

Diabetes & Pregnancy

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Outline

- ▶ Classification of diabetes in pregnancy
- ▶ Pre-existing diabetes
 - ▶ Risks, pre-conception counselling, AN care, delivery, post-partum
- ▶ Testing in pregnancy
 - ▶ Early vs routine, who to test and why
- ▶ Diabetes Mellitus in Pregnancy
- ▶ Gestational Diabetes
 - ▶ Diagnosis, risks, AN care, delivery, post-partum

Resources

- ▶ ADIPS Consensus Guidelines for the Testing and Diagnosis of Hyperglycaemia in Pregnancy in Australia and New Zealand (modified November 2014)
- ▶ Diagnostic Criteria and Classification of Hyperglycaemia First Detected in Pregnancy, WHO (2013)
- ▶ IADPSG Recommendations on the diagnosis and classification of hyperglycemia in pregnancy (2010)
- ▶ SA PPG Diabetes Mellitus and Gestational Diabetes (2019)

Classification

- ▶ Pre-existing diabetes
 - ▶ Type 1
 - ▶ Type 2
- ▶ Gestational diabetes is characterised by glucose intolerance of varying severity, which develops or is first recognised during pregnancy, mostly in the second or third trimester
- ▶ Hyperglycaemia 1st detected at any time in pregnancy (ADIPS/WHO)
 - ▶ Diabetes mellitus in pregnancy
 - ▶ Gestational diabetes mellitus

Pre-existing Diabetes

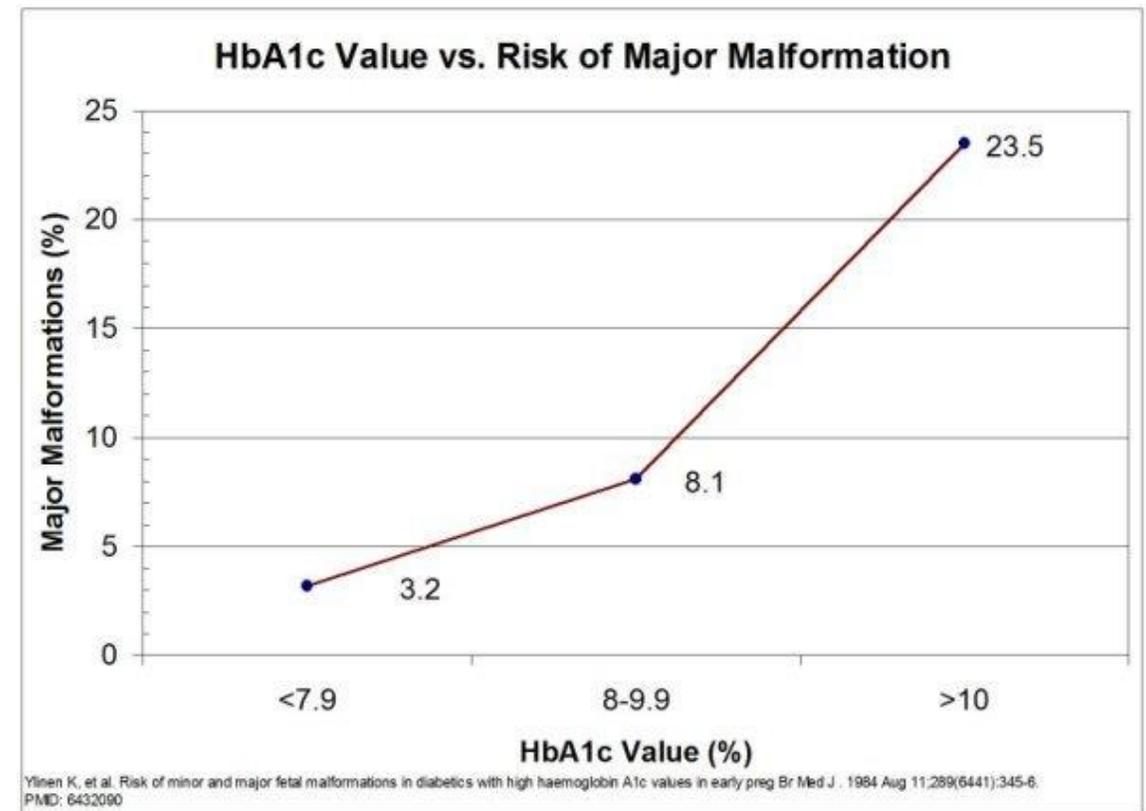
Pre-existing diabetes



- ▶ Affects approx. 1% of pregnancies
- ▶ Risks:
 - ▶ Congenital malformations:
 - ▶ caudal regression syndrome, anencephaly, meningomyelocele, cleft palate, hydrocephalus, pulmonary valve atresia
 - ▶ Pregnancy complications:
 - ▶ macrosomia, IUGR, polyhydramnios, PTB, PET, shoulder dystocia, IUFD
 - ▶ Newborn complications:
 - ▶ hypoglycaemia, jaundice, respiratory distress

Pre-conception Counselling

- ▶ Control of blood glucose
- ▶ Risks of poor control
 - ▶ Congenital malformations, pregnancy complications, newborn complications
- ▶ HbA1c $\leq 6.5\%$
 - ▶ HbA1c $\geq 8\%$ increases risk of birth defects
- ▶ Possible contraindications to pregnancy
 - ▶ Eg IHD, severe renal disease, advanced retinopathy, severe gastropathy, uncontrolled HTN
- ▶ Refer to other specialists, eg ophthalmologist



