BACKGROUND

During this unprecedented severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, there has been a growing focus on how to minimise contagion while maintaining excellent clinical care. Non-urgent surgery and routine clinical appointments have been postponed and resources have been diverted to those with possible or diagnosed SARS-CoV-2.

Diabetes is a major risk factor for SARS-CoV-2 associated mortality. At the time of writing, unlike with SARS-CoV-1, there was no evidence that pregnant women or their fetuses are more severely affected than the general population if they are infected with SARS-CoV-2. However, given the pandemic only commenced in December 2019, there has been insufficient time to assess the full impact on babies. Neither diagnosed nor undiagnosed gestational diabetes mellitus (GDM) has yet been shown to be associated with either an increased risk of contraction of, or worse outcomes with, SARS-CoV-2.

The background risk from infection and of infecting others, particularly those with an already heightened risk, remains a significant concern. As a result, models of GDM antenatal care have largely shifted from group and face-to-face interactions to online and telephone consults. These new approaches, without the interactive interdisciplinary team approach and real-time data...
sharing that are considered best practice, have not been evaluated. Diminished GDM care must also be considered a risk for increased pre-eclampsia, stillbirth, shoulder dystocia, birth trauma and postnatal depression.4,6

One aspect of GDM of immediate concern is the use of the 75 g two-hour oral glucose tolerance test (OGTT) to diagnose GDM during a time of social isolation and risk of SARS-CoV-2 contagion. The aim of this report is to summarise the options and the rationale behind recommendations designed to minimise the risks to pregnant women.

**RISK OF SARS-COV-2 CONTAGION DURING THE OGTT**

Close contacts of persons with SARS-CoV-2 are most at risk.7 SARS-CoV-2 was detected for up to 72 and 48 h on plastic and stainless steel surfaces, respectively, and remains viable in aerosols for 3 h with an exponential decay in virus titre over time.8 Each visit to a pathology centre may therefore represent a risk during pregnancy, particularly if a stay in excess of two hours is required.

Current Australian recommendations require 1.5 m between persons and 4 m² area for each person in an enclosed space.9 However, it is unknown whether a greater risk to the pregnant woman ensues from a single 2.5 hours visit to a pathology collection centre or from multiple short visits. Beyond implementing the standard SARS-CoV-2 contagion control recommendations, the general principles are, therefore, to minimise the need to attend a pathology centre (ie one attendance rather than two), the duration of attendance (ie single sampling rather than multiple sampling), and the number of women likely to attend at once (eg fasting sample).

**CURRENT OPTIONS FOR REPLACING THE OGTT**

The need to diagnose GDM using an OGTT, which assesses both fasting and post-prandial glycaemia, is now considered best practice by all relevant international organisations, with the International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic criteria for GDM (fasting glucose ≥ 5.1 mmol/L, one hour ≥ 10.0 mmol/L, two hours ≥ 8.5 mmol/L) most used in Australia.10 Table 1 summarises the disadvantages of each alternative option. These alternatives either exclude an assessment of post-prandial glycaemia (fasting blood glucose (FBG)) or are dependent on a variable prandial state (random blood glucose (RBG)), erythrocyte physiology (HbA1c) or albumin turnover (fructosamine).

Complexity is compounded by ethnic differences in both OGTT profiles and the HbA1c. At 24–28 weeks gestation in the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study, the proportion of women diagnosed by the fasting criterion alone ranged from 26% in Hong Kong to 74% in Barbados.11 Therefore, dependence on FBG alone is problematic in multiethnic cities, such as Sydney and Melbourne. Even where populations are of largely European descent, a significant proportion (40–50%) of women with GDM will be missed with use of FBG alone. The FBG is particularly problematic in early pregnancy when it drops over time, making threshold definition difficult.12 The HbA1c is also affected by ethnic differences in glycation and individual variation in red cell turnover13 and has remarkably low sensitivity for IADPSG-defined GDM in both early and late pregnancy14,15 and for adverse pregnancy outcomes (as shown in the HAPO study16).

