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Strategies to address the intergenerational nature of type 2 diabetes in Aboriginal and Torres Strait Islander communities:

The NT & FNQ Diabetes in Pregnancy Partnership

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discovery for a healthy tomorrow

Outline

- Youth-onset Type 2 diabetes
  - Characteristics
  - Challenges

- Strategies to reduce the inter-generational nature of Type 2 diabetes:
  - pre & inter – pregnancy
  - During pregnancy
  - Breast-feeding

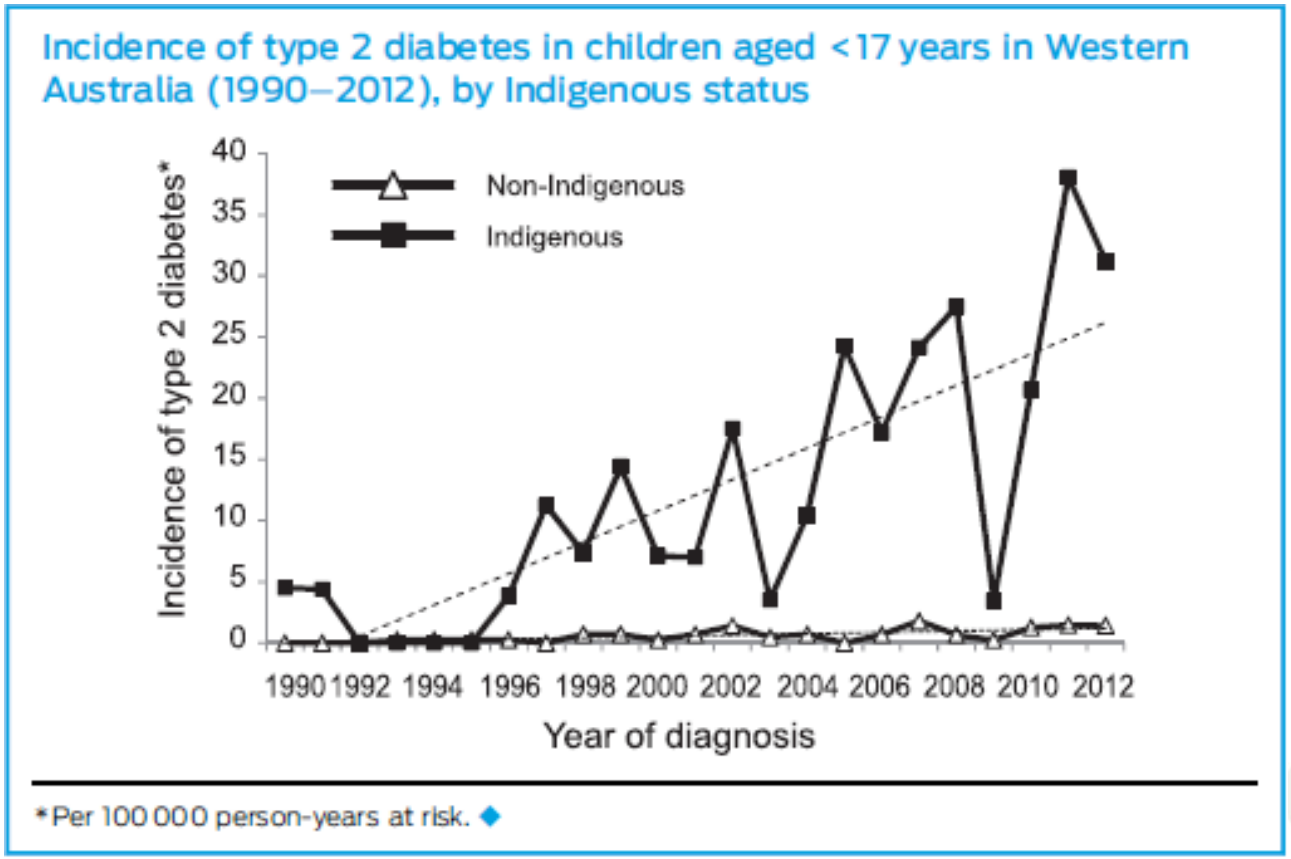
- NT & FNQ Diabetes in Pregnancy Partnership

Indigenous Australian youths

- T2DM occurs at a younger age
- assoc with socio-economic disadvantage
- Greater ↑rates of T2DM recently
- Assoc with central obesity
- Co-morbidities very common → ↑cv risk

Diabetes data: WA study

Type 2 diabetes diagnosed each yr per 100 000 population < 17 yrs in WA [1]



For the Indigenous group, incidence increased from 4.1 (1990) to 31.1 (2012)

For the non-Indigenous group, incidence increased from 0 (1990) to 1.4 (2012)

20-fold higher mean incidence in Indigenous than non-Indigenous children

Similar annual increase in both groups: 12.5% (Indigenous), 10.9% (non-Indigenous)

1. Haynes, Med J Aus 2016.

FNQ Case Report

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Case Report

A 5-year-old girl with type 2 diabetes

Dev Kevat, Dyanne Wilson, Ashim Sinha

Lancet 2014; 383: 1268

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In August, 2013, a 5-year-old Indigenous girl accompanied her mother to her diabetes outreach appointment in a remote community in Australia. Towards the end of her consultation, the mother mentioned concerns about non-healing sores on her daughter's thighs. Noting the child's obesity, two random blood glucose level tests were done, showing concentrations of 19·2 mmol/L and 18·7 mmol/L. A urine dipstick test was negative for ketones. The girl's mother reported that the sores had been present for roughly 5 weeks, and bedwetting for the past 12 months. There was no history of diarrhoea or vomiting. The child was born macrosomic (4·5 kg) at 38 weeks by caesarean section after a pregnancy complicated by poorly controlled gestational diabetes. Her diet was high in large portions of refined carbohydrates and simple sugars. There was a strong family history of type 2 diabetes.

