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Implications of the introduction of new criteria for the diagnosis of gestational diabetes: a health outcome and economic analysis

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Abstract

Objective

To identify effects on health outcomes from implementing new criteria diagnosing gestational diabetes (GDM) and to analyse costs-of-care associated with this change.

Design

Large retrospective cohort study comparing data from the calendar year before (2014) and after (2016) the change.

Setting

Single, tertiary level, university-affiliated, maternity hospital.

Participants

All women giving birth in the hospital, excluding those with pre-existing diabetes or multiple pregnancy.

Main outcome measures

Primary outcomes were caesarean section, birthweight > 90th percentile for gestation, hypertensive disorder of pregnancy and pre-term birth less than 37 weeks. A number of secondary outcomes reported to be associated with GDM were also analysed were also analysed.

Care packages were derived for those without GDM, diet-controlled GDM and GDM requiring insulin. The Institutional Business Reporting Unit data for average occasions of service, pharmacy schedule for the costs of consumables and medications, and Medicare Benefits Schedule ultrasound services were used for costing each package. All costs were estimated in figures from the end of 2016 negating the need to adjust for Consumer Price Index increases.

Results

There was an increase in annual incidence of GDM of 74% without overall improvements in primary health outcomes. This incurred a gross cost increase of \$904 178 and net of \$560 093

Conclusion

New criteria for the diagnosis of GDM have not resulted in significant improvements in key health outcomes in a large tertiary maternity hospital but have significantly increased the incidence of GDM and the overall cost of GDM care.

Strengths and limitations of this study

- Australia is one of the only major Western countries to introduce universal screening for GDM by new International Association of Diabetes in Pregnancy Study Group criteria and is uniquely poised to assess concerns about increased annual incidence and costs of care compared to any potential improvement in health outcomes.
- Concerns about an increase in diagnoses and “over-medicalisation” of women who erstwhile would have been considered normal have given many countries reason for caution in adopting the new criteria: our findings may assist in decision making regarding this public health policy.
- As with any large retrospective audit, there are potential methodological flaws in data analysis, however we have assessed the implication of adopting this criteria on an entire cohort (not a specific subgroup) minimising the risks of selection bias.
- A major problem with assessing changes in diagnostic criteria in GDM lies within being unable to retrospectively identify those who were potentially underdiagnosed under older systems and assess their outcomes. We have thus assessed the impact on a large tertiary hospital as a whole and quantified the costs associated with the increased burden or care.

Introduction

Diagnostic criteria for gestational diabetes (GDM) in Australia changed following a 2014 consensus statement by the Australian Diabetes in Pregnancy Society (ADIPS)¹ ratifying support for the International Association of Diabetes in Pregnancy Study Group's recommendations² (see table 1). These, in turn, used data from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) trial,³ which was a large, prospective, multi-centre study examining the influence of increasing blood glucose levels on a fasting glucose tolerance test on eventual adverse pregnancy outcome.

Previously, diagnostic criteria for GDM in Australia were derived from an earlier ADIPS consensus statement published in 1991⁴ and re-endorsed in 1998⁵ (see Table 1). It was based on the observed distributions of blood glucose levels tested in pregnant women at various maternity centres. These older criteria had been widely utilised for the last two decades in many Australian maternity centres including our own.

(Table 1 goes about here).

Since the introduction of the new criteria, concerns have focussed on the anticipated increase in annual incidence of GDM that these new criteria will cause and the resultant implications for workload. Early estimates of an annual increase of 35%⁶ were followed by later data suggesting an almost doubling in some populations.⁷ Although many major maternity centres in Australia have adopted the new criteria, a 2016 survey found variable adoption in Australia⁶ and the criteria have not yet found international acceptance despite WHO endorsement.^{9, 10, 11}

While it was never the intention of the HAPO authors to suggest a specific annual incidence for GDM, it is important to remember that the new criteria and the suggested relative risk reductions were derived from an untreated population. They were not derived from comparing the new criteria to any other existing methods of diagnosis. While the change may be important for uniformity in diagnosis and may result in clinically important outcomes in individuals previously not diagnosed with GDM, it is also important to assess whether any improvements are seen across large populations and, if so, whether they justify any increase in costs-of-care.

We aimed to estimate the impact of this change in a large tertiary maternity hospital by examining an entire cohort of pregnant women immediately before and immediately after the new criteria were adopted. Specifically, we wished to examine the increase in annual incidence of GDM, assign an appropriate cost-of-care to the high-risk model employed for GDM and compare this to any hospital-wide change in the HAPO outcomes upon which the new criteria are based.

Patients and Methods

As the new criteria for diagnosing GDM were introduced in our hospital in mid 2015, we selected 2014 as the last full calendar year of diagnosis under 1991/1998 ADIPS criteria^{4,5} and 2016 as the first full year of diagnosis under the new IADPSG criteria.² All women having care and delivering within the hospital were included for analysis, with exclusion limited

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3 only to pre-existing diabetes (i.e. those who did not undergo screening for GDM) and
4 multiple pregnancy (an exclusion criterion in the HAPO trial).
5

6 Clinical care during the periods of study was divided into three groups: those without GDM,
7 GDM managed with dietary measures, and GDM requiring insulin. For occasions of clinical
8 review, such as antenatal clinic consultations, group class and phone-call consultations, and
9 pregnancy day care admissions, cost was estimated from “average occasion of service”
10 figures for the relevant health professional, as collected by the institutional Business
11 Performance Reporting Unit. The pharmacy schedule was consulted for the costs of
12 consumables and medications. The Medicare Benefits Schedule was considered the most
13 reproducible and valid estimation for the cost of ultrasound services. All costs were
14 estimated in figures from the end of 2016, thus negating the need to adjust 2014 figures for
15 consumer price index (CPI) or other potential inflationary changes.
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19 Women diagnosed with GDM receive a three-hour group class with a diabetes educator,
20 dietician and physiotherapist. In addition, most have a follow-up one-on-one session with a
21 dietician, phone consultations with diabetes educators, two extra antenatal clinics,
22 assessment by consultant obstetricians rather than by midwives or junior medical staff, and
23 a growth ultrasound. They also require a glucometer and testing strips.
24

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26 If dietary measures fail to control blood glucose levels (BGLs) at acceptable levels, they also
27 require insulin, a one-on-one session with a diabetes educator, an extra antenatal clinic,
28 often a second growth scan and sometimes fetal heart rate monitoring via cardiotocography
29 (CTG).
30

31 Demographic data were collected for each group, including age, body mass index (BMI), pre-
32 existing polycystic ovarian syndrome (PCOS), smoking, parity and previous caesarean
33 section (LUSCS).
34
35

36 Primary outcomes were those upon which the new criteria were based, namely caesarean
37 section rates, hypertensive disorder of pregnancy, birthweight greater than the 90th
38 percentile, pre-term birth less than 37 weeks.²
39

40
41 Additional maternal outcomes were induction of labour, instrumental birth, third degree
42 tear and post-partum haemorrhage. Additional fetal outcomes were greater than the 95th
43 percentile, less than the 10th percentile, admission to special care nursery (SCN) or neonatal
44 intensive care (NICU), estimated gestational age, pre-term birth less than 34 weeks, birth
45 trauma, respiratory distress, jaundice requiring phototherapy, hypoglycaemia, stillbirth,
46 neonatal death, and Apgar score less than 7 at 5 minutes.
47

48
49 Neonatal birthweights were plotted by percentile as described by the latest Australian birth
50 charts.¹⁵ Neonatal hypoglycaemia was defined as any ward-measured BGL less than 2.6
51 mmol/L.
52

53 Data were collected prospectively by the institutional Quality and Safety Unit from the
54 Maternity Care Information System (“MCIS”, GE Healthcare, Little Chanfont, UK) and
55 collated in MS Excel spreadsheets (Microsoft, Redmond, USA). Data were analysed after
56 selecting the demographics and outcomes of interest. Maternal and neonatal
57 characteristics were compared using descriptive statistics. Discrete variables are reported in
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3 the tables as a mean percentage and continuous variables are reported as mean (95%
4 confidence interval). For univariate analyses, discrete variables were analysed using Fisher's
5 exact test or Pearson's chi-squared test and continuous variables using Student's t-test.
6 Multivariate analysis with logistic regression was planned for any outcome which met
7 statistical and clinical significance and had documented risk factors other than GDM. P-
8 values are reported in the final column of all tables with less than 0.05 considered
9 statistically significant and highlighted in bold. Statistical analysis was performed using
10 STATA 9.2 (StataCorp, Texas, USA).
11

12
13 The study was approved as an anonymised audit by the Institutional Research and Ethics
14 Committee with identifying information removed before analysis.
15

16 *Patient and Public Involvement*

17
18 This was an anonymised retrospective audit, thus patients and the public were not required
19 to be directly involved in recruitment or conduct of the study. Indeed, emphasis was given
20 toward assessing the implications of this public health policy on a patient cohort as a whole
21 rather than subgroup or individual outcomes.
22
23

24 **Results**

25 *Demographics and Health Outcomes*

26
27 In 2014, there were 7010 pregnant women of whom 416 were diagnosed with GDM
28 (incidence 5.93%) and in 2016, there were 7488 pregnant women of whom 774 were
29 diagnosed with GDM (incidence 10.3%). The demographics of the two cohorts are shown in
30 Table 2.
31
32

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34
35 (Table 2 goes about here).
36

37 Although the second cohort was statistically significantly older, this was only by a mean of
38 four months. The diagnosis of PCOS was higher but overall rates were low and possibly
39 under-reported. These two findings were statistically significant but unlikely to be clinically
40 relevant. The relative increase of 73.7% in the annual incidence of GDM is most likely
41 attributable to the change in diagnosis rather than to any changed demographic factors.
42
43

44 The maternal outcomes are shown in Table 3 and the fetal outcomes in Table 4, with the
45 HAPO/IADPSG outcomes highlighted in bold.
46

47
48 (Tables 3 and 4 go about here).
49

50 Following the introduction of the new GDM criteria, there has not been a hospital-wide
51 decrease in the main outcomes reported in the sub-analysis of the HAPO trial, most
52 particularly in birthweight >90th percentile for gestation, caesarean section, hypertensive
53 disorder of pregnancy or pre-term birth <37 weeks. However, there has been a hospital-
54 wide decrease in documented birth trauma, neonatal death and birthweight greater than
55 the 95th percentile in the fetal outcomes and an increase in induction of labour and
56 instrumental birth in the maternal outcomes.
57
58

The decrease in birth trauma was due to a change in coding practices between 2014 and 2016 allowing only those injuries directly related to the mode of birth and requiring treatment to be recorded. The decrease in neonatal death rates was unexplained and, on further analysis, only confined to the non-diabetic population. Therefore, the change may have resulted in a small reduction in very large babies but seemed to have no relevant clinical reduction in any other outcome.

Costs of care

The average antenatal care package for women without GDM costs \$923 and for the 15% that require post-dates care this is \$1742 (when extra clinics, and CTG and amniotic fluid monitoring are required). The care package for women with GDM who do not need insulin is \$2026 and for those that do need insulin is \$2534 (or \$3826 if CTG monitoring from 36 weeks is undertaken: on audit during the study period, this occurred in 50% of patients).

In 2014, 210 women with GDM were controlled with dietary measures and 206 required insulin. The costs of care for GDM was calculated as follows:

GDM diet controlled: $210 \times \$2026 = \$425\ 460$

GDM insulin controlled: $0.5 \times 206 \times \$2534 + 0.5 \times 206 \times \$3826 = \$655\ 080$

Total = \$1 080 540

In 2016, 413 women with GDM were controlled with dietary measures and 361 required insulin. The costs of care for GDM was calculated as follows:

GDM diet controlled: $413 \times \$2026 = \$836\ 738$

GDM insulin controlled: $0.5 \times 361 \times \$2534 + 0.5 \times 361 \times \$3826 = \$1\ 147\ 980$

Total = \$1 984 718

The gross cost increase for care of women with GDM was thus \$904 178. The net cost increase can be determined by attributing the cost of standard care to the excess diagnoses of GDM. If we round the incidence of GDM in 2014 up to 6% and use this with the total number of deliveries in 2016 ($n=7420$), the approximate number of women diagnosed with GDM if the criteria did not change would have been: $0.06 \times 7420 = 445$. The approximate excess number of cases of GDM is the total in 2016 ($n = 774$) minus this figure ($n = 445$) which is: $774 - 445 = 329$. We can then apply this number to routine care (bearing in mind 15% of those undergoing routine care require post-dates monitoring) as follows:

$$0.85 \times 329 \times \$923 + 0.15 \times 329 \times \$1742 = \$344\ 085$$

The net cost increase is then the gross cost increase minus this figure:

$$\$904\ 178 - \$344\ 085 = \$560\ 093$$

The hospital has thus spent a gross of **\$904 178** or a net of **\$560 093** caring for women with GDM because of the change in criteria.

Discussion

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3 The HAPO trial³ was a landmark study for several reasons, namely its sheer size (over 25 000
4 pregnant women), its robust statistical methods, and its aim to unify disparate international
5 views about the significance of GDM and the best way to diagnose it. The IADPSG sub-
6 analysis² used important clinical outcomes in identifying a “best-fit” for cut-off values within
7 the 75-gram glucose tolerance test (GTT) to diagnose GDM: most are routinely measured in
8 clinical care (with the exception of cord C-peptide and fetal fat distribution). The resulting
9 recommendation was for a 75-gram GTT for all women (regardless of baseline risk) with
10 levels of greater than 5.1 mmol/L at fasting, 10 mmol/L at one-hour and 8.5 mmol/L at two-
11 hours considered diagnostic.
12
13

14 Despite a WHO statement endorsing the new criteria,¹⁶ there has been a failure of
15 international acceptance to screen for GDM in this way. The National Institute of Clinical
16 Excellence which guides care in the United Kingdom is perhaps the most striking example,
17 recommending only screening those patients with risk factors and using levels of greater
18 than or equal to 5.6 mmol/L at fasting and 7.8 mmol/L at two-hours.⁹ A sophisticated
19 economic evaluation found this approach to be superior in their population.¹⁷ The latest
20 Cochrane review concluded that there is insufficient evidence to prefer any particular
21 screening method for GDM over another.¹⁸
22
23

24 The new criteria were a major change to established practice in Australia. The abolition of
25 the non-fasting glucose challenge test (GCT) and the introduction of the one-hour BGL on
26 the GTT were both new. The fasting BGL was tightened from greater than or equal to 5.5
27 mmol/L to 5.1 mmol/L and the two-hour level eased from greater than or equal to 8.0
28 mmol/L to 8.5 mmol/L. Some studies have tried to examine outcomes in patients who may
29 have been diagnosed with GDM under the new system but not under the old.^{19,20,21}
30 Generally, they have reported groups at higher risk of adverse outcome (particularly
31 caesarean section and large babies) who may have been previously underdiagnosed, but
32 such an approach is flawed because of the abolition of the glucose challenge test and the
33 introduction of the previously untested one-hour BGL. It thus is not possible to
34 retrospectively examine the outcomes of those who may have had a false negative on the
35 GCT or those who may have only tested positive on the new one-hour level.
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39 A separate approach, one adopted by this study, is to quantify any overall changes in clinical
40 outcomes and attribute a cost to the increased burden of care and a saving to any potential
41 outcome improvements.
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44 The strengths of this study include using a single, large, tertiary centre with a uniform urban
45 catchment area and relatively stable demographics over the study period. The numbers
46 were large with over 7000 births per year in each cohort, and the costs of care were
47 quantifiable by an established institutional Business Performance Reporting Unit. Outcomes
48 were readily identified from existing data management systems and were usually
49 categorical (often binary) and not requiring extensive further investigation or statistical
50 analysis. The weaknesses of the study are those always inherent within retrospective data,
51 including the potential for treatment or ascertainment bias. However, as the outcomes of
52 the entire cohort (rather than just those diagnosed with GDM were analysed) this was likely
53 to be minimised. The latter point is important as the aim of the study was to estimate a
54 public health impact overall, as a result of a public health policy change.
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3 We demonstrated a relative increased incidence of GDM of 74%, but we were unable to
4 demonstrate any statistically significant improvements in major outcomes across the
5 hospital as a whole. There was possibly a small improvement in the incidence of very large
6 babies (greater than the 95th percentile) but the absolute changes were small (0.7%) and
7 there was no change in babies greater than the 90th percentile. An apparent improvement
8 in birth trauma was due to a change in coding practices, and an improvement in the
9 neonatal death rate was isolated to the non-diabetic population and also low in absolute
10 terms (0.2%).
11

12
13 We have also demonstrated an increase in gross costs of over A\$900 000 and in net costs of
14 over A\$500 000 per annum. This is primarily due to employing a “high-risk” model of care to
15 all women with GDM.
16

17
18 While the new criteria are laudable in their efforts at uniformity of diagnosis and adverse
19 outcome avoidance, and possibly have improved clinical outcomes in sub-groups of women
20 previously not diagnosed with GDM, there is lack of quality evidence supporting their
21 superiority over other systems of diagnosis. Thus, further research is needed in three main
22 areas. Firstly, it would be desirable to have prospective (and ideally randomised controlled
23 trial) evidence examining the impact of this system of diagnosis over others employed
24 around the world. Secondly, long-term outcomes of the women with GDM and their
25 children may uncover health benefits not accounted for in immediate analyses like those
26 presented in this study. Finally, it is important to investigate more economic ways of
27 antenatally managing women with GDM particularly in the lower risk group, for example
28 those easily controlled with simple dietary measures.
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31 **Conclusion**

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34 The annual incidence of GDM has immediately and markedly increased due to the change in
35 diagnostic criteria with a substantial increase in cost of care and with no overall
36 improvement in clinical outcomes. We suggest that these results tell a cautionary tale about
37 the routine adoption of even internationally endorsed clinical guidelines which have not
38 been validated by rigorous randomized studies. In the present case, countries like the UK
39 which chose not to adopt the new criteria for diagnosing GDM will have saved considerable
40 resources without resultant clinical detriment. On the other hand, countries like Australia
41 which adopted these new criteria in good faith have incurred considerable extra costs
42 without commensurate clinical improvement.
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45

46 **Declaration of Interests**

47
48
49 There were no conflicts of interest with regards to any of the three authors.
50

51 **Contributor and guarantor information**

52 The corresponding author (TC) was responsible for the study design, literature review,
53 collection and analysis of data, interpretation of clinical findings, writing of the manuscript
54 and decision for submission. TC is responsible for the overall content and acts as guarantor.
55 SB supervised the project and contributed to all of the above in a consulting role. AP
56 contributed to planning and executing appropriate statistical analysis and with
57
58
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3 interpretation of the data. All authors contributed to the final manuscript review and final
4 submission.
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Role of the funding source

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Transparency Declaration

The corresponding author (TC) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted.

