresholds used by the most important international organizations worldwide, updated to the latest recommendations [4, 5, 8–12].

We found a large number of studies in international literature comparing One-Step and Two-Step test and different glucose thresholds. When evaluating the best screening method, clinically significant improvements in maternal and neonatal outcomes were analyzed. Two are the most significant studies:

- (1) Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group: the aim was to determine whether treatment of GDM reduced the risk of perinatal complications.
- (2) National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network Study: the intent was to determine whether treatment of women with mild GDM reduces perinatal and obstetrical complications.

Both trials agree with the rule of IADPSG criteria adoption on reducing fetal birth weight over the 90th percentile and the risk of developing maternal preeclampsia.

Furthermore, to compare the One-Step test to the Two-Step test, several possible study designs have been evaluated in the literature. We can summarize the literature in five groups.

(1) RCTs in which women underwent both the One-Step and the Two-Step tests and the women positive for the One-Step but negative for the Two-Step test were randomized to treatment of GDM versus no treatment: the only such RCT is by Weiss et al. [12], who unfortunately do not report outcomes specific to this group of women.

(2) RCTs of treatment versus no treatment of GDM, focusing on women positive for the One-Step but negative for the Two-Step test: we found 6 RCTs comparing insulin or glyburide to placebo or routine care, and all of them used a Two-Step approach with different glucose thresholds (Table 2) [13–18]. In this group, ACHOIS trial by Crowther

TABLE 1: Criteria for GDM screening and diagnosis.

|                    | Population to screen | Time to screen | Test                 | Number of abnormal values required for diagnosis | Fasting glucose (mg/dL) | 1 hour after loading (mg/dL) | 2 hours after loading (mg/dL) | 3 hours after loading (mg/dL) |
|--------------------|----------------------|----------------|----------------------|--|-------------------------|------------------------------|-------------------------------|-------------------------------|
| ACOG 2013 C&C [4]  | Selective screening  | First visit    | Two-Step, 3 h, 100 g | $\geq 2$   | 95                      | 180                          | 155                           | 140                           |
| ACOG 2013 NDDG [4] | Selective screening  | First visit    | Two-Step, 3 h, 100 g | $\geq 2$   | 105                     | 190                          | 165                           | 145                           |
| ADA 2015 [9]       | Universal screening  | 24–28 weeks    | One-Step, 2 h, 75 g  | $\geq 2$   | 95                      | 180                          | 155                           | Not required                  |
| ADA 2015 [9]       | Universal screening  | First visit    | Two-Step, 3 h, 100 g | $\geq 2$   | 95                      | 180                          | 155                           | 140                           |
| ADIPS 2013 [52]    | Selective screening  | 24–28 weeks    | One-Step, 2 h, 75 g  | $\geq 1$   | 92                      | 180                          | 153                           | Not required                  |
| CDA 2013 [10]      | Universal screening  | First visit    | Two-Step, 2 h, 75 g  | $\geq 2$   | 95                      | 191                          | 160                           | Not required                  |
| FIGO 2013 [5]      | Universal screening  | 24–28 weeks    | One-Step, 2 h, 75 g  | $\geq 1$   | 92                      | 180                          | 153                           | Not required                  |
| IADPSG 2010 [7]    | Universal screening  | 24–28 weeks    | One-Step, 2 h, 75 g  | $\geq 1$   | 92                      | 180                          | 153                           | Not required                  |
| NICE 2015 [11]     | Selective screening  | 24–28 weeks    | One-Step, 2 h, 75 g  | $\geq 1$   | 101                     | Not required                 | 140                           | Not required                  |
| WHO 2013 [8]       | Universal screening  | 24–28 weeks    | One-Step, 2 h, 75 g  | $\geq 1$   | 92                      | 180                          | 153                           | Not required                  |

ACOG: American College of Obstetricians and Gynecologists; ADA: American Diabetes Association; ADIPS: Australasian Diabetes in Pregnancy Society; CDA: Canadian Diabetes Association; C&C: Carpenter and Coustan; FIGO: International Federation of Gynecology and Obstetrics; IADPSG: International Association of Diabetes Pregnancy Study Group; NICE: National Institute for Health and Care Excellence; NDDG: National Diabetes Data Group; WHO: World Health Organization.

TABLE 2: RCTs of treatment versus no treatment of GDM, focusing on women positive for the One-Step but negative for the Two-Step test.

| Study                                  | Screening test   | Diagnostic test                        | Values for diagnosis              | Intervention group | Control group | Primary outcome                 |
|--|--|--|-----------------------------------|--------------------|---------------|---------------------------------|
| O'Sullivan et al., 1966 (USA) [13]     | 50 g GCT: positive if $\geq 130$ mg/dl                 | 100 g, 3 h (110-170-120-110)           | 2 or more values                  | Insulin            | Routine care  | LGA                             |
| Coustan and Lewis, 1978 (USA) [14]     | 50 g GCT: positive if $\geq 130$ mg/dl                 | 100 g, 3 h (95-180-160-135)            | 2 or more values                  | Insulin            | Routine care  | Macrosomia                      |
| Thompson et al., 1990 (USA) [15]       | 50 g GCT: positive if F > 105 mg/dL or 1 h > 140 mg/dL | 100 g, 3 h (105-190-165-145)           | 2 or more values                  | Insulin            | Routine care  | Maternal and neonatal morbidity |
| Crowther et al., 2005 (Australia) [16] | 50 g GCT: positive if $\geq 140$ mg/dl                 | 75 g OGTT (F > 7.8; 2 h 7.8–10 mmol/L) | Both values                       | Insulin            | Routine care  | Perinatal complications         |
| Landon et al., 2009 (USA) [17]         | 50 g GCT: positive if $\geq 135$ mg/dl                 | 100 g, 3 h (95-180-155-140)            | 2 or more values but F < 95 mg/dL | Insulin            | Routine care  | Perinatal outcome               |
| Casey et al., 2015 (USA) [18]          | 50 g GCT: positive if $\geq 140$ mg/dL                 | 100 g, 3 h (105-190-165-145)           | 2 values                          | Glyburide          | Placebo       | Birth weight                    |

et al. [16] is included, mentioned before. The main common outcome was lower rate of fetal birth weight over the 90th percentile and macrosomia.