The patient was above the 95th centile for weight (36 kg), body-mass index (24·5 kg/m²) and height (123 cm). Crusted sores on both upper thighs and right axilla were consistent with impetigo. The rest of the examination was unremarkable except for acanthosis nigricans in the axillae and around the neck (figure). The patient had high concentrations of HbA_{1c} (11·9%, normal range 4·3–6·0; or 107 mmol/mol, 23–42), plasma glucose (19·5 mmol/L, 3·0–7·8), C-peptide (1·6 nmol/L, 0·3–1·4), and insulin (201 pmol/L, 14–160). Urine albumin:creatinine ratio was normal (0·3 g/mol creatinine, normal <1·0). Tests for type 1 diabetes autoantibodies and genetic tests for *MODY1* (*HNF4A*) and *MODY3* (*HNF1A*) were negative. The patient was transferred to a tertiary centre and given intravenous antibiotics for infection, and metformin and insulin for type 2 diabetes. When seen for follow-up in November, 2013, she was no longer taking metformin because of intolerance, but remained on insulin. Blood glucose concentrations remained above target levels at 10–13 mmol/L.

Driven by increased urbanisation, high calorie diets, and increasingly sedentary lifestyles, the worldwide rise in the incidence of type 2 diabetes has predominantly occurred in adults. However, children are also being affected.[1] The continued burden of infectious diseases (eg, respiratory and diarrhoeal illnesses) coupled with an increasing prevalence of chronic diseases (particularly cardiovascular disease and type 2 diabetes) has resulted in Indigenous Australians having an additional 70% disease burden compared with the general Australian population.[2] Remote Indigenous communities are generally socioeconomically poor yet pay high prices for fresh food because of transport costs and limited competition. In addition to adverse socioeconomic determinants, genetic factors and in-utero exposure to hyperglycaemia[3] probably contributed to this child's risk of developing type 2 diabetes. The US SEARCH study[4] provides epidemiological data about the incidence of diabetes in young people. In our experience with this population, compliance and good diabetic control is often difficult to achieve and sustain—the TODAY trial[5] showed that even under trial conditions 52% of children on metformin alone, and 39% of children on combination oral treatment lost glycaemic control (HbA_{1c} >8% for 6 months or required insulin), over an average follow-up period of 3·9 years. Further long-term outcome studies are needed to determine the most efficacious combinations of interventions for type 2 diabetes in children who have extra decades to accrue disabling complications.

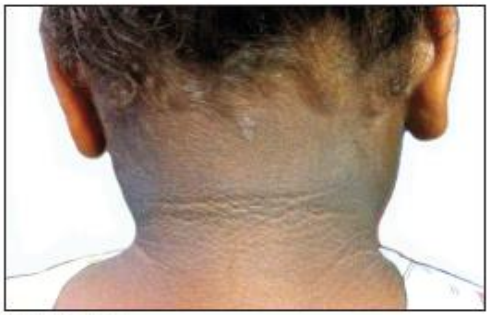


Figure: Acanthosis nigricans

Contributors

DK wrote the report and initially managed the patient. DW and AS helped revise the report and assisted with references, and have provided ongoing care to the patient. Written consent to publish was obtained.

Declaration of interests

AS has been on advisory boards for Sanofi-Aventis and AstraZeneca-BMS; been on speakers bureaux for Eli Lilly, AstraZeneca-BMS, Novo Nordisk, Sanofi-Aventis, Merck Sharp & Dohme, Takeda, Servier, and Novartis; and received research grants from Novo Nordisk and Merck. DK and DW declare that they have no competing interests.

References

1 Pinhas-Hamiel O, Zeitler P. The global spread of type 2 diabetes in children and adolescents. *J Pediatr* 2005; 146: 693–700.

2 Vos T, Barker B, Begg S, Stanley L, Lopez A. Burden of disease and injury in Aboriginal and Torres Strait Islander Peoples: the Indigenous health gap. *Int J Epidemiol* 2009; 38: 470–77.

3 Dabelea D, Hanson R, Lindsay R, et al. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. *Diabetes* 2000; 49: 2208–11.

4 The Writing Group for the SEARCH for Diabetes in Youth Study Group. Incidence of diabetes in youth in the United States. *JAMA* 2007; 297: 2716–24.

5 TODAY Study Group. Clinical trial to maintain glycemic control in youth with type 2 diabetes. *N Engl J Med* 2012; 366: 2247–56.

T2D Complications Australian Youth

n=68, 15% Aboriginal/Torres Strait Islander youth

Table 1—*Comparison of clinical characteristics and complication rates in youth with type 1 and type 2 diabetes in New South Wales from 1996 to 2005*

	Type 1 diabetes	Type 2 diabetes	*P* value
n	1,433	68	
Age at last assessment (years)	15.7 (13.9–17.0)	15.3 (13.6–16.4)	0.23
Age at diagnosis (years)	8.1 (4.8–10.8)	13.2 (11.6–15.0)	<0.0001
Sex (male/female)	674/759	34/34	0.63
Duration (years)	6.8 (4.7–9.6)	1.3 (0.6–3.1)	<0.0001
A1C (%)	8.5 (7.8–9.5)	7.3 (6.0–8.3)	<0.0001
A1C <7.5%	230/1,393 (17)	42/66 (64)	<0.0001
Insulin/weight	1.15 (0.96–1.39)	0.89 (0.51–1.31) (*n* = 9)	0.063
BMI SD score	0.80 (0.25–1.27)	1.86 (1.28–2.40)	<0.0001
Social disadvantage risk score	0.23 (−0.17–0.80)	0.14 (−0.47–0.56	0.058
From urban area	957/1,419 (67)	46/63 (73)	0.56
Microalbuminuria	81/1,325 (6)	10/36 (28)	<0.0001
Hypertension	223/1,393 (16)	21/58 (36)	<0.0001
Retinopathy	254/1,264 (20)	1/25 (4)	0.043
Peripheral nerve abnormality	375/1,376 (27)	5/24 (21)	0.48
Pupillary abnormality	568/928 (61)	13/23 (57)	0.65
Overweight	452/1,411 (32)	16/64 (25)	0.24
Obese	100/1,411 (7)	36/64 (56)	<0.0001