Tables

Table 1 1991/1998 ADIPS versus 2014 IADPSG Criteria for diagnosing GDM

| | 1991/1998 ADIPS | | 2014 IADPSG | | 2015 NICE | |
|------------------------|---|---|---|--|---|--|
| | Type of test | Positive criteria | Type of test | Positive criteria | Type of test | Positive criteria |
| Screening test | 50g non-fasting glucose challenge test or 75g non-fasting glucose challenge test | ≥ 7.8mmol/L ≥ 8.0mmol/L | Nil | N/A | Clinical risk assessment | Any one of five clinical risk factors ⁹ |
| Diagnostic test | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.5mmol/L 2 hour ≥ 8.0mmol/L | 75g, 2-hour fasting glucose tolerance test (three levels) | Fasting ≥ 5.1mmol/L 1 hour ≥ 10mmol/L 2 hour ≥ 8.5mmol/L | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.6mmol/L 2 hour ≥ 7.8mmol/L |

Table 2 Demographics of the 2014 and 2016 cohorts

| | 2014 | 2016 | p-value |
|--------------------------|--------------------|--------------------|---------------|
| Total Deliveries | 7010 | 7488 | n/a |
| Age (yr) | 30.9 (30.8 – 31.0) | 31.2 (31.1 – 31.3) | 0.0016 |
| BMI (kg.m ²) | 24.8 (24.7 – 24.9) | 24.7 (24.6 – 24.8) | 0.28 |
| PCOS | 110 (1.57%) | 151 (2.02%) | 0.043 |
| Smoking | 326 (4.65%) | 303 (4.05%) | 0.075 |
| Parity ≥ 1 | 3228 (46.1%) | 3365 (44.9%) | 0.18 |
| Previous LUSCS | 960 (13.7%) | 1027 (13.7%) | 0.45 |

Table 3 Overall Maternal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------|--------------|--------------|-------------|
| Hypertensive disorder | 332 (4.74%) | 361 (4.82%) | 0.81 |
| Induction of labour | 2407 (34.3%) | 2725 (36.4%) | 0.01 |
| Overall LUSCS rate | 1963 (28.0%) | 2070 (27.6%) | 0.63 |
| Emergency LUSCS rate | 1088 (15.5%) | 1076 (14.3%) | 0.05 |
| Instrumental birth | 1316 (18.8%) | 1513 (20.2%) | 0.03 |
| Third degree tear | 217 (3.1%) | 197 (2.6%) | 0.09 |
| PPH | 1685 (24.0%) | 1765 (23.6%) | 0.51 |

Table 4 Overall Fetal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------------|--------------------|--------------------|-------------------|
| EGA | 38.6 (38.6 – 38.7) | 38.6 (38.5 – 38.6) | 0.18 |
| Stillbirth | 36 (0.51%) | 40 (0.53%) | 0.86 |
| NND | 29 (0.41%) | 16 (0.21%) | 0.03 |
| Hypoglycaemia | 154 (2.20%) | 170 (2.27%) | 0.77 |
| Respiratory distress | 140 (2.00%) | 170 (2.27%) | 0.26 |
| Jaundice requiring phototherapy | 112 (1.60%) | 135 (1.80%) | 0.34 |
| Birth trauma | 142 (2.03%) | 28 (0.37%) | < 0.001 |
| Apgar < 7 at 5 min | 280 (3.99%) | 286 (3.82%) | 0.59 |
| Birth < 37 weeks | 645 (9.20%) | 671 (8.96%) | 0.62 |
| Birth < 34 weeks | 292 (4.17%) | 325 (4.34%) | 0.61 |
| Shoulder dystocia | 102 (1.46%) | 131 (1.75%) | 0.16 |
| Admission to NICU | 320 (4.56%) | 366 (4.89%) | 0.36 |
| Admission to SCN | 534 (7.62%) | 537 (7.17%) | 0.31 |
| Birthweight (g) | 3289 (3274 – 3304) | 3275 (3271 – 3293) | 0.21 |
| Birthweight > 95% | 300 (4.31%) | 269 (3.61%) | 0.03 |
| Birthweight > 90% | 577 (8.28%) | 586 (7.86%) | 0.36 |
| Birthweight < 10% | 570 (8.18%) | 616 (8.27%) | 0.85 |

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Yes (page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found Yes (page 2) |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Yes (page 3) |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Yes (page 3) |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Yes (page 3-4) |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes (page 3) |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Yes – no exclusion criteria (page 3) (b) For matched studies, give matching criteria and number of exposed and unexposed N/A |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes (page 4) |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes (page 4) |
| Bias | 9 | Describe any efforts to address potential sources of bias Yes (page 4 and 7) |
| Study size | 10 | Explain how the study size was arrived at Yes (entire cohort, page 4) |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes (page 4) |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Yes, confounding not particularly relevant as outcomes were examined across whole cohorts (page 4-5) (b) Describe any methods used to examine subgroups and interactions N/A (no subgroups) (c) Explain how missing data were addressed N/A (nil was missing) (d) If applicable, explain how loss to follow-up was addressed N/A (nil lost to follow-up) (e) Describe any sensitivity analyses N/A (not required) |
| Results | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Yes (page 5) (b) Give reasons for non-participation at each stage N/A (retrospective analysis with no possibility for non-participation) (c) Consider use of a flow diagram Not used |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Yes (page 5 and Table 2) (b) Indicate number of participants with missing data for each variable of interest Nil missing |

| | | |
|--------------------------|-----|---|
| | | (c) Summarise follow-up time (eg, average and total amount) N/A (examined at time of delivery – no long-term follow up) |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time Yes (page 5-6) |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Yes (page 5-6, tables 3-4) (b) Report category boundaries when continuous variables were categorized N/A (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives Yes (page 6-7) |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes (page 7) |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes (page 7-8) |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results Yes (page 8) |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Yes (page 8) |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

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Implications of the introduction of new criteria for the diagnosis of gestational diabetes: a health outcome and economic analysis

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Implications of the introduction of new criteria for the diagnosis of gestational diabetes: a health outcome and economic analysis

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Abstract

Objective

To identify effects on health outcomes from implementing new criteria diagnosing gestational diabetes (GDM) and to analyse costs-of-care associated with this change.

Design

Large retrospective cohort study comparing data from the calendar year before (2014) and after (2016) the change.

Setting

Single, tertiary level, university-affiliated, maternity hospital.

Participants

All women giving birth in the hospital, excluding those with pre-existing diabetes or multiple pregnancy.

Main outcome measures

Primary outcomes were caesarean section, birthweight > 90th percentile for gestation, hypertensive disorder of pregnancy and pre-term birth less than 37 weeks. A number of secondary outcomes reported to be associated with GDM were also analysed were also analysed.

Care packages were derived for those without GDM, diet-controlled GDM and GDM requiring insulin. The Institutional Business Reporting Unit data for average occasions of service, pharmacy schedule for the costs of consumables and medications, and Medicare Benefits Schedule ultrasound services were used for costing each package. All costs were estimated in figures from the end of 2016 negating the need to adjust for Consumer Price Index increases.

Results

There was an increase in annual incidence of GDM of 74% without overall improvements in primary health outcomes. This incurred a gross cost increase of \$904 178 and net of \$560 093. Babies of women with GDM had lower rates of neonatal hypoglycaemia and special care nursery admissions after the change, suggesting a milder spectrum of disease.

Conclusion

New criteria for the diagnosis of GDM have not resulted in significant improvements in key health outcomes in a large tertiary maternity hospital but have significantly increased the incidence of GDM and the overall cost of GDM care.

Strengths and limitations of this study

- Australia is one of the only major Western countries to introduce universal screening for GDM by new International Association of Diabetes in Pregnancy Study Group criteria and is uniquely poised to assess concerns about increased annual incidence and costs of care compared to any potential improvement in health outcomes.
- Concerns about an increase in diagnoses and “over-medicalisation” of women who erstwhile would have been considered normal have given many countries reason for caution in adopting the new criteria: our findings may assist in decision making regarding this public health policy.
- As with any large retrospective audit, there are potential methodological flaws in data analysis, however we have assessed the implication of adopting this criteria on an entire cohort (not a specific subgroup) minimising the risks of selection bias.
- A major problem with assessing changes in diagnostic criteria in GDM lies within being unable to retrospectively identify those who were potentially underdiagnosed under older systems and assess their outcomes. We have thus assessed the impact on a large tertiary hospital as a whole and quantified the costs associated with the increased burden or care.

Introduction

Diagnostic criteria for gestational diabetes (GDM) in Australia changed following a 2014 consensus statement by the Australian Diabetes in Pregnancy Society (ADIPS)¹ ratifying support for the International Association of Diabetes in Pregnancy Study Group's recommendations² (see table 1). These, in turn, used data from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) trial,³ which was a large, prospective, multi-centre study examining the influence of increasing blood glucose levels on a fasting glucose tolerance test on eventual adverse pregnancy outcome.

Previously, diagnostic criteria for GDM in Australia were derived from an earlier ADIPS consensus statement published in 1991⁴ and re-endorsed in 1998⁵ (see Table 1). It was based on the observed distributions of blood glucose levels tested in pregnant women at various maternity centres. These older criteria had been widely utilised for the last two decades in many Australian maternity centres including our own.

(Table 1 goes about here).

Since the introduction of the new criteria, concerns have focussed on the anticipated increase in annual incidence of GDM that these new criteria will cause and the resultant implications for workload. Early estimates of an annual increase of 35%⁶ were followed by later data suggesting an almost doubling in some populations.⁷ Although many major maternity centres in Australia have adopted the new criteria, a 2016 survey found variable adoption in Australia⁸ and the criteria have not yet found international acceptance despite WHO endorsement.^{9, 10, 11}

While it was never the intention of the HAPO authors to suggest a specific annual incidence for GDM, it is important to remember that the new criteria and the suggested relative risk reductions were derived from an untreated population. They were not derived from comparing the new criteria to any other existing methods of diagnosis. While the change may be important for uniformity in diagnosis and may result in clinically important outcomes in individuals previously not diagnosed with GDM, it is also important to assess whether any improvements are seen across large populations and, if so, whether they justify any increase in costs-of-care.

We aimed to estimate the impact of this change in a large tertiary maternity hospital by examining an entire cohort of pregnant women immediately before and immediately after the new criteria were adopted. Specifically, we wished to examine the increase in annual incidence of GDM, assign an appropriate cost-of-care to the high-risk model employed for GDM and compare this to any hospital-wide change in the HAPO outcomes upon which the new criteria are based.

Patients and Methods

As the new criteria for diagnosing GDM were introduced in our hospital in mid 2015, we selected 2014 as the last full calendar year of diagnosis under 1991/1998 ADIPS criteria^{4,5} and 2016 as the first full year of diagnosis under the new IADPSG criteria.² All women having care and delivering within the hospital were included for analysis, with exclusion limited

1
2
3 only to pre-existing diabetes (i.e. those who did not undergo screening for GDM) and
4 multiple pregnancy (an exclusion criterion in the HAPO trial). Women in Australia have
5 universal screening for GDM between 24 and 28 weeks.
6

7
8 Clinical care during the periods of study was divided into three groups: those without GDM,
9 GDM managed with dietary measures, and GDM requiring insulin. For occasions of clinical
10 review, such as antenatal clinic consultations, group class and phone-call consultations, and
11 pregnancy day care admissions, cost was estimated from “average occasion of service”
12 figures for the relevant health professional, as collected by the institutional Business
13 Performance Reporting Unit. The pharmacy schedule was consulted for the costs of
14 consumables and medications. The Medicare Benefits Schedule was considered the most
15 reproducible and valid estimation for the cost of ultrasound services. All costs were
16 estimated in figures from the end of 2016, thus negating the need to adjust 2014 figures for
17 consumer price index (CPI) or other potential inflationary changes.
18

19
20 Women diagnosed with GDM receive a three-hour group class with a diabetes educator,
21 dietician and physiotherapist. In addition, most have a follow-up one-on-one session with a
22 dietician, phone consultations with diabetes educators, two extra antenatal clinics,
23 assessment by consultant obstetricians rather than by midwives or junior medical staff, and
24 a growth ultrasound. They also require a glucometer and testing strips.
25

26
27 If dietary measures fail to control blood glucose levels (BGLs) at acceptable levels, they also
28 require insulin, a one-on-one session with a diabetes educator, an extra antenatal clinic,
29 often a second growth scan and sometimes fetal heart rate monitoring via cardiotocography
30 (CTG).
31

32
33 Demographic data were collected for each group, including age, body mass index (BMI), pre-
34 existing polycystic ovarian syndrome (PCOS), smoking, parity and previous caesarean
35 section (LUSCS).
36

37
38 Primary outcomes were those upon which the new criteria were based, namely caesarean
39 section rates, hypertensive disorder of pregnancy, birthweight greater than the 90th
40 percentile, pre-term birth less than 37 weeks.²
41

42
43 Additional maternal outcomes were induction of labour, instrumental birth, third degree
44 tear and post-partum haemorrhage. Additional fetal outcomes were greater than the 95th
45 percentile, less than the 10th percentile, admission to special care nursery (SCN) or neonatal
46 intensive care (NICU), estimated gestational age, pre-term birth less than 34 weeks,
47 respiratory distress, jaundice requiring phototherapy, hypoglycaemia, stillbirth, neonatal
48 death, and Apgar score less than 7 at 5 minutes. Birth trauma was initially included as an
49 outcome but subsequently removed due to a change in coding practices midway through
50 the study period which artificially lowered overall recorded rates.
51

52
53 Neonatal birthweights were plotted by percentile as described by the latest Australian birth
54 charts.¹² Neonatal hypoglycaemia was defined as any ward-measured BGL less than 2.6
55 mmol/L.
56
57
58
59

1
2
3 Maternal and neonatal outcomes were examined for the entire hospital cohort (to examine
4 the change as a public health policy) and for just women diagnosed with GDM in 2014
5 (before the change) compared to those in 2016 (after the change).
6

7
8 Data were collected prospectively by the institutional Quality and Safety Unit from the
9 Maternity Care Information System ("MCIS", GE Healthcare, Little Chalfont, UK) and
10 collated in MS Excel spreadsheets (Microsoft, Redmond, USA). Data were analysed after
11 selecting the demographics and outcomes of interest. Maternal and neonatal
12 characteristics were compared using descriptive statistics. Discrete variables are reported in
13 the tables as total numbers with percentage in parentheses and continuous variables are
14 reported as the mean with 95% confidence intervals in parentheses. For univariate analyses,
15 discrete variables were analysed using Fisher's exact test or Pearson's chi-squared test and
16 continuous variables using Student's t-test. Multivariate analysis with logistic regression was
17 planned for any outcome which met statistical and clinical significance and had documented
18 risk factors other than GDM. P-values are reported in the final column of all tables with less
19 than 0.05 considered statistically significant and highlighted in bold. Statistical analysis was
20 performed using STATA 9.2 (StataCorp, Texas, USA).
21
22

23
24 The study was approved as an anonymised audit by the Institutional Research and Ethics
25 Committee with identifying information removed before analysis.
26

27 *Patient and Public Involvement*

28
29 This was an anonymised retrospective audit, thus patients and the public were not required
30 to be directly involved in recruitment or conduct of the study. Indeed, emphasis was given
31 toward assessing the implications of this public health policy on a patient cohort as a whole
32 rather than subgroup or individual outcomes.
33
34

35 **Results**

36 *Demographics and Health Outcomes*

37
38 In 2014, there were 7010 pregnant women of whom 416 were diagnosed with GDM
39 (incidence 5.93%) and in 2016, there were 7488 pregnant women of whom 774 were
40 diagnosed with GDM (incidence 10.3%). The demographics of the two cohorts are shown in
41 Table 2.
42
43

44
45 (Table 2 goes about here).
46

47
48 Although the second cohort was statistically significantly older, this was only by a mean of
49 four months. The diagnosis of PCOS was higher but overall rates were low and possibly
50 under-reported. These two findings were statistically significant but unlikely to be clinically
51 relevant. The relative increase of 73.7% in the annual incidence of GDM is most likely
52 attributable to the change in diagnosis rather than to any changed demographic factors.
53

54
55 The maternal outcomes for the entire cohort are shown in Table 3 and the fetal outcomes in
56 Table 4, with the HAPO/IADPSG outcomes highlighted in bold.
57

58 (Tables 3 and 4 go about here).
59

1
2
3
4 Following the introduction of the new GDM criteria, there has not been a hospital-wide
5 decrease in the main outcomes reported in the sub-analysis of the HAPO trial, most
6 particularly in birthweight >90th percentile for gestation, caesarean section, hypertensive
7 disorder of pregnancy or pre-term birth <37 weeks. However, there has been a hospital-
8 wide decrease in neonatal death and birthweight greater than the 95th percentile in the
9 fetal outcomes and an increase in induction of labour and instrumental birth in the maternal
10 outcomes. The decrease in neonatal death rates was unexplained, almost always occurs at
11 the extreme of prematurity and the absolute difference was low at 0.2%. The change most
12 likely attributable to tightening GDM diagnoses is a small reduction in very large babies.
13
14

15 The maternal and fetal outcomes for the women with GDM are shown in Tables 5 and 6
16 respectively. There was a reduction in the annual incidence of third degree tears from 5.29%
17 to 2.58% in the mothers with GDM. There was also a reduction in the incidence of neonatal
18 hypoglycaemia (from 9.62% to 5.94%) and admissions to special care nursery (from 12.5% to
19 7.75%).
20
21

22 (Tables 5 and 6 go about here)
23
24

25 *Costs of care*

26
27 The average antenatal care package for women without GDM costs \$923 and for the 15%
28 that require post-dates care this is \$1742 (when extra clinics, and CTG and amniotic fluid
29 monitoring are required). The care package for women with GDM who do not need insulin is
30 \$2026 and for those that do need insulin is \$2534 (or \$3826 if CTG monitoring from 36
31 weeks is undertaken: on audit during the study period, this occurred in 50% of patients).
32
33

34 In 2014, 210 women with GDM were controlled with dietary measures and 206 required
35 insulin. The costs of care for GDM was calculated as follows:
36

37 GDM diet controlled: $210 \times \$2026 = \$425\ 460$

38 GDM insulin controlled: $0.5 \times 206 \times \$2534 + 0.5 \times 206 \times \$3826 = \$655\ 080$

39 **Total = \$1 080 540**
40
41

42 In 2016, 413 women with GDM were controlled with dietary measures and 361 required
43 insulin. The costs of care for GDM was calculated as follows:
44

45 GDM diet controlled: $413 \times \$2026 = \$836\ 738$

46 GDM insulin controlled: $0.5 \times 361 \times \$2534 + 0.5 \times 361 \times \$3826 = \$1\ 147\ 980$

47 **Total = \$1 984 718**
48
49

50 The gross cost increase for care of women with GDM was thus \$904 178. The net cost
51 increase can be determined by attributing the cost of standard care to the excess diagnoses
52 of GDM. If we round the incidence of GDM in 2014 up to 6% and use this with the total
53 number of deliveries in 2016 ($n=7420$), the approximate number of women diagnosed with
54 GDM if the criteria did not change would have been: $0.06 \times 7420 = 445$. The approximate
55 excess number of cases of GDM is the total in 2016 ($n = 774$) minus this figure ($n = 445$)
56 which is: $774 - 445 = 329$. We can then apply this number to routine care (bearing in
57 mind 15% of those undergoing routine care require post-dates monitoring) as follows:
58
59

$$0.85 \times 329 \times \$923 + 0.15 \times 329 \times \$1742 = \$344\,085$$

The net cost increase is then the gross cost increase minus this figure:

$$\$904\,178 - \$344\,085 = \$560\,093$$

The hospital has thus spent a gross of **\$904 178** or a net of **\$560 093** caring for women with GDM because of the change in criteria.