(3) RCTs comparing the One-Step to the Two-Step methods: we found 3 RCTs by Meltzer et al. [19], Sevket et al. [20], and Scifres et al. [21] (Table 3). In each one, there are

a study group undergoing One-Step 75 g test and a control group undergoing Two-Step 100 g test. Regarding GDM rate, Sevket et al.'s and Scifres et al.'s RCTs reveal an incidence more than double in the study group with respect to control group (14.5% versus 6%; 4.3% versus 0.0%), while in Meltzer et al.'s RCT, there are no differences (3.6% versus 3.7%). Maternal

TABLE 3: RCTs comparing the One-Step to the Two-Step methods.

| Author (origin)                    | Study group          | Control group (1)                | Control group (2)               | GDM rate                     | Primary outcome                |
|------------------------------------|----------------------|----------------------------------|---------------------------------|------------------------------|--------------------------------|
| Meltzer et al., 2010 (Canada) [19] | One-Step (2 h, 75 g) | Two-Step (50 g, 1 h; 100 g, 3 h) | Two-Step (50 g, 1 h; 75 g, 3 h) | 3.6% versus 3.7% versus 3.7% | Costs of screening             |
| Sevket et al., 2013 (Turkey) [20]  | One-Step (2 h, 75 g) | Two-Step (50 g, 1 h; 100 g, 3 h) |                                 | 14.5% versus 6%              | Maternal and neonatal outcomes |
| Scifres et al., 2014 (USA) [21]    | One-Step (2 h, 75 g) | Two-Step (50 g, 1 h; 100 g, 3 h) |                                 | 4.3% versus 0.0%             | Maternal and neonatal outcomes |

and neonatal outcomes have been analyzed only in 2 studies. Sevket et al.'s RCT reveals that GDM-negative women by IADPSG had better perinatal outcomes than GCT-negative women and GCT-positive women with a negative OGTT; Scifres et al.'s RCT concludes that rates of macrosomia, cesarean delivery, and pregnancy-induced hypertension were also similar between groups.

Interestingly, Meltzer et al.'s RCT analyzed costs of the One-Step compared to the Two-Step test: while the Two-Step test involved the lowest costs, the One-Step test recognized higher GDM rate. The authors' conclusion was in favor of the Two-Step test because the universal glucose screen with 50 g glucose load is an inexpensive, easy-to-administer tool for GDM screening, especially with the use of a lower diagnostic cut-off.

(4) Prospective non-RCTs or retrospective studies comparing incidence of GDM and/or outcomes between the One-Step and Two-Step methods: we found 9 retrospective studies comparing the One-Step approach with IADPSG criteria and Two-Step approach with ACOG criteria (Table 4) [22–30]. Regarding GDM rate, the incidence is higher for women undergoing the One-Step test in all the studies analyzing this issue. Only two studies concluded that IADPSG One-Step approach is useful to avoid worse pregnancy outcomes, in particular LGA and macrosomia [22, 27], while five studies did not find statistically significant differences between the two approaches on outcomes [23–26, 28].

(5) Prospective non-RCTs or retrospective studies reporting outcomes of women meeting criteria for GDM based on the One-Step test but not on the Two-Step test: we found 8 retrospective cohort studies (Tables 5 and 6) [31–38], but no study evaluated whether treatment of women meeting criteria for GDM by IADPSG criteria (One-Step test) but not by other less strict criteria has an effect on adverse pregnancy outcomes compared to no treatment. When analyzing outcomes, macrosomia was more common in women positive on 75 g IADPSG criteria but negative on CDA criteria and positive on 75 g IADPSG criteria but negative on NICE criteria.

### 3. Conclusion

Despite continuing controversy regarding whether the One-Step test or the Two-Step test should be used for GDM screening, we identified very limited evidence regarding whether treatment of women meeting criteria for GDM by IADPSG criteria (One-Step test) but not by other less strict criteria has an effect on adverse pregnancy outcomes compared to no

treatment. Moreover, in none of the included studies was the study group with milder disease treated for GDM (positive for IADPSG criteria, but negative for less stringent criteria). We also found a large variety of different criteria (IADPSG, WHO, NICE, CDA, and C&C) for screening for GDM used in the literature. Therefore, it is not surprising that societies such as IADPSG, WHO, and FIGO recommend the One-Step approach (assuming that identification of women with milder GDM might have benefits for them and their babies), while others such as ACOG still recommend the Two-Step approach for screening.

Only well designed RCTs comparing the One-Step versus the Two-Step approach including huge populations could answer this question.

### 4. Management Controversies

The aim of management is to reduce the risk of adverse outcomes for the mother and the fetus. Several studies demonstrated that treatment can be effective in reducing adverse outcomes in GDM patients.

Regarding the effect of management on obstetrical outcomes, there are many variables that can play a role; these include

- (i) criteria to start therapy after diet alone: once GDM has been diagnosed, patients start nonpharmacological therapy, that is, well balanced diet based on BMI and physical exercise, but it is unclear how long this evaluation period should last before deciding to start pharmacological treatment; a recent systematic review found inconclusive evidence for the threshold value to start medical therapy [4];
- (ii) type of initial therapy: insulin and oral hypoglycemic agents are equally effective and can be used as first-line therapy [5];
- (iii) dose and frequency of initial therapy: therapy should start at the lower effective dose and then increase based on glucose monitoring;
- (iv) frequency of glucose monitoring: when patients start therapy, either diet or pharmacological therapy is important to establish whether glycemic control has been reached; while patients in pharmacological therapy should perform glycemic checks at least four times daily (fasting and after 1 or 2 hours from three main meals: breakfast, lunch, and dinner), there



TABLE 4: Prospective non-RCTs or retrospective studies comparing incidence of GDM and/or outcomes between the One-Step and Two-Step methods.