Pre-conception counselling

- ▶ Folate 5mg daily for at least 6wks pre-conception
- ▶ Cease or change any medication contraindicated in pregnancy
 - ▶ Eg some oral hypoglycaemic agents, ACEI, statins
- ▶ Type 2 DM – consider adding or changing to insulin for improved control
- ▶ Type 1 DM - consider changing to insulin infusion pump pre-pregnancy
- ▶ Consider obstetric physician or endocrinology referral
- ▶ Reproductive carrier screening



Antenatal Care



- ▶ Early referral to high-risk care
 - ▶ Endocrinologist/obstetric physician, obstetrician, diabetic educator, GP
- ▶ Bloods
 - ▶ Booking bloods, HbA1c, TFTs, EUC/LFTs/urate, random glucose
- ▶ Urine protein/creatinine ratio, plus MCS
- ▶ Review medications
- ▶ Commence low dose aspirin
- ▶ Education
 - ▶ Diet, physical activity, BSL monitoring (+ ketones for T1DM), increased insulin requirements

Antenatal Care

- ▶ All visits with obstetric medical officer
 - ▶ Frequency according to stability of BSLs and complications
- ▶ Weekly diabetes educator monitoring
- ▶ BSLs – fasting and 2hr post meals
 - ▶ ≤ 5.0 mmol/L before breakfast (fasting)
 - ▶ ≤ 6.7 mmol/L two hours after a meal
 - ▶ Remain >4.0 mmol/L
 - ▶ Perinatal outcomes better when control based on PP BSLs
 - ▶ Blood ketones if BSL >15 mmo/L, or unwell
- ▶ Bloods/urine 2-3monthly
- ▶ BP and urine dipstick for protein each visit



Ultrasounds

- ▶ Routine dating and 12wk NT/anatomy US
- ▶ Consider 16wk early morph US
- ▶ Tertiary level morph US
- ▶ Fetal echo 20-22wks if HbA1c >10%
- ▶ Growth scans



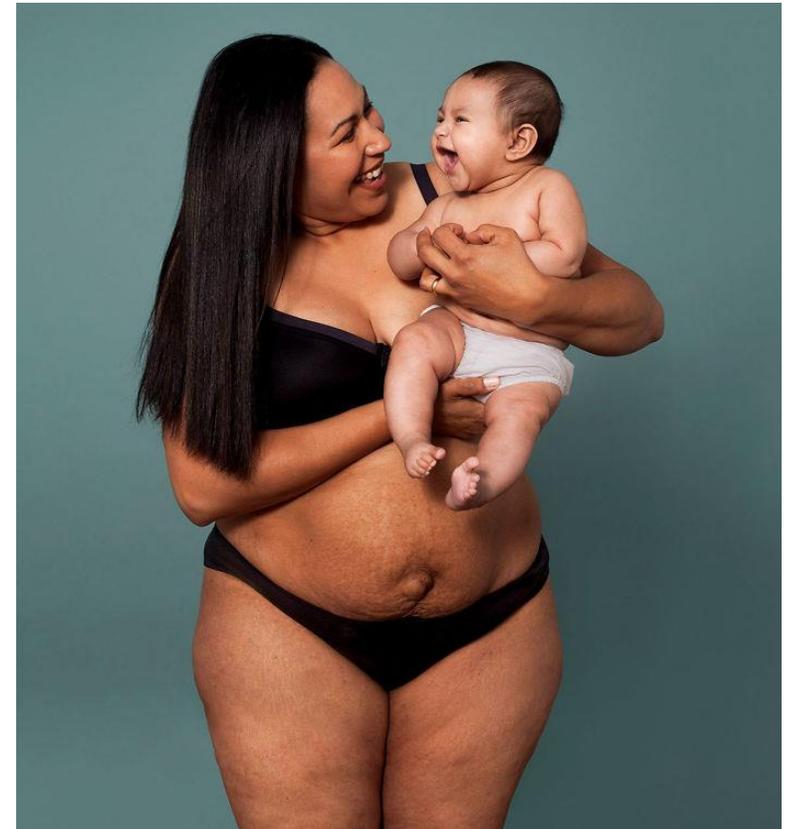
Delivery



- ▶ Planned delivery
 - ▶ Type 1 DM - Level 4, 5, 6 birth suite
 - ▶ Type 2 DM - Level 4, 5, 6 birth suite, possibly level 3
- ▶ Balance between risk of IUFD and neonatal morbidity
- ▶ Individualised decision based on range of factors
 - ▶ Gestation, EFW, growth pattern, BSL control, obs hx, co-morbidities

Post-partum

- ▶ Send placenta for histopathology
- ▶ Review medication
 - ▶ Immediate fall in insulin resistance after placental delivery
- ▶ Usual diabetic diet
- ▶ BSL monitoring
- ▶ Physician/endocrinologist/diabetic educator f/u
- ▶ Encourage breastfeeding
 - ▶ May require smaller insulin doses due to energy consumption of BF
 - ▶ Insulin and metformin safe to use
- ▶ Contraception