Discussion

The HAPO trial³ was a landmark study for several reasons, namely its sheer size (over 25 000 pregnant women), its robust statistical methods, and its aim to unify disparate international views about the significance of GDM and the best way to diagnose it. The IADPSG sub-analysis² used important clinical outcomes in identifying a “best-fit” for cut-off values within the 75-gram glucose tolerance test (GTT) to diagnose GDM: most are routinely measured in clinical care (with the exception of cord C-peptide and fetal fat distribution). The resulting recommendation was for a 75-gram GTT for all women (regardless of baseline risk) with levels of greater than 5.1 mmol/L at fasting, 10 mmol/L at one-hour and 8.5 mmol/L at two-hours considered diagnostic.

Despite a WHO statement endorsing the new criteria,¹³ there has been a failure of international acceptance to screen for GDM in this way. The National Institute of Clinical Excellence which guides care in the United Kingdom is perhaps the most striking example, recommending only screening those patients with risk factors and using levels of greater than or equal to 5.6 mmol/L at fasting and 7.8 mmol/L at two-hours.⁹ A sophisticated economic evaluation found this approach to be superior in their population¹⁴, and an earlier economic evaluation found that it was not currently cost-effective to routinely identify pregnant women for hyperglycaemia¹⁵. This latter also suggested further research into longer term health-outcomes of women and babies affected by GDM and more cost-effective ways of treating GDM, a sentiment reiterated by the findings of our manuscript.

Economic evaluations in American populations have also tended to favour existing screening criteria^{16,17,18}, albeit with less robust methodology and with different existing screening methods to both the UK and Australia. The latest Cochrane review concluded that there is insufficient evidence to prefer any particular screening method for GDM over another.¹⁹

The new criteria were a major change to established practice in Australia. The abolition of the non-fasting glucose challenge test (GCT) and the introduction of the one-hour BGL on the GTT were both new. The fasting BGL was tightened from greater than or equal to 5.5 mmol/L to 5.1 mmol/L and the two-hour level eased from greater than or equal to 8.0 mmol/L to 8.5 mmol/L. Some studies have tried to examine outcomes in patients who may have been diagnosed with GDM under the new system but not under the old.^{20,21,22} Generally, they have reported groups at higher risk of adverse outcome (particularly caesarean section and large babies) who may have been previously underdiagnosed, but such an approach is flawed because of the abolition of the glucose challenge test and the introduction of the previously untested one-hour BGL. It thus is not possible to retrospectively examine the outcomes of those who may have had a false negative on the GCT or those who may have only tested positive on the new one-hour level.

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4 A separate approach, one adopted by this study, is to quantify any overall changes in clinical
5 outcomes and attribute a cost to the increased burden of care and a saving to any potential
6 outcome improvements.
7

8
9 The strengths of this study include using a single, large, tertiary centre with a uniform urban
10 catchment area and relatively stable demographics over the study period. The numbers
11 were large with over 7000 births per year in each cohort, and the costs of care were
12 quantifiable by an established institutional Business Performance Reporting Unit. Outcomes
13 were readily identified from existing data management systems and were usually
14 categorical (often binary) and not requiring extensive further investigation or statistical
15 analysis. The weaknesses of the study are those always inherent within retrospective data,
16 including the potential for treatment or ascertainment bias. However, as the outcomes of
17 the entire cohort (rather than just those diagnosed with GDM were analysed) this was likely
18 to be minimised. The latter point is important as the aim of the study was to estimate a
19 public health impact overall, as a result of a public health policy change.
20
21

22 We demonstrated a relative increased incidence of GDM of 74%, but we were unable to
23 demonstrate any statistically significant improvements in major outcomes across the
24 hospital as a whole. There was possibly a small improvement in the incidence of very large
25 babies (greater than the 95th percentile) but the absolute changes were small (0.7%) and
26 there was no change in babies greater than the 90th percentile. An apparent improvement
27 in birth trauma was due to a change in coding practices (and removed as an outcome), and
28 an improvement in the neonatal death rate was unexplained but very low in absolute terms
29 (0.2%). This latter tended to be confined to babies of extreme prematurity born well before
30 routine screening for GDM.
31
32

33
34 It is reasonable to hypothesise that, with such minimal overall hospital-wide changes, that it
35 is simply a lower-risk cohort being now diagnosed with GDM. This is somewhat, but not
36 completely, borne out by analysing the same outcomes in women with GDM before and
37 after the change. While major outcomes such as caesarean section rates, hypertensive
38 disorders, pre-term birth and macrosomia have not changed, there has been a reduction in
39 third degree tears and a substantial decrease in the number of babies diagnosed with
40 hypoglycaemia and admitted to SCN. This is suggestive of an increase in diagnoses
41 represented by women on the milder end of the spectrum of GDM.
42
43

44 We have also demonstrated an increase in gross costs of over A\$900 000 and in net costs of
45 over A\$500 000 per annum. This is primarily due to employing a “high-risk” model of care to
46 all women with GDM.
47
48

49 While the new criteria are laudable in their efforts at uniformity of diagnosis and adverse
50 outcome avoidance, and possibly have improved clinical outcomes in sub-groups of women
51 previously not diagnosed with GDM, there is lack of quality evidence supporting their
52 superiority over other systems of diagnosis. Thus, further research is needed in three main
53 areas. Firstly, it would be desirable to have prospective (and ideally randomised controlled
54 trial) evidence examining the impact of this system of diagnosis over others employed
55 around the world. Secondly, long-term outcomes of the women with GDM and their
56 children may uncover health benefits not accounted for in immediate analyses like those
57 presented in this study, for instance with improvements in childhood obesity rates. There
58
59

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3 may indeed be economic benefits that can be compared with the initial increase in costs of
4 care but appropriate budgetary measures to ensure the initial hospitals of care are
5 adequately reimbursed are essential. Finally, it is important to investigate more economic
6 ways of antenatally managing women with GDM particularly in the lower risk group, for
7 example those easily controlled with simple dietary measures or the increasing use of
8 metformin in those currently being prescribed insulin.
9

10 **Conclusion**

11
12
13 The annual incidence of GDM has immediately and markedly increased due to the change in
14 diagnostic criteria with a substantial increase in cost of care and with no overall
15 improvement in immediate clinical outcomes. Most particularly, macrosomia rates (>90th%),
16 caesarean section rates and pre-term birth less than 37 weeks remain unchanged. We
17 suggest that these results tell a cautionary tale about the routine adoption of even
18 internationally endorsed clinical guidelines which have not been validated by rigorous
19 randomized studies. In the present case, countries like the UK which chose not to adopt the
20 new criteria for diagnosing GDM may have saved considerable resources without short-term
21 clinical detriment. On the other hand, countries like Australia which adopted these new
22 criteria in good faith have incurred considerable extra costs without proven commensurate
23 clinical improvement. Further validation of long-term outcomes such as childhood obesity
24 rates are important to assist with the justification of adopting the new criteria and lower
25 risk models-of-care would make the economic case more robust.
26
27
28
29

30 **Declaration of Interests**

31
32
33 There were no conflicts of interest with regards to any of the three authors.
34

35 **Contributor and guarantor information**

36 The corresponding author (TC) was responsible for the study design, literature review,
37 collection and analysis of data, interpretation of clinical findings, writing of the manuscript
38 and decision for submission. TC is responsible for the overall content and acts as guarantor.
39 SB supervised the project and contributed to all of the above in a consulting role. AP
40 contributed to planning and executing appropriate statistical analysis and with
41 interpretation of the data. All authors contributed to the final manuscript review and final
42 submission.
43
44

45 **Data Sharing Statement**

46
47
48 There are no unpublished data from the study.
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60

Role of the funding source

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Transparency Declaration

The corresponding author (TC) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted.

Tables

Table 1 1991/1998 ADIPS versus 2014 IADPSG Criteria for diagnosing GDM

| | 1991/1998 ADIPS | | 2014 IADPSG | | 2015 NICE | |
|------------------------|---|---|---|--|---|--|
| | Type of test | Positive criteria | Type of test | Positive criteria | Type of test | Positive criteria |
| Screening test | 50g non-fasting glucose challenge test or 75g non-fasting glucose challenge test | ≥ 7.8mmol/L ≥ 8.0mmol/L | Nil | N/A | Clinical risk assessment | Any one of five clinical risk factors ⁹ |
| Diagnostic test | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.5mmol/L 2 hour ≥ 8.0mmol/L | 75g, 2-hour fasting glucose tolerance test (three levels) | Fasting ≥ 5.1mmol/L 1 hour ≥ 10mmol/L 2 hour ≥ 8.5mmol/L | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.6mmol/L 2 hour ≥ 7.8mmol/L |

Table 2 Demographics of the 2014 and 2016 cohorts

| | 2014 | 2016 | p-value |
|--------------------------|--------------------|--------------------|---------------|
| Total Deliveries | 7010 | 7488 | n/a |
| Age (yr) | 30.9 (30.8 – 31.0) | 31.2 (31.1 – 31.3) | 0.0016 |
| BMI (kg.m ²) | 24.8 (24.7 – 24.9) | 24.7 (24.6 – 24.8) | 0.28 |
| PCOS | 110 (1.57%) | 151 (2.02%) | 0.043 |
| Smoking | 326 (4.65%) | 303 (4.05%) | 0.075 |
| Parity ≥ 1 | 3228 (46.1%) | 3365 (44.9%) | 0.18 |
| Previous LUSCS | 960 (13.7%) | 1027 (13.7%) | 0.45 |

Table 3 Overall Maternal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------|--------------|--------------|-------------|
| Hypertensive disorder | 332 (4.74%) | 361 (4.82%) | 0.81 |
| Induction of labour | 2407 (34.3%) | 2725 (36.4%) | 0.01 |
| Overall LUSCS rate | 1963 (28.0%) | 2070 (27.6%) | 0.63 |
| Emergency LUSCS rate | 1088 (15.5%) | 1076 (14.3%) | 0.05 |
| Instrumental birth | 1316 (18.8%) | 1513 (20.2%) | 0.03 |
| Third degree tear | 217 (3.1%) | 197 (2.6%) | 0.09 |
| PPH | 1685 (24.0%) | 1765 (23.6%) | 0.51 |

Table 4 Overall Fetal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------------|--------------------|--------------------|-------------|
| EGA | 38.6 (38.6 – 38.7) | 38.6 (38.5 – 38.6) | 0.18 |
| Stillbirth | 36 (0.51%) | 40 (0.53%) | 0.86 |
| NND | 29 (0.41%) | 16 (0.21%) | 0.03 |
| Hypoglycaemia | 154 (2.20%) | 170 (2.27%) | 0.77 |
| Respiratory distress | 140 (2.00%) | 170 (2.27%) | 0.26 |
| Jaundice requiring phototherapy | 112 (1.60%) | 135 (1.80%) | 0.34 |
| Apgar < 7 at 5 min | 280 (3.99%) | 286 (3.82%) | 0.59 |
| Birth < 37 weeks | 645 (9.20%) | 671 (8.96%) | 0.62 |
| Birth < 34 weeks | 292 (4.17%) | 325 (4.34%) | 0.61 |
| Shoulder dystocia | 102 (1.46%) | 131 (1.75%) | 0.16 |
| Admission to NICU | 320 (4.56%) | 366 (4.89%) | 0.36 |
| Admission to SCN | 534 (7.62%) | 537 (7.17%) | 0.31 |
| Birthweight (g) | 3289 (3274 – 3304) | 3275 (3271 – 3293) | 0.21 |
| Birthweight > 95% | 300 (4.31%) | 269 (3.61%) | 0.03 |
| Birthweight > 90% | 577 (8.28%) | 586 (7.86%) | 0.36 |
| Birthweight < 10% | 570 (8.18%) | 616 (8.27%) | 0.85 |
| | | | |

Table 5 Maternal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|-----------------------|-------------|-------------|----------------|
| Total | 416 | 774 | N/A |
| Hypertensive disorder | 20 (4.80%) | 35 (4.52%) | 0.85 |
| Induction of labour | 204 (49.0%) | 379 (49.0%) | 0.98 |
| Overall LUSCS rate | 162 (38.9%) | 289 (37.3%) | 0.59 |
| Emergency LUSCS rate | 71 (17.1%) | 121 (15.6%) | 0.52 |
| Instrumental birth | 83 (20.0%) | 134 (17.3%) | 0.26 |
| Third degree tear | 22 (5.29%) | 20 (2.58%) | 0.016 |
| PPH | 121 (29.1%) | 205 (26.5%) | 0.34 |

Table 6 Fetal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|---------------------------------|--------------------|--------------------|----------------|
| EGA | 37.8 (37.6 – 38.1) | 38.0 (37.9 – 38.2) | 0.13 |
| Stillbirth | 5 (1.20%) | 3 (0.39%) | 0.10 |
| NND | 0.00% | 1 (0.13%) | N/A |
| Hypoglycaemia | 40 (9.62%) | 46 (5.94%) | 0.02 |
| Respiratory distress | 11 (2.64%) | 12 (1.55%) | 0.19 |
| Jaundice requiring phototherapy | 9 (2.16%) | 12 (1.55) | 0.44 |
| Apgar < 7 at 5 mins | 19 (4.57%) | 26 (3.36%) | 0.30 |
| Birth < 37 weeks | 51 (12.3%) | 83 (10.7%) | 0.42 |
| Birth < 34 weeks | 25 (6.01%) | 30 (3.88%) | 0.10 |
| Shoulder dystocia | 7 (1.68%) | 5 (0.65%) | 0.09 |
| Admission to NICU | 27 (6.49%) | 39 (5.04%) | 0.30 |
| Admission to SCN | 52 (12.5%) | 60 (7.75%) | 0.007 |
| Birthweight | 3151 (3089 – 3213) | 3207 (3167 – 3248) | 0.12 |
| Birthweight > 95% | 27 (6.49%) | 35 (4.52%) | 0.15 |
| Birthweight > 90% | 48 (11.5%) | 74 (9.56%) | 0.28 |
| Birthweight < 10% | 38 (9.13%) | 60 (7.75%) | 0.41 |

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Yes (page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found Yes (page 2) |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Yes (page 3) |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Yes (page 3) |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Yes (page 3-4) |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes (page 3) |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Yes – no exclusion criteria (page 3) (b) For matched studies, give matching criteria and number of exposed and unexposed N/A |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes (page 4) |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes (page 4) |
| Bias | 9 | Describe any efforts to address potential sources of bias Yes (page 4 and 7) |
| Study size | 10 | Explain how the study size was arrived at Yes (entire cohort, page 4) |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes (page 4) |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Yes, confounding not particularly relevant as outcomes were examined across whole cohorts (page 4-5) (b) Describe any methods used to examine subgroups and interactions N/A (no subgroups) (c) Explain how missing data were addressed N/A (nil was missing) (d) If applicable, explain how loss to follow-up was addressed N/A (nil lost to follow-up) (e) Describe any sensitivity analyses N/A (not required) |
| Results | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Yes (page 5) (b) Give reasons for non-participation at each stage N/A (retrospective analysis with no possibility for non-participation) (c) Consider use of a flow diagram Not used |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Yes (page 5 and Table 2) (b) Indicate number of participants with missing data for each variable of interest Nil missing |

| | | |
|--------------------------|-----|---|
| | | (c) Summarise follow-up time (eg, average and total amount) N/A (examined at time of delivery – no long-term follow up) |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time Yes (page 5-6) |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Yes (page 5-6, tables 3-4) (b) Report category boundaries when continuous variables were categorized N/A (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives Yes (page 6-7) |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes (page 7) |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes (page 7-8) |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results Yes (page 8) |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Yes (page 8) |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

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

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| | |

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Manuscripts

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

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Abstract

Objective

To identify effects on health outcomes from implementing new criteria diagnosing gestational diabetes (GDM) and to analyse costs-of-care associated with this change.

Design

Quasi-experimental study comparing data from the calendar year before (2014) and after (2016) the change.

Setting

Single, tertiary level, university-affiliated, maternity hospital.

Participants

All women giving birth in the hospital, excluding those with pre-existing diabetes or multiple pregnancy.

Main outcome measures

Primary outcomes were caesarean section, birthweight > 90th percentile for gestation, hypertensive disorder of pregnancy and pre-term birth less than 37 weeks. A number of secondary outcomes reported to be associated with GDM were also analysed were also analysed.