| Author (origin)                       | Study design         | Two-Step group  | One-Step group                       | GDM rate           | Primary outcome                 |
|---------------------------------------|----------------------|---|--------------------------------------|--------------------|---------------------------------|
| Duran et al., 2014 (Spain) [22]       | Retrospective cohort | ACOG: 50 g 1 h GCT; if >140 mg/dL followed by 100 g 3 h GTT (C&C) | IADPSG: 75 g 2 h GTT                 | 10.6% versus 35.5% | Pregnancy outcomes              |
| Fuller and Borgida, 2014 (USA) [23]   | Retrospective cohort | ACOG: 50 g 1 h GCT; if >135 mg/dL followed by 100 g 3 h GTT (C&C) | IADPSG: 75 g 2 h GTT                 | 7.0% versus 11.7%  | Maternal and delivery outcomes  |
| Liu et al., 2014 (China) [24]         | Retrospective cohort | ACOG: 50 g 1 h GCT; if >140 mg/dL followed by 100 g 3 h GTT (C&C) | IADPSG: 75 g 2 h GTT                 | 7.0% versus 20.4%  | Maternal and perinatal outcomes |
| Oriot et al., 2014 (Belgium) [25]     | Retrospective cohort | ACOG: 50 g 1 h GCT; if >140 mg/dL followed by 100 g 3 h GTT (C&C) | IADPSG: 75 g 2 h GTT                 | 8.0% versus 23.0%  | CS, macrosomia                  |
| Wei et al., 2014 (China) [26]         | Retrospective cohort | ACOG: 50 g 1 h GCT; if >135 mg/dL followed by 75 g 3 h GTT (NDDG) | IADPSG: 75 g 2 h GTT                 | 18.3% versus 21.0% | CS, macrosomia                  |
| Hung and Hsieh, 2015 (Taiwan) [27]    | Retrospective cohort | ACOG: 50 g 1 h GCT; if >140 mg/dL followed by 100 g 3 h GTT (C&C) | IADPSG: 75 g 2 h GTT                 | 4.6% versus 12.4%  | Macrosomia, LGA                 |
| Kong et al., 2015 (Canada) [28]       | Retrospective cohort | ACOG: 50 g 1 h GCT; if >140 mg/dL followed by 100 g 3 h GTT (C&C) | IADPSG: 75 g 2 h GTT                 | 7.9% versus 9.4%   | Maternal and fetal outcomes     |
| Assaf-Balut et al., 2016 (Spain) [29] | Retrospective cohort | ADA: 50 g 1 h GCT; if >140 mg/dL followed by 100 g 3 h GTT (C&C)  | IADPSG: 75 g 2 h GTT                 | Not stated         | Postpartum disorders            |
| Klara Feldman et al., 2016 (USA) [30] | Retrospective cohort | ACOG: 50 g 1 h GCT; if >130 mg/dL followed by 100 g 3 h GTT (C&C) | IADPSG: 75 g 2 h GTT if HbA1c < 5.7% | 17.0% versus 27.0% | Pregnancy outcomes              |

is uncertainty for women in nonpharmacological therapy [5];

- (v) target glucose values: RCTs to identify ideal glycemic targets have not been performed, but ADA and ACOG recommend a threshold of 140 mg/dL at 1 hour postprandially or 120 mg/dL at 2 hours postprandially as glycemic targets to reduce the risk of macrosomia [5, 9];
- (vi) criteria for pharmacologic therapy dose adjustment: when choosing between tight versus very tight glycemic control, we have to consider risk of hypoglycemia, effects of non-well-controlled GDM, and women compliance;
- (vii) criteria for adding or switching pharmacologic therapy;
- (viii) fetal monitoring;

(ix) time to delivery: women with GDM with good glycemic control and no other complications can be managed expectantly, while if GDM is not well controlled with therapy, induction of delivery could be considered [5].

We analyzed the literature to figure out which management is the best to follow. When evaluating RCTs [16, 17, 39–51] which included criteria for starting pharmacologic therapy in women with GDM, the most common frequency for glucose monitoring was four times per day (i.e., when fasting and after each main meal). The effect of therapy on GDM was assessed using fasting of 90 (or 95) mg/dL and 2 hours of 120 mg/dL as blood glucose target values. Importantly, we found several different criteria for starting pharmacologic therapy after a period of diet alone, with the majority using very tight criteria of either 1 or 2 values in one- or two-week period higher than the target values, of which

TABLE 5: Prospective non-RCT or retrospective studies reporting outcomes of women meeting criteria for GDM based on the One-Step test but not on the Two-Step test.

| Author (origin)                       | Study design         | GDM screening  | 50 g GCT criteria                              | 75 g OGTT criteria   | 100 g OGTT criteria  |
|---------------------------------------|----------------------|--|--|--|--|
| Lapolla et al., 2011 (Italy) [31]     | Retrospective cohort | <i>Two-Step: 50 g 1 h; if &gt;140 mg/dL: 100 g 3 h GTT</i> | ≥140 mg/dL: 100 g 3 h GTT                      | <i>Not done</i>  | 2 abnormal values of fasting ≥ 95 mg/dL, or<br>1 h 180 mg/dL; 2 h 155 mg/dL; 3 h 140 mg/dL |
| Bodmer-Roy et al., 2012 (Canada) [32] | Retrospective cohort | <i>Two-Step: 50 g 1 h; if 137–184 mg/dL: 75 g 2 h GTT</i>  | 137–184 mg/dL: 75 g GTT;<br>>184 mg/dL: GDM    | 1 abnormal value of fasting ≥ 96 mg/dL;<br>1 h: ≥191 mg/dL; 2 h: ≥160 mg/dL* | <i>Not done</i>  |
| Benhalima et al., 2013 (Belgium) [33] | Retrospective cohort | <i>Two-Step: 50 g 1 h; if ≥140 mg/dL: 100 g 3 h GTT</i>    | ≥140 mg/dL: 100 g 3 h GTT                      | <i>Not done</i>  | 2 abnormal values of fasting ≥ 95 mg/dL, or<br>1 h 180 mg/dL; 2 h 155 mg/dL; 3 h 140 mg/dL |
| Ethridge et al., 2014 (USA) [34]      | Retrospective cohort | <i>Two-Step: 50 g 1 h; if ≥135 mg/dL: 100 g 3 h GTT</i>    | ≥135 mg/dL: 100 g 3 h GTT                      | <i>Not done</i>  | 2 abnormal values of fasting ≥ 95 mg/dL, or<br>1 h 180 mg/dL; 2 h 155 mg/dL; 3 h 140 mg/dL |
| Liao et al., 2014 (China) [35]        | Retrospective cohort | <i>Two-Step: 50 g 1 h; if ≥140 mg/dL: 100 g 3 h GTT</i>    | ≥140 mg/dL: 100 g 3 h GTT                      | <i>Not done</i>  | 2 abnormal values of fasting ≥ 95 mg/dL, or 1 h 180 mg/dL; 2 h 155 mg/dL; 3 h 140 mg/dL    |
| Mayo et al., 2015 (Canada) [36]       | Retrospective cohort | <i>Two-Step: 50 g 1 h; if 140–184 mg/dL: 75 g 2 h GTT</i>  | If 140–184 mg/dL: 75 g GTT;<br>>184 mg/dL: GDM | 1 abnormal value of fasting ≥ 95 mg/dL;<br>1 h: ≥191 mg/dL; 2 h: ≥160 mg/dL* | <i>Not done</i>  |
| Meek et al., 2015 (UK) [37]           | Retrospective cohort | <i>Two-Step: 50 g 1 h; if &gt;138 mg/dL: 75 g 2 h GTT</i>  | >138 mg/dL: 75 g 2 h GTT                       | 1 abnormal value of fasting ≥ 110/128 mg/dL; 2 h: ≥140 mg/dL**               | <i>Not done</i>  |
| Tward et al., 2016 (Canada) [38]      | Retrospective cohort | <i>Two-Step: 50 g 1 h; if &gt;140 mg/dL: 75 g 2 h GTT</i>  | ≥140 mg/dL: 75 g 2 h GTT                       | 2 abnormal values of fasting ≥ 95 mg/dL;<br>1 h: ≥191 mg/dL; 2 h: ≥160 mg/dL | <i>Not done</i>  |