There have been several attempts to reduce the time burden of the OGTT, including either dropping the two-hour timepoint, which will miss ~12% of women with IADPSG-defined GDM,17 or using an algorithmic approach to the FBG results.18 An FBG-based algorithm defining GDM (≥5.1 mmol/L) and low risk (≤4.4 mmol/L), with OGTT only among those with an FBG 4.5–5.0 mmol/L, can reduce the number of OGTTs required at the end of the second trimester by ~57% among women of Middle Eastern descent.18 This differs from the 4.7 mmol/L threshold recommended in the FBG-based algorithm of the Australasian Diabetes in Pregnancy Society (ADIPS)19 temporary guidelines (Table 1). Differences between ‘optimal’ thresholds using different datasets from different populations may at least partly explain this difference. Further issues with the FBG-based algorithm based approach arise from the need for rapid laboratory turnaround to prevent a return visit to the pathology centre requires a capability improbable in most centres. Therefore, two-step algorithms are associated with both delayed treatment and a proportion (estimated at 10%) not returning for the OGTT.20 The use of point-of-care testing has been suggested,18 but most glucose meters are relatively imprecise during pregnancy.21

**CURRENT TEMPORARY GUIDELINES FOR GDM DIAGNOSTIC AND POSTPARTUM TESTING DURING THE SARS-COV-2 PANDEMIC**

Table S1 shows some of the current temporary international guidelines for diagnosing GDM during the SARS-CoV-2 pandemic.19,22–25 Various options for the diagnosis of early/booking GDM are recommended, including HbA1c, RBG and immediate self blood glucose monitoring (SBGM). In early pregnancy, all recommend the use of HbA1c ≥ 5.9% (41 mmol/mol), with RBG and FBG as possible alternatives. The purpose of early testing is to identify undiagnosed type 2 diabetes. In Australia, ADIPS19 also targets milder forms of hyperglycaemia in early pregnancy, although without defining the exact thresholds for diagnosis/treatment, currently the focus of the Treatment Of Booking GDM (TOBOGM) randomised controlled trial.26 ADIPS and The New Zealand Society for the Study of Diabetes (NZSSD) recommend the immediate commencement of SBGM (usually involving a referral to a diabetes in pregnancy service) for women with prior GDM.23

At 24–28 weeks gestation, the five guidelines show a wider range of strategies. The Canadian and Royal College of Obstetrics
and Gynaecology guidelines include HbA1c/RBG and HbA1c/ FBG combinations to maintain the single, short visit approach, with reported sensitivities for GDM of 25%22 and 41%24, respectively. In Australia, Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommends FBG alone,25 whereas ADIPS recommends an FBG-based two-step algorithm.19 Unpublished data from four Sydney public hospitals with multiethnic catchments indicate sensitivities of 38–64% for RANZCOG’s approach, and 60–80% for ADIPS’ approach, the latter of which is anticipated to reduce the OGTT rate by 82% (Table 1).

Table 1: Disadvantages of alternative options to the 75 g OGTT during pregnancy to diagnose GDM†