Care packages were derived for those without GDM, diet-controlled GDM and GDM requiring insulin. The Institutional Business Reporting Unit data for average occasions of service, pharmacy schedule for the costs of consumables and medications, and Medicare Benefits Schedule ultrasound services were used for costing each package. All costs were estimated in figures from the end of 2016 negating the need to adjust for Consumer Price Index increases.

Results

There was an increase in annual incidence of GDM of 74% without overall improvements in primary health outcomes. This incurred a gross cost increase of \$904 178 and net of \$560 093. Babies of women with GDM had lower rates of neonatal hypoglycaemia and special care nursery admissions after the change, suggesting a milder spectrum of disease.

Conclusion

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

Strengths and limitations of this study

- Australia is one of the only major Western countries to introduce universal screening for GDM by new International Association of Diabetes in Pregnancy Study Group criteria and is uniquely poised to assess concerns about increased annual incidence and costs of care compared to any potential improvement in health outcomes.
- Concerns about an increase in diagnoses and “over-medicalisation” of women who erstwhile would have been considered normal have given many countries reason for caution in adopting the new criteria. Our findings may assist in decision making regarding this public health policy, and may highlight the need for longer-term follow-up of women with GDM and their babies treated under this system.
- As with any large retrospective audit, there are potential methodological flaws in data analysis, including unexplained selection bias and confounding. We have assessed the implication of adopting this criteria on a large entire cohort (not a specific subgroup) in an attempt to assess outcomes and costs as a surrogate for public health policy “en masse”, however it is noted that no social determinants of health were defined or analysed as part of the study.
- A major problem with assessing changes in diagnostic criteria in GDM lies within being unable to retrospectively identify those who were potentially underdiagnosed under older systems and assess their outcomes. We have thus assessed the impact on a large tertiary hospital as a whole and quantified the costs associated with the increased burden or care.

Introduction

Diagnostic criteria for gestational diabetes (GDM) in Australia changed following a 2014 consensus statement by the Australian Diabetes in Pregnancy Society (ADIPS)¹ ratifying support for the International Association of Diabetes in Pregnancy Study Group's recommendations² (see table 1). These, in turn, used data from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study,³ which was a large, prospective, observational study examining the influence of increasing blood glucose levels on a fasting glucose tolerance test on eventual adverse pregnancy outcome.

Previously, diagnostic criteria for GDM in Australia were derived from an earlier ADIPS consensus statement published in 1991⁴ and re-endorsed in 1998⁵ (see Table 1). It was based on the observed distributions of blood glucose levels tested in pregnant women at various maternity centres. These older criteria had been widely utilised for the last two decades in many Australian maternity centres including our own.

(Table 1 goes about here).

Since the introduction of the new criteria, concerns have focussed on the anticipated increase in annual incidence of GDM that these new criteria will cause and the resultant implications for workload. Early estimates of an annual increase of 35%⁶ were followed by later data suggesting an almost doubling in some populations.⁷ Although many major maternity centres in Australia have adopted the new criteria, a 2016 survey found variable adoption in Australia⁸ and the criteria have not yet found international acceptance despite WHO endorsement.^{9, 10, 11}

While it was never the intention of the HAPO authors to suggest a specific annual incidence for GDM, it is important to remember that the new criteria and the suggested relative risk reductions were derived from an untreated population. They were not derived from comparing the new criteria to any other existing methods of diagnosis. While the change may be important for uniformity in diagnosis and may result in clinically important outcomes in individuals previously not diagnosed with GDM, it is also important to assess whether any improvements are seen across large populations and, if so, whether they justify any increase in costs-of-care.

We aimed to estimate the impact of this change in a large tertiary maternity hospital by examining an entire cohort of pregnant women immediately before and immediately after the new criteria were adopted. Specifically, we wished to examine the increase in annual incidence of GDM, assign an appropriate cost-of-care to the high-risk model employed for GDM and compare this to any hospital-wide change in the HAPO outcomes upon which the new criteria are based.

Patients and Methods

As the new criteria for diagnosing GDM were introduced in our hospital in mid 2015, we selected 2014 as the last full calendar year of diagnosis under 1991/1998 ADIPS criteria^{4,5} and 2016 as the first full year of diagnosis under the new IADPSG criteria.² All women having care and delivering within the hospital were included for analysis, with exclusion limited

1
2
3 only to pre-existing diabetes (i.e. those who did not undergo screening for GDM) and
4 multiple pregnancy (an exclusion criterion in the HAPO trial). Women in Australia have
5 universal screening for GDM between 24 and 28 weeks.
6

7
8 Clinical care during the periods of study was divided into three groups: those without GDM,
9 GDM managed with dietary measures, and GDM requiring insulin. For occasions of clinical
10 review, such as antenatal clinic consultations, group class and phone-call consultations, and
11 pregnancy day care admissions, cost was estimated from “average occasion of service”
12 figures for the relevant health professional, as collected by the institutional Business
13 Performance Reporting Unit. The pharmacy schedule was consulted for the costs of
14 consumables and medications. The Medicare Benefits Schedule was considered the most
15 reproducible and valid estimation for the cost of ultrasound services. All costs were
16 estimated in figures from the end of 2016, thus negating the need to adjust 2014 figures for
17 consumer price index (CPI) or other potential inflationary changes.
18

19
20 Women diagnosed with GDM receive a three-hour group class with a diabetes educator,
21 dietician and physiotherapist. In addition, most have a follow-up one-on-one session with a
22 dietician, phone consultations with diabetes educators, two extra antenatal clinics,
23 assessment by consultant obstetricians rather than by midwives or junior medical staff, and
24 a growth ultrasound. They also require a glucometer and testing strips.
25

26
27 If dietary measures fail to control blood glucose levels (BGLs) at acceptable levels, they also
28 require insulin, a one-on-one session with a diabetes educator, an extra antenatal clinic,
29 often a second growth scan and sometimes fetal heart rate monitoring via cardiotocography
30 (CTG).
31

32
33 Demographic data were collected for each group, including age, body mass index (BMI), pre-
34 existing polycystic ovarian syndrome (PCOS), smoking, parity and previous caesarean
35 section (LUSCS).
36

37
38 Primary outcomes were those upon which the new criteria were based, namely caesarean
39 section rates, hypertensive disorder of pregnancy, birthweight greater than the 90th
40 percentile, pre-term birth less than 37 weeks.²
41

42
43 Additional maternal outcomes were induction of labour, instrumental birth, third degree
44 tear and post-partum haemorrhage. Additional fetal outcomes were greater than the 95th
45 percentile, less than the 10th percentile, admission to special care nursery (SCN) or neonatal
46 intensive care (NICU), estimated gestational age, pre-term birth less than 34 weeks,
47 respiratory distress, jaundice requiring phototherapy, hypoglycaemia, stillbirth, neonatal
48 death, and Apgar score less than 7 at 5 minutes. Birth trauma was initially included as an
49 outcome but subsequently removed due to a change in coding practices midway through
50 the study period which artificially lowered overall recorded rates.
51

52
53 Neonatal birthweights were plotted by percentile as described by the latest Australian birth
54 charts.¹² Neonatal hypoglycaemia was defined as any ward-measured BGL less than 2.6
55 mmol/L.
56
57
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59

1
2
3 Maternal and neonatal outcomes were examined for the entire hospital cohort (to examine
4 the change as a public health policy) and for just women diagnosed with GDM in 2014
5 (before the change) compared to those in 2016 (after the change).
6

7
8 Data were collected prospectively by the institutional Quality and Safety Unit from the
9 Maternity Care Information System ("MCIS", GE Healthcare, Little Chalfont, UK) and
10 collated in MS Excel spreadsheets (Microsoft, Redmond, USA). Data were analysed after
11 selecting the demographics and outcomes of interest. Maternal and neonatal
12 characteristics were compared using descriptive statistics. Discrete variables are reported in
13 the tables as total numbers with percentage in parentheses and continuous variables are
14 reported as the mean with 95% confidence intervals in parentheses. For univariate analyses,
15 discrete variables were analysed using Fisher's exact test or Pearson's chi-squared test and
16 continuous variables using Student's t-test. Multivariate analysis with logistic regression was
17 planned for any outcome which met statistical and clinical significance and had documented
18 risk factors other than GDM. P-values are reported in the final column of all tables with less
19 than 0.05 considered statistically significant and highlighted in bold. Statistical analysis was
20 performed using STATA 9.2 (StataCorp, Texas, USA).
21
22

23
24 The study was approved as an anonymised audit by the Institutional Research and Ethics
25 Committee with identifying information removed before analysis.
26

27 *Patient and Public Involvement*

28
29 This was an anonymised retrospective audit, thus patients and the public were not required
30 to be directly involved in recruitment or conduct of the study. Indeed, emphasis was given
31 toward assessing the implications of this public health policy on a patient cohort as a whole
32 rather than subgroup or individual outcomes.
33
34

35 **Results**

36 *Demographics and Health Outcomes*

37
38 In 2014, there were 7010 pregnant women of whom 416 were diagnosed with GDM
39 (incidence 5.93%) and in 2016, there were 7488 pregnant women of whom 774 were
40 diagnosed with GDM (incidence 10.3%). The demographics of the two cohorts are shown in
41 Table 2.
42
43

44
45 (Table 2 goes about here).
46

47
48 Although the second cohort was statistically significantly older, this was only by a mean of
49 four months. The diagnosis of PCOS was higher but overall rates were low and possibly
50 under-reported. These two findings were statistically significant but unlikely to be clinically
51 relevant. The relative increase of 73.7% in the annual incidence of GDM is most likely
52 attributable to the change in diagnosis rather than to any changed demographic factors.
53

54
55 The maternal outcomes for the entire cohort are shown in Table 3 and the fetal outcomes in
56 Table 4, with the HAPO/IADPSG outcomes highlighted in bold.
57

58 (Tables 3 and 4 go about here).
59

Following the introduction of the new GDM criteria, there has not appeared to be a hospital-wide decrease in the main outcomes reported in the sub-analysis of the HAPO trial, most particularly in birthweight >90th percentile for gestation, caesarean section, hypertensive disorder of pregnancy or pre-term birth <37 weeks. However, there has been a hospital-wide decrease in neonatal death and birthweight greater than the 95th percentile in the fetal outcomes and an increase in induction of labour and instrumental birth in the maternal outcomes. The decrease in neonatal death rates was unexplained, almost always occurs at the extreme of prematurity and the absolute difference was low at 0.2%. The change most likely attributable to tightening GDM diagnoses is a small reduction in very large babies.

The maternal and fetal outcomes for the women with GDM are shown in Tables 5 and 6 respectively. There was a reduction in the annual incidence of third degree tears from 5.29% to 2.58% in the mothers with GDM. There was also a reduction in the incidence of neonatal hypoglycaemia (from 9.62% to 5.94%) and admissions to special care nursery (from 12.5% to 7.75%).

(Tables 5 and 6 go about here)

Costs of care

The average antenatal care package for women without GDM costs \$923 and for the 15% that require post-dates care this is \$1742 (when extra clinics, and CTG and amniotic fluid monitoring are required). The care package for women with GDM who do not need insulin is \$2026 and for those that do need insulin is \$2534 (or \$3826 if CTG monitoring from 36 weeks is undertaken: on audit during the study period, this occurred in 50% of patients).

In 2014, 210 women with GDM were controlled with dietary measures and 206 required insulin. The costs of care for GDM was calculated as follows:

GDM diet controlled: $210 \times \$2026 = \$425\ 460$

GDM insulin controlled: $0.5 \times 206 \times \$2534 + 0.5 \times 206 \times \$3826 = \$655\ 080$

Total = \$1 080 540

In 2016, 413 women with GDM were controlled with dietary measures and 361 required insulin. The costs of care for GDM was calculated as follows:

GDM diet controlled: $413 \times \$2026 = \$836\ 738$

GDM insulin controlled: $0.5 \times 361 \times \$2534 + 0.5 \times 361 \times \$3826 = \$1\ 147\ 980$

Total = \$1 984 718

The gross cost increase for care of women with GDM was thus \$904 178. The net cost increase can be determined by attributing the cost of standard care to the excess diagnoses of GDM. If we round the incidence of GDM in 2014 up to 6% and use this with the total number of deliveries in 2016 (n=7420), the approximate number of women diagnosed with GDM if the criteria did not change would have been: $0.06 \times 7420 = 445$. The approximate excess number of cases of GDM is the total in 2016 (n = 774) minus this figure (n = 445)

1
2
3 which is: $774 - 445 = 329$. We can then apply this number to routine care (bearing in
4 mind 15% of those undergoing routine care require post-dates monitoring) as follows:

$$0.85 \times 329 \times \$923 + 0.15 \times 329 \times \$1742 = \$344\,085$$

5
6
7 The net cost, which greater represents the change in antenatal resources, is then the gross
8 cost increase minus this figure:

$$\$904\,178 - \$344\,085 = \$560\,093$$

9
10
11 The hospital has thus spent approximately **\$560 093** caring for women with GDM because
12 of the change in criteria.

13 14 15 16 Discussion

17
18
19 HAPO³ was a landmark study for several reasons, namely its sheer size (over 25 000
20 pregnant women), its robust statistical methods, and its aim to unify disparate international
21 views about the significance of GDM and the best way to diagnose it. The IADPSG sub-
22 analysis² used important clinical outcomes in identifying a “best-fit” for cut-off values within
23 the 75-gram glucose tolerance test (GTT) to diagnose GDM: most are routinely measured in
24 clinical care (with the exception of cord C-peptide and fetal fat distribution). The resulting
25 recommendation was for a 75-gram GTT for all women (regardless of baseline risk) with
26 levels of greater than 5.1 mmol/L at fasting, 10 mmol/L at one-hour and 8.5 mmol/L at two-
27 hours considered diagnostic.

28
29
30 Despite a WHO statement endorsing the new criteria,¹³ there has been a failure of
31 international acceptance to screen for GDM in this way. The National Institute of Clinical
32 Excellence which guides care in the United Kingdom is perhaps the most striking example,
33 recommending only screening those patients with risk factors and using levels of greater
34 than or equal to 5.6 mmol/L at fasting and 7.8 mmol/L at two-hours.⁹ A sophisticated
35 economic evaluation found this approach to be superior in their population¹⁴, and an
36 earlier economic evaluation found that it was not currently cost-effective to routinely
37 identify pregnant women for hyperglycaemia¹⁵. This latter also suggested further research
38 into longer term health-outcomes of women and babies affected by GDM and more cost-
39 effective ways of treating GDM, a sentiment reiterated by the findings of our manuscript.

40
41
42 Economic evaluations in American populations have also tended to favour existing screening
43 criteria^{16,17,18}, albeit with less robust methodology and with different existing screening
44 methods to both the UK and Australia. The latest Cochrane review concluded that there is
45 insufficient evidence to prefer any particular screening method for GDM over another.¹⁹

46
47
48 The new criteria were a major change to established practice in Australia. The abolition of
49 the non-fasting glucose challenge test (GCT) and the introduction of the one-hour BGL on
50 the GTT were both new. The fasting BGL was tightened from greater than or equal to 5.5
51 mmol/L to 5.1 mmol/L and the two-hour level eased from greater than or equal to 8.0
52 mmol/L to 8.5 mmol/L. Some studies have tried to examine outcomes in patients who may
53 have been diagnosed with GDM under the new system but not under the old.^{20,21,22}

54
55 Generally, they have reported groups at higher risk of adverse outcome (particularly
56 caesarean section and large babies) who may have been previously underdiagnosed, but
57 such an approach is flawed because of the abolition of the glucose challenge test and the
58

1
2
3 introduction of the previously untested one-hour BGL. It thus is not possible to
4 retrospectively examine the outcomes of those who may have had a false negative on the
5 GCT or those who may have only tested positive on the new one-hour level.
6

7 A separate approach, one adopted by this study, is to quantify any overall changes in clinical
8 outcomes and attribute a cost to the increased burden of care and a saving to any potential
9 outcome improvements.
10

11
12 The strengths of this study include using a single, large, tertiary centre with a uniform urban
13 catchment area and relatively stable demographics over the study period. The numbers
14 were large with over 7000 births per year in each cohort, and the costs of care were
15 quantifiable by an established institutional Business Performance Reporting Unit. Outcomes
16 were readily identified from existing data management systems and were usually
17 categorical (often binary) and not requiring extensive further investigation or statistical
18 analysis. The weaknesses of the study are those always inherent within retrospective data,
19 including the potential for treatment or ascertainment bias. However, as the outcomes of
20 the entire cohort (rather than just those diagnosed with GDM were analysed) this was likely
21 to be minimised. The latter point is important as the aim of the study was to estimate a
22 public health impact overall, as a result of a public health policy change.
23
24

25
26 We demonstrated a relative increased incidence of GDM of 74%, but we were unable to
27 demonstrate any statistically significant improvements in major outcomes across the
28 hospital as a whole. There was possibly a small improvement in the incidence of very large
29 babies (greater than the 95th percentile) but the absolute changes were small (0.7%) and
30 there was no change in babies greater than the 90th percentile. An apparent improvement
31 in birth trauma was due to a change in coding practices (and removed as an outcome), and
32 an improvement in the neonatal death rate was unexplained but very low in absolute terms
33 (0.2%). This latter tended to be confined to babies of extreme prematurity born well before
34 routine screening for GDM. It is important to note that these findings, in a retrospective
35 analysis, may be subject to unrecognised selection bias or confounding and form part of a
36 larger debate into the care for women with GDM.
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39
40 It may be reasonable to hypothesise that, with such minimal overall hospital-wide changes,
41 that it is simply a lower-risk cohort being now diagnosed with GDM. This is somewhat, but
42 not completely, borne out by analysing the same outcomes in women with GDM before and
43 after the change. While major outcomes such as caesarean section rates, hypertensive
44 disorders, pre-term birth and macrosomia have seemingly not changed, there has been a
45 reduction in third degree tears and a substantial decrease in the number of babies
46 diagnosed with hypoglycaemia and admitted to SCN. This is suggestive of an increase in
47 diagnoses represented by women on the milder end of the spectrum of GDM.
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49

50 We have also demonstrated an increase in gross costs of over A\$900 000 and in net costs of
51 over A\$500 000 per annum. This is primarily due to employing a "high-risk" model of care to
52 all women with GDM. While these costs are seemingly not redeemed in the short term by
53 marked improved outcomes, better health care is not always defined by more economic
54 models and there may be unquantified health outcomes demonstrable in longer term
55 analysis of women with GDM and their babies treated under this system.
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3 While the new criteria are laudable in their efforts at uniformity of diagnosis and adverse
4 outcome avoidance, and possibly have improved clinical outcomes in sub-groups of women
5 previously not diagnosed with GDM, there is lack of quality evidence supporting their
6 superiority over other systems of diagnosis. Thus, further research is needed in three main
7 areas. Firstly, it would be desirable to have prospective (and ideally randomised controlled
8 trial) evidence examining the impact of this system of diagnosis over others employed
9 around the world. Secondly, long-term outcomes of the women with GDM and their
10 children may uncover health benefits not accounted for in immediate analyses like those
11 presented in this study, for instance with improvements in childhood obesity rates. There
12 may indeed be economic benefits that can be compared with the initial increase in costs of
13 care but appropriate budgetary measures to ensure the initial hospitals of care are
14 adequately reimbursed are essential. Finally, it is important to investigate more economic
15 ways of antenatally managing women with GDM particularly in the lower risk group, for
16 example those easily controlled with simple dietary measures or the increasing use of
17 metformin in those currently being prescribed insulin.
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19
20

21 **Conclusion**

22
23 The annual incidence of GDM has immediately and markedly increased due to the change in
24 diagnostic criteria with a substantial increase in cost of care and with seemingly no clear
25 changes in immediate clinical outcomes. Most particularly, macrosomia rates (>90th%),
26 caesarean section rates and pre-term birth less than 37 weeks remain unchanged. We
27 suggest that these results add weight to the need for longer-term data before confirming
28 that HAPO/IADPSG criteria are superior to other systems of diagnosis. Such data would need
29 to be derived from cohorts undergoing universal routine screening with these criteria, and
30 quantifiable health benefits compared against increases in immediate costs of care such as
31 we report here.
32
33
34

35 **Declaration of Interests**

36
37 There were no conflicts of interest with regards to any of the three authors.
38
39

40 **Contributor and guarantor information**

41 The corresponding author (TC) was responsible for the study design, literature review,
42 collection and analysis of data, interpretation of clinical findings, writing of the manuscript
43 and decision for submission. TC is responsible for the overall content and acts as guarantor.
44 SB supervised the project and contributed to all of the above in a consulting role. AP
45 contributed to planning and executing appropriate statistical analysis and with
46 interpretation of the data. All authors contributed to the final manuscript review and final
47 submission.
48
49

50 **Data Sharing Statement**

51
52 There are no unpublished data from the study.
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Role of the funding source

The Royal Australian and New Zealand College of Obstetrics and Gynaecology, who awarded the Luke Proposch Perinatal Research Scholarship to the corresponding author to financially support this research, had no role in the study design, data collection, analysis and interpretation, writing of the report or decision to submit for publication. The corresponding author had full access to the data in the study and final responsibility for the decision to submit for publication.