\*2008 Canadian Diabetes Association criteria (ref.). \*\*WHO 1999 criteria until 2007 (fasting, 148 mg/dL), modified WHO 1999 criteria (fasting, 130 mg/dL).

half used only 1 value and half used 2 values, while any RCT used less tight criteria (i.e., >50% glucose values higher than target values) (Table 7) [16, 17, 39–51].

Finally, when analyzing international organizations guidelines on management of GDM, while there is consensus about glycemic targets, we found different opinions about therapy, monitoring, and time of delivery (Table 8). Moreover, there is limited information regarding other important criteria about dose and frequency of therapy, dose adjustment, and adding or switching pharmacologic therapy.

Moreover, the application of the IADPSG was associated with an increase in GDM prevalence up to 3.5-fold, as well as significant improvements in pregnancy outcomes (gestational hypertension, prematurity, CD, number of LGA and

SGA, and 1-minute Apgar scores <7), and was cost-effective. This could be presumably by permitting the treatment of a greater number of women at risk for pregnancy complications [22].

## 5. Conclusion

There are many unsolved questions concerning GDM management. Analyzing the literature in detail, we found different criteria for screening for GDM, for monitoring GDM, and for starting pharmacological therapy. The hope is to reach universally approved and shared recommendations to improve health care and reduce costs and adverse outcomes for women with GDM and their babies.

TABLE 6: Continues on the same studies as in Table 5.

| Author (origin)                          | Study group   | Control  | Primary outcome                       |
|--|---|--|---------------------------------------|
| Lapolla et al., 2011 (Italy) [31]        | 100 g IADPSG-positive,<br>C&C-negative<br>(fasting: 92–94 mg/dL; 2 h:<br>153–154 mg/dL; <i>not treated</i> )<br>[n = 112]                       | IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h:<br><153 mg/dL)<br>[n = 1815]  | Perinatal outcomes                    |
| Bodmer-Roy et al., 2012<br>(Canada) [32] | 75 g IADPSG-positive,<br>CDA-negative<br>(fasting: 92–95 mg/dL; 1 h:<br>180–190 mg/dL; 2 h:<br>153–159 mg/dL; <i>not treated</i> )<br>[n = 186] | GCT-negative (50 g 1 h <<br>137 mg/dL)<br>[n = 186]<br>Or<br>IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h:<br><153 mg/dL)<br>[n = 186]  | LGA > 90th percentile                 |
| Benhalima et al., 2013<br>(Belgium) [33] | 100 g IADPSG-positive,<br>C&C-negative<br>(fasting: 92–94 mg/dL; 2 h:<br>153–154 mg/dL; <i>not treated</i> )<br>[n = 160]                       | GCT-negative (50 g 1 h <<br>140 mg/dL)<br>And<br>IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h:<br><153 mg/dL)<br>[n = 6345]             | Pregnancy outcomes                    |
| Ethridge et al., 2014 (USA)<br>[34]      | 100 g IADPSG-positive,<br>C&C-negative<br>(fasting: 92–94 mg/dL; 2 h:<br>153–154 mg/dL; <i>not treated</i> )<br>[n = 281]                       | GCT-negative (50 g 1 h <<br>135 mg/dL)<br>[n = 6999]<br>Or<br>IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h:<br><153 mg/dL)<br>[n = 772] | Birth weight and neonatal<br>outcomes |
| Liao et al., 2014 (China) [35]           | 100 g IADPSG-positive,<br>C&C-negative<br>(fasting: 92–94 mg/dL; 2 h:<br>153–154 mg/dL; <i>not treated</i> )<br>[n = 1314]                      | GCT-negative (50 g 1 h <<br>140 mg/dL)<br>And<br>IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h:<br><153 mg/dL)<br>[n = 2662]             | Maternal and neonatal<br>outcomes     |
| Mayo et al., 2015 (Canada)<br>[36]       | 75 g IADPSG-positive,<br>CDA-negative<br>(fasting: 92–95 mg/dL; 1 h:<br>180–190 mg/dL; 2 h:<br>153–159 mg/dL; <i>not treated</i> )<br>[n = 155] | GCT-negative<br>(50 g 1 h < 140 mg/dL)<br>[n = 4183]<br>Or<br>IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h: <153<br>mg/dL)<br>[n = 526] | Not stated                            |
| Meek et al., 2015 (USA) [37]             | 75 g IADPSG-positive,<br>NICE-negative<br>(fasting: 92–101 mg/dL; 1 h:<br>≥153 mg/dL; <i>not treated</i> )<br>[n = 387]                         | IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h:<br><153 mg/dL)<br>[n = 2406]  | Delivery and neonatal<br>outcomes     |
| Tward et al., 2016 (Canada)<br>[38]      | 75 g IADPSG-positive,<br>CDA-negative<br>(fasting: 92–95 mg/dL; 1 h:<br>180–190 mg/dL; 2 h:<br>153–159 mg/dL; <i>not treated</i> )<br>[n = 99]  | GCT-negative<br>(50 g 1 h < 140 mg/dL)<br>[n = 1021]<br>Or<br>IADPSG-negative<br>(fasting: <92 mg/dL; 1 h:<br><180 mg/dL; 2 h:<br><153 mg/dL)<br>[n = 184] | Fetal growth in twins                 |



TABLE 7: Management of women included in RCTs.

