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# The 2019 Flemish consensus on screening for overt diabetes in early pregnancy and screening for gestational diabetes mellitus

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**ABSTRACT**

Screening for gestational diabetes mellitus (GDM) is important to improve pregnancy outcomes and to prevent type 2 diabetes after pregnancy. The 'International Association of Diabetes and Pregnancy Study Groups' (IADPSG) recommends a universal one-step approach with the 75 g oral glucose tolerance test (OGTT) for screening of GDM. The IADPSG recommendation remains controversial due to the important increase in GDM prevalence and increased workload. After review of the latest evidence and based on data from the 'Belgian Diabetes in Pregnancy' study, members of the Diabetes Liga, the Flemish associations of general physicians (Domus Medica), obstetricians (VVOG), midwives (VVOB), diabetes nurse educators (BVVDV) and clinical chemists (RBSLM) have reached a new consensus on screening for GDM in Flanders. This new consensus recommends universal screening for overt diabetes when planning pregnancy or at the latest at first prenatal contact, preferably by measuring the fasting plasma glucose by using the same diagnostic criteria as in the non-pregnant state. In women with impaired fasting glycaemia, but also in normoglycemic obese women and women with a previous history of GDM, lifestyle counselling is advised with screening for GDM with a 75 g OGTT at 24 weeks. In all other women, we recommend a two-step screening strategy with a 50 g glucose challenge test (GCT) at 24 weeks followed by a 75 g OGTT when the glucose level 1 hour after the GCT ≥130 mg/dl. Diagnosis of GDM is made using the IADPSG criteria for GDM. Postpartum screening for subsequent glucose abnormalities should be advocated and organized for every woman with GDM.

**KEYWORDS**

Gestational diabetes mellitus; screening; pregnancy; consensus; type 2 diabetes

## Introduction

Gestational diabetes mellitus (GDM) is defined as diabetes diagnosed in the second or third trimester of pregnancy provided that overt diabetes early in pregnancy has been excluded [1]. Screening and treatment of GDM between 24 and 28 weeks of pregnancy reduces the risk for pregnancy complications such as large-for-gestational age infants (LGA) and preeclampsia [2,3]. Women with a history of GDM and their offspring are at increased risk to develop type 2 diabetes (T2DM) later in life [4,5].

The 'International Association of Diabetes and Pregnancy Study Groups' (IADPSG) recommends a universal one-step approach with the 75 g oral glucose tolerance test (OGTT) for screening of GDM with the use of more stringent diagnostic criteria [6]. Since the adoption of the IADPSG recommendation by the World Health Organization (WHO), the IADPSG criteria are commonly referred to as the 2013 WHO criteria [7]. The IADPSG recommendation remains controversial due to the important increase in GDM prevalence, increased workload, the need for a fasting test and the risk for increased medicalization of care [8–10]. As a consequence, there still is a large variation in screening strategies for GDM used across Europe. A survey in 2015 demonstrated that the majority of European societies still recommended screening based on risk factors, about one third recommended a universal one–step approach with a 75 g OGTT [11].

After weighing of the advantages and disadvantages, the 2012 Flemish consensus on screening for GDM

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recommended not to implement the IADPSG screening strategy for GDM but to continue with a universal two-step screening strategy with the 50 g glucose challenge test (GCT) and 3-hour 100 g OGTT with the Carpenter & Coustan criteria for GDM [12]. To obtain data on the impact of the IADPSG screening strategy in Belgium and to evaluate the diagnostic accuracy of different screening strategies for GDM, the 'Belgian Diabetes in Pregnancy-North' study (BEDIP-N) was performed from 2014 to 2018. After review of the evidence including data from the completed BEDIP-N study, the 2012 Flemish consensus on screening for GDM was now revised. A discussion meeting was held on 22–01–2019 between members of the Diabetes Liga, the Flemish associations of general physicians (Domus Medica), obstetricians (Vlaamse Vereniging voor Obstetrie en Gynaecologie 'VVOG'), midwives (Vlaamse Beroepsvereniging voor Vroedvrouwen 'VBOV'), diabetes nurse educators (Beroepsvereniging Vlaamse diabetesverpleegkundigen 'BVVDV') and clinical chemists (Royal Belgian Society Laboratory Medicine 'RBSLM') which led to current consensus statement on screening for GDM in Flanders. Before the consensus meeting, data on the BEDIP-N study were made available to all attendees and the consensus paper was further revised based on the comments given after the consensus meeting.