Transparency Declaration

The corresponding author (TC) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted.

Tables

Table 1 1991/1998 ADIPS versus 2014 IADPSG Criteria for diagnosing GDM

| | 1991/1998 ADIPS | | 2014 IADPSG | | 2015 NICE | |
|------------------------|---|---|---|--|---|--|
| | Type of test | Positive criteria | Type of test | Positive criteria | Type of test | Positive criteria |
| Screening test | 50g non-fasting glucose challenge test or 75g non-fasting glucose challenge test | ≥ 7.8mmol/L ≥ 8.0mmol/L | Nil | N/A | Clinical risk assessment | Any one of five clinical risk factors ⁹ |
| Diagnostic test | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.5mmol/L 2 hour ≥ 8.0mmol/L | 75g, 2-hour fasting glucose tolerance test (three levels) | Fasting ≥ 5.1mmol/L 1 hour ≥ 10mmol/L 2 hour ≥ 8.5mmol/L | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.6mmol/L 2 hour ≥ 7.8mmol/L |

Table 2 Demographics of the 2014 and 2016 cohorts

| | 2014 | 2016 | p-value |
|--------------------------|--------------------|--------------------|---------------|
| Total Deliveries | 7010 | 7488 | n/a |
| Age (yr) | 30.9 (30.8 – 31.0) | 31.2 (31.1 – 31.3) | 0.0016 |
| BMI (kg.m ²) | 24.8 (24.7 – 24.9) | 24.7 (24.6 – 24.8) | 0.28 |
| PCOS | 110 (1.57%) | 151 (2.02%) | 0.043 |
| Smoking | 326 (4.65%) | 303 (4.05%) | 0.075 |
| Parity ≥ 1 | 3228 (46.1%) | 3365 (44.9%) | 0.18 |
| Previous LUSCS | 960 (13.7%) | 1027 (13.7%) | 0.45 |

Table 3 Overall Maternal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------|--------------|--------------|-------------|
| Hypertensive disorder | 332 (4.74%) | 361 (4.82%) | 0.81 |
| Induction of labour | 2407 (34.3%) | 2725 (36.4%) | 0.01 |
| Overall LUSCS rate | 1963 (28.0%) | 2070 (27.6%) | 0.63 |
| Emergency LUSCS rate | 1088 (15.5%) | 1076 (14.3%) | 0.05 |
| Instrumental birth | 1316 (18.8%) | 1513 (20.2%) | 0.03 |
| Third degree tear | 217 (3.1%) | 197 (2.6%) | 0.09 |
| PPH | 1685 (24.0%) | 1765 (23.6%) | 0.51 |

Table 4 Overall Fetal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------------|--------------------|--------------------|-------------|
| EGA | 38.6 (38.6 – 38.7) | 38.6 (38.5 – 38.6) | 0.18 |
| Stillbirth | 36 (0.51%) | 40 (0.53%) | 0.86 |
| NND | 29 (0.41%) | 16 (0.21%) | 0.03 |
| Hypoglycaemia | 154 (2.20%) | 170 (2.27%) | 0.77 |
| Respiratory distress | 140 (2.00%) | 170 (2.27%) | 0.26 |
| Jaundice requiring phototherapy | 112 (1.60%) | 135 (1.80%) | 0.34 |
| Apgar < 7 at 5 min | 280 (3.99%) | 286 (3.82%) | 0.59 |
| Birth < 37 weeks | 645 (9.20%) | 671 (8.96%) | 0.62 |
| Birth < 34 weeks | 292 (4.17%) | 325 (4.34%) | 0.61 |
| Shoulder dystocia | 102 (1.46%) | 131 (1.75%) | 0.16 |
| Admission to NICU | 320 (4.56%) | 366 (4.89%) | 0.36 |
| Admission to SCN | 534 (7.62%) | 537 (7.17%) | 0.31 |
| Birthweight (g) | 3289 (3274 – 3304) | 3275 (3271 – 3293) | 0.21 |
| Birthweight > 95% | 300 (4.31%) | 269 (3.61%) | 0.03 |
| Birthweight > 90% | 577 (8.28%) | 586 (7.86%) | 0.36 |
| Birthweight < 10% | 570 (8.18%) | 616 (8.27%) | 0.85 |
| | | | |

Table 5 Maternal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|-----------------------|-------------|-------------|----------------|
| Total | 416 | 774 | N/A |
| Hypertensive disorder | 20 (4.80%) | 35 (4.52%) | 0.85 |
| Induction of labour | 204 (49.0%) | 379 (49.0%) | 0.98 |
| Overall LUSCS rate | 162 (38.9%) | 289 (37.3%) | 0.59 |
| Emergency LUSCS rate | 71 (17.1%) | 121 (15.6%) | 0.52 |
| Instrumental birth | 83 (20.0%) | 134 (17.3%) | 0.26 |
| Third degree tear | 22 (5.29%) | 20 (2.58%) | 0.016 |
| PPH | 121 (29.1%) | 205 (26.5%) | 0.34 |

Table 6 Fetal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|---------------------------------|--------------------|--------------------|----------------|
| EGA | 37.8 (37.6 – 38.1) | 38.0 (37.9 – 38.2) | 0.13 |
| Stillbirth | 5 (1.20%) | 3 (0.39%) | 0.10 |
| NND | 0.00% | 1 (0.13%) | N/A |
| Hypoglycaemia | 40 (9.62%) | 46 (5.94%) | 0.02 |
| Respiratory distress | 11 (2.64%) | 12 (1.55%) | 0.19 |
| Jaundice requiring phototherapy | 9 (2.16%) | 12 (1.55) | 0.44 |
| Apgar < 7 at 5 mins | 19 (4.57%) | 26 (3.36%) | 0.30 |
| Birth < 37 weeks | 51 (12.3%) | 83 (10.7%) | 0.42 |
| Birth < 34 weeks | 25 (6.01%) | 30 (3.88%) | 0.10 |
| Shoulder dystocia | 7 (1.68%) | 5 (0.65%) | 0.09 |
| Admission to NICU | 27 (6.49%) | 39 (5.04%) | 0.30 |
| Admission to SCN | 52 (12.5%) | 60 (7.75%) | 0.007 |
| Birthweight | 3151 (3089 – 3213) | 3207 (3167 – 3248) | 0.12 |
| Birthweight > 95% | 27 (6.49%) | 35 (4.52%) | 0.15 |
| Birthweight > 90% | 48 (11.5%) | 74 (9.56%) | 0.28 |
| Birthweight < 10% | 38 (9.13%) | 60 (7.75%) | 0.41 |

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Yes (page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found Yes (page 2) |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Yes (page 3) |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Yes (page 3) |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Yes (page 3-4) |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes (page 3) |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Yes – no exclusion criteria (page 3) (b) For matched studies, give matching criteria and number of exposed and unexposed N/A |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes (page 4) |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes (page 4) |
| Bias | 9 | Describe any efforts to address potential sources of bias Yes (page 4 and 7) |
| Study size | 10 | Explain how the study size was arrived at Yes (entire cohort, page 4) |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes (page 4) |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Yes, confounding not particularly relevant as outcomes were examined across whole cohorts (page 4-5) (b) Describe any methods used to examine subgroups and interactions N/A (no subgroups) (c) Explain how missing data were addressed N/A (nil was missing) (d) If applicable, explain how loss to follow-up was addressed N/A (nil lost to follow-up) (e) Describe any sensitivity analyses N/A (not required) |
| Results | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Yes (page 5) (b) Give reasons for non-participation at each stage N/A (retrospective analysis with no possibility for non-participation) (c) Consider use of a flow diagram Not used |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Yes (page 5 and Table 2) (b) Indicate number of participants with missing data for each variable of interest Nil missing |

| | | |
|--------------------------|-----|---|
| | | (c) Summarise follow-up time (eg, average and total amount) N/A (examined at time of delivery – no long-term follow up) |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time Yes (page 5-6) |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Yes (page 5-6, tables 3-4) (b) Report category boundaries when continuous variables were categorized N/A (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives Yes (page 6-7) |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes (page 7) |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes (page 7-8) |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results Yes (page 8) |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Yes (page 8) |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

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

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| | |

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Manuscripts

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

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For peer review only

Abstract

Objective

To identify effects on health outcomes from implementing new criteria diagnosing gestational diabetes (GDM) and to analyse costs-of-care associated with this change.

Design

Quasi-experimental study comparing data from the calendar year before (2014) and after (2016) the change.

Setting

Single, tertiary level, university-affiliated, maternity hospital.

Participants

All women giving birth in the hospital, excluding those with pre-existing diabetes or multiple pregnancy.

Main outcome measures

Primary outcomes were caesarean section, birthweight > 90th percentile for gestation, hypertensive disorder of pregnancy and pre-term birth less than 37 weeks. A number of secondary outcomes reported to be associated with GDM were also analysed were also analysed.

Care packages were derived for those without GDM, diet-controlled GDM and GDM requiring insulin. The Institutional Business Reporting Unit data for average occasions of service, pharmacy schedule for the costs of consumables and medications, and Medicare Benefits Schedule ultrasound services were used for costing each package. All costs were estimated in figures from the end of 2016 negating the need to adjust for Consumer Price Index increases.

Results

There was an increase in annual incidence of GDM of 74% without overall improvements in primary health outcomes. This incurred a net cost increase of \$560 093. Babies of women with GDM had lower rates of neonatal hypoglycaemia and special care nursery admissions after the change, suggesting a milder spectrum of disease.

Conclusion

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

Strengths and limitations of this study

- Australia is one of the only major Western countries to introduce universal screening for GDM by new International Association of Diabetes in Pregnancy Study Group criteria and is uniquely poised to assess concerns about increased annual incidence and costs of care compared to any potential improvement in health outcomes.
- Concerns about an increase in diagnoses and “over-medicalisation” of women who erstwhile would have been considered normal have given many countries reason for caution in adopting the new criteria. Our findings may assist in decision making regarding public health policy, albeit with findings applicable to clinical policy change within a single large centre. It may also highlight the need for longer-term follow-up of women with GDM and their babies treated under this system.
- As with any large retrospective audit, there are potential methodological flaws in data analysis, including unrecognised selection bias and confounding. We have assessed the implication of adopting this criteria on a large entire cohort (not a specific subgroup) in an attempt to assess outcomes and costs as a surrogate for public health policy “en masse”, however it is noted that no social determinants of health were defined or analysed as part of the study. Findings should be interpreted with respect to clinical policy change within a single centre and add to the debate about adopting this policy on a wider public scale.
- A major problem with assessing changes in diagnostic criteria in GDM lies within being unable to retrospectively identify those who were potentially underdiagnosed under older systems and assess their outcomes. We have thus assessed the impact on a large tertiary hospital as a whole and quantified the costs associated with the increased burden or care.

Introduction

Diagnostic criteria for gestational diabetes (GDM) in Australia changed following a 2014 consensus statement by the Australian Diabetes in Pregnancy Society (ADIPS)¹ ratifying support for the International Association of Diabetes in Pregnancy Study Group's recommendations² (see table 1). These, in turn, used data from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study,³ which was a large, prospective, observational study examining the influence of increasing blood glucose levels on a fasting glucose tolerance test on eventual adverse pregnancy outcome.

Previously, diagnostic criteria for GDM in Australia were derived from an earlier ADIPS consensus statement published in 1991⁴ and re-endorsed in 1998⁵ (see Table 1). It was based on the observed distributions of blood glucose levels tested in pregnant women at various maternity centres. These older criteria had been widely utilised for the last two decades in many Australian maternity centres including our own.

(Table 1 goes about here).

Since the introduction of the new criteria, concerns have focussed on the anticipated increase in annual incidence of GDM that these new criteria will cause and the resultant implications for workload. Early estimates of an annual increase of 35%⁶ were followed by later data suggesting an almost doubling in some populations.⁷ Although many major maternity centres in Australia have adopted the new criteria, a 2016 survey found variable adoption in Australia⁸ and the criteria have not yet found international acceptance despite WHO endorsement.^{9, 10, 11}

While it was never the intention of the HAPO authors to suggest a specific annual incidence for GDM, it is important to remember that the new criteria and the suggested relative risk reductions were derived from an untreated population. They were not derived from comparing the new criteria to any other existing methods of diagnosis. While the change may be important for uniformity in diagnosis and may result in clinically important outcomes in individuals previously not diagnosed with GDM, it is also important to assess whether any improvements are seen across large populations and, if so, whether they justify any increase in costs-of-care.

We aimed to estimate the impact of this change in a large tertiary maternity hospital by examining two pre-screening cohorts of pregnant women immediately before and immediately after the new criteria were adopted. Specifically, we wished to examine the increase in annual incidence of GDM, assign an appropriate cost-of-care to the high-risk model employed for GDM and compare this to any hospital-wide change in the HAPO outcomes upon which the new criteria are based.

Patients and Methods

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3 As the new criteria for diagnosing GDM were introduced in our hospital in mid 2015, we
4 selected 2014 as the last full calendar year of diagnosis under 1991/1998 ADIPS criteria^{4,5} and
5 2016 as the first full year of diagnosis under the new IADPSG criteria.² All women having care
6 and delivering within the hospital were included for analysis, with exclusion limited only to pre-
7 existing diabetes (i.e. those who did not undergo screening for GDM) and multiple pregnancy
8 (an exclusion criterion in the HAPO trial). Women in Australia have universal screening for GDM
9 between 24 and 28 weeks.
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13 Clinical care during the periods of study was divided into three groups: those without GDM,
14 GDM managed with dietary measures, and GDM requiring insulin. For occasions of clinical
15 review, such as antenatal clinic consultations, group class and phone-call consultations, and
16 pregnancy day care admissions, cost was estimated from “average occasion of service” figures
17 for the relevant health professional, as collected by the institutional Business Performance
18 Reporting Unit. The pharmacy schedule was consulted for the costs of consumables and
19 medications. The Medicare Benefits Schedule was considered the most reproducible and valid
20 estimation for the cost of ultrasound services. All costs were estimated in figures from the end
21 of 2016, thus negating the need to adjust 2014 figures for consumer price index (CPI) or other
22 potential inflationary changes.
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27 Costs of in-patient care in our hospital consist mainly of “bed-days” for the mother (increased
28 mainly by caesarean section compared to vaginal birth) or admissions to special care nursery or
29 neonatal intensive care for the infant. In-patient costs were to be assessed if any differences
30 were found in these two outcomes. The only difference in care for women with GDM compared
31 to those without was a self-collected bi-daily BGL for one to two days which was not deemed a
32 significant enough cost for quantification.
33
34

35
36 Women diagnosed with GDM receive a three-hour group class with a diabetes educator,
37 dietician and physiotherapist. In addition, most have a follow-up one-on-one session with a
38 dietician, phone consultations with diabetes educators, two extra antenatal clinics, assessment
39 by consultant obstetricians rather than by midwives or junior medical staff, and a growth
40 ultrasound. They also require a glucometer and testing strips.
41

42
43 If dietary measures fail to control blood glucose levels (BGLs) at acceptable levels, they also
44 require insulin, a one-on-one session with a diabetes educator, an extra antenatal clinic, often a
45 second growth scan and sometimes fetal heart rate monitoring via cardiotocography (CTG).
46

47
48 Demographic data were collected for each group, including age, body mass index (BMI), pre-
49 existing polycystic ovarian syndrome (PCOS), smoking, parity and previous caesarean section
50 (LUSCS).
51