|                                 | Glucose monitoring         | Target value for glycemic control   | Type of diet   | Recommendations about exercise | Glucose values used for starting pharmacologic therapy based on target values   |
|---------------------------------|----------------------------|---|--|--------------------------------|---|
| Garner et al., 1997 [39]        | 4 times daily <sup>A</sup> | F: <4.4 mmol/l (80 mg/dL);<br>1 h: <7.8 mmol/l (140 mg/dL)  | 35 kcal/kg IBW/day   | Not stated                     | 2 or more values higher in 2 weeks  |
| Langer et al., 2000 [40]        | 7 times daily <sup>B</sup> | F: <5.0 mmol/l (90 mg/dL);<br>preprandial: <5.3 mmol/l (95 mg/dl)<br>2 h: <6.7 mmol/l (120 mg/dL)   | (i) 25 kcal/kg BW/day for obese women<br>(ii) 35 kcal/kg BW/day for nonobese women<br>(iii) 3 meals and 4 snacks<br>(iv) 40–45% of calories from carbohydrates | Not stated                     | 1 or more preprandial or 2 h values higher in 1 week  |
| Mecacci et al., 2003 [41]       | 9 times daily <sup>C</sup> | F: <5.0 mmol/l (90 mg/dL);<br>1 h: <6.7 mmol/l (120 mg/dL)  | ADA recommendations*   | Not stated                     | More than 50% values higher after 1 week  |
| Schaefer-Graf et al., 2004 [42] | 6 times daily <sup>D</sup> | Intervention group:<br>F: <4.5 mmol/l (80 mg/dL);<br>1 h: <6.1 mmol/l (110 mg/dL)<br>Control group:<br>F: <5.0 mmol/l (90 mg/dL);<br>1 h: <6.7 mmol/l (120 mg/dL) | (i) 25 kcal/kg BW/day for overweight women<br>(ii) 30 kcal/kg BW/day for normal weight women   | Exercise after meals           | Intervention group:<br>(i) AC > 75th $p < 36$ weeks<br>(ii) F $\geq 120$ mg/dL<br>(iii) 2 h $\geq 200$ mg/dL<br>Control group:<br>(iv) 2 or more values<br>(v) 4 profiles with at least 1 value higher in 2 weeks |
| Crowther et al., 2005 [16]      | 4 times daily <sup>E</sup> | F: <5.5 mmol/l (99 mg/dL);<br>2 h: <7.0 mmol/l (126 mg/dL)  | Dietary advice from a qualified dietician  | Not stated                     | (i) 2 values higher in 2 weeks <35 weeks<br>(ii) 2 h >8.0 mmol/l (144 mg/dl) in 2 weeks >35 weeks<br>(iii) 1 value >9.0 mmol/l (162 mg/dl) in 2 weeks   |
| Anjalakshi et al., 2007 [43]    | Not specified              | 2 h: <6.7 mmol/l (120 mg/dL)  | Medical Nutrition Therapy (MNT)  | Not stated                     | 1 value 2 h higher in 2 weeks   |
| Landon et al., 2009 [17]        | 4 times daily <sup>E</sup> | F: <5.3 mmol/l (95 mg/dL);<br>2 h: <6.7 mmol/l (120 mg/dL)  | ADA recommendations**  | Not stated                     | (i) >50% values higher between 2 study visits<br>(ii) 1 random value >160 mg/dl (8.9 mmol/l)<br>(iii) 1 F > 95 mg/dl; the patient's caregiver initiated treatment (more or less 7 visits)                         |

TABLE 7: Continued.

|                                | Glucose monitoring         | Target value for glycemic control   | Type of diet   | Recommendations about exercise | Glucose values used for starting pharmacologic therapy based on target values |
|--------------------------------|----------------------------|---|--|--------------------------------|---|
| Ijäs et al., 2011 [44]         | 4 times daily <sup>F</sup> | F: <5.3 mmol/l (95 mg/dL);<br>1.5 h: <6.7 mmol/l (120 mg/dL)                    | Dietary and lifestyle counselling  | Not stated                     | 2 values higher in 2–4 weeks  |
| Balaji et al., 2012 [45]       | 4 times daily <sup>E</sup> | F: <5.0 mmol/l (90 mg/dL);<br>2 h: <6.7 mmol/l (120 mg/dL);<br>HbA1c: <6.0 g/dL | Medical Nutrition Therapy (MNT)  | Not stated                     | 1 value higher in 2 weeks   |
| Mukhopadhyay et al., 2012 [46] | 7 times daily <sup>B</sup> | F: <5.0 mmol/l (90 mg/dL);<br>2 h: <6.7 mmol/l (120 mg/dL)                      | (i) 25 kcal/kg BW for obese women<br>(ii) 35 kcal/kg BW for nonobese women<br>(iii) 3 daily meals; 40–45% of calories from carbohydrates   | Not stated                     | 1 value higher in 2 weeks   |
| Niromanesh et al., 2012 [47]   | 4 times daily <sup>E</sup> | F: <5.3 mmol/l (95 mg/dL);<br>2 h: <6.7 mmol/l (120 mg/dL)                      | (i) 15 kcal/kg BW for obese women<br>(ii) 22 kcal/kg BW for overweight women<br>(iii) 30 kcal/kg BW for normal weight women<br>(iv) 40 kcal/kg BW for underweight women<br>(v) 45% of calories from carbohydrates, 20% from protein, and 35% from fat<br>(vi) 3 meals and 3 snacks<br>(vii) Calories: 10% breakfast, 30% each lunch and dinner, and 30% snacks | 30 minutes of walking per day  | 2 values higher in one week   |
| Silva et al., 2010 [48]        | 4 times daily <sup>A</sup> | F: <5.0 mmol/l (90 mg/dL);<br>1 h: <6.7 mmol/l (120 mg/dL)                      | (i) 25 kcal/kg BW/day for overweight women<br>(ii) 35 kcal/kg BW/day for normal weight women<br>(iii) 3 full meals and 4 light meals<br>(iv) 35–45% of calories from carbohydrates   | Not stated                     | 2 values higher after 1 week  |
| Mesdaghinia et al., 2013 [49]  | 4 times daily <sup>E</sup> | F: <5.3 mmol/l (95 mg/dL);<br>2 h: <6.7 mmol/l (120 mg/dL)                      | Dietary changes***   | Not stated                     | 1 value higher in 1 week  |
| Spaulonci et al., 2013 [50]    | 4 times daily <sup>E</sup> | F: <5.3 mmol/l (95 mg/dL);<br>2 h: <6.7 mmol/l (120 mg/dL)                      | (i) 25–35 kcal/kg IBW based on pregestational BMI<br>(ii) 55% carbohydrates, 15% proteins, and 30% fat   | 30-minute walk 3 times a week  | >30% values higher in 1 week  |

TABLE 7: Continued.

|                            | Glucose monitoring         | Target value for glycemic control                          | Type of diet                                       | Recommendations about exercise                     | Glucose values used for starting pharmacologic therapy based on target values |
|----------------------------|----------------------------|--|--|--|---|
| Behrashi et al., 2016 [53] | 4 times daily <sup>E</sup> | F: <5.0 mmol/l (90 mg/dL);<br>2 h: <6.7 mmol/l (120 mg/dL) | Education for lifestyle change (exercise and diet) | Education for lifestyle change (exercise and diet) | 1 value higher in 1 week  |

F: fasting; GA: gestational age; IBW: ideal body weight; BW: body weight; BMI: body mass index.