Testing in Pregnancy

Testing in pregnancy

- ▶ Universal screening with 75g GTT after at least 8hr fast (water OK)
- ▶ No need for 3 day high carb diet
- ▶ GCT no longer used – poor sensitivity and specificity
- ▶ Alternative to GTT
 - ▶ HbA1c may be considered in areas with high rates of undiagnosed T2DM, or where GTT logistically difficult
 - ▶ >6.5% diagnostic
 - ▶ Contraindicated - Gastric bypass surgery -> risk of dumping syndrome (gastric banding generally OK)
 - ▶ Unable to tolerate GTT (eg vomit after drink)
 - ▶ Patient declines
 - ▶ Home BSL monitoring for 1-2wks
 - ▶ More cost to patient due to test strips and hire/buy machine



Collection of Glucose Tolerance Test

Caution

If insulin levels are requested along with the GTT, the collection staff will draw blood for this in a separate tube, at the same time that each glucose blood sample is collected.

Special Requirements

- You are to remain on a normal, unrestricted diet for at least 3 days prior to the test.
- You have had no significant illness for 2 weeks prior to the test.
- Fasting is required for a period of 10-12 hours prior to the test - no food or fluids such as tea, coffee, or fruit juice. You may have sips of water if you are thirsty.
- Due to the nature of the test, testing is generally done in the morning.
- Certain centres will require you to make an appointment; please telephone your chosen collection centre to check.
- Maintain normal activity prior to the test.
- Avoid smoking for one hour before and during the test.
- Before drinking the glucose, please inform the collection staff if you have any allergies.

What to do during the procedure

- You must remain seated quietly during the test.
- You will be at the collection centre for a minimum of 2 hours.
- You are required to remain in the collection centre until the procedure is completed.
- Bring some reading material or other activity to pass the time.
- If you feel unwell during the test, please inform the collection staff, as you may wish to lie down.

Testing in pregnancy

- ▶ Early testing:
 - ▶ Woman with risk factors for hyperglycaemia in pregnancy but not known to have pre-existing glucose abnormalities
 - ▶ Approx 12-14wks
- ▶ Routine testing:
 - ▶ 24-28 wks gestation

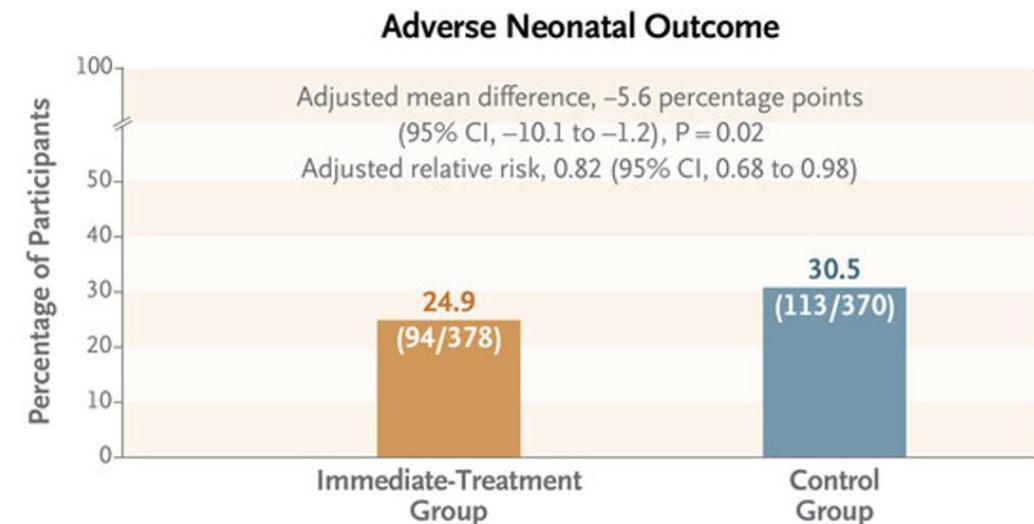


Who should we test early?

- ▶ Previous hyperglycaemia in pregnancy
- ▶ Previously elevated blood glucose level
- ▶ Maternal age ≥ 40 years
- ▶ Ethnicity: Asian, Indian subcontinent, Aboriginal, Torres Strait Islander, Pacific Islander, Maori, Middle Eastern, non-white African
- ▶ Family history DM (1st degree relative with diabetes or a sister with hyperglycaemia in pregnancy)
- ▶ Pre-pregnancy BMI > 30
- ▶ Previous macrosomia (baby with birth weight > 4500 g or > 90 th centile)
- ▶ Polycystic ovarian syndrome
- ▶ Medications: corticosteroids, antipsychotics

Why test early?

- ▶ 2017 meta-analysis of 13 cohort studies in women with early GDM
 - ▶ greater perinatal mortality (RR 3.58) compared to women diagnosed with GDM in later pregnancy, despite treatment
- ▶ TOBOGM (NEJM 2023)
 - ▶ RCT, 802 women, randomised to immediate/delayed/no treatment for early GDM
 - ▶ Immediate treatment
 - ▶ modestly lower incidence of a composite of adverse neonatal outcomes than no immediate treatment
 - ▶ No differences were observed for pregnancy-related hypertension or neonatal lean body mass.