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53 Primary outcomes were those upon which the new criteria were based, namely caesarean
54 section rates, hypertensive disorder of pregnancy, birthweight greater than the 90th percentile,
55 pre-term birth less than 37 weeks.²
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3 Additional maternal outcomes were induction of labour, instrumental birth, third degree tear
4 and post-partum haemorrhage. Additional fetal outcomes were greater than the 95th
5 percentile, less than the 10th percentile, admission to special care nursery (SCN) or neonatal
6 intensive care (NICU), estimated gestational age, pre-term birth less than 34 weeks, respiratory
7 distress, jaundice requiring phototherapy, hypoglycaemia, stillbirth, neonatal death, and Apgar
8 score less than 7 at 5 minutes. Birth trauma was initially included as an outcome but
9 subsequently removed due to a change in coding practices midway through the study period
10 which artificially lowered overall recorded rates.
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13
14 Neonatal birthweights were plotted by percentile as described by the latest Australian birth
15 charts.¹² Neonatal hypoglycaemia was defined as any ward-measured BGL less than 2.6
16 mmol/L.
17
18

19 Maternal and neonatal outcomes were examined for the entire hospital cohort (to examine the
20 change as a hospital health policy) and for just women diagnosed with GDM in 2014 (before the
21 change) compared to those in 2016 (after the change).
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23

24 Data were collected prospectively by the institutional Quality and Safety Unit from the
25 Maternity Care Information System ("MCIS", GE Healthcare, Little Chalfont, UK) and collated in
26 MS Excel spreadsheets (Microsoft, Redmond, USA). Data were analysed after selecting the
27 demographics and outcomes of interest. Maternal and neonatal characteristics were compared
28 using descriptive statistics. Discrete variables are reported in the tables as total numbers with
29 percentage in parentheses and continuous variables are reported as the mean with 95%
30 confidence intervals in parentheses. For univariate analyses, discrete variables were analysed
31 using Fisher's exact test or Pearson's chi-squared test and continuous variables using Student's
32 t-test. Multivariate analysis with logistic regression was planned for any outcome which met
33 statistical and clinical significance and had documented risk factors other than GDM. P-values
34 are reported in the final column of all tables with less than 0.05 considered statistically
35 significant and highlighted in bold. Statistical analysis was performed using STATA 9.2
36 (StataCorp, Texas, USA).
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40

41 The study was approved as an anonymised audit by the Institutional Research and Ethics
42 Committee with identifying information removed before analysis.
43
44

45 *Patient and Public Involvement*

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47 This was an anonymised retrospective audit, thus patients and the public were not required to
48 be directly involved in recruitment or conduct of the study. Indeed, emphasis was given toward
49 assessing the implications of this clinical health policy on a patient cohort as a whole rather
50 than subgroup or individual outcomes.
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53 **Results**

54

55 *Demographics and Health Outcomes*

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3 In 2014, there were 7010 pregnant women of whom 416 were diagnosed with GDM (incidence
4 5.93%) and in 2016, there were 7488 pregnant women of whom 774 were diagnosed with GDM
5 (incidence 10.3%). The demographics of the two cohorts are shown in Table 2.
6
7

8 (Table 2 goes about here).
9

10 Although the second cohort was statistically significantly older, this was only by a mean of four
11 months. The diagnosis of PCOS was higher but overall rates were low and possibly under-
12 reported. These two findings were statistically significant but unlikely to be clinically relevant.
13 The relative increase of 73.7% in the annual incidence of GDM is most likely attributable to the
14 change in diagnosis rather than to any changed demographic factors.
15
16

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18 The maternal outcomes for the entire cohort are shown in Table 3 and the fetal outcomes in
19 Table 4, with the HAPO/IADPSG outcomes highlighted in bold.
20

21 (Tables 3 and 4 go about here).
22
23

24 Following the introduction of the new GDM criteria, there has not appeared to be a hospital-
25 wide decrease in the main outcomes reported in the sub-analysis of the HAPO study, most
26 particularly in birthweight >90th percentile for gestation, caesarean section, hypertensive
27 disorder of pregnancy or pre-term birth <37 weeks. However, there has been a hospital-wide
28 decrease in neonatal death and birthweight greater than the 95th percentile in the fetal
29 outcomes and an increase in induction of labour and instrumental birth in the maternal
30 outcomes. The decrease in neonatal death rates was unexplained, almost always occurs at the
31 extreme of prematurity and the absolute difference was low at 0.2%. The change most likely
32 attributable to tightening GDM diagnoses is a small reduction in very large babies.
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36 The maternal and fetal outcomes for the women with GDM are shown in Tables 5 and 6
37 respectively. There was a reduction in the annual incidence of third degree tears from 5.29% to
38 2.58% in the mothers with GDM. There was also a reduction in the incidence of neonatal
39 hypoglycaemia (from 9.62% to 5.94%) and admissions to special care nursery (from 12.5% to
40 7.75%).
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42

43 (Tables 5 and 6 go about here)
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46 *Costs of care* 47

48 The average antenatal care package for women without GDM costs \$923 and for the 15% that
49 require post-dates care this is \$1742 (when extra clinics, and CTG and amniotic fluid monitoring
50 are required). The care package for women with GDM who do not need insulin is \$2026 and for
51 those that do need insulin is \$2534 (or \$3826 if CTG monitoring from 36 weeks is undertaken:
52 on audit during the study period, this occurred in 50% of patients).
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56 In 2014, 210 women with GDM were controlled with dietary measures and 206 required insulin.
57 The costs of care for GDM was calculated as follows:
58
59

GDM diet controlled: $210 \times \$2026 = \$425\ 460$

GDM insulin controlled: $0.5 \times 206 \times \$2534 + 0.5 \times 206 \times \$3826 = \$655\ 080$

Total = \$1 080 540

In 2016, 413 women with GDM were controlled with dietary measures and 361 required insulin. The costs of care for GDM was calculated as follows:

GDM diet controlled: $413 \times \$2026 = \$836\ 738$

GDM insulin controlled: $0.5 \times 361 \times \$2534 + 0.5 \times 361 \times \$3826 = \$1\ 147\ 980$

Total = \$1 984 718

The gross cost increase for care of women with GDM was thus \$904 178. The net cost increase can be determined by attributing the cost of standard care to the excess diagnoses of GDM. If we round the incidence of GDM in 2014 up to 6% and use this with the total number of deliveries in 2016 ($n=7420$), the approximate number of women diagnosed with GDM if the criteria did not change would have been: $0.06 \times 7420 = 445$. The approximate excess number of cases of GDM is the total in 2016 ($n = 774$) minus this figure ($n = 445$) which is: $774 - 445 = 329$. We can then apply this number to routine care (bearing in mind 15% of those undergoing routine care require post-dates monitoring) as follows:

$$0.85 \times 329 \times \$923 + 0.15 \times 329 \times \$1742 = \$344\ 085$$

The net cost, which represents the change in antenatal resources, is then the gross cost increase minus this figure:

$$\$904\ 178 - \$344\ 085 = \$560\ 093$$

The hospital has thus spent approximately **\$560 093** caring for women with GDM because of the change in criteria.

Discussion

HAPO³ was a landmark study for several reasons, namely its sheer size (over 25 000 pregnant women), its robust statistical methods, and its aim to unify disparate international views about the significance of GDM and the best way to diagnose it. The IADPSG sub-analysis² used important clinical outcomes in identifying a “best-fit” for cut-off values within the 75-gram glucose tolerance test (GTT) to diagnose GDM: most are routinely measured in clinical care (with the exception of cord C-peptide and fetal fat distribution). The resulting recommendation was for a 75-gram GTT for all women (regardless of baseline risk) with levels of greater than 5.1 mmol/L at fasting, 10 mmol/L at one-hour and 8.5 mmol/L at two-hours considered diagnostic.

Despite a WHO statement endorsing the new criteria,¹³ there has been a failure of international acceptance to screen for GDM in this way. The National Institute of Clinical Excellence which guides care in the United Kingdom is perhaps the most striking example, recommending only screening those patients with risk factors and using levels of greater than or equal to 5.6

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3 mmol/L at fasting and 7.8 mmol/L at two-hours.⁹ A sophisticated economic evaluation found
4 this approach to be superior in their population¹⁴, and an earlier economic evaluation found
5 that it was not currently cost-effective to routinely identify pregnant women for
6 hyperglycaemia¹⁵. This latter also suggested further research into longer term health-outcomes
7 of women and babies affected by GDM and more cost-effective ways of treating GDM, a
8 sentiment reiterated by the findings of our manuscript.
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12 Economic evaluations in American populations have also tended to favour existing screening
13 criteria^{16,17,18}, albeit with less robust methodology and with different existing screening
14 methods to both the UK and Australia. The latest Cochrane review concluded that there is
15 insufficient evidence to prefer any particular screening method for GDM over another.¹⁹
16
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18 The new criteria were a major change to established practice in Australia. The abolition of the
19 non-fasting glucose challenge test (GCT) and the introduction of the one-hour BGL on the GTT
20 were both new. The fasting BGL was tightened from greater than or equal to 5.5 mmol/L to 5.1
21 mmol/L and the two-hour level eased from greater than or equal to 8.0 mmol/L to 8.5 mmol/L.
22 Some studies have tried to examine outcomes in patients who may have been diagnosed with
23 GDM under the new system but not under the old.^{20,21,22} Generally, they have reported groups
24 at higher risk of adverse outcome (particularly caesarean section and large babies) who may
25 have been previously underdiagnosed, but such an approach is flawed because of the abolition
26 of the glucose challenge test and the introduction of the previously untested one-hour BGL. It
27 thus is not possible to retrospectively examine the outcomes of those who may have had a false
28 negative on the GCT or those who may have only tested positive on the new one-hour level.
29 Unfortunately, this is a major inherent weakness in all studies retrospectively examining GDM
30 when screening is changed (rather than modified) and would only be overcome by a large
31 prospective study examining two different systems of diagnosis. This would require at least
32 multi-centre or more likely international collaboration to recruit suitable numbers: a prospect
33 which seems unlikely given the international disagreement over different diagnostic criteria and
34 the immense time and planning a trial with somewhat similar methodology (albeit with two
35 groups for comparison) to the HAPO study would require.
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41 A separate approach, one adopted by this study, is to quantify any overall changes in clinical
42 outcomes and attribute a cost to the increased burden of care and to identify any overall
43 outcome improvements.
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46 The strengths of this study include using a single, large, tertiary centre with a uniform urban
47 catchment area and relatively stable demographics over the study period. The numbers were
48 large with over 7000 births per year in each cohort, and the costs of care were quantifiable by
49 an established institutional Business Performance Reporting Unit. Outcomes were readily
50 identified from existing data management systems and were usually categorical (often binary)
51 and not requiring extensive further investigation or statistical analysis.
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54 The weaknesses of the study are those always inherent within retrospective data, including the
55 potential for treatment or ascertainment bias. Retrospectively comparing two large cohorts
56 with different methodologies for diagnosis will always carry greater uncertainty than usual when
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3 compared with well-designed prospective trials. As it is impossible to determine which of the
4 2014 “screen-negative” cohort would screen-positive under new criteria (and vice-versa), many
5 assumptions about the background demographic being the same must be made. As we
6 examined a large cohort, within a single centre, with strict zoning boundaries which did not
7 change between the two years and with an analysis of all feasibly collected background data,
8 we have attempted to satisfy the assumption of equal demographics but this will always remain
9 an uncertainty.
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13 We demonstrated a relative increased incidence of GDM of 74%, but we were unable to
14 demonstrate any statistically significant improvements in major outcomes across the hospital
15 as a whole. There was possibly a small improvement in the incidence of very large babies
16 (greater than the 95th percentile) but the change was small (0.7%) and there was no change in
17 babies greater than the 90th percentile. An apparent improvement in birth trauma was due to a
18 change in coding practices (and removed as an outcome), and an improvement in the neonatal
19 death rate was unexplained but very low in absolute terms (0.2%). This latter tended to be
20 confined to babies of extreme prematurity born well before routine screening for GDM. It is
21 important to note that these findings, in a retrospective analysis, may be subject to
22 unrecognised selection bias or confounding and form part of a larger debate into the care for
23 women with GDM.
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28 It may be reasonable to hypothesise that, with such minimal overall hospital-wide changes, that
29 it is simply a lower-risk cohort being now diagnosed with GDM. This is somewhat, but not
30 completely, borne out by analysing the same outcomes in women with GDM before and after
31 the change. While major outcomes such as caesarean section rates, hypertensive disorders,
32 pre-term birth and macrosomia have seemingly not changed, there has been a reduction in
33 third degree tears and a substantial decrease in the number of babies diagnosed with
34 hypoglycaemia and admitted to SCN. This is suggestive of an increase in diagnoses represented
35 by women on the milder end of the spectrum of GDM.
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39 We have also demonstrated an increase in net costs of over A\$500 000 per annum. This is
40 primarily due to employing a “high-risk” model of care to all women with GDM. As no overall
41 changes were discovered in mode of delivery or admission to NICU/SCN, in-patient costs were
42 not examined. In smaller cohorts, especially those analysed prospectively, it would be
43 worthwhile to examine patient-level data and directly assign costs of care in both the antenatal
44 and immediate post-partum period. While the overall costs are seemingly not redeemed in the
45 short term by marked improved outcomes, there may be unquantified health outcomes
46 demonstrable in longer term analysis of women with GDM and their babies treated under this
47 system.
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51 While the new criteria are laudable in their efforts at uniformity of diagnosis and adverse
52 outcome avoidance, and possibly have improved clinical outcomes in sub-groups of women
53 previously not diagnosed with GDM, there is lack of quality evidence supporting their
54 superiority over other systems of diagnosis. Thus, further research is needed in three main
55 areas. Firstly, it would be desirable to have prospective (and ideally randomised controlled trial)
56 evidence examining the impact of this system of diagnosis over others employed around the
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3 world. Secondly, long-term outcomes of the women with GDM and their children may uncover
4 health benefits not accounted for in immediate analyses like those presented in this study, for
5 instance with improvements in childhood obesity rates. There may indeed be quantifiable cost
6 savings that can be compared with the initial increase in costs of care but appropriate
7 budgetary measures to ensure the initial hospitals of care are adequately reimbursed are
8 essential. Finally, it is important to investigate more economic ways of antenatally managing
9 women with GDM particularly in the lower risk group, for example those easily controlled with
10 simple dietary measures or the increasing use of metformin in those currently being prescribed
11 insulin.
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15 **Conclusion**

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18 The annual incidence of GDM has immediately and markedly increased due to the change in
19 diagnostic criteria with an increase in cost of care and with seemingly no clear changes in
20 immediate clinical outcomes. Most particularly, macrosomia rates (>90th%), caesarean section
21 rates and pre-term birth less than 37 weeks remain unchanged. We suggest that these results
22 add weight to the need for longer-term data before confirming that HAPO/IADPSG criteria are
23 superior to other systems of diagnosis. Such data would need to be derived from cohorts
24 undergoing universal routine screening with these criteria, and quantifiable health benefits
25 compared against increases in immediate costs of care such as we report here.
26
27
28

29 **Declaration of Interests**

30
31 There were no conflicts of interest with regards to any of the three authors.
32
33

34 **Contributor and guarantor information**

35 The corresponding author (TC) was responsible for the study design, literature review,
36 collection and analysis of data, interpretation of clinical findings, writing of the manuscript and
37 decision for submission. TC is responsible for the overall content and acts as guarantor. SB
38 supervised the project and contributed to all of the above in a consulting role. AP contributed
39 to planning and executing appropriate statistical analysis and with interpretation of the data.
40 All authors contributed to the final manuscript review and final submission.
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44 **Data Sharing Statement**

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46 There are no unpublished data from the study.
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Role of the funding source

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Transparency Declaration

The corresponding author (TC) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted.

Tables

Table 1 1991/1998 ADIPS versus 2014 IADPSG Criteria for diagnosing GDM

| | 1991/1998 ADIPS | | 2014 IADPSG | | 2015 NICE | |
|------------------------|---|---|---|--|---|--|
| | Type of test | Positive criteria | Type of test | Positive criteria | Type of test | Positive criteria |
| Screening test | 50g non-fasting glucose challenge test <i>or</i> 75g non-fasting glucose challenge test | ≥ 7.8mmol/L ≥ 8.0mmol/L | Nil | N/A | Clinical risk assessment | Any one of five clinical risk factors ⁹ |
| Diagnostic test | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.5mmol/L 2 hour ≥ 8.0mmol/L | 75g, 2-hour fasting glucose tolerance test (three levels) | Fasting ≥ 5.1mmol/L 1 hour ≥ 10mmol/L 2 hour ≥ 8.5mmol/L | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting ≥ 5.6mmol/L 2 hour ≥ 7.8mmol/L |

Table 2 Demographics of the 2014 and 2016 cohorts

| | 2014 | 2016 | p-value |
|--------------------------|--------------------|--------------------|---------------|
| Total Deliveries | 7010 | 7488 | n/a |
| Age (yr) | 30.9 (30.8 – 31.0) | 31.2 (31.1 – 31.3) | 0.0016 |
| BMI (kg.m ²) | 24.8 (24.7 – 24.9) | 24.7 (24.6 – 24.8) | 0.28 |
| PCOS | 110 (1.57%) | 151 (2.02%) | 0.043 |
| Smoking | 326 (4.65%) | 303 (4.05%) | 0.075 |
| Parity ≥ 1 | 3228 (46.1%) | 3365 (44.9%) | 0.18 |
| Previous LUSCS | 960 (13.7%) | 1027 (13.7%) | 0.45 |

Table 3 Overall Maternal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------|--------------|--------------|-------------|
| Hypertensive disorder | 332 (4.74%) | 361 (4.82%) | 0.81 |
| Induction of labour | 2407 (34.3%) | 2725 (36.4%) | 0.01 |
| Overall LUSCS rate | 1963 (28.0%) | 2070 (27.6%) | 0.63 |
| Emergency LUSCS rate | 1088 (15.5%) | 1076 (14.3%) | 0.05 |
| Instrumental birth | 1316 (18.8%) | 1513 (20.2%) | 0.03 |
| Third degree tear | 217 (3.1%) | 197 (2.6%) | 0.09 |
| PPH | 1685 (24.0%) | 1765 (23.6%) | 0.51 |