Data are median (interquartile range) or *n* (%) and are from last complications assessment

Table 2—*Multivariate analyses (using GEEs) of microalbuminuria and glycemic control in youth with type 1 and type 2 diabetes*

Outcomes	OR*	95% CI	*P* value
Microalbuminuria			
Type 1 diabetes			
Age (years)	1.30	1.15–1.46	<0.001
A1C (%)	1.17	1.00–1.38	0.06
Systolic hypertension	3.63	2.01–6.30	<0.001
Type 2 diabetes			
A1C (%)	1.67	1.26–2.94	0.003
A1C >7.5%			
Type 1 diabetes			
Age (years)	0.94	0.90–0.98	0.005
Diabetes duration (years)	1.06	1.02–1.09	0.003
Type 2 diabetes			
Treatment with OHAs and diet/exercise vs. insulin	0.12	0.05–0.31	<0.001
Resident in urban area	22.78	4.06–127.89	<0.001
Aboriginal/Polynesian ethnic group	4.20	0.85–20.72	0.08
Social disadvantage risk score	0.41	0.21–0.79	0.03

*Explanatory variables from the multivariate GEE models are expressed as adjusted OR (95% CI). OHAs, oral hypoglycemic agents.

Eppens, Diabetes Care 2006

Challenges: Systems & Setting

- Health care in remote Australia
  - High staff turnover
  - Limited resources
  - Limited specialist support
- Setting of socio-economic disadvantage
  - Poverty
  - Over-crowding
  - Food insecurity

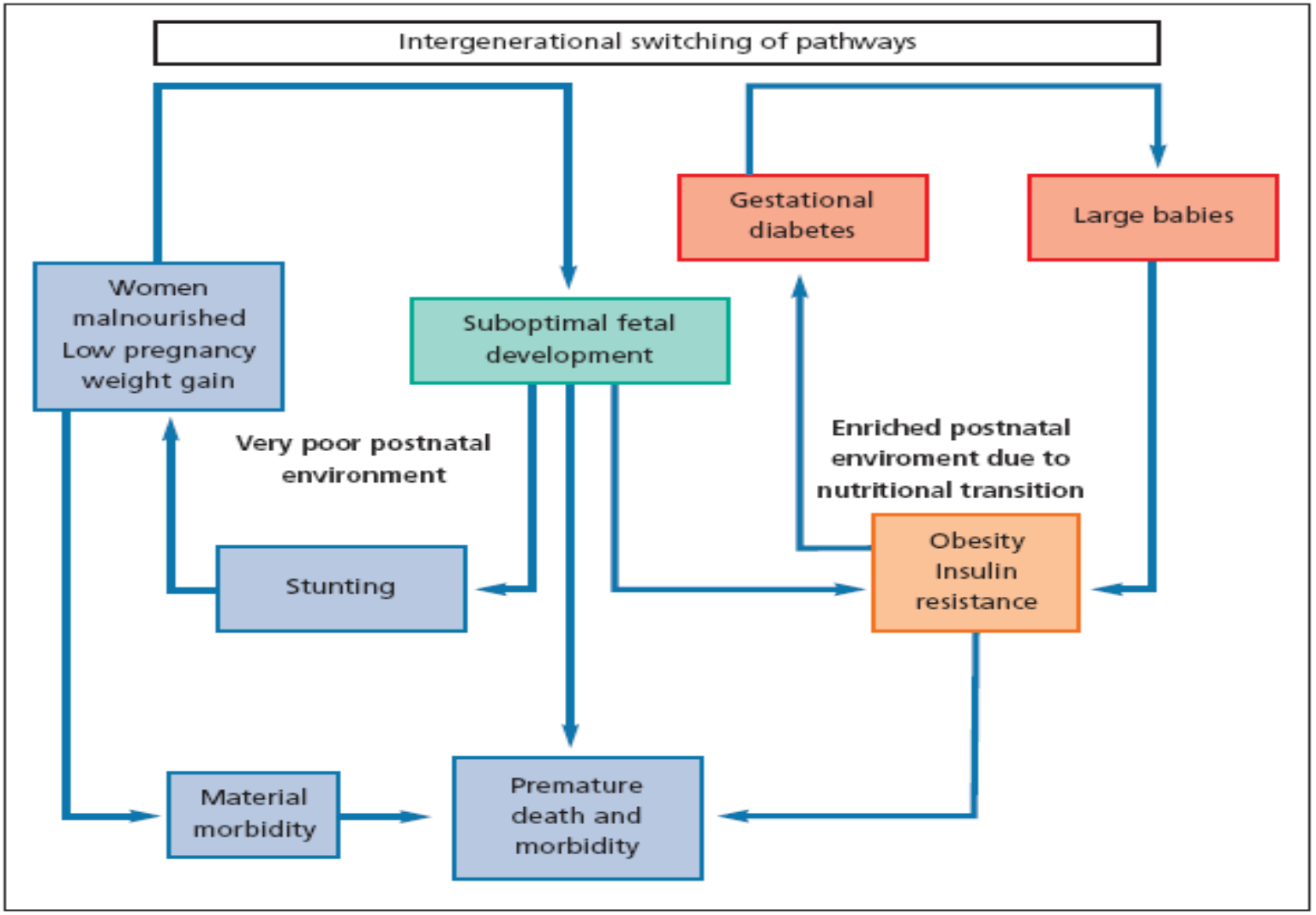
Azzopardi P et al, Med J Aus 2012; 197 (1): 32-36. Gibson O et al, Implement Sci 2015; 10: 71.