Diabetes Mellitus in Pregnancy

Diabetes mellitus in pregnancy

- ▶ One or more of:
 - ▶ Fasting plasma glucose ≥ 7.0 mmol/l
 - ▶ 2-h plasma glucose ≥ 11.1 mmol/l following a 75 g oral glucose load
 - ▶ a random plasma glucose ≥ 11.1 mmol/l in the presence of diabetes symptoms
- ▶ Diagnostic of diabetes in non-pregnant adults
- ▶ Management requires assessment of chronic complications
- ▶ More likely to require pharmacological intervention
- ▶ May not be confirmed as diabetes in the post-partum period
 - ▶ More likely to be if was diagnosed early and/or degree of hyperglycaemia was marked

Have a stretch!

Gestational Diabetes

Diagnosis

- ▶ One or more at any time of pregnancy:
 - ▶ Fasting plasma glucose 5.1–6.9 mmol/l
 - ▶ 1-h post 75 g oral glucose load >10.0 mmol/l
 - ▶ 2-h post 75 g oral glucose load 8.5–11.0 mmol/l
- ▶ ACHOIS trial (2005)
 - ▶ Treating GDM reduces rates of serious perinatal complications without increasing CS delivery
- ▶ HAPO (2008)
 - ▶ Strong correlation between increasing maternal glucose levels at 24-32wks and a range of adverse maternal and fetal outcomes
- ▶ IADPSG formulated guidelines (2010)
- ▶ Endorsed by WHO (2013)
- ▶ ADIPS guidelines (modified 2014)
- ▶ Pre-2014: 2-step = non-fasting GCT then GTT (F \geq 5.5, 2hr \geq 8)