Table 4 Overall Fetal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------------|--------------------|--------------------|-------------|
| EGA | 38.6 (38.6 – 38.7) | 38.6 (38.5 – 38.6) | 0.18 |
| Stillbirth | 36 (0.51%) | 40 (0.53%) | 0.86 |
| NND | 29 (0.41%) | 16 (0.21%) | 0.03 |
| Hypoglycaemia | 154 (2.20%) | 170 (2.27%) | 0.77 |
| Respiratory distress | 140 (2.00%) | 170 (2.27%) | 0.26 |
| Jaundice requiring phototherapy | 112 (1.60%) | 135 (1.80%) | 0.34 |
| Apgar < 7 at 5 min | 280 (3.99%) | 286 (3.82%) | 0.59 |
| Birth < 37 weeks | 645 (9.20%) | 671 (8.96%) | 0.62 |
| Birth < 34 weeks | 292 (4.17%) | 325 (4.34%) | 0.61 |
| Shoulder dystocia | 102 (1.46%) | 131 (1.75%) | 0.16 |
| Admission to NICU | 320 (4.56%) | 366 (4.89%) | 0.36 |
| Admission to SCN | 534 (7.62%) | 537 (7.17%) | 0.31 |
| Birthweight (g) | 3289 (3274 – 3304) | 3275 (3271 – 3293) | 0.21 |
| Birthweight > 95% | 300 (4.31%) | 269 (3.61%) | 0.03 |
| Birthweight > 90% | 577 (8.28%) | 586 (7.86%) | 0.36 |
| Birthweight < 10% | 570 (8.18%) | 616 (8.27%) | 0.85 |

| | | | |
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Table 5 Maternal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|-----------------------|-------------|-------------|--------------|
| Total | 416 | 774 | N/A |
| Hypertensive disorder | 20 (4.80%) | 35 (4.52%) | 0.85 |
| Induction of labour | 204 (49.0%) | 379 (49.0%) | 0.98 |
| Overall LUSCS rate | 162 (38.9%) | 289 (37.3%) | 0.59 |
| Emergency LUSCS rate | 71 (17.1%) | 121 (15.6%) | 0.52 |
| Instrumental birth | 83 (20.0%) | 134 (17.3%) | 0.26 |
| Third degree tear | 22 (5.29%) | 20 (2.58%) | 0.016 |
| PP H | 121 (29.1%) | 205 (26.5%) | 0.34 |

Table 6 Fetal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|---------------------------------|--------------------|--------------------|--------------|
| EGA | 37.8 (37.6 – 38.1) | 38.0 (37.9 – 38.2) | 0.13 |
| Stillbirth | 5 (1.20%) | 3 (0.39%) | 0.10 |
| NND | 0.00% | 1 (0.13%) | N/A |
| Hypoglycaemia | 40 (9.62%) | 46 (5.94%) | 0.02 |
| Respiratory distress | 11 (2.64%) | 12 (1.55%) | 0.19 |
| Jaundice requiring phototherapy | 9 (2.16%) | 12 (1.55) | 0.44 |
| Apgar < 7 at 5 mins | 19 (4.57%) | 26 (3.36%) | 0.30 |
| Birth < 37 weeks | 51 (12.3%) | 83 (10.7%) | 0.42 |
| Birth < 34 weeks | 25 (6.01%) | 30 (3.88%) | 0.10 |
| Shoulder dystocia | 7 (1.68%) | 5 (0.65%) | 0.09 |
| Admission to NICU | 27 (6.49%) | 39 (5.04%) | 0.30 |
| Admission to SCN | 52 (12.5%) | 60 (7.75%) | 0.007 |

| | | | |
|-------------------|--------------------|--------------------|------|
| Birthweight | 3151 (3089 – 3213) | 3207 (3167 – 3248) | 0.12 |
| Birthweight > 95% | 27 (6.49%) | 35 (4.52%) | 0.15 |
| Birthweight > 90% | 48 (11.5%) | 74 (9.56%) | 0.28 |
| Birthweight < 10% | 38 (9.13%) | 60 (7.75%) | 0.41 |

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Yes (page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found Yes (page 2) |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Yes (page 3) |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Yes (page 3) |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Yes (page 3-4) |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes (page 3) |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Yes – no exclusion criteria (page 3) (b) For matched studies, give matching criteria and number of exposed and unexposed N/A |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes (page 4) |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes (page 4) |
| Bias | 9 | Describe any efforts to address potential sources of bias Yes (page 4 and 7) |
| Study size | 10 | Explain how the study size was arrived at Yes (entire cohort, page 4) |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes (page 4) |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Yes, confounding not particularly relevant as outcomes were examined across whole cohorts (page 4-5) (b) Describe any methods used to examine subgroups and interactions N/A (no subgroups) (c) Explain how missing data were addressed N/A (nil was missing) (d) If applicable, explain how loss to follow-up was addressed N/A (nil lost to follow-up) (e) Describe any sensitivity analyses N/A (not required) |
| Results | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Yes (page 5) (b) Give reasons for non-participation at each stage N/A (retrospective analysis with no possibility for non-participation) (c) Consider use of a flow diagram Not used |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Yes (page 5 and Table 2) (b) Indicate number of participants with missing data for each variable of interest Nil missing |

| | | |
|--------------------------|-----|---|
| | | (c) Summarise follow-up time (eg, average and total amount) N/A (examined at time of delivery – no long-term follow up) |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time Yes (page 5-6) |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Yes (page 5-6, tables 3-4) (b) Report category boundaries when continuous variables were categorized N/A (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives Yes (page 6-7) |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes (page 7) |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes (page 7-8) |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results Yes (page 8) |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Yes (page 8) |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

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

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Manuscripts

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

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Abstract

Objective

To identify effects on health outcomes from implementing new criteria diagnosing gestational diabetes (GDM) and to analyse costs-of-care associated with this change.

Design

Quasi-experimental study comparing data from the calendar year before (2014) and after (2016) the change.

Setting

Single, tertiary level, university-affiliated, maternity hospital.

Participants

All women giving birth in the hospital, excluding those with pre-existing diabetes or multiple pregnancy.

Main outcome measures

Primary outcomes were caesarean section, birthweight > 90th percentile for gestation, hypertensive disorder of pregnancy and pre-term birth less than 37 weeks. A number of secondary outcomes reported to be associated with GDM were also analysed were also analysed.

Care packages were derived for those without GDM, diet-controlled GDM and GDM requiring insulin. The Institutional Business Reporting Unit data for average occasions of service, pharmacy schedule for the costs of consumables and medications, and Medicare Benefits Schedule ultrasound services were used for costing each package. All costs were estimated in figures from the end of 2016 negating the need to adjust for Consumer Price Index increases.

Results

There was an increase in annual incidence of GDM of 74% without overall improvements in primary health outcomes. This incurred a net cost increase of \$560 093. Babies of women with GDM had lower rates of neonatal hypoglycaemia and special care nursery admissions after the change, suggesting a milder spectrum of disease.

Conclusion

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

Strengths and limitations of this study

- Australia is one of the only major Western countries to introduce universal screening for GDM by new International Association of Diabetes in Pregnancy Study Group criteria and is uniquely poised to assess concerns about increased annual incidence and costs of care compared to any potential improvement in health outcomes.
- Concerns about an increase in diagnoses and “over-medicalisation” of women who erstwhile would have been considered normal have given many countries reason for caution in adopting the new criteria. Our findings may assist in decision making regarding public health policy, albeit with findings applicable to clinical policy change within a single large centre. It may also highlight the need for longer-term follow-up of women with GDM and their babies treated under this system.
- As with any large retrospective audit, there are potential methodological flaws in data analysis, including unrecognised selection bias and confounding. We have assessed the implication of adopting this criteria on a large entire cohort (not a specific subgroup) in an attempt to assess outcomes and costs as a surrogate for public health policy “en masse”. Findings should be interpreted with respect to clinical policy change within a single centre and add to the debate about adopting this policy on a wider public scale.
- A major problem with assessing changes in diagnostic criteria in GDM lies within being unable to retrospectively identify those who were potentially underdiagnosed under older systems and assess their outcomes. We have thus assessed the impact on a large tertiary hospital as a whole and quantified the costs associated with the increased burden or care.

Introduction

Diagnostic criteria for gestational diabetes (GDM) in Australia changed following a 2014 consensus statement by the Australian Diabetes in Pregnancy Society (ADIPS)¹ ratifying support for the International Association of Diabetes in Pregnancy Study Group's recommendations² (see table 1). These, in turn, used data from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study,³ which was a large, prospective, observational study examining the influence of increasing blood glucose levels on a fasting glucose tolerance test on eventual adverse pregnancy outcome.

Previously, diagnostic criteria for GDM in Australia were derived from an earlier ADIPS consensus statement published in 1991⁴ and re-endorsed in 1998⁵ (see Table 1). It was based on the observed distributions of blood glucose levels tested in pregnant women at various maternity centres. These older criteria had been widely utilised for the last two decades in many Australian maternity centres including our own.

(Table 1 goes about here).

Since the introduction of the new criteria, concerns have focussed on the anticipated increase in annual incidence of GDM that these new criteria will cause and the resultant implications for workload. Early estimates of an annual increase of 35%⁶ were followed by later data suggesting an almost doubling in some populations.⁷ Although many major maternity centres in Australia have adopted the new criteria, a 2016 survey found variable adoption in Australia⁸ and the criteria have not yet found international acceptance despite WHO endorsement.^{9, 10, 11}

While it was never the intention of the HAPO authors to suggest a specific annual incidence for GDM, it is important to remember that the new criteria and the suggested relative risk reductions were derived from an untreated population. They were not derived from comparing the new criteria to any other existing methods of diagnosis. While the change may be important for uniformity in diagnosis and may result in clinically important outcomes in individuals previously not diagnosed with GDM, it is also important to assess whether any improvements are seen across large populations and, if so, whether they justify any increase in costs-of-care.

We aimed to estimate the impact of this change in a large tertiary maternity hospital by examining two pre-screening cohorts of pregnant women immediately before and immediately after the new criteria were adopted. Specifically, we wished to examine the increase in annual incidence of GDM, assign an appropriate cost-of-care to the high-risk model employed for GDM and compare this to any hospital-wide change in the HAPO outcomes upon which the new criteria are based.

Patients and Methods

As the new criteria for diagnosing GDM were introduced in our hospital in mid 2015, we selected 2014 as the last full calendar year of diagnosis under 1991/1998 ADIPS criteria^{4,5} and 2016 as the first full year of diagnosis under the new IADPSG criteria.² All women having care and delivering within the hospital were included for analysis, with exclusion limited

1
2
3 only to pre-existing diabetes (i.e. those who did not undergo screening for GDM) and
4 multiple pregnancy (an exclusion criterion in the HAPO trial). Women in Australia have
5 universal screening for GDM between 24 and 28 weeks.
6
7

8 Clinical care during the periods of study was divided into three groups: those without GDM,
9 GDM managed with dietary measures, and GDM requiring insulin. For occasions of clinical
10 review, such as antenatal clinic consultations, group class and phone-call consultations, and
11 pregnancy day care admissions, cost was estimated from “average occasion of service”
12 figures for the relevant health professional, as collected by the institutional Business
13 Performance Reporting Unit. The pharmacy schedule was consulted for the costs of
14 consumables and medications. The Medicare Benefits Schedule was considered the most
15 reproducible and valid estimation for the cost of ultrasound services. All costs were
16 estimated in figures from the end of 2016, thus negating the need to adjust 2014 figures for
17 consumer price index (CPI) or other potential inflationary changes.
18
19
20

21 Costs of in-patient care in our hospital consist mainly of “bed-days” for the mother
22 (increased mainly by caesarean section compared to vaginal birth) or admissions to special
23 care nursery or neonatal intensive care for the infant. In-patient costs were to be assessed if
24 any differences were found in these two outcomes. The only difference in care for women
25 with GDM compared to those without was a self-collected bi-daily BGL for one to two days
26 which was not deemed a significant enough cost for quantification.
27
28
29

30 Women diagnosed with GDM receive a three-hour group class with a diabetes educator,
31 dietician and physiotherapist. In addition, most have a follow-up one-on-one session with a
32 dietician, phone consultations with diabetes educators, two extra antenatal clinics,
33 assessment by consultant obstetricians rather than by midwives or junior medical staff, and
34 a growth ultrasound. They also require a glucometer and testing strips.
35
36

37 If dietary measures fail to control blood glucose levels (BGLs) at acceptable levels, they also
38 require insulin, a one-on-one session with a diabetes educator, an extra antenatal clinic,
39 often a second growth scan and sometimes fetal heart rate monitoring via cardiotocography
40 (CTG).
41
42

43 Demographic data were collected for each group, including age, body mass index (BMI), pre-
44 existing polycystic ovarian syndrome (PCOS), smoking, parity and previous caesarean
45 section (LUSCS).
46
47

48 Primary outcomes were those upon which the new criteria were based, namely caesarean
49 section rates, hypertensive disorder of pregnancy, birthweight greater than the 90th
50 percentile, pre-term birth less than 37 weeks.²
51
52

53 Additional maternal outcomes were induction of labour, instrumental birth, third degree
54 tear and post-partum haemorrhage. Additional fetal outcomes were greater than the 95th
55 percentile, less than the 10th percentile, admission to special care nursery (SCN) or neonatal
56 intensive care (NICU), estimated gestational age, pre-term birth less than 34 weeks,
57 respiratory distress, jaundice requiring phototherapy, hypoglycaemia, stillbirth, neonatal
58 death, and Apgar score less than 7 at 5 minutes. Birth trauma was initially included as an
59 outcome but subsequently removed due to a change in coding practices midway through
60 the study period which artificially lowered overall recorded rates.

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2
3
4 Neonatal birthweights were plotted by percentile as described by the latest Australian birth
5 charts.¹² Neonatal hypoglycaemia was defined as any ward-measured BGL less than 2.6
6 mmol/L.
7
8

9 Maternal and neonatal outcomes were examined for the entire hospital cohort (to examine
10 the change as a hospital health policy) and for just women diagnosed with GDM in 2014
11 (before the change) compared to those in 2016 (after the change).
12
13

14 Data were collected prospectively by the institutional Quality and Safety Unit from the
15 Maternity Care Information System ("MCIS", GE Healthcare, Little Chalfont, UK) and
16 collated in MS Excel spreadsheets (Microsoft, Redmond, USA). Data were analysed after
17 selecting the demographics and outcomes of interest. Maternal and neonatal
18 characteristics were compared using descriptive statistics. Discrete variables are reported in
19 the tables as total numbers with percentage in parentheses and continuous variables are
20 reported as the mean with 95% confidence intervals in parentheses. For univariate analyses,
21 discrete variables were analysed using Fisher's exact test or Pearson's chi-squared test and
22 continuous variables using Student's t-test. Multivariate analysis with logistic regression was
23 planned for any outcome which met statistical and clinical significance and had documented
24 risk factors other than GDM. P-values are reported in the final column of all tables with less
25 than 0.05 considered statistically significant and highlighted in bold. Statistical analysis was
26 performed using STATA 9.2 (StataCorp, Texas, USA).
27
28
29
30

31 The study was approved as an anonymised audit by the Institutional Research and Ethics
32 Committee with identifying information removed before analysis.
33
34

35 *Patient and Public Involvement*

36
37 This was an anonymised retrospective audit, thus patients and the public were not required
38 to be directly involved in recruitment or conduct of the study. Indeed, emphasis was given
39 toward assessing the implications of this clinical health policy on a patient cohort as a whole
40 rather than subgroup or individual outcomes.
41
42

43 **Results**

44 *Demographics and Health Outcomes*

45
46 In 2014, there were 7010 pregnant women of whom 416 were diagnosed with GDM
47 (incidence 5.93%) and in 2016, there were 7488 pregnant women of whom 774 were
48 diagnosed with GDM (incidence 10.3%). The demographics of the two cohorts are shown in
49 Table 2.
50
51
52

53
54 (Table 2 goes about here).
55
56

57 Although the second cohort was statistically significantly older, this was only by a mean of
58 four months. The diagnosis of PCOS was higher but overall rates were low and possibly
59 under-reported. These two findings were statistically significant but unlikely to be clinically
60 relevant. The relative increase of 73.7% in the annual incidence of GDM is most likely
attributable to the change in diagnosis rather than to any changed demographic factors.

The maternal outcomes for the entire cohort are shown in Table 3 and the fetal outcomes in Table 4, with the HAPO/IADPSG outcomes highlighted in bold.

(Tables 3 and 4 go about here).

Following the introduction of the new GDM criteria, there has not appeared to be a hospital-wide decrease in the main outcomes reported in the sub-analysis of the HAPO study, most particularly in birthweight >90th percentile for gestation, caesarean section, hypertensive disorder of pregnancy or pre-term birth <37 weeks. However, there has been a hospital-wide decrease in neonatal death and birthweight greater than the 95th percentile in the fetal outcomes and an increase in induction of labour and instrumental birth in the maternal outcomes. The decrease in neonatal death rates was unexplained, almost always occurs at the extreme of prematurity and the absolute difference was low at 0.2%. The change most likely attributable to tightening GDM diagnoses is a small reduction in very large babies.

The maternal and fetal outcomes for the women with GDM are shown in Tables 5 and 6 respectively. There was a reduction in the annual incidence of third degree tears from 5.29% to 2.58% in the mothers with GDM. There was also a reduction in the incidence of neonatal hypoglycaemia (from 9.62% to 5.94%) and admissions to special care nursery (from 12.5% to 7.75%).

(Tables 5 and 6 go about here)

Costs of care

The average antenatal care package for women without GDM costs \$923 and for the 15% that require post-dates care this is \$1742 (when extra clinics, and CTG and amniotic fluid monitoring are required). The care package for women with GDM who do not need insulin is \$2026 and for those that do need insulin is \$2534 (or \$3826 if CTG monitoring from 36 weeks is undertaken: on audit during the study period, this occurred in 50% of patients).