## Counselling when planning pregnancy

Several studies have shown that both maternal GDM and obesity are independently associated with adverse pregnancy outcomes [13,14]. Since the placenta may already be programmed in early pregnancy, achieving optimal metabolic health before a planned pregnancy, might be the best strategy to obtain good pregnancy outcomes. Although several randomized controlled trials (RCTs) investigating lifestyle interventions in overweight or obese women during pregnancy demonstrated a significant reduction in gestational weight gain, this was generally not associated with a reduction in the rate of GDM or other pregnancy complications [15–18]. The consensus recommends therefore that overweight and obese women should lose weight before pregnancy to improve pregnancy outcomes. In addition, since excessive weight gain during pregnancy is also an independent risk factor for adverse pregnancy outcomes in normal-weight women, lifestyle counselling should be considered for all woman before pregnancy [19]. Lifestyle counselling can be given by a general physician, dietician or midwife. Lifestyle advice should be in line with the general Belgian recommendations for a healthy lifestyle (if overweight weight loss ≥5% of body weight, ≥30 minutes of moderate exercise per day and food recommendations according to the food triangle (www.gezondleven.be/themas/voeding/voedingsdriehoek).

## Screening for overt diabetes in early pregnancy

Due to the increasing prevalence of T2DM in women of childbearing age, many international associations recommend to screen for overt diabetes when planning pregnancy or at first prenatal contact [1,6]. Women with diabetes are at an increased risk for congenital anomalies and diabetes complications due to their greater degree of hyperglycaemia earlier in pregnancy [1]. These women need rapid treatment with insulin and close follow-up during and after pregnancy. The current consensus endorses therefore the recommendation of 2012 to universally screen for overt diabetes at the latest at first prenatal contact, preferably by measuring the fasting plasma glucose (FPG) by using the same diagnostic criteria as in the non-pregnant state [12] (Figure 1). In addition, a novel (pre-clinical) autoimmune type 1 diabetes should be excluded when alarm signs are present such as weight loss, symptoms related to the rapid development of hyperglycaemia (polyuria, thirst), important glucosuria, the presence of polyhydramnios and fetal macrosomia.

The OGTT is considered to be the golden standard for diagnosis of diabetes but is not practical as a screening test, as it is difficult to implement in out-patient clinics, has a low reproducibility and a high cost. The consensus recommends therefore to screen with an FPG since this has the advantage that it is relatively easy to perform at a low cost. In addition, FPG has shown to diagnose more people with T2DM than HbA1c [20]. Moreover, the Hba1c test is not reimbursed for screening in Belgium. However, when it is not possible to come fasting for the test, HbA1c can be used as an alternative to diagnose T2DM (HbA1c ≥6.5%). The measurement of glycosuria is not recommended as this has a very low sensitivity to detect diabetes and is frequently false positive in pregnancy [21].

To limit excessive gestational weight gain, lifestyle counselling is also recommended in early pregnancy, especially in overweight and obese women. The 2009 Institute of Medicine (IOM) targets for gestational weight gain are recommended [22] (Table 1). More recent research has shown that obese women who can limit gestational weight gain ≤5 kg have a lower LGA rate [23,24]. Lower weight gain targets for obese women than the 2009 IOM guidelines might therefore be considered.