Figure 3: Incidence of gestational diabetes, 2000-01 to 2016-17

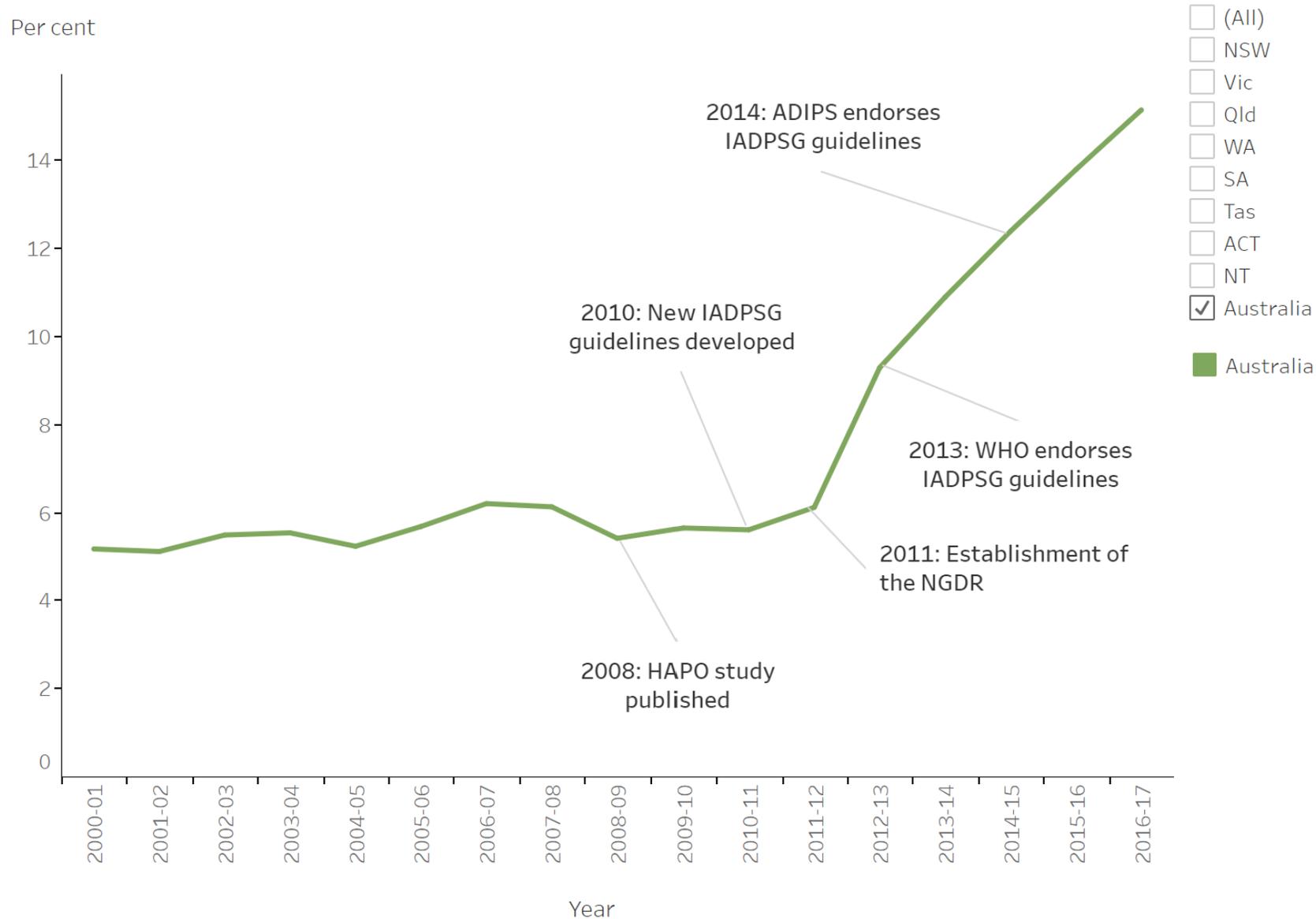


Figure 3: Incidence of gestational diabetes, 2000–01 to 2016–17

Per cent

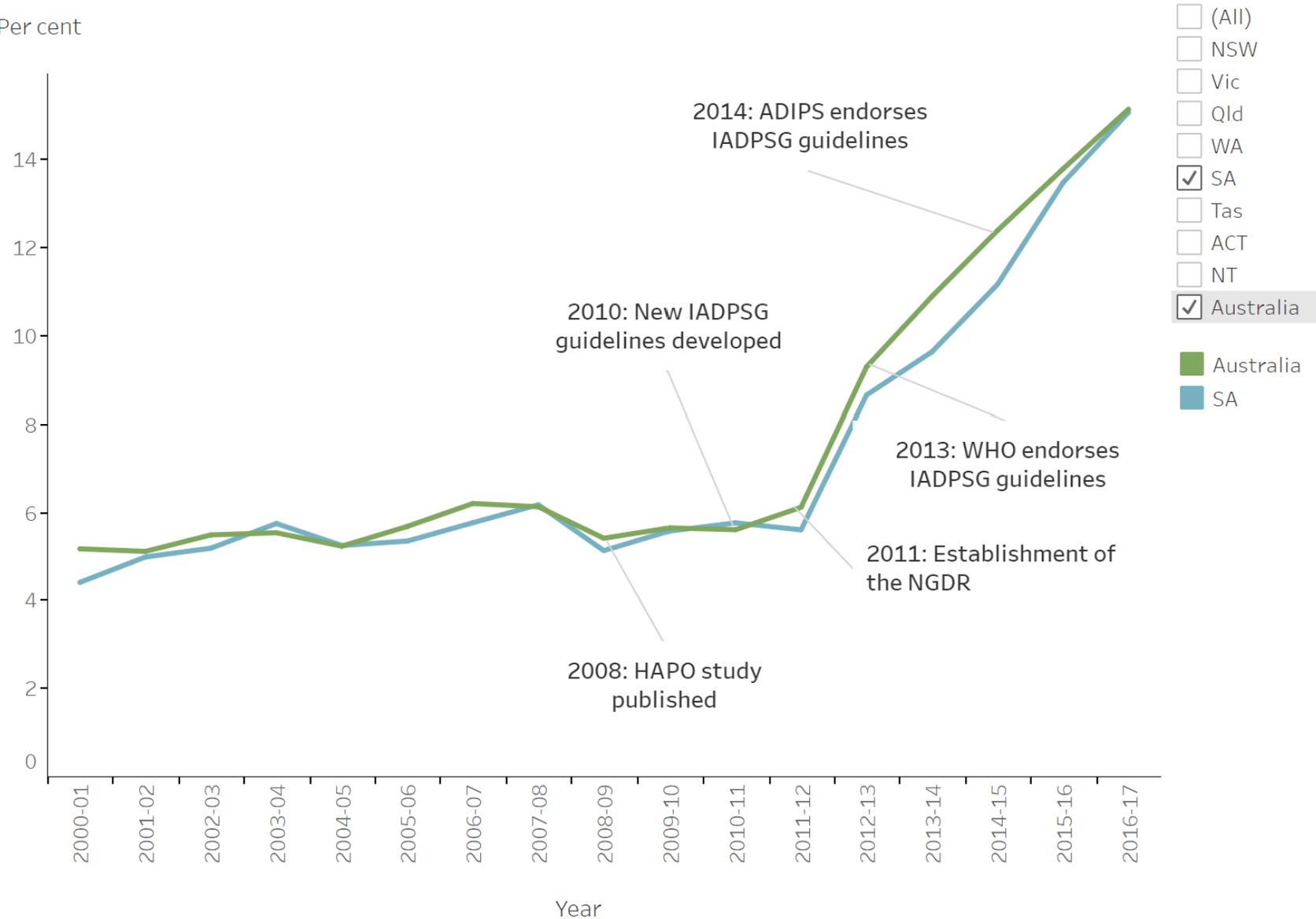
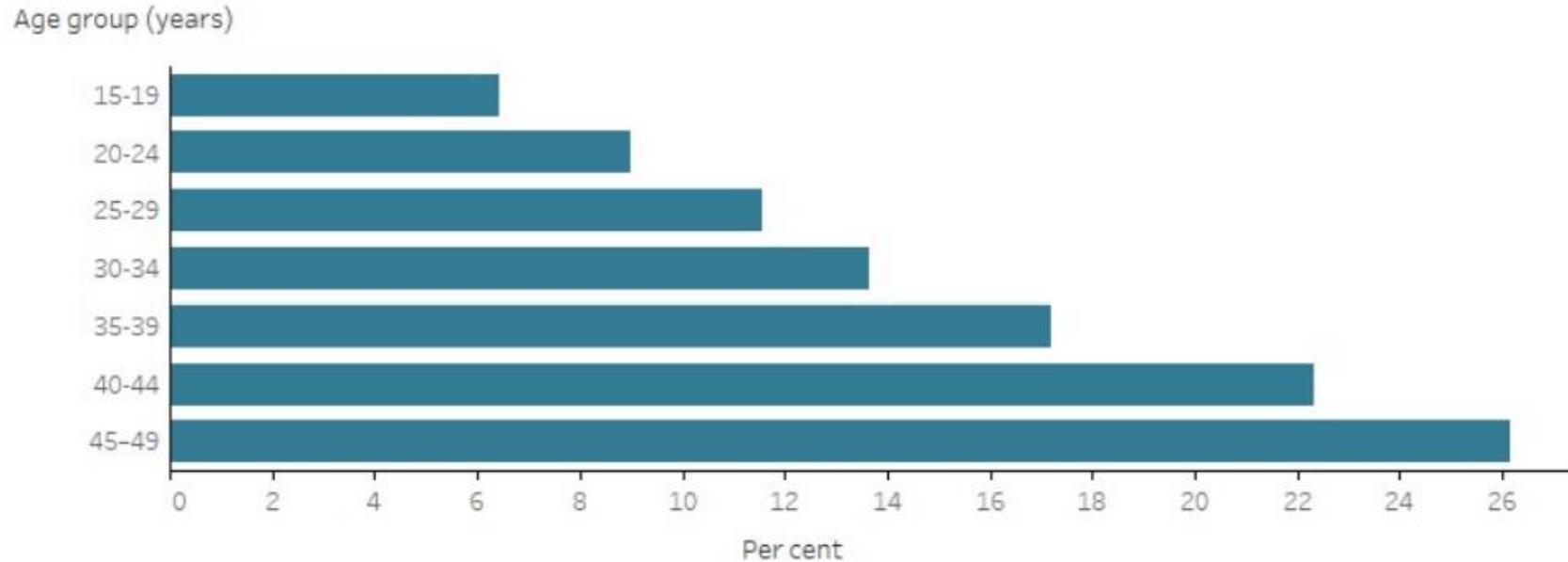