<sup>A</sup> Fasting and 1 hour after each main meal: breakfast, lunch, and dinner.

<sup>B</sup> Fasting, before lunch and dinner, 2 hours after main meals, breakfast, lunch, and dinner, and at bedtime.

<sup>C</sup> Fasting, preprandial before lunch and dinner, 1 and 2 hours after each main meal: breakfast, lunch, and dinner.

<sup>D</sup> Fasting, preprandial before lunch and dinner, 1 hour after each main meal: breakfast, lunch, and dinner.

<sup>E</sup> Fasting and 2 hours after each main meal: breakfast, lunch, and dinner.

<sup>F</sup> Fasting and 1.5 hours after each main meal: breakfast, lunch, and dinner.

\* American Diabetes Association, Medical Management of Pregnancy Complicated by Diabetes, 3rd Edition, Alexandria, Virginia; ADA, 2000, pp. 70–86.

\*\* American Diabetes Association, Nutrition Recommendations and Interventions for Diabetes: A Position Statement of the American Diabetes Association; Diabetes Care 2008 Jan. 31 (Suppl. 1): S61–S78.

\*\*\* Cheung NW, The Management of Gestational Diabetes: A Review Article; Vasc Health Risk Manag. 2009; 5:153–64.

TABLE 8: Management of GDM, international guidelines.

|   | ACOG 2013 [4]  | CDA 2013 [10]  | ADA 2015 [9]   | FIGO 2015 [5]  | NICE 2015 [11]  |
|---|--|--|--|--|---|
| <i>Criteria to start therapy after diet alone</i>             | Inconclusive evidence  | Glycemic control not achieved after 2 weeks of nutritional therapy alone | NR   | NR   | Glycemic control not achieved after 1-2 weeks of diet and exercise                    |
| <i>Type of initial therapy</i>                                | Insulin or oral medications  | Insulin or oral medications  | Insulin or glyburide                                 | Glyburide inferior to both insulin and metformin, while metformin performs better than insulin | Metformin   |
| <i>Dose and frequency of initial therapy</i>                  | NR   | NR   | NR   | NR   | NR  |
| <i>Frequency of glucose monitoring</i>                        | 4 times daily as fasting and either 1 h or 2 h after each meal               | 4 times daily as fasting and either 1 h or 2 h after each meal           | NR   | 4 times daily as fasting and 2 h after each meal   | 7 times daily as fasting, premeal, 1 h after each meal, bedtime                       |
| <i>Target glucose values</i>                                  | 1 h ≤ 140 mg/dL, 2 h ≤ 120 mg/dL   | Fasting ≤ 95 mg/dL, 1 h ≤ 140 mg/dL, 2 h ≤ 120 mg/dL                     | Fasting ≤ 95 mg/dL, 1 h ≤ 140 mg/dL, 2 h ≤ 120 mg/dL | Fasting ≤ 95 mg/dL, 1 h ≤ 140 mg/dL, 2 h ≤ 120 mg/dL   | Fasting ≤ 95 mg/dL, 1 h ≤ 140 mg/dL, 2 h ≤ 116 mg/dL                                  |
| <i>Criteria for pharmacologic therapy dose adjustment</i>     | NR   | NR   | NR   | NR   | NR  |
| <i>Criteria for adding or switching pharmacologic therapy</i> | NR   | NR   | NR   | NR   | NR  |
| <i>Pregnancy monitoring</i>                                   | No consensus   | NR   | NR   | NR   | Ultrasound monitoring of fetal growth and AF volume every 4 weeks from 28 to 36 weeks |
| <i>Time to delivery</i>                                       | Well-controlled: >39 weeks; insufficient data for others; CD if EFW > 4500 g | NR   | NR   | Consider induction at 38-39 weeks  | Delivery no later than 40 + 6 weeks   |

NR: not reported.

## Conflicts of Interest

The authors report no conflicts of interest.