## Impaired fasting glycaemia in early pregnancy

There is currently not enough evidence to recommend screening and treatment of GDM before 24–28 weeks of gestation. The IADPSG Consensus Panel initially recommended that a fasting glucose ≥92 mg/dl in early pregnancy should be classified as GDM [6]. This

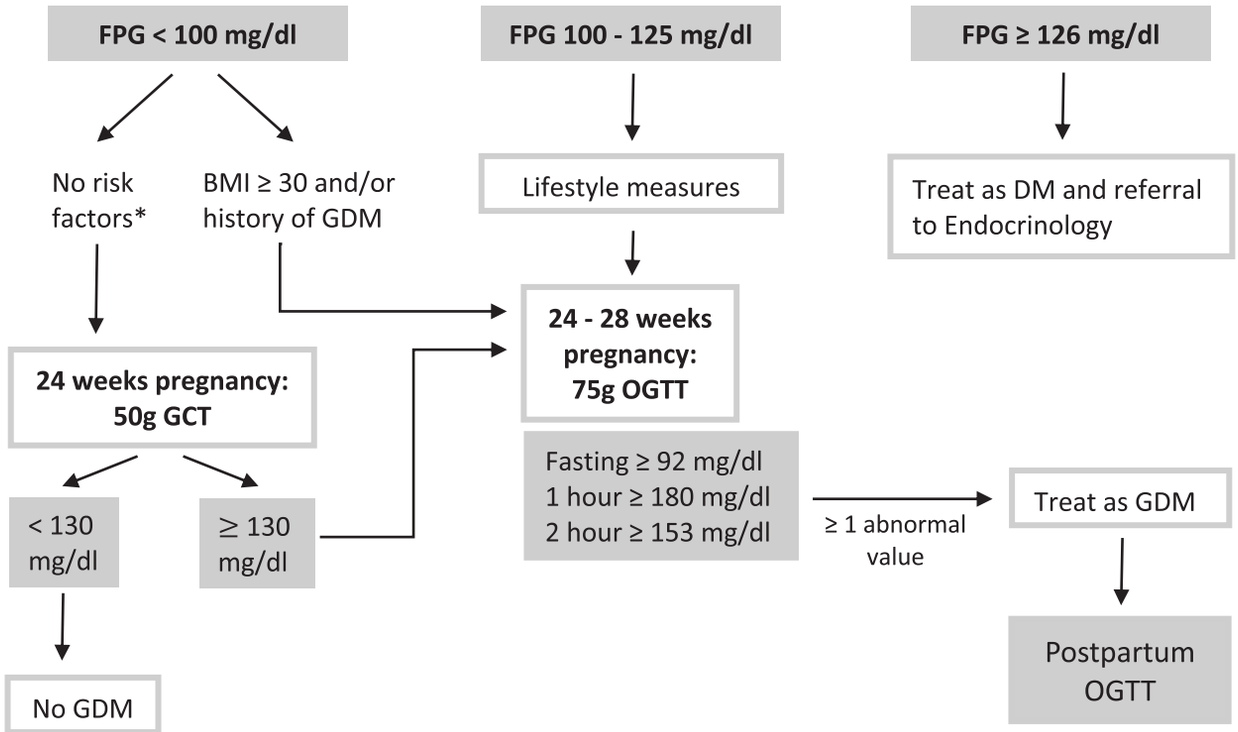


**Figure 1.** The 2019 consensus on screening for overt diabetes and gestational diabetes mellitus. GDM: gestational diabetes mellitus; FPG: fasting plasma glucose; GCT: glucose challenge test; OGTT: oral glucose tolerance test; BMI: body mass index (kg/m$^2$); * no risk factors: if BMI <30 and/or no previous history of GDM.

**Table 1.** The 2009 institute of medicine targets for gestational weight gain.

| | BMI (Kg/m$^2$) | Desired weight Gain (Kg) |
|---|---|---|
| Underweight | <18.5 | 12.5–18 |
| Normal weight | 18.5–24.9 | 11.5–16 |
| Overweight | 25–29.9 | 7–11.5 |
| Obese | ≥30 | 5–9 |