Strategies

- To prevent intergenerational impacts of diabetes:
  - Pre-pregnancy
  - During pregnancy
  - Breast-feeding

Cycles of disease risk

Figure 7: Cycles of disease risk



Pre-existing DIP vs GDM

- Major congenital anomalies & stillbirth:
  - Pre-existing type 1 or 2 diabetes [1, 2] : rates are up to 4x> general pop'n
  - GDM: similar to background pop'n[1]

  - Type 2 diabetes diagnosed in pregnancy[1]

  =Similar risk to those with pre-existing diabetes

- ↑ risk with ↑ peri-conception/first trimester HbA1c[3]
- ↓congenital anomalies & stillbirth rate with pre-pregnancy care[4]

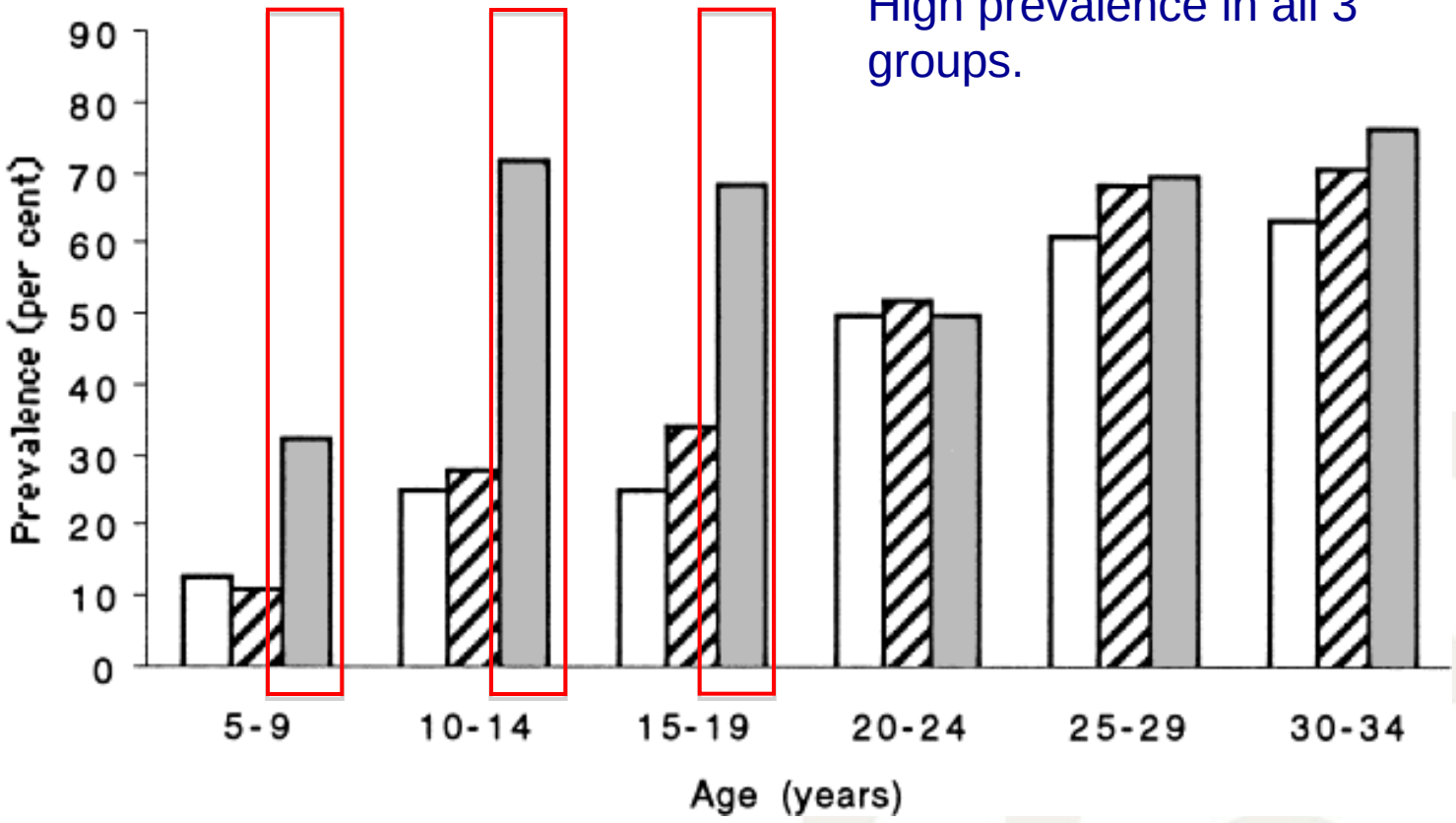
1. *Farrell T et al. Diab Med 2002.* 2. *McElduff A et al. Diab Care 2005.*
3. *Jensen et al. Diab Care, 2009.* 4. *Murphy H et al. Diab Care 2010.*

Future risk after DIP: babies

- Risk for babies of women with DIP:
  - ↑obesity in adolescence [1]
  - ↑ CV risk factors, independent of adiposity [2]
  - ↑type 2 diabetes, at all ages
- Maternal breastfeeding associated with ↓DM among Pima & Native Canadian children[3]