| Test                  | Timing | Collection centre duration | Disadvantages                                                                 |
|-----------------------|--------|---------------------------|-------------------------------------------------------------------------------|
| 75 g 2-h OGTT         | Fasting| >2 h                      | Three blood samples, potential increased exposure                             |
| 75 g 1-h OGTT         | Fasting| >1 h                      | Two blood samples, potential intermediate exposure, ~12% GDM missed11         |
| Fasting glucose       | Fasting| <15 min                   | Misses women with GDM diagnosed on the post-load glucose, ethnic differences15 |
| HbA1c                 | Any time| <15 min                   | Early pregnancy-FBG drops over the first trimester, making it unreliable      |
|                       |        |                           | depending on criteria/population12                                              |
|                       |        |                           | Early pregnancy-FBG diagnostic criterion not defined - 6.1 mmol/L most       |
|                       |        |                           | valid currently12                                                              |
|                       |        |                           | Turnaround time, re-attendance if using laboratory measure to decide on      |
|                       |        |                           | need for post-load test18                                                       |
|                       |        |                           | Late pregnancy sensitivity at 4.7 mmol/L 79.5%/5.1 mmol/L 64.1% for GDM-       |
|                       |        |                           | Greater Western Sydney#1                                                        |
| Random glucose        | Any time| <15 min                   | Low sensitivity for outcomes at 24–32 weeks16                                  |
| Fructosamine          | Any time| <15 min                   | Substantially influenced by albumin turnover                                   |
| Capillary testing     | Any time| <15 min                   | Lab or clinic point-of-care testing; capillary blood thresholds not defined   |
|                       |        |                           | for IADPSG criteria; vary with temperature/haematocrit; potential user error;|
|                       |        |                           | meter variability in pregnancy21                                               |
| Prior GDM             | No lab test required | 0                           | GDM does not recur in 30–70% women, especially of European descent27          |
| SBGM                  | No lab test required | 0                           | Exposes women without GDM to GDM testing and education/follow up at a         |
|                       |        |                           | time when staff and clinic appointments should be minimised-women with       |
|                       |        |                           | past GDM will already be familiar with SBGM and will need less time/input;    |
|                       |        |                           | costs; no validity                                                             |

Greater Western Sydney-unpublished data: #1 Bankstown-Lidcombe Hospital, #2 Liverpool Hospital, #3 Westmead Hospital.
Central Sydney - unpublished data: #4 Royal Prince Alfred Hospital.
FBG, fasting blood glucose; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test; SBGM, self blood glucose monitoring.
†Gold standard = IADPSG International Association of Diabetes and Pregnancy Society: fasting, 1, 2 h criteria (mmol/L): 1 = 5.1/10.0/8.5 mmol/L
into the two-step pitfalls, with the FBG used to determine who requires an OGTT on another day. NZSSD attempts to avoid the OGTT altogether, instead referring women with an indeterminate FBG to the diabetes specialist clinic for 1–2 weeks of SBGM. This approach will lead to a proportion of women without GDM undertaking SBGM (a relatively costly activity) and increased work for diabetes specialist teams (although women with past GDM will already be familiar with SBGM and will need less time/input).

Post-partum testing policy in Australia and Canada is generally to await the end of the pandemic before re-testing, unless women have a high short-term risk of type two diabetes, in which case, ADIPS recommends measurement of HbA1c 4–6 months post-partum if undertaking an OGTT remains a risk.

**RECOMMENDATIONS**

All organisations are to be commended for releasing guidance within weeks of the SARS-CoV-2 pandemic. Each has attempted to reduce contagion exposure through combining
different non-OGTT testing approaches, which will inevitably reduce the sensitivity of diagnosing GDM. The reliance on the HbA1c, a low sensitivity, high specificity test, is likely to have a particular impact in this regard.12–15 Conversely, of the women with prior GDM, 30–70% will be commenced on SBGM despite GDM not being present, with resultant increasing costs, diabetes service workload and potentially over-medicalising some pregnancies.27

However, it is clear that the SARS-CoV-2 context differs across Australia and it is recommended that more emphasis be placed on encouraging organisations and practitioners, in collaboration with the women, to choose the GDM diagnostic pathway that best suits their population and situation. In many collection centres, there is sufficient room for adherence to social distancing rules and for the OGTT to occur.

Two major refinements could be made to the temporary ADIPS guidelines for women who decline the OGTT and/or where risk of contagion is significant (Figure 1). Firstly, adding an RBG ≥ 9.0 mmol/L or FBG ≥ 6.1 mmol/L12 to early HbA1c testing would ensure that more high-risk women are identified.28 Secondly, at 24–28 weeks gestation, while the temporary ADIPS guidelines are the most sensitive, they still require the woman to return for an OGTT if the FBG is 4.7–5.0 mmol/L. A better approach might be to ask the woman whether she would prefer (after advising that there is a possibility of the diagnosis being missed with any of the abridged forms of testing):

- The full OGTT with attendance of 2–2.5 hours (100% sensitivity). Women could perhaps be allowed to wait outside the collection centre, such as in their own car, which may reduce the sensitivity (inaccurate timing and physical activity) but may be more acceptable to some women. (Some laboratories may also baulk at not being able to observe women for adverse effects of a glucose load.)