## References

- [1] A. D. Mackeen and M. Lott, "Gestational diabetes," in *Maternal-Fetal Evidence Based Guidelines*, V. Berghella, Ed., chapter 5, CRC Press, 3rd edition, 2017.
- [2] C. Kim, K. M. Newton, and R. H. Knopp, "Gestational diabetes and the incidence of type 2 diabetes: a systematic review," *Diabetes Care*, vol. 25, no. 10, pp. 1862–1868, 2002.
- [3] D. Di Mascio, E. R. Magro-Malosso, G. Saccone, G. D. Marhefka, and V. Berghella, "Exercise during pregnancy in normal-weight women and risk of preterm birth: A systematic review and meta-analysis of randomized controlled trials," *American Journal of Obstetrics and Gynecology*, 2016.
- [4] Committee on Practice Bulletins-Obstetrics, "Practice Bulletin No. 137: Gestational diabetes mellitus," *Obstetrics & Gynecology*, vol. 122, article 406, 2013.
- [5] M. Hod, A. Kapur, D. A. Sacks et al., "The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: a pragmatic guide for diagnosis, management, and care," *International Journal of Gynecology and Obstetrics*, vol. 131, supplement 3, pp. S173–S211, 2015.
- [6] HAPO Study Cooperative Research Group, B. E. Metzger, L. P. Lowe et al., "Hyperglycemia and adverse pregnancy outcomes," *The New England Journal of Medicine*, vol. 358, article 1991, 2008.
- [7] International Association of Diabetes and Pregnancy Study Groups Consensus Panel, B. E. Metzger, S. G. Gabbe et al., "International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy," *Diabetes Care*, vol. 33, no. 3, pp. 676–682, 2010.
- [8] World Health Organization, *Diagnostic Criteria and Classification of Hyperglycaemia First Detected in Pregnancy*, 2013.
- [9] American Diabetes Association, "2. Classification and diagnosis of diabetes," *Diabetes Care*, vol. 40, article S11, 2017.
- [10] Canadian Diabetes Association Clinical Practice Guidelines Expert Committee and A. Y. Cheng, "Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. Introduction," *Canadian Journal of Diabetes*, vol. 37, supplement 1, pp. S1–S3, 2013.
- [11] NICE, *NICE Guidelines. Diabetes in Pregnancy: Management from Preconception to the Postnatal Period*, 2015.
- [12] P. A. M. Weiss, M. Haeusler, F. Kainer, P. Purstner, and J. Haas, "Toward universal criteria for gestational diabetes: relationships between seventy-five and one hundred gram glucose loads and between capillary and venous glucose concentrations," *American Journal of Obstetrics and Gynecology*, vol. 178, no. 4, pp. 830–835, 1998.
- [13] J. B. O'Sullivan, S. S. Gellis, and B. O. Tenney, "Gestational blood glucose levels in normal and potentially diabetic women related to the birth weight of their infants," *Diabetes*, vol. 15, no. 7, pp. 466–470, 1966.
- [14] D. R. Coustan and S. B. Lewis, "Insulin therapy for gestational diabetes," *Obstetrics and Gynecology*, vol. 51, no. 3, pp. 306–310, 1978.
- [15] D. J. Thompson, K. B. Porter, D. J. Gunnells, P. C. Wagner, and J. A. Spinnato, "Prophylactic insulin in the management of gestational diabetes," *Obstetrics and Gynecology*, vol. 75, no. 6, pp. 960–964, 1990.
- [16] C. A. Crowther, J. E. Hiller, J. R. Moss, A. J. McPhee, W. S. Jeffries, and J. S. Robinson, "Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes," *New England Journal of Medicine*, vol. 352, no. 24, pp. 2477–2486, 2005.
- [17] M. B. Landon, C. Y. Spong, E. Thom et al., "A multicenter, randomized trial of treatment for mild gestational diabetes," *New England Journal of Medicine*, vol. 361, no. 14, pp. 1339–1348, 2009.
- [18] B. M. Casey, E. L. Duryea, M. Abbassi-Ghanavati et al., "Glyburide in women with mild gestational diabetes: a randomized controlled trial," *Obstetrics and Gynecology*, vol. 126, no. 2, pp. 303–309, 2015.
- [19] S. J. Meltzer, J. Snyder, J. R. Penrod, M. Nudi, and L. Morin, "Gestational diabetes mellitus screening and diagnosis: a prospective randomised controlled trial comparing costs of one-step and two-step methods," *BJOG*, vol. 117, no. 4, pp. 407–415, 2010.
- [20] O. Sevketic, S. Ates, O. Uysal, T. Molla, R. Dansuk, and S. Kelekci, "To evaluate the prevalence and clinical outcomes using a one-step method versus a two-step method to screen gestational diabetes mellitus," *Journal of Maternal-Fetal and Neonatal Medicine*, vol. 27, no. 1, pp. 36–41, 2014.
- [21] C. M. Scifres, K. Z. Abebe, K. A. Jones et al., "Gestational Diabetes Diagnostic Methods (GD2M) pilot randomized trial," *Maternal and Child Health Journal*, vol. 19, no. 7, pp. 1472–1480, 2014.
- [22] A. Duran, S. Sáenz, and M. Torrejón, "Introduction of IADPSG criteria for the screening and diagnosis of gestational diabetes mellitus results in improved pregnancy outcomes at a lower cost in a large cohort of pregnant women: the St. Carlos Gestational Diabetes study," *Diabetes Care*, vol. 37, pp. 2442–2450, 2014.
- [23] K. P. Fuller and A. F. Borgida, "Gestational diabetes mellitus screening using the one-step versus two-step method in a high-risk practice," *Clinical Diabetes*, vol. 32, no. 4, pp. 148–150, 2014.
- [24] X. Liu, Y. Chen, Q. Zhou, H. Shi, and W. W. Cheng, "Utilization of International Association of Diabetes and Pregnancy Study Groups criteria vs. a two-step approach to screening for gestational diabetes mellitus in Chinese women with twin pregnancies," *Diabetic Medicine*, vol. 32, no. 3, pp. 367–373, 2015.
- [25] P. Oriot, P. Selvais, J. Radikov et al., "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," *Acta Clinica Belgica*, vol. 69, no. 1, pp. 8–11, 2014.
- [26] Y.-M. Wei, H.-X. Yang, W.-W. Zhu, H.-Y. Yang, H.-X. Li, and A. Kapur, "Effects of intervention to mild GDM on outcomes," *Journal of Maternal-Fetal and Neonatal Medicine*, vol. 28, no. 8, pp. 928–931, 2015.
- [27] T.-H. Hung and T.-T. Hsieh, "The Effects of Implementing the International Association of Diabetes and Pregnancy Study Groups Criteria for diagnosing gestational diabetes on maternal and neonatal outcomes," *PLoS ONE*, vol. 10, no. 3, Article ID e0122261, 2015.
- [28] J. M. Kong, K. Lim, and D. M. Thompson, "Evaluation of the International Association of the Diabetes in Pregnancy Study Group New Criteria: gestational diabetes project," *Canadian Journal of Diabetes*, vol. 39, no. 2, pp. 128–132, 2015.
- [29] C. Assaf-Balut, E. Bordiú, L. Del Valle et al., "The impact of switching to the one-step method for GDM diagnosis on the rates of postpartum screening attendance and glucose disorder