1. Fetita LS, JCEM 2006. 2. Blunt JC, JCEM 2005.
3. Pettit DJ, Diab Care, 1998.

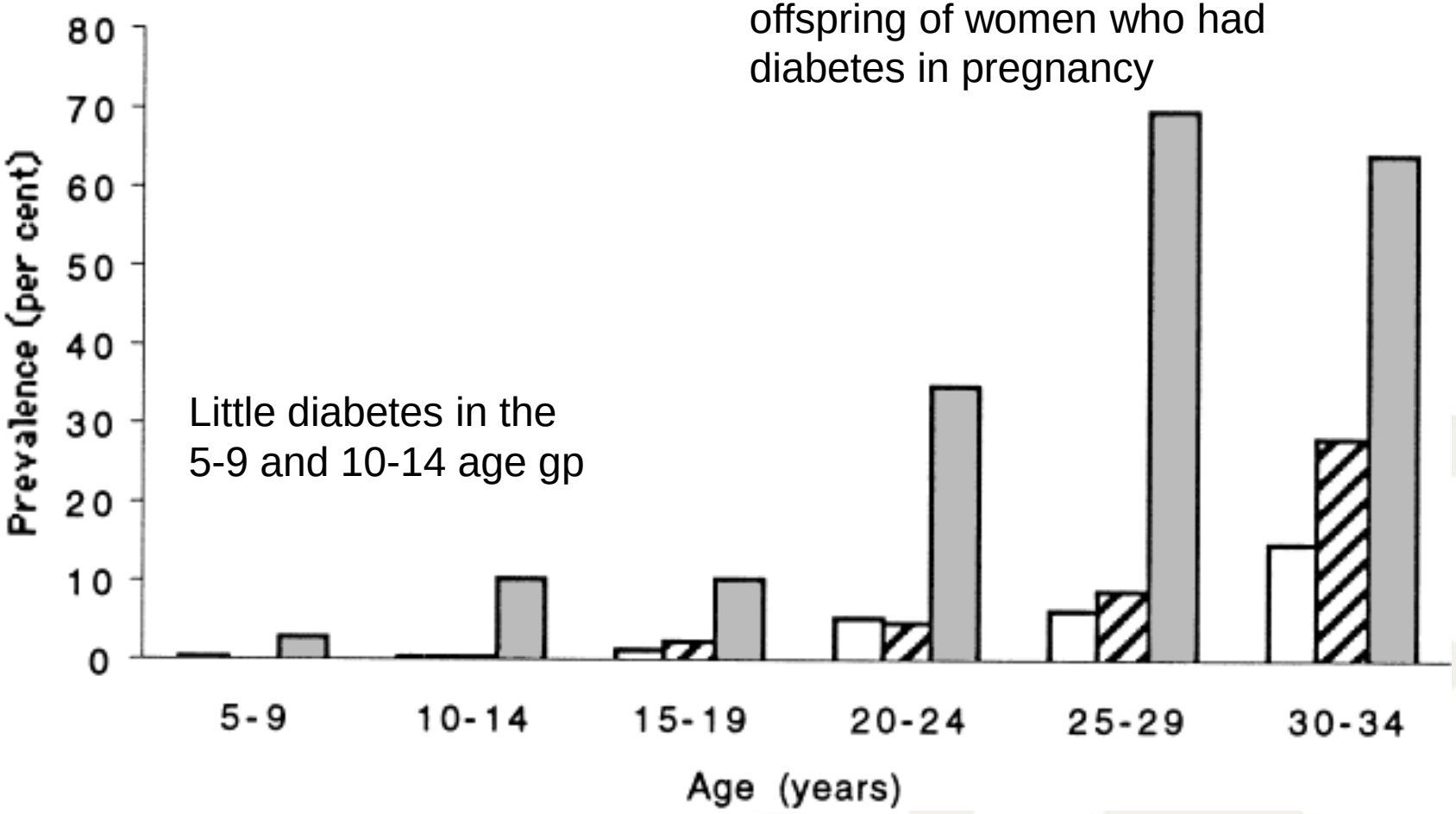
Pima: obesity in children



Dabelea et al. J Mat-Fet Med 2000

High prevalence of T2DM in offspring

Prevalence much higher in offspring of women who had diabetes in pregnancy



Dabelea et al. J Mat-Fet Med 2000

Follow-up of babies

- Pima: 70% of offspring have diabetes age 25-34yr vs <15% in offspring of non-diab mothers [1]
- Canadian First Nations: in children of mothers with pre-preg DM (<18yo):
  - at age 10-19 years, 43% DM [2]
- Continuing cycle of diabetes & DIP:
  - Offspring have diabetes at younger age than their parents
  - then diabetes pre-conception in mother & father & during mother's pregnancy

1. Dabelea et al. J Mat-Fet Med 2000 *2. Mendelson M, Pediatr Diabetes 2011*

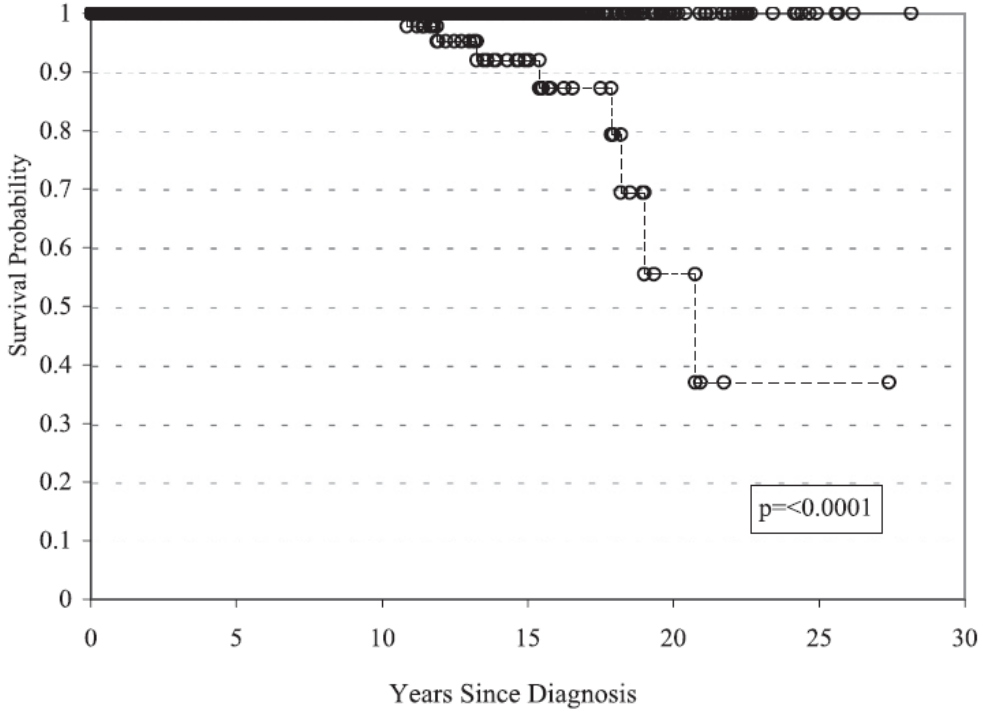
DIP, Youth type 2, renal

- SEARCH case-control study: 47% of type 2 diabetes in youth attributed to intra-uterine exposure to maternal diabetes & obesity[1]