BMI: body mass index

recommendation is much debated as this was reached by consensus only and is merely based on data extrapolated from the cut-off value used on the 75 g OGTT later in pregnancy. In 2016, the IADPSG stated that it can no longer recommend screening for GDM in early pregnancy due to lack of data from intervention studies on GDM in early pregnancy and the fact that the fasting glucose generally further decreases by the end of the first trimester and is therefore a poor predictor for GDM later in pregnancy [25]. There are currently no data from RCTs demonstrating benefit of early screening and treatment of GDM to improve pregnancy outcomes but several studies are ongoing (NCT1926457, NCT01864564 and NCT02708758). In the BEDIP-N study, women with impaired fasting glycaemia in early pregnancy were often obese and/or had a metabolic syndrome (unpublished data). Due to the lack of evidence, we propose a pragmatic approach using the definition of impaired fasting glycaemia (100-125 mg/dl) in early pregnancy according to American Diabetes Association (ADA) criteria for prediabetes as in the non-pregnant state. The consensus recommends that women with impaired fasting glycaemia in early pregnancy should receive lifestyle counselling, with screening for GDM with a 75 g OGTT at 24 weeks using the IADPSG criteria (Figure 1). There is currently no evidence that women with impaired fasting glycaemia in early pregnancy would benefit from self-monitoring of blood glucose (SMBG). In addition, since this is also not reimbursed and to avoid increased medicalization of care, the consensus does not recommend SMBG in these women.

Not all gestational hyperglycaemia has the same aetiology. Autoimmune type 1 diabetes and undetected monogenetic forms of diabetes such as the maturity-onset diabetes of the young MODY-2 can be first revealed during pregnancy masquerading as impaired fasting glycaemia or GDM. People with MODY-2 have an inactivating mutation of the glucokinase gene, leading to a defect in glucose sensing and their glucose homeostasis is therefore maintained at a higher set point, resulting in a mild asymptomatic fasting hyperglycaemia [26]. Since glucose-lowering therapy is ineffective in people with MODY-2 and because of the lack of long-term complications, treatment is not recommended outside pregnancy. When both mother and child have the genetic mutation predisposing to MODY-2, the fetus has poor insulin secretion and treating maternal hyperglycaemia may result in inadequate intrauterine growth. In pregnancy, insulin treatment of the mother is therefore only appropriate when increased fetal growth on scanning suggests the fetus is unaffected [27].

## Screening for GDM at 24 weeks of pregnancy

The 'Hyperglycemia and Adverse Pregnancy Outcomes' (HAPO) study showed a continuous and graded relationship between maternal hyperglycaemia and the risk for an adverse perinatal outcome [28]. Based on the HAPO study, the IADPSG recommended a universal one-step approach with the 75 g OGTT for screening of GDM with the use of more stringent diagnostic criteria for GDM [6]. However, the IADPSG recommendation for screening for GDM remains controversial due to the important increase in the number of women labelled and treated as GDM. The BEDIP-N study has shown that the prevalence of GDM would double to 12.5% in Belgium using the one-step approach with 75 g OGTT and IADPSG criteria compared to a two-step screening strategy with a 50 g GCT with a subsequent 75 g OGTT only when the GCT is abnormal [29,30]. In addition, since the one-step diagnostic approach with the 75 g OGTT will lead to an important increase in workload, alternative screening strategies need to be investigated that can limit the number of OGTTs [8]. The GCT has the advantage that it can be performed in the non-fasting state and can easily be organized in primary care. By using a two-step screening strategy with a GCT, the OGTT could be avoided in many women but data were lacking on the sensitivity and specificity of the GCT with the IADPSG criteria.

The BEDIP-N study was a large Belgian multicentric prospective cohort study enrolling 2006 pregnant women in early pregnancy to evaluate the diagnostic accuracy of different screening strategies for GDM based on the IADPSG criteria. During the study, both healthcare providers and participants were blinded for the GCT. Al participants received therefore a 75 g OGTT irrespective of the result of the GCT. The BEDIP-N study has recently shown that the GCT has a moderate diagnostic accuracy in a universal two-step screening strategy for GDM using the IADPSG criteria and that the threshold of the GCT would need to be reduced to at least 130 mg/dl to achieve a sensitivity ≥72% [29]. By using a GCT ≥130 mg/dl as cut-off, 65% of all OGTTs could be avoided [29]. In addition, the BEDIP-N study has demonstrated that a modified two-step screening strategy combining the GCT ≥130 mg/dl with clinical risk factors may be a practical alternative to the universal one-step approach with the 75 g OGTT [31]. In this modified two-step screening strategy, women with a BMI ≥30 Kg/m$^2$ and/or a previous history of GDM would immediately receive an OGTT at 24 weeks since they are at high risk for GDM while women without any of these risk factors would be screened with a GCT [31]. This strategy can reduce the workload and the need for an OGTT in nearly 60% of women while reducing the number of women that would be missed with GDM (Figure 2). Moreover, the BEDIP-N study showed that the GCT was generally better tolerated than an OGTT and more women preferred a GCT [31].