- in women with prior GDM. The San Carlos Gestational Study," *Journal of Diabetes and Its Complications*, vol. 30, no. 7, pp. 1360–1364, 2016.
- [30] R. Klara Feldman, R. S. Tieu, and L. Yasumura, "Gestational diabetes screening the international association of the diabetes and pregnancy study groups compared with carpenter-coustan screening," *Obstetrics and Gynecology*, vol. 127, no. 1, pp. 10–17, 2016.
- [31] A. Lapolla, M. G. Dalfrà, E. Ragazzi, A. P. De Cata, and D. Fedele, "New International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommendations for diagnosing gestational diabetes compared with former criteria. retrospective study on pregnancy outcome," *Diabetic Medicine*, vol. 28, no. 9, pp. 1074–1077, 2011.
- [32] S. Bodmer-Roy, L. Morin, J. Cousineau, and E. Rey, "Pregnancy outcomes in women with and without gestational diabetes mellitus according to the international association of the diabetes and pregnancy study groups criteria," *Obstetrics and Gynecology*, vol. 120, no. 4, pp. 746–752, 2012.
- [33] K. Benhalima, M. Hanssens, R. Devlieger, J. Verhaeghe, and C. Mathieu, "Analysis of pregnancy outcomes using the new IADPSG recommendation compared with the carpenter and coustan criteria in an area with a low prevalence of gestational diabetes," *International Journal of Endocrinology*, vol. 2013, Article ID 248121, 2013.
- [34] J. K. Ethridge, P. M. Catalano, and T. P. Waters, "Perinatal outcomes associated with the diagnosis of gestational diabetes made by the international association of the diabetes and pregnancy study groups criteria," *Obstetrics and Gynecology*, vol. 124, no. 3, pp. 571–578, 2014.
- [35] S. Liao, J. Mei, W. Song et al., "The impact of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) fasting glucose diagnostic criterion on the prevalence and outcomes of gestational diabetes mellitus in Han Chinese women," *Diabetic Medicine*, vol. 31, no. 3, pp. 341–351, 2014.
- [36] K. Mayo, N. Melamed, H. Vandenbergh, and H. Berger, "The impact of adoption of the International Association of Diabetes in Pregnancy Study Group criteria for the screening and diagnosis of gestational diabetes," *American Journal of Obstetrics and Gynecology*, vol. 212, no. 2, pp. 224–224.e9, 2015.
- [37] C. L. Meek, H. B. Lewis, C. Patient, H. R. Murphy, and D. Simmons, "Diagnosis of gestational diabetes mellitus: falling through the net," *Diabetologia*, vol. 58, no. 9, pp. 2003–2012, 2015.
- [38] C. Tward, J. Barrett, H. Berger et al., "Does gestational diabetes affect fetal growth and pregnancy outcome in twin pregnancies?" *American Journal of Obstetrics and Gynecology*, vol. 214, no. 5, pp. 653.e1–653.e8, 2016.
- [39] P. Garner, N. Okun, E. Keely et al., "A randomized controlled trial of strict glycemic control and tertiary level obstetric care versus routine obstetric care in the management of gestational diabetes: a pilot study," *American Journal of Obstetrics and Gynecology*, vol. 177, no. 1, pp. 190–195, 1997.
- [40] O. Langer, D. L. Conway, M. D. Berkus, E. M.-J. Xenakis, and O. Gonzales, "A comparison of glyburide and insulin in women with gestational diabetes mellitus," *New England Journal of Medicine*, vol. 343, no. 16, pp. 1134–1138, 2000.
- [41] F. Mecacci, L. Carignani, R. Cioni et al., "Maternal metabolic control and perinatal outcome in women with gestational diabetes treated with regular or lispro insulin: comparison with non-diabetic pregnant women," *European Journal of Obstetrics and Reproductive Biology*, vol. 111, no. 1, pp. 19–24, 2003.
- [42] U. M. Schaefer-Graf, S. L. Kjos, O. H. Fauzan et al., "A randomized trial evaluating a predominately fetal growth-based strategy to guide management of gestational diabetes in Caucasian women," *Diabetes Care*, vol. 27, no. 2, pp. 297–302, 2004.
- [43] C. Anjalakshi, V. Balaji, M. S. Balaji, and V. Seshiah, "A prospective study comparing insulin and glibenclamide in gestational diabetes mellitus in Asian Indian women," *Diabetes Research and Clinical Practice*, vol. 76, no. 3, pp. 474–475, 2007.
- [44] H. Ijäs, M. Väärasmäki, L. Morin-Papunen et al., "Metformin should be considered in the treatment of gestational diabetes: a prospective randomised study," *BJOG*, vol. 118, no. 7, pp. 880–885, 2011.
- [45] V. Balaji, M. S. Balaji, C. Alexander et al., "Premixed insulin aspart 30 (BIAsp 30) versus premixed human insulin 30 (BHI 30) in gestational diabetes mellitus: a randomized open-label controlled study," *Gynecological Endocrinology*, vol. 28, no. 7, pp. 529–532, 2012.
- [46] P. Mukhopadhyay, T. B. Sankar, A. Kyal, and P. D. Saha, "Oral hypoglycemic glibenclamide: can it be a substitute to insulin in the management of gestational diabetes mellitus? A comparative study," *Journal of South Asian Federation of Obstetrics and Gynaecology*, vol. 4, no. 1, pp. 28–31, 2012.
- [47] S. Niromanesh, A. Alavi, F. R. Sharbaf, N. Amjadi, S. Moosavi, and S. Akbari, "Metformin compared with insulin in the management of gestational diabetes mellitus: a randomized clinical trial," *Diabetes Research and Clinical Practice*, vol. 98, no. 3, pp. 422–429, 2012.
- [48] J. C. Silva, C. Pacheco, J. Bizato, B. V. de Souza, T. E. Ribeiro, and A. M. Bertini, "Metformin compared with glyburide for the management of gestational diabetes," *International Journal of Gynecology and Obstetrics*, vol. 111, no. 1, pp. 37–40, 2010.
- [49] E. Mesdaghinia, M. Samimi, Z. Homaei, F. Saberi, S. G. A. Moosavi, and M. Yaribakht, "Comparison of newborn outcomes in women with gestational diabetes mellitus treated with metformin or insulin: a randomised blinded trial," *International Journal of Preventive Medicine*, vol. 4, no. 3, pp. 327–333, 2013.
- [50] C. P. Spaulonci, L. S. Bernardes, T. C. Trindade, M. Zugaib, and R. P. V. Francisco, "Randomized trial of metformin vs insulin in the management of gestational diabetes," *American Journal of Obstetrics and Gynecology*, vol. 209, no. 1, pp. 34.e1–34.e7, 2013.
- [51] W. K. Nicholson, L. M. Wilson, C. T. Witkop et al., "Therapeutic management, delivery, and postpartum risk assessment and screening in gestational diabetes," *Evidence Report/Technology Assessment*, no. 162, pp. 1–96, 2008.
- [52] A. Nankervis, H. D. McIntyre, R. G. Moses, G. P. Ross, and L. K. Callaway, "Testing for gestational diabetes mellitus in Australia," *Diabetes Care*, vol. 36, no. 5, p. e64, 2013.
- [53] M. Behrashi, M. Samimi, T. Ghasemi, F. Saberi, and F. Atoof, "Comparison of glibenclamide and insulin on neonatal outcomes in pregnant women with gestational diabetes," *International Journal of Preventive Medicine*, vol. 7, no. 1, p. 88, 2016.