Figure 1: Incidence of gestational diabetes 2016–17, by age group



Note:

Population (women aged 15–49 giving birth in Australian hospitals) based on ICD-10-AM diagnosis codes. Refer to statistical notes for method.

Chart: AIHW. Source: National Hospital Morbidity Database.

Risks

▶ Maternal

- ▶ Gestational HTN/PET
- ▶ IOL
- ▶ Operative birth
- ▶ Caesarean section
- ▶ PTB
- ▶ Polyhydramnios
- ▶ PPH
- ▶ Infection
- ▶ Birth trauma

▶ Fetal/Neonatal

- ▶ Prematurity
- ▶ Macrosomia
- ▶ Higher BW and adiposity
- ▶ Birth trauma – bone fracture/nerve palsy
- ▶ Hypoglycaemia
- ▶ RDS
- ▶ Jaundice
- ▶ Hypocalcaemia
- ▶ Polycythaemia
- ▶ Cardiac anomalies
- ▶ IUFD

Management

- ▶ Patient education – diet, physical activity, BSL monitoring
 - ▶ SALHN – 1-1.5hr group session (diabetic educator/dietician)
 - ▶ Glucometer/strips, NDSS form for chemist
 - ▶ Private – individual session
- ▶ QID BSLs – fasting, 2hrs post break/lunch/dinner
- ▶ Targets/treatment vary, different centres, clinicians
 - ▶ $\leq 5.0\text{mmol/L}$ before breakfast (fasting)
 - ▶ $\leq 6.7\text{mmol/L}$ two hours after meals
 - ▶ 2SD above the mean values for pregnant women without known risk factors
- ▶ Consider BD/OD testing if persistently in target range



Obstetric physician/endocrinologist

- ▶ BSLs not within target despite diet/physical activity
- ▶ Consider additional treatment if ≥ 2 elevated levels at a given testing point in 1 week
 - ▶ After considering dietary factors
- ▶ Pregnancy complications or other co-morbidity
- ▶ Fetal growth concerns

Metformin

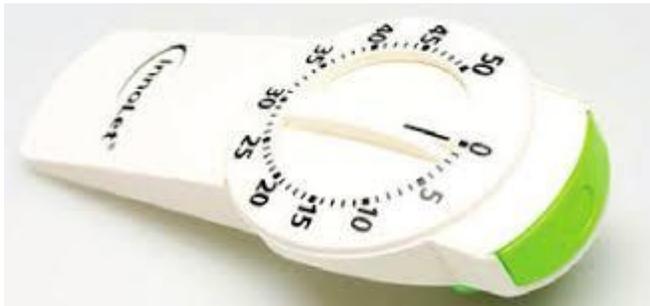
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- ▶ Evidence supports safety of use in pregnancy
- ▶ MiG Trial (NEJM 2008)
 - ▶ metformin (alone or combo with insulin) is not associated with inc perinatal comps as compared to insulin alone
 - ▶ women preferred metformin
- ▶ MiG TOFU (BMJ Open Diabetes Res Care 2018)
 - ▶ metformin or insulin for GDM was associated with similar offspring total and abdominal body fat percent and metabolic measures at 7-9 years.
- ▶ NICE guidelines support its use as 1st line pharmacological management
 - ▶ Not currently endorsed by Australian bodies
- ▶ Not recommended in growth restriction
 - ▶ Crosses placenta and hypothetically impact on insulin's effect as a promotor of fetal growth
 - ▶ Evidence for higher rates of SGA
- ▶ Used in consultation with obstetric physician/endocrinologist
- ▶ When patients decline or are unable to take insulin
- ▶ Can be added with insulin – reduces insulin requirements

Insulin

- ▶ Used in consultation with obstetric physician/endocrinologist
- ▶ Does not cross the placenta
- ▶ Risk of maternal hypoglycaemia and excessive gestational weight gain
- ▶ Rapid acting eg Novorapid, Humalog
- ▶ Intermediate acting eg Protophane
- ▶ Basal bolus regimen with long acting eg Lantus or Levemir



Metformin information



Great state. Great opportunity.