- Youth Type 2[2]:
  - 4x ↑ risk of renal failure vs youth T1
  - 23 x ↑ risk of renal failure vs age, sex, post-code matched controls
  - 39 x ↑ risk of dialysis vs age, sex, post-code matched controls

1. Dabelea et al, Diab Care 2008; 2. Dart et al, Diab Care 2012

Renal Survival: Youth T1 vs T2



Patients at risk

T1DM	1,011	608	365	152	37	4
T2DM	342	153	56	25	6	1

Figure 1—*Renal survival in youth-onset diabetic cohorts. Patients at risk are the number of patients in each group with follow-up to that time period. T1DM, ——; T2DM, - - - -.*

- Renal Survival: 100% for T1 & T2 at 10yrs since diagnosis
  - 15yrs: 92% T2 vs 100% T1
  - 20yrs: 55% T2 vs 100% T1

Dart et al, Diab Care 2012

Potential Intervention points

1. Pre-pregnancy: optimise pre-conception & inter-conception health in Indigenous women of child-bearing age

2. During pregnancy: enhance current DIP practice
   - early detection of diabetes in pregnancy
   - management of diabetes in pregnancy

3. After pregnancy: improve rates of breastfeeding to ↓ risk of obesity & diabetes in children of women with DIP

Strategy 1: Pre-pregnancy care

- Pre-pregnancy care in type 1 & 2 diabetes has benefits beyond glucose control[1]
  - ↓ adverse outcomes (stillbirth, congenital malformation, neonatal death)

    1.3 vs 7.8% (p=0.009)
  - Pre-pregnancy care was stronger predictor of pregnancy outcomes than maternal obesity, ethnicity or social disadvantage in this study across 10 UK regional maternity units
- ATLANTIC-DIP: change in clinical care for women with DIP resulted in significantly improved outcomes (↑ live births, ↓perinatal mortality)[2]

1. Murphy H et al, Diab Care, 2010. 2. Owens LA, Diab Care, 2012

Pre-& inter-conception health

- Diagnose diabetes & treat to ↓HbA1c
  - Discuss contraception until ↓HbA1c
- Diagnose & treat other metabolic risks:
  - Obesity
  - BP
- Assess other risks:
  - STIs
  - Smoking
  - Alcohol
  - Weight, diet, exercise
- Folic acid: ↓ neural tube defects[1]

1. Lumley J et al, Cochrane Database Syst Rev, 2001.

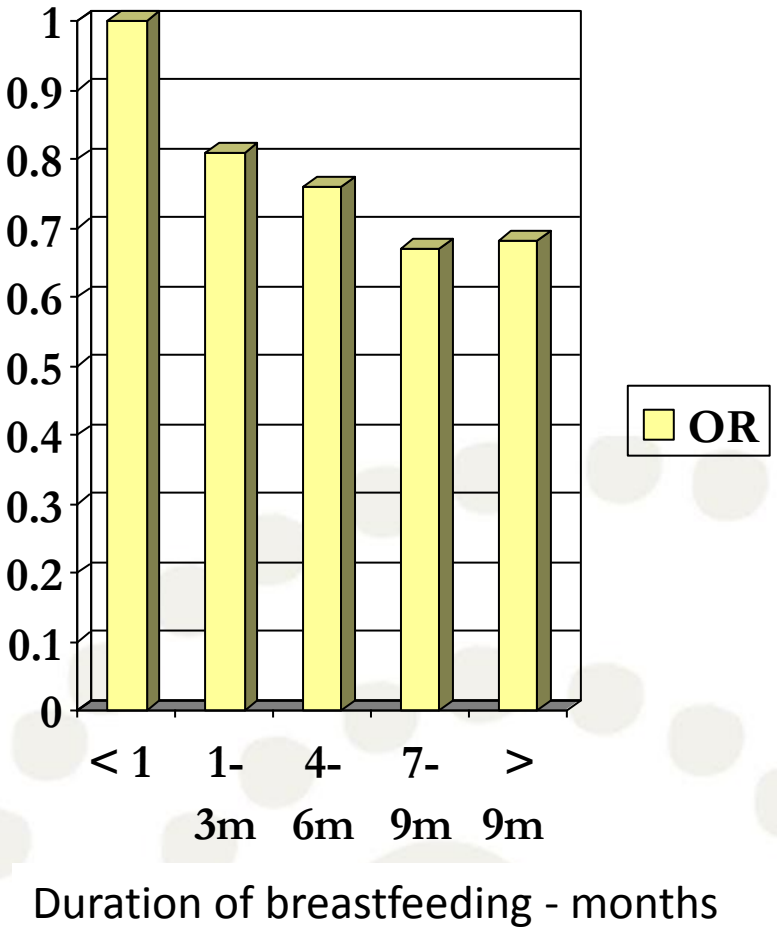
Strategy 2: During pregnancy

- Early screening to detect undiagnosed type 2 diabetes
  - Treat to ↓HbA1c & thus ↓risk
- Optimise management of DIP:
  - Pre-existing
  - GDM
- NT & FNQ DIP Partnership: to improve systems & care for all women with DIP

Breastfeeding & risk of overweight

- Case-control studies from Pima Indian & Native Canadian populations[1,2]

- Meta-analysis 17 studies[3]
  - Duration of breastfeeding was inversely associated with risk of overweight
  - Risk of overweight was reduced by 4% for each month of breastfeeding
  - Exclusively formula-fed subjects were the referent