In contrast to the 2012 consensus, the current consensus recommends a 75 g OGTT with the IADPSG criteria for the diagnosis of GDM since these criteria are the first diagnostic criteria based on pregnancy outcomes. However, data on the cost-effectiveness of a universal one-step approach with 75 g OGTT and IADPSG are conflicting and the one-step screening strategy labels milder forms of hyperglycaemia as GDM with an increased risk for medicalization of care during pregnancy and possibly a lower long-term risk for glucose intolerance postpartum [8,19]. The consensus recommends therefore a universal two-step screening strategy with a GCT in women without obesity and without a history of GDM [8,32]. Since the BEDIP-N study has demonstrated that the threshold of the GCT should be reduced to 130 mg/dl when used with the IADPSG criteria, the current recommendation is to use a universal two-step screening strategy with a 50 g GCT at 24 weeks followed by a 75 g OGTT when GCT ≥130 mg/dl with the use of the IADPSG criteria for GDM (Figure 1). In line with the BEDIP-N results on a modified two-step screening strategy, for obese women and women with a history of GDM, a universal one-step approach with a 75 g OGTT at 24 weeks is now recommended (Figure 1–2). In addition, the recommendation is to screen for GDM rather earlier around 24 weeks and certainly before 28 weeks to allow for timely treatment of GDM.

## Screening for GDM in women after bariatric surgery

Since bariatric surgery is currently the most successful way to achieve maintained weight loss, increasing numbers of obese women of childbearing age receive bariatric surgery. Bariatric surgery performed before pregnancy significantly reduces the risk to develop GDM but the risk in these women is generally still higher compared to normal weight pregnant women [33]. Women after bariatric surgery therefore still require screening for GDM, which is challenging. The standard screening tests (GCT and OGTT) are often not well tolerated and wide variations in glucose excursions make the diagnosis difficult [33]. The poor tolerance of the OGTT in patients with bariatric surgery is due to the high risk for early dumping and postprandial hyperinsulinemic hypoglycaemia after ingestion of the glucose load. A large retrospective cohort study showed that pregnant women after a gastric bypass had more often a high glucose excursion at 1 hour and 55% had a reactive hypoglycaemia at 2 hours [34]. Since there