Commencing insulin therapy



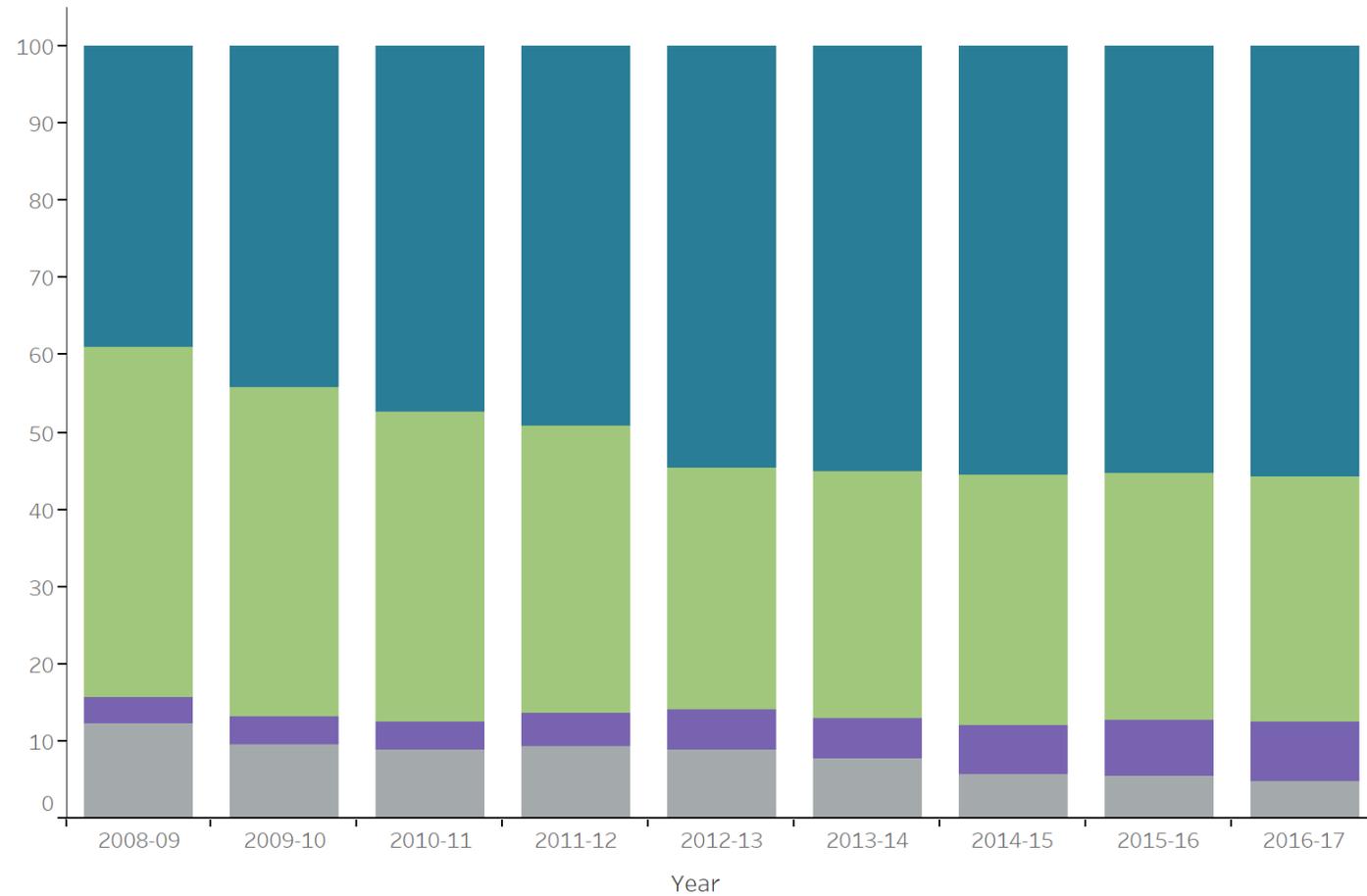
Great state. Great opportunity.



Figure 5: Gestational diabetes management type 2008–09 to 2016–17

- Diet, exercise, lifestyle management
- Insulin treated
- Oral hypoglycaemic therapy
- Unspecified

Per cent



Notes:

Population (women aged 15–49 giving birth in Australian hospitals) based on ICD-10-AM diagnosis codes. Refer to statistical notes for method.

Chart: AIHW. Source: National Hospital Morbidity Database.