1. Pettitt et al, 1995. 2. Young et al, 2002. 3. Harder et al, 2005

Strategy 3 : breastfeeding

- Breastfeeding:
  - Target young disadvantaged women in urban settings
  - nurse home visiting programs
  - Start discussion re importance of breastfeeding early in pregnancy

Summary

1. Pre-pregnancy: optimise pre-conception & inter-conception health in Indigenous women of child-bearing age

2. During pregnancy: enhance current DIP practice
   - early detection of DIP
   - management of DIP

3. After pregnancy: improve rates of breastfeeding to ↓ risk of obesity & diabetes in children of women with DIP

NT and FNQ DIP Partnership

- To improve models of care & health outcomes by reducing risk *as early as possible in life course*
- Partners:
  - NT Department of Health, Queensland Health
  - Menzies School of Health Research
  - Baker IDI, SAHMRI
  - Aboriginal Medical Service Alliance NT
  - Apunipima Cape York Health Council
- Chief Investigators: Louise Maple-Brown, Alex Brown, Mark Wenitong, Ashim Sinha, Christine Connors, Jeremy Oats, David McIntyre, Paul Zimmet, Jonathan Shaw, Kerin O'Dea

NT & FNQ DIP Partnership Aims

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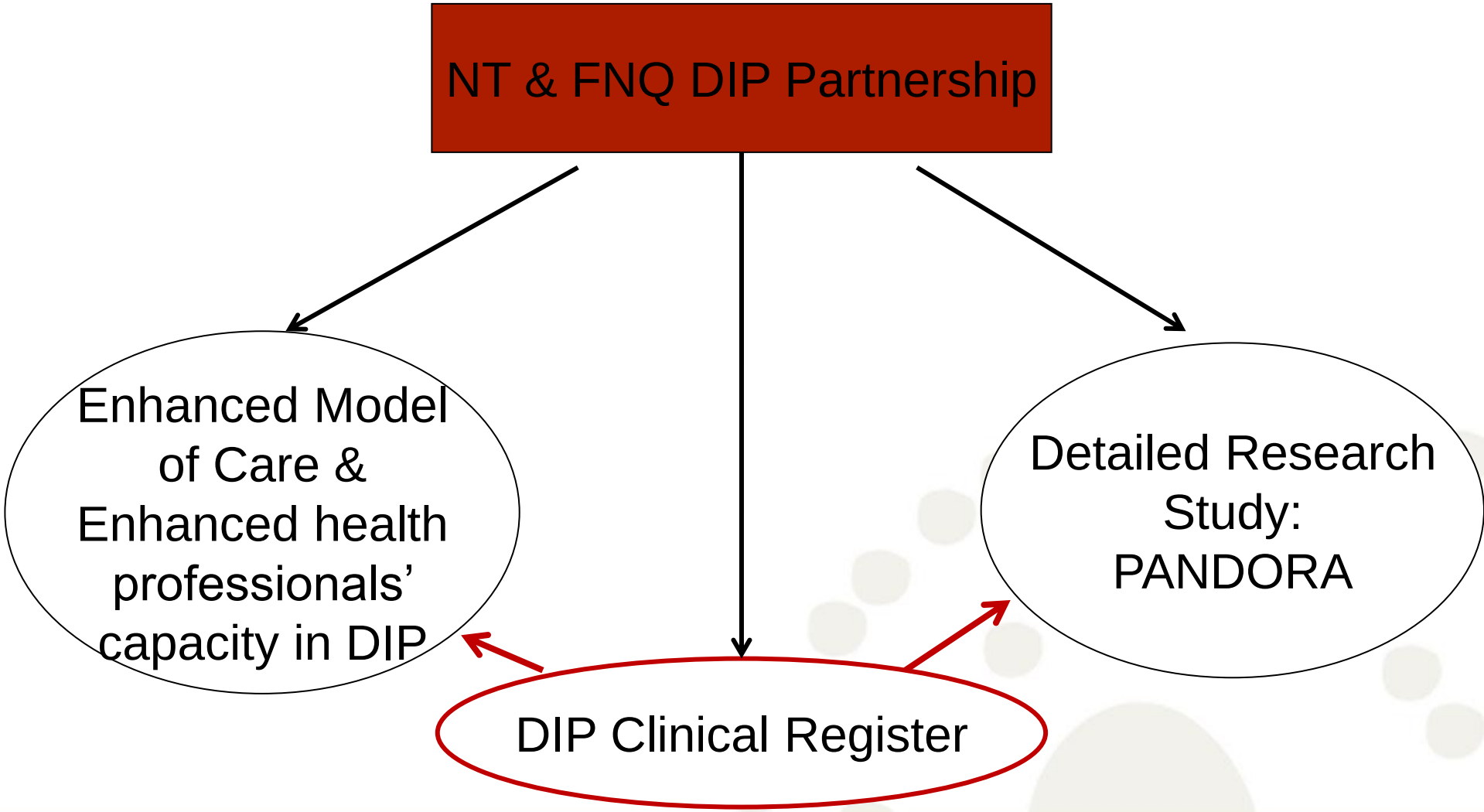
1. Improve systems & service delivery for all women with DIP

2. Reduce gap b/w evidence & practice for screening, management & post-partum follow-up of women with DIP

3. Establish systems that enable close monitoring of relevant clinical outcomes for mothers & babies, thereby providing reliable information around future health risk for the NT

DIP Partnership Methods

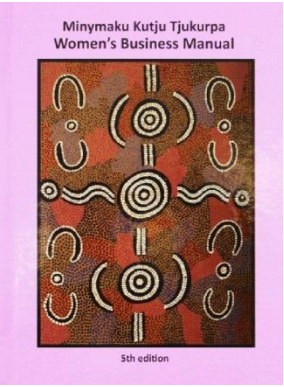


Progress

- Partnership commenced in NT in 2011
- Global Alliance Chronic Diseases funding (2016-2020) :
  - Extend clinical register & models of care work within NT
  - expand clinical register & models of care work to FNQ
  - post-partum intervention to improve maternal health inter-pregnancy
    - Systems-based intervention using clinical register
    - Case management pilot intervention for Aboriginal women in PANDORA