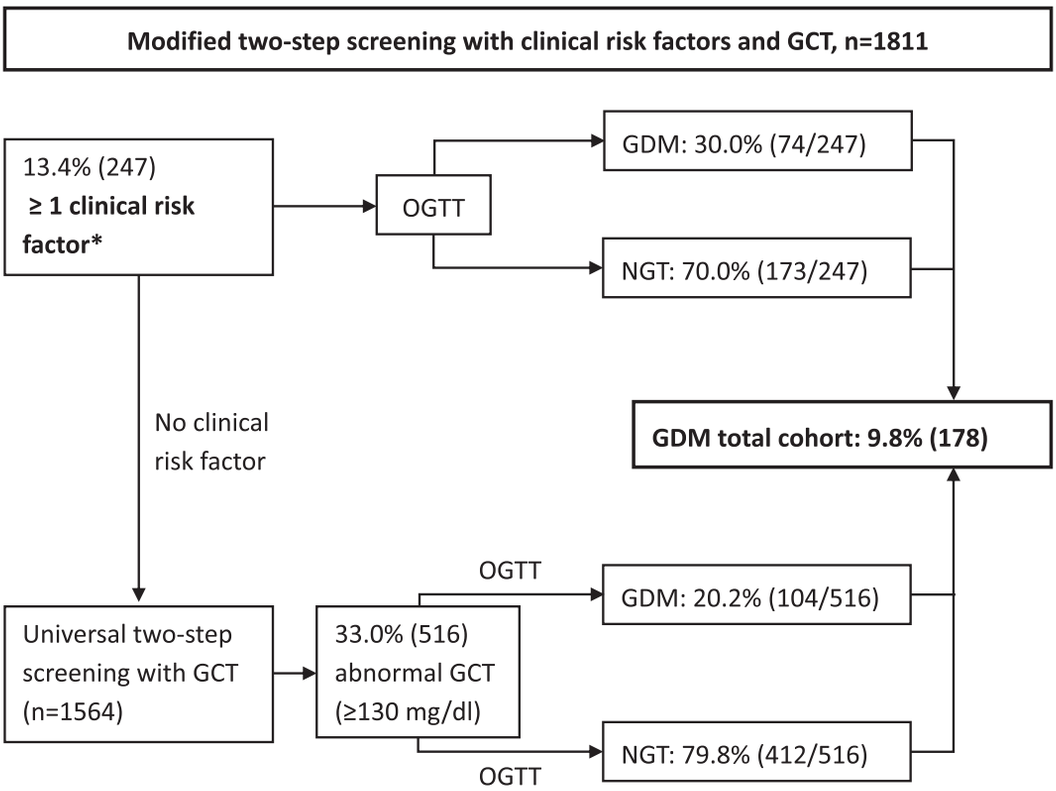


**Figure 2.** Modified two-step screening for gestational diabetes applied to the BEDIP-N study. BEDIP-N: Belgian Diabetes in Pregnancy-North study; OGTT: oral glucose tolerance test; GCT: 50g glucose challenge test; GDM: gestational diabetes mellitus; NGT: normal glucose tolerance test. *clinical risk factor: BMI ≥ 30Kg/m$^2$ or a previous history of GDM.

- Universal screening with 2-h 75g OGTT 6-12 weeks postpartum (ADA criteria)
- Registration in 'Zoet Zwanger' project with yearly measurement of fasting plasma glucose by general physician

| | **Normal** | **Impaired glucose regulation** | **diabetes** |
|---|---|---|---|
| Fasting | <100mg/dl | ≥100 and <126mg/dl | ≥ 126mg/dl |
| 2-hour glucose on OGTT | <140mg/dl | ≥140 en <200mg/dl | ≥200mg/dl |

**Figure 3.** Postpartum follow-up. OGTT: oral glucose tolerance test; ADA: American Diabetes Association.

are currently no good tests available to screen for GDM, the consensus suggests a pragmatic approach to evaluate dysglycaemia in pregnant women with bariatric surgery [33]. Women with bariatric surgery should first receive screening for overt diabetes at first prenatal visit by measuring the fasting glycaemia. To evaluate dysglycaemia later in pregnancy, the recommendation is to record capillary blood glucose daily before and 1 or 2 hours after each meal during 3–7 days at 24–28 weeks of pregnancy. For the diagnostic glycaemic targets, we propose to use the same targets recommended by the ADA for the treatment of GDM (fasting glycaemia < 95 mg/dl, 1 hour after the meal < 140 mg/dl or 2 hours after the meal < 120 mg/dl) [33].

## Treatment of GDM

Initial treatment of GDM involves diet modification, glucose monitoring (fasting and 1 hour or 2 hours after each meal) and moderate exercise. Evidence-based data concerning nutritional treatment for GDM are limited. In general the recommendation is to reduce the caloric intake of obese women by approximately one-third while maintaining a minimum intake of 1600–1800 kcal per day, to limit the carbohydrate intake to 35–45% of total calories without compensatory increased intake of saturated fat, to avoid the intake of carbohydrates with a high glycaemic index and to perform daily moderate exercise for 30 minutes or more [19]. The generally recommended glycaemic targets for the treatment of

GDM are fasting glycaemia < 95 mg/dl, 1 hour after the meal <140 mg/dl or 2 hours after the meal < 120 mg/dl [1].