In 2014, 210 women with GDM were controlled with dietary measures and 206 required insulin. The costs of care for GDM was calculated as follows:

GDM diet controlled: $210 \times \$2026 = \$425\ 460$

GDM insulin controlled: $0.5 \times 206 \times \$2534 + 0.5 \times 206 \times \$3826 = \$655\ 080$

Total = \$1 080 540

In 2016, 413 women with GDM were controlled with dietary measures and 361 required insulin. The costs of care for GDM was calculated as follows:

GDM diet controlled: $413 \times \$2026 = \$836\ 738$

GDM insulin controlled: $0.5 \times 361 \times \$2534 + 0.5 \times 361 \times \$3826 = \$1\ 147\ 980$

Total = \$1 984 718

The gross cost increase for care of women with GDM was thus \$904 178. The net cost increase can be determined by attributing the cost of standard care to the excess diagnoses

of GDM. If we round the incidence of GDM in 2014 up to 6% and use this with the total number of deliveries in 2016 (n=7420), the approximate number of women diagnosed with GDM if the criteria did not change would have been: $0.06 \times 7420 = 445$. The approximate excess number of cases of GDM is the total in 2016 (n = 774) minus this figure (n = 445) which is: $774 - 445 = 329$. We can then apply this number to routine care (bearing in mind 15% of those undergoing routine care require post-dates monitoring) as follows:

$$0.85 \times 329 \times \$923 + 0.15 \times 329 \times \$1742 = \$344\,085$$

The net cost, which represents the change in antenatal resources, is then the gross cost increase minus this figure:

$$\$904\,178 - \$344\,085 = \$560\,093$$

The hospital has thus spent approximately **\$560 093** caring for women with GDM because of the change in criteria.

Discussion

HAPO³ was a landmark study for several reasons, namely its sheer size (over 25 000 pregnant women), its robust statistical methods, and its aim to unify disparate international views about the significance of GDM and the best way to diagnose it. The IADPSG sub-analysis² used important clinical outcomes in identifying a “best-fit” for cut-off values within the 75-gram glucose tolerance test (GTT) to diagnose GDM: most are routinely measured in clinical care (with the exception of cord C-peptide and fetal fat distribution). The resulting recommendation was for a 75-gram GTT for all women (regardless of baseline risk) with levels of greater than 5.1 mmol/L at fasting, 10 mmol/L at one-hour and 8.5 mmol/L at two-hours considered diagnostic.

Despite a WHO statement endorsing the new criteria,¹³ there has been a failure of international acceptance to screen for GDM in this way. The National Institute of Clinical Excellence which guides care in the United Kingdom is perhaps the most striking example, recommending only screening those patients with risk factors and using levels of greater than or equal to 5.6 mmol/L at fasting and 7.8 mmol/L at two-hours.⁹ A sophisticated economic evaluation found this approach to be superior in their population¹⁴, and an earlier economic evaluation found that it was not currently cost-effective to routinely identify pregnant women for hyperglycaemia¹⁵. This latter also suggested further research into longer term health-outcomes of women and babies affected by GDM and more cost-effective ways of treating GDM, a sentiment reiterated by the findings of our manuscript.

Economic evaluations in American populations have also tended to favour existing screening criteria^{16,17,18}, albeit with less robust methodology and with different existing screening methods to both the UK and Australia. The latest Cochrane review concluded that there is insufficient evidence to prefer any particular screening method for GDM over another.¹⁹

The new criteria were a major change to established practice in Australia. The abolition of the non-fasting glucose challenge test (GCT) and the introduction of the one-hour BGL on the GTT were both new. The fasting BGL was tightened from greater than or equal to 5.5 mmol/L to 5.1 mmol/L and the two-hour level eased from greater than or equal to 8.0 mmol/L to 8.5 mmol/L. Some studies have tried to examine outcomes in patients who may

1
2
3 have been diagnosed with GDM under the new system but not under the old.^{20,21,22}
4 Generally, they have reported groups at higher risk of adverse outcome (particularly
5 caesarean section and large babies) who may have been previously underdiagnosed, but
6 such an approach is flawed because of the abolition of the glucose challenge test and the
7 introduction of the previously untested one-hour BGL. It thus is not possible to
8 retrospectively examine the outcomes of those who may have had a false negative on the
9 GCT or those who may have only tested positive on the new one-hour level. Unfortunately,
10 this is a major inherent weakness in all studies retrospectively examining GDM when
11 screening is changed (rather than modified) and would only be overcome by a large
12 prospective study examining two different systems of diagnosis. This would require at least
13 multi-centre or more likely international collaboration to recruit suitable numbers: a
14 prospect which seems unlikely given the international disagreement over different
15 diagnostic criteria and the immense time and planning a trial with somewhat similar
16 methodology (albeit with two groups for comparison) to the HAPO study would require.
17
18
19
20

21 A separate approach, one adopted by this study, is to quantify any overall changes in clinical
22 outcomes and attribute a cost to the increased burden of care and and to identify any
23 overall outcome improvements.
24
25

26 The strengths of this study include using a single, large, tertiary centre with a uniform urban
27 catchment area and relatively stable demographics over the study period. The numbers
28 were large with over 7000 births per year in each cohort, and the costs of care were
29 quantifiable by an established institutional Business Performance Reporting Unit. Outcomes
30 were readily identified from existing data management systems and were usually
31 categorical (often binary) and not requiring extensive further investigation or statistical
32 analysis.
33
34
35

36 The weaknesses of the study are those always inherent within retrospective data, including
37 the potential for treatment or ascertainment bias. Retrospectively comparing two large
38 cohorts with different methodologies for diagnosis will always carry greater uncertainty than
39 usual when compared with well-designed prospective trials. As it is impossible to determine
40 which of the 2014 “screen-negative” cohort would screen-positive under new criteria (and
41 vice-versa), many assumptions about the background demographic being the same must be
42 made. As we examined a large cohort, within a single centre, with strict zoning boundaries
43 which did not change between the two years and with an analysis of all feasibly collected
44 background data, we have attempted to satisfy the assumption of equal demographics but
45 this will always remain an uncertainty.
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50 We demonstrated a relative increased incidence of GDM of 74%, but we were unable to
51 demonstrate any statistically significant improvements in major outcomes across the
52 hospital as a whole. There was possibly a small improvement in the incidence of very large
53 babies (greater than the 95th percentile) but the change was small (0.7%) and there was no
54 change in babies greater than the 90th percentile. An apparent improvement in birth trauma
55 was due to a change in coding practices (and removed as an outcome), and an improvement
56 in the neonatal death rate was unexplained but very low in absolute terms (0.2%). This
57 latter tended to be confined to babies of extreme prematurity born well before routine
58 screening for GDM. It is important to note that these findings, in a retrospective analysis,
59 may be subject to unrecognised selection bias or confounding and form part of a larger
60 debate into the care for women with GDM.

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5 It may be reasonable to hypothesise that, with such minimal overall hospital-wide changes,
6 that it is simply a lower-risk cohort being now diagnosed with GDM. This is somewhat, but
7 not completely, borne out by analysing the same outcomes in women with GDM before and
8 after the change. While major outcomes such as caesarean section rates, hypertensive
9 disorders, pre-term birth and macrosomia have seemingly not changed, there has been a
10 reduction in third degree tears and a substantial decrease in the number of babies
11 diagnosed with hypoglycaemia and admitted to SCN. This is suggestive of an increase in
12 diagnoses represented by women on the milder end of the spectrum of GDM.
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15 We have also demonstrated an increase in net costs of over A\$500 000 per annum. This is
16 primarily due to employing a “high-risk” model of care to all women with GDM. As no
17 overall changes were discovered in mode of delivery or admission to NICU/SCN, in-patient
18 costs were not examined. In smaller cohorts, especially those analysed prospectively, it
19 would be worthwhile to examine patient-level data and directly assign costs of care in both
20 the antenatal and immediate post-partum period. Some outcome differences noted in
21 Tables 5 and 6 in the outcomes of screen-positive women would be accounted for in such
22 prospective data and unrecognised variation in costs (including inpatient care) may come to
23 light. While the overall costs are seemingly not redeemed in the short term by marked
24 improved outcomes, there may be unquantified health outcomes demonstrable in longer
25 term analysis of women with GDM and their babies treated under this system.
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30 While the new criteria are laudable in their efforts at uniformity of diagnosis and adverse
31 outcome avoidance, and possibly have improved clinical outcomes in sub-groups of women
32 previously not diagnosed with GDM, there is lack of quality evidence supporting their
33 superiority over other systems of diagnosis. Thus, further research is needed in three main
34 areas. Firstly, it would be desirable to have prospective (and ideally randomised controlled
35 trial) evidence examining the impact of this system of diagnosis over others employed
36 around the world. Secondly, long-term outcomes of the women with GDM and their
37 children may uncover health benefits not accounted for in immediate analyses like those
38 presented in this study, for instance with improvements in childhood obesity rates. There
39 may indeed be quantifiable cost savings that can be compared with the initial increase in
40 costs of care but appropriate budgetary measures to ensure the initial hospitals of care are
41 adequately reimbursed are essential. Finally, it is important to investigate more economic
42 ways of antenatally managing women with GDM particularly in the lower risk group, for
43 example those easily controlled with simple dietary measures or the increasing use of
44 metformin in those currently being prescribed insulin.
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50 Conclusion

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52 The annual incidence of GDM has immediately and markedly increased due to the change in
53 diagnostic criteria with an increase in cost of care and with seemingly no clear changes in
54 immediate clinical outcomes. Most particularly, macrosomia rates (>90th%), caesarean
55 section rates and pre-term birth less than 37 weeks remain unchanged. We suggest that
56 these results add weight to the need for longer-term data before confirming that
57 HAPO/IADPSG criteria are superior to other systems of diagnosis. Such data would need to
58 be derived from cohorts undergoing universal routine screening with these criteria, and
59 quantifiable health benefits compared against increases in immediate costs of care such as
60 we report here.

Declaration of Interests

There were no conflicts of interest with regards to any of the three authors.

Contributor and guarantor information

The corresponding author (TC) was responsible for the study design, literature review, collection and analysis of data, interpretation of clinical findings, writing of the manuscript and decision for submission. TC is responsible for the overall content and acts as guarantor. SB supervised the project and contributed to all of the above in a consulting role. AP contributed to planning and executing appropriate statistical analysis and with interpretation of the data. All authors contributed to the final manuscript review and final submission.

Data Sharing Statement

There are no unpublished data from the study.

Role of the funding source

The Royal Australian and New Zealand College of Obstetrics and Gynaecology, who awarded the Luke Proposch Perinatal Research Scholarship to the corresponding author to financially support this research, had no role in the study design, data collection, analysis and interpretation, writing of the report or decision to submit for publication. The corresponding author had full access to the data in the study and final responsibility for the decision to submit for publication.

Transparency Declaration

The corresponding author (TC) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted.

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Tables

Table 1 1991/1998 ADIPS versus 2014 IADPSG Criteria for diagnosing GDM

| | 1991/1998 ADIPS | | 2014 IADPSG | | 2015 NICE | |
|------------------------|---|---|---|---|---|---|
| | Type of test | Positive criteria | Type of test | Positive criteria | Type of test | Positive criteria |
| Screening test | 50g non-fasting glucose challenge test or 75g non-fasting glucose challenge test | \geq 7.8mmol/L \geq 8.0mmol/L | Nil | N/A | Clinical risk assessment | Any one of five clinical risk factors ⁹ |
| Diagnostic test | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting \geq 5.5mmol/L 2 hour \geq 8.0mmol/L | 75g, 2-hour fasting glucose tolerance test (three levels) | Fasting \geq 5.1mmol/L 1 hour \geq 10mmol/L 2 hour \geq 8.5mmol/L | 75g, 2-hour fasting glucose tolerance test (two levels) | Fasting \geq 5.6mmol/L 2 hour \geq 7.8mmol/L |

Table 2 Demographics of the 2014 and 2016 cohorts

| | 2014 | 2016 | p-value |
|--------------------------|--------------------|--------------------|---------------|
| Total Deliveries | 7010 | 7488 | n/a |
| Age (yr) | 30.9 (30.8 – 31.0) | 31.2 (31.1 – 31.3) | 0.0016 |
| BMI (kg.m ²) | 24.8 (24.7 – 24.9) | 24.7 (24.6 – 24.8) | 0.28 |
| PCOS | 110 (1.57%) | 151 (2.02%) | 0.043 |
| Smoking | 326 (4.65%) | 303 (4.05%) | 0.075 |
| Parity \geq 1 | 3228 (46.1%) | 3365 (44.9%) | 0.18 |
| Previous LUSCS | 960 (13.7%) | 1027 (13.7%) | 0.45 |

Table 3 Overall Maternal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------|--------------|--------------|-------------|
| Hypertensive disorder | 332 (4.74%) | 361 (4.82%) | 0.81 |
| Induction of labour | 2407 (34.3%) | 2725 (36.4%) | 0.01 |
| Overall LUSCS rate | 1963 (28.0%) | 2070 (27.6%) | 0.63 |
| Emergency LUSCS rate | 1088 (15.5%) | 1076 (14.3%) | 0.05 |
| Instrumental birth | 1316 (18.8%) | 1513 (20.2%) | 0.03 |
| Third degree tear | 217 (3.1%) | 197 (2.6%) | 0.09 |
| PPH | 1685 (24.0%) | 1765 (23.6%) | 0.51 |

Table 4 Overall Fetal Outcomes in 2014 and 2016

| | 2014 | 2016 | p-value |
|------------------------------------|--------------------|--------------------|-------------|
| EGA | 38.6 (38.6 – 38.7) | 38.6 (38.5 – 38.6) | 0.18 |
| Stillbirth | 36 (0.51%) | 40 (0.53%) | 0.86 |
| NND | 29 (0.41%) | 16 (0.21%) | 0.03 |
| Hypoglycaemia | 154 (2.20%) | 170 (2.27%) | 0.77 |
| Respiratory distress | 140 (2.00%) | 170 (2.27%) | 0.26 |
| Jaundice requiring phototherapy | 112 (1.60%) | 135 (1.80%) | 0.34 |
| Apgar < 7 at 5 min | 280 (3.99%) | 286 (3.82%) | 0.59 |
| Birth < 37 weeks | 645 (9.20%) | 671 (8.96%) | 0.62 |
| Birth < 34 weeks | 292 (4.17%) | 325 (4.34%) | 0.61 |
| Shoulder dystocia | 102 (1.46%) | 131 (1.75%) | 0.16 |
| Admission to NICU | 320 (4.56%) | 366 (4.89%) | 0.36 |
| Admission to SCN | 534 (7.62%) | 537 (7.17%) | 0.31 |
| Birthweight (g) | 3289 (3274 – 3304) | 3275 (3271 – 3293) | 0.21 |
| Birthweight > 95% | 300 (4.31%) | 269 (3.61%) | 0.03 |
| Birthweight > 90% | 577 (8.28%) | 586 (7.86%) | 0.36 |
| Birthweight < 10% | 570 (8.18%) | 616 (8.27%) | 0.85 |
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Table 5 Maternal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|-----------------------|-------------|-------------|--------------|
| Total | 416 | 774 | N/A |
| Hypertensive disorder | 20 (4.80%) | 35 (4.52%) | 0.85 |
| Induction of labour | 204 (49.0%) | 379 (49.0%) | 0.98 |
| Overall LUSCS rate | 162 (38.9%) | 289 (37.3%) | 0.59 |
| Emergency LUSCS rate | 71 (17.1%) | 121 (15.6%) | 0.52 |
| Instrumental birth | 83 (20.0%) | 134 (17.3%) | 0.26 |
| Third degree tear | 22 (5.29%) | 20 (2.58%) | 0.016 |
| PP H | 121 (29.1%) | 205 (26.5%) | 0.34 |

Table 6 Fetal Outcomes of Women with GDM in 2014 compared to 2016

| | 2014 | 2016 | p-value |
|---------------------------------|--------------------|--------------------|--------------|
| EGA | 37.8 (37.6 – 38.1) | 38.0 (37.9 – 38.2) | 0.13 |
| Stillbirth | 5 (1.20%) | 3 (0.39%) | 0.10 |
| NND | 0.00% | 1 (0.13%) | N/A |
| Hypoglycaemia | 40 (9.62%) | 46 (5.94%) | 0.02 |
| Respiratory distress | 11 (2.64%) | 12 (1.55%) | 0.19 |
| Jaundice requiring phototherapy | 9 (2.16%) | 12 (1.55) | 0.44 |
| Apgar < 7 at 5 mins | 19 (4.57%) | 26 (3.36%) | 0.30 |
| Birth < 37 weeks | 51 (12.3%) | 83 (10.7%) | 0.42 |
| Birth < 34 weeks | 25 (6.01%) | 30 (3.88%) | 0.10 |
| Shoulder dystocia | 7 (1.68%) | 5 (0.65%) | 0.09 |
| Admission to NICU | 27 (6.49%) | 39 (5.04%) | 0.30 |
| Admission to SCN | 52 (12.5%) | 60 (7.75%) | 0.007 |
| Birthweight | 3151 (3089 – 3213) | 3207 (3167 – 3248) | 0.12 |
| Birthweight > 95% | 27 (6.49%) | 35 (4.52%) | 0.15 |
| Birthweight > 90% | 48 (11.5%) | 74 (9.56%) | 0.28 |
| Birthweight < 10% | 38 (9.13%) | 60 (7.75%) | 0.41 |

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Yes (page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found Yes (page 2) |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Yes (page 3) |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Yes (page 3) |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Yes (page 3-4) |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes (page 3) |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Yes – no exclusion criteria (page 3) (b) For matched studies, give matching criteria and number of exposed and unexposed N/A |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes (page 4) |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes (page 4) |
| Bias | 9 | Describe any efforts to address potential sources of bias Yes (page 4 and 7) |
| Study size | 10 | Explain how the study size was arrived at Yes (entire cohort, page 4) |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes (page 4) |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Yes, confounding not particularly relevant as outcomes were examined across whole cohorts (page 4-5) (b) Describe any methods used to examine subgroups and interactions N/A (no subgroups) (c) Explain how missing data were addressed N/A (nil was missing) (d) If applicable, explain how loss to follow-up was addressed N/A (nil lost to follow-up) (e) Describe any sensitivity analyses N/A (not required) |
| Results | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Yes (page 5) (b) Give reasons for non-participation at each stage N/A (retrospective analysis with no possibility for non-participation) (c) Consider use of a flow diagram Not used |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Yes (page 5 and Table 2) (b) Indicate number of participants with missing data for each variable of interest Nil missing |

| | | |
|--------------------------|-----|---|
| | | (c) Summarise follow-up time (eg, average and total amount) N/A (examined at time of delivery – no long-term follow up) |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time Yes (page 5-6) |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Yes (page 5-6, tables 3-4) (b) Report category boundaries when continuous variables were categorized N/A (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives Yes (page 6-7) |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes (page 7) |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes (page 7-8) |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results Yes (page 8) |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Yes (page 8) |

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.