Impact of NT DIP Partnership

- Key areas of change:
  - Improved communication
  - Strengthened networks
  - Integration of quality improvement activities
  - Contribution writing & promotion of guidelines
  - Improved collaboration & relationships between health professionals
  - Improved access to specialist services
  - More education opportunities: regional workshops

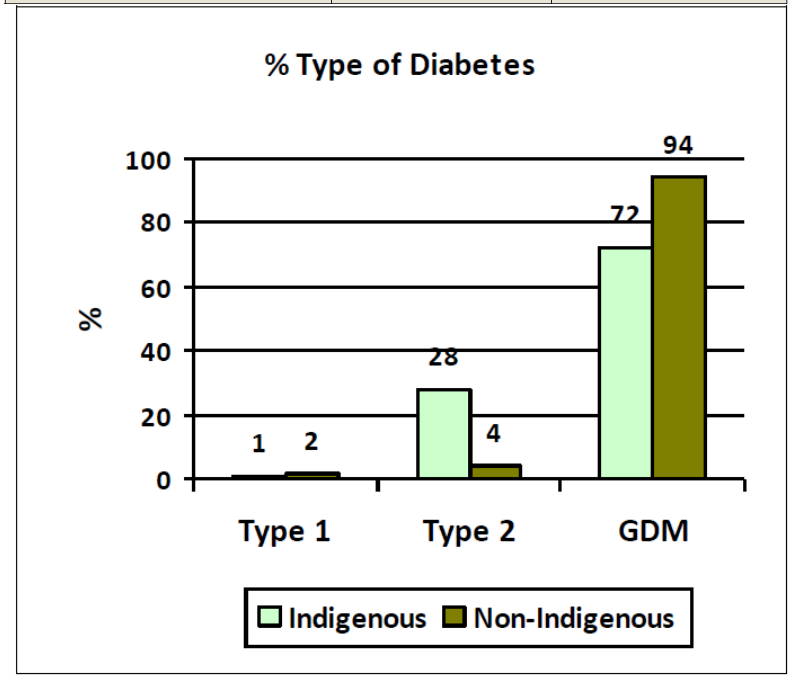


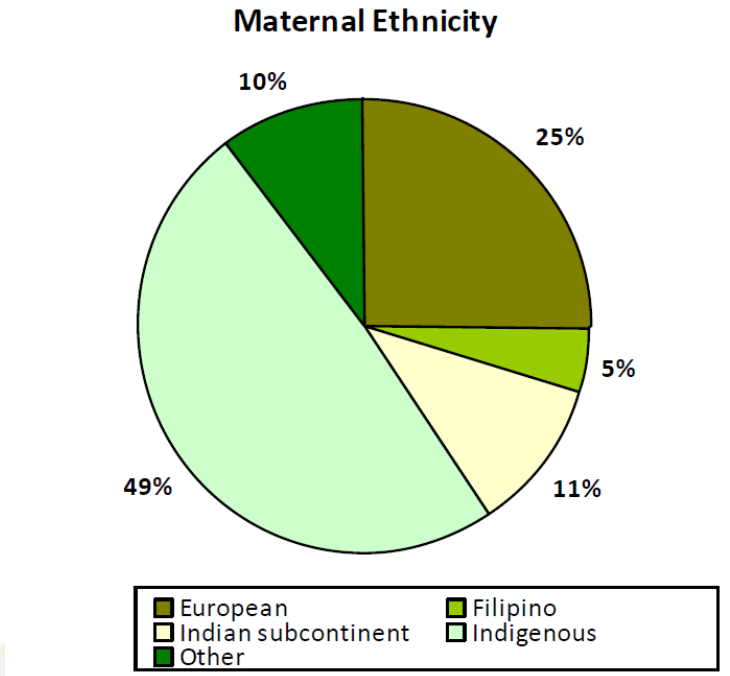
Kirkham R, BMC Health Services, in press

NT DIP Clinical Register Report 2011 – 16

No of Births	1721
Twin pregnancies	27
2 pregnancies within timeframe	88

	Indigenous	Non-Indigenous
No. of Births	846	875
Average Age (years)	29.3	31.7
Regional/Remote	75%	9%





NT DIP Clinical Register Report 2011 – 16

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3. Birth Outcomes

Births	Type 2	GDM
No. of Births	277	1445
Live birth	95%	100%
Caesarean section	62%	43%
Still birth/neonatal death (n)	7	2
Miscarriage/abortion (n)	8	1

Weight and Gestational Age	Type 2	GDM
Birth weight (gm)	3337	3252
Gestational age (wks)	37	38.3
% LGA	38%	14%
% SGA	7%	11%

Congenital Malformations	Type 2	GDM
Major malformation	3%	1%
Minor malformation	8%	5%

Clinical Register Evaluation

- 80% ↑ GDM prevalence in NT Midwives Data Collection among Aboriginal women (2011-13)
  - Prior to adoption new definition 2014
  - Most women met both GDM def'ns (81% in 2012 & 74% in 2015) thus unlikely changes in diagnostic criteria contributed to ↑ prevalence
- 57% of health prof reported ↑ knowledge of DIP epidemiology since establishment of the register
- 32% of health prof reported ↑ care-coordination
- Regions with similar challenges in context & high risk populations for DIP may benefit from experience of implementing a register

Kirkham R, PlosOne, in press

Thank you

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Thank you

- **NT & FNQ DIP Partners:** Menzies, Apunipima, QH, SAHMRI, Baker, AMSANT, NT DoH, Healthy Living NT
- **NT & FNQ DIP Investigators:** A Brown, C Connors, K O'Dea, HD McIntyre, J Oats, J Shaw, P Zimmet, M Wenitong, A Sinha, S Eades, J Boyle, J Mein, A McLean, S Campbell, R McDermott, S Corpus, S Chitturi, E Moore, C Inglis, C Whitbread
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