If lifestyle is insufficient to maintain the glycaemic targets after 1-2 weeks, pharmacological therapy with insulin becomes necessary. Recent studies have suggested that metformin and glibenclamide (glyburide) may be safe and acceptable alternatives for insulin for the treatment of GDM [19]. However, the need for supplemental insulin in women on metformin is around 30% and increased risks for neonatal hypoglycaemia and macrosomia have been reported in women treated with glibenclamide [35]. Moreover, there is a paucity of long-term follow-up data on children exposed to oral agents in utero and recent data suggest that exposure to metformin in utero might be associated with increased offspring weight [36,37]. Insulin remains therefore the first choice when lifestyle measures are insufficient to achieve good glycemic control. The long-acting insulins, human neutral protamine Hagedorn (NPH) and insulin analogue detemir as well as the short-acting insulins, human regular and insulin analogues lispro and aspart (including the faster acting aspart), are all approved for use during pregnancy [1]. Detemir is however only reimbursed for the treatment of type 1 diabetes in Belgium. The long-acting insulin analogue glargine is not approved for use in pregnancy but there are a large number of observational data showing no adverse effects when used in pregnancy [12]. The recommendation of the 'Belgium Federal Agency of Medicinal Agents ' is that when considered necessary, the use of glargine in pregnancy can be considered [12]. There are no data yet on the safety of the long-acting insulin analogues glargine U300 and degludec in pregnancy.

## Follow-up postpartum

By diagnosing GDM, a group of women at high risk to develop T2DM and cardiovascular disease later in life is identified [4]. Lifestyle interventions and metformin can prevent progression to T2DM on the long term [38]. A healthy lifestyle postpartum should therefore be stimulated in all women with a history of GDM. However, outside clinical studies attendance rates at screening tests postpartum are often low, with only 30–50% of women with recent GDM receiving an OGTT and follow-up rates after one year dropping further [39]. This is a missed opportunity to timely identify and treat high-risk women for glucose intolerance. The 'Zoet Zwanger ' project is a Flemish GDM recall register coordinated by the Diabetes Liga with the aim to increase the awareness on the long-term risk for diabetes. Women registered in 'Zoet Zwanger', receive annual reminders to get a yearly screening test in primary care [39].

Data on the risk to develop T2DM in women with GDM diagnosed by the one-step approach and IADPSG criteria are limited. Before the introduction of the IADPSG screening strategy, studies have shown that 30–50% of women with GDM develop T2DM within the first 10 years after the index pregnancy [4]. The use of the IADPSG criteria for GDM results in a greater proportion of women diagnosed with mild forms of GDM, which might lead to a lower proportion at risk for postpartum glucose intolerance. In the BEDIP-N study, nearly 20% of women with GDM based on a universal one-step approach with the IADPSG criteria had glucose intolerance in early postpartum [40]. In contrast, research from UZ Leuven has shown glucose intolerance in 42% three months postpartum in women with GDM diagnosed by a two-step screening strategy with the IADPSG criteria [30]. The majority of women with glucose intolerance had an abnormal 2 hour glucose level on the OGTT (Impaired glucose tolerance). IGT is an important risk factor for T2DM, since the highest cumulative incidence to develop T2DM is seen in people with combined impaired fasting glycaemia/IGT, followed by isolated IGT with the lowest incidence in patients with impaired fasting glycaemia [41]. Moreover, the BEDIP-N study shows that combining FPG and HbA1c in early postpartum does not improve the accuracy to detect glucose intolerance [40]. The consensus recommends therefore a 75 g OGTT 6–12 weeks postpartum in all women with a history of GDM (Figure 1). In addition, all women should be offered registration in 'Zoet Zwanger' (Figure 3). On the long term, OGTTs result in lower costs per case detected than FPG or HbA1c [42]. When glucose intolerance is found, the frequency of screening should be increased to at least annually [43].

Breastfeeding (at least 3–6 months) should be stimulated, since this is associated with a reduced risk to develop T2DM [44]. The postpartum OGTT should ideally be planned when breastfeeding is stopped and should at the latest be planned 6 months postpartum.

## Conclusion

The 2019 Flemish consensus on GDM recommends universal screening for overt diabetes when planning pregnancy or at first prenatal contact, preferably by measuring FPG. In women with impaired fasting glycaemia, but also in normoglycemic obese women and women with a history of GDM, lifestyle counselling is advised with screening for GDM with a 75 g OGTT at 24 weeks. In all other women, the consensus recommends the use of a universal two-step screening strategy with a 50 g GCT at 24 weeks followed by a 75 g OGTT when GCT ≥130 mg/dl with the use of the IADPSG criteria for GDM.

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