Antenatal Care

- ▶ If GDM and adequate glycaemic control with diet/physical activity then can remain under MW
- ▶ Any form of medication required -> obstetric medical officer/GP
- ▶ Routine AN care intervals +/- obstetric physician/endocrinologist
- ▶ 36wk review by obstetric consultant/registrar for birth plan
- ▶ U/S
 - ▶ no need if adequately managed by diet alone
 - ▶ 32-36wk scan if suboptimal control, pharmacological treatment or fetal growth concerns

Delivery

- ▶ Location
 - ▶ Level 3, 4, 5, 6 birth suite if diet/exercise controlled
 - ▶ Level 4, 5, 6 birth suite if on metformin +/- insulin
- ▶ Timing
 - ▶ Up to 40+10 if diet/lifestyle managed and no complications
 - ▶ 38-39wk
 - ▶ Poor glycaemic control
 - ▶ Polyhydramnios/oligohydramnios
 - ▶ Macrosomia or growth restriction
 - ▶ Inc BMI requiring high doses of insulin
 - ▶ HTN/PET (or earlier as indicated)
 - ▶ Good peripartum BSL control to reduce risk of neonatal hypoglycaemia
- ▶ Mode
 - ▶ Vaginal if EFW <4.5kg



Post-partum

- ▶ Neonate requires BSL at 1hr of age
- ▶ Resume normal diet
- ▶ Cease metformin +/- insulin
- ▶ BSL profile day 2-3
 - ▶ Fasting ≥ 6 mmol/l or 2hr PP ≥ 10 mmol/l
 - > consult with obstetric physician/endocrinologist
- ▶ 75g GTT at 6-12 weeks
- ▶ Contraception



Did you have gestational diabetes during pregnancy?



Most women who had gestational diabetes will no longer have diabetes after the baby is born but they are at greater risk of developing type 2 diabetes, heart disease and stroke than women who did not have this condition.



Long-term health

- ▶ Pregnancy is the ultimate stress test for the body
- ▶ 30% risk of recurrence in subsequent pregnancy
- ▶ 50% risk of developing Type 2 DM within 10-20yrs
- ▶ Encourage breastfeeding
 - ▶ Lower estrogen levels may have protective effect on glucose metabolism and reduce risk of developing diabetes
 - ▶ Lower risk of T2DM in offspring BF for ≥ 2 months
- ▶ Annual GTT if contemplating another pregnancy
- ▶ HbA1c when Medicare funded (high risk of diabetes, 1 per 12mnth period)
- ▶ Lower risk women could have fasting glucose every 1-2 years
- ▶ NDSS Gestational Diabetes Register
- ▶ Offspring – increased risk of obesity, IGT and diabetes



Conclusion

- ▶ Pre-conception counselling is important to optimise maternal and fetal outcomes in women with pre-existing diabetes
 - ▶ Early referral for high-risk care in pregnancy
- ▶ Women with risk factors for hyperglycaemia in pregnancy should be screened with a GTT at 12-14wks, and everyone else at 26-28wks
 - ▶ Early testing and treating decreases adverse neonatal outcomes
- ▶ GDM is associated with a range of maternal, fetal and neonatal adverse outcomes
- ▶ GDM can be managed by diet alone in over half of cases but metformin and insulin can safely be used in the majority when pharmacological means are required
- ▶ GDM increases long term health risk in both the women and their offspring

Articles

- ▶ Australian Institute of Health and Welfare (AIHW) 2019, Incidence of gestational diabetes in Australia, viewed 9 June 2024, <https://www.aihw.gov.au/reports/diabetes/incidence-of-gestational-diabetes-in-australia>
- ▶ Immanuel J, Simmons D. Screening and Treatment for Early-Onset Gestational Diabetes Mellitus: a Systematic Review and Meta-analysis. *Curr Diab Rep.* 2017 Oct 2;17(11):115. doi: 10.1007/s11892-017-0943-7. PMID: 28971305.
- ▶ Simmons D, Immanuel J, Hague WM, Teede H, Nolan CJ, Peek MJ, Flack JR, McLean M, Wong V, Hibbert E, Kautzky-Willer A, Harreiter J, Backman H, Gianatti E, Sweeting A, Mohan V, Enticott J, Cheung NW; TOBOGM Research Group. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. *N Engl J Med.* 2023 Jun 8;388(23):2132-2144. doi: 10.1056/NEJMoa2214956. Epub 2023 May 5. PMID: 37144983.
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- ▶ Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS; Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med.* 2005 Jun 16;352(24):2477-86. doi: 10.1056/NEJMoa042973. Epub 2005 Jun 12. PMID: 15951574.
- ▶ Lowe WL Jr, Scholtens DM, Kuang A, Linder B, Lawrence JM, Lebenthal Y, McCance D, Hamilton J, Nodzinski M, Talbot O, Brickman WJ, Clayton P, Ma RC, Tam WH, Dyer AR, Catalano PM, Lowe LP, Metzger BE; HAPO Follow-up Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study (HAPO FUS): Maternal Gestational Diabetes Mellitus and Childhood Glucose Metabolism. *Diabetes Care.* 2019 Mar;42(3):372-380. doi: 10.2337/dc18-1646. Epub 2019 Jan 17. PMID: 30655380; PMCID: PMC6385693.
- ▶ The First International Association of Diabetes and Pregnancy Study Groups (IADPSG) summit on the diagnosis of gestational diabetes in early pregnancy: TOBOGM Summit Report Sweeting A, MacMillan F, Simmons D for the TOBOGM Summit attendees. (2023)



Questions?