Or

- A one-hour 75 g OGTT with attendance of just over one hour (88–91% sensitivity based upon unpublished data from two hospitals in Greater Western Sydney and HAPO 11).

Or

- An FBG only with attendance of <15 minutes (38–64% sensitivity; current RANZCOG advice) with a need for 18% of women to return for an OGTT (60–80% sensitivity; current ADIPS advice).

Offering such options may be particularly difficult for those women who do not have English as a first language, or with health literacy or cultural barriers, but could be supported by a pictorial guide. Organisational/clinician decision-making can be supported by a risk guide (Table 2). Alternatively, each organisation may decide to select one of these as the default option most appropriate for their population and logistics.

**TABLE 2  Traffic Lights (Red-Amber-Green) approach to GDM testing cognisant of SARS-CoV2 risk**

| Definition | Early pregnancy | 24–28 weeks - single visit strategy | 24–28 weeks - double visit strategy | GDM missed | Predicted annual excess number of babies with serious adverse perinatal outcomes/100 000† |
|------------|----------------|-------------------------------------|-------------------------------------|------------|------------------------------------------------------------------|
| Green      | Collection site able to provide social distancing or contagion risk is low | • Usual practice | • OGTT | - | 0% | 0 |
|            |                  |                                    |                                    |            |                                                                  |
| Amber      | Collection site limited ability to provide social distancing and contagion risk is moderate-high | • HbA1c ≥ 5.9% (41 mmol/mol) | • OGTT where capacity | • FBG ≥ 5.1 mmol/L: GDM - no further testing | • 1-h OGTT | • 12% | • 35 | • 58–109 | (up to 176 depending on attendance) |
|            |                  | • RBG ≥ 9.0 mmol/L | • 1-h OGTT | • FBG 4.7–5.0 mmol/L: return for OGTT | • Double visit (assuming 100% attendance) | 20–40% |
|            |                  | • FBG ≥ 6.1 mmol/L | • Immediate SMBG if prior GDM | • FBG < 4.7 mmol/L: no further testing | | |
|            |                  | • Refer to alternative collection centre where possible | • Move to ‘Red’ status when collection site capacity is severely limited | | | |
| Red        | Collection site unable to provide social distancing and contagion risk is high | • HbA1c ≥ 5.9% (41 mmol/mol) | • FBG ≥ 5.1 mmol/L | - | 35–60%‡ | 103–176 |
|            |                  | • RBG ≥ 9.0 mmol/L | • Refer to alternative collection centre where possible | | | |
|            |                  | • FBG ≥ 6.1 mmol/L | | | | |

FBG, fasting blood glucose; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test; SBGM, self blood glucose monitoring.

†Assumes 10% GDM: number needed to treat to avoid one severe adverse perinatal outcome (death, shoulder dystocia, bone fracture, and nerve palsy) was 1:34 in the Australian Carbohydrate Intolerance Study in Pregnant Women Trial (5).‡Particularly in Asian communities.
CONCLUSION

During the SARS-CoV-2 pandemic, we need to find a balance between reducing the exposure of pregnant women to SARS-CoV-2 and still enabling early screening for ‘diabetes in pregnancy’ and 24–28 weeks screening for GDM, both of which we know lead to improved pregnancy outcomes. Where pathology centres can allow sufficient social distancing, the OGTT remains the gold standard for diagnosis throughout pregnancy and, as ADIPS suggests, should still be offered to all women. If social distancing requirements cannot be observed, there are alternative diagnostic approaches, which should identify the majority of women with GDM while limiting the potential within-laboratory exposure to the virus. It is essential that organisations and practitioners be supported to choose the GDM diagnostic pathway which best suits their population and situation.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Table S1.** National and international guidelines to replace current oral glucose tolerance test (OGTT) during SARS-CoV-2 pandemic.