

The Rise and rise of diabetes: Pay now or pay (more) later



AUT
UNIVERSITY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

Visiting
Professor
2012

David Simmons Institute of Metabolic Science,
Cambridge University Hospitals, UK

Diabetes epidemic takes a rising toll

Diabetes sweeps Australia

Diabetes epidemic worsens

Diabetes epidemic hits NSW
By JANELLE MILES



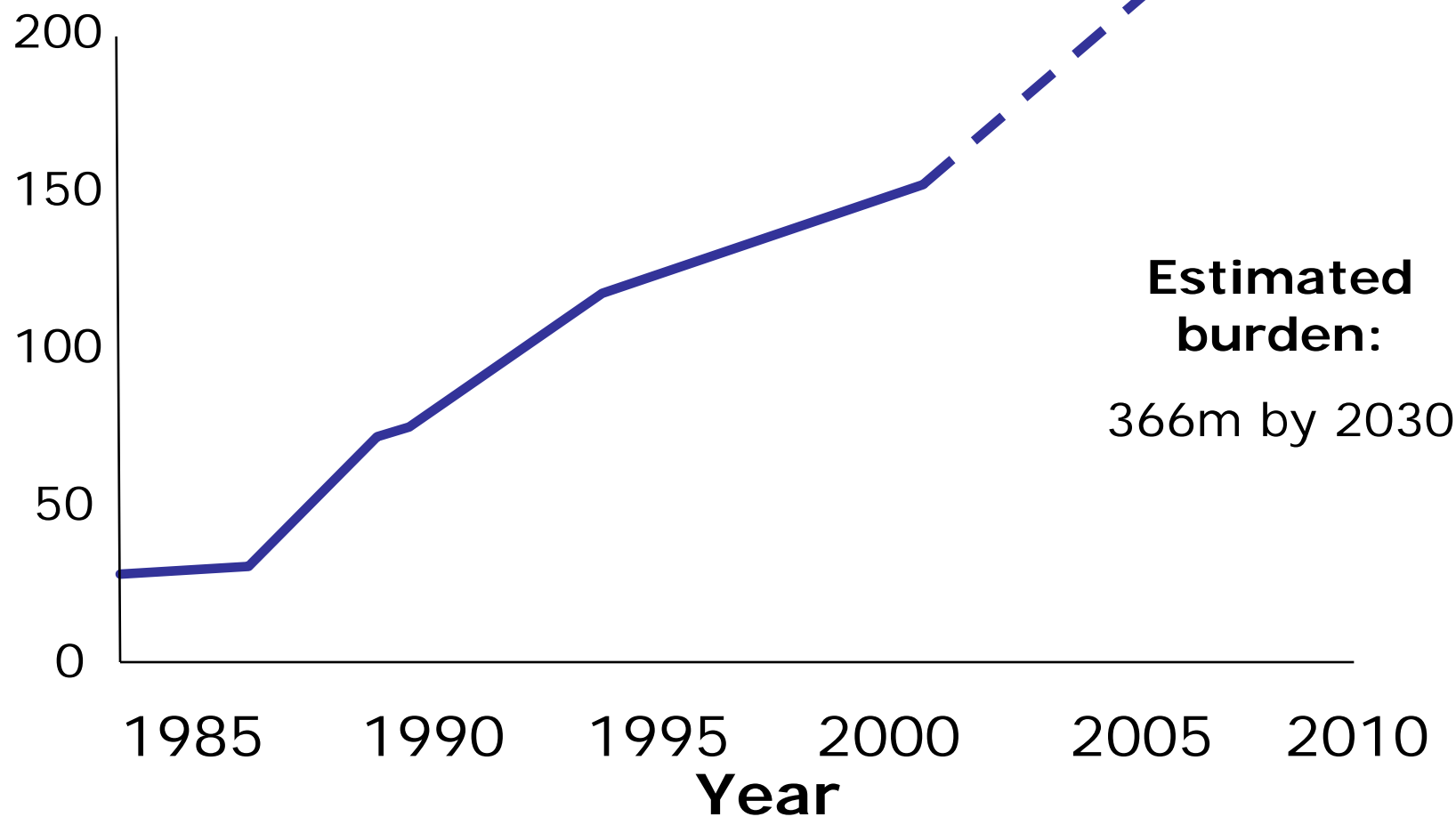
Public health bodies issue warning over the growing number of cases of diabetes

James Meikle, health correspondent

The Rise and rise of diabetes: Pay now or pay (more) later

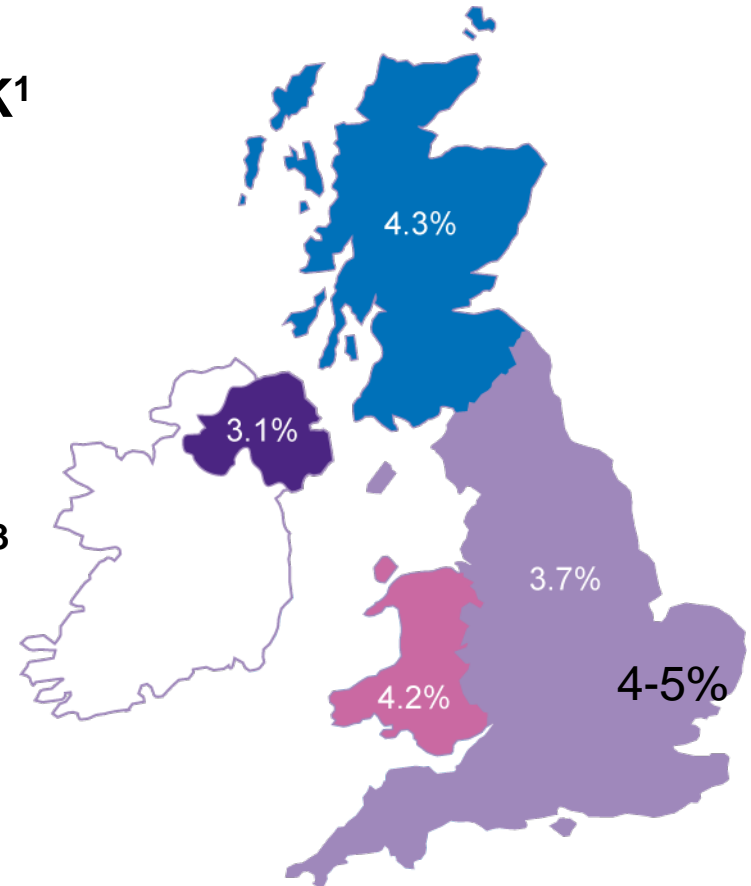
- Is there really an epidemic?
- What are the current costs of diabetes?
- What is the evidence that we can do something to address the epidemic?
- What can we do?

Diabetes is Increasing:



Prevalence of diabetes is increasing

- Around 2.3 million people are diagnosed with diabetes in the UK¹
- By 2025, it is estimated that there will be more than 4 million people with diabetes in the UK^{1,2}
- Type 2 diabetes accounts for approximately 90% of all cases and is recording the most growth³
- In addition, there are more than 500,000 who have type 2 diabetes but are not aware of it¹



Adapted from: Diabetes UK (2008). Diabetes. Beware The Silent Assassin.

1. Diabetes UK (2008). Diabetes. Beware The Silent Assassin. Available at: www.diabetes.org.uk/Documents/Reports/Silent_assassin_press_report.pdf. Date accessed: August 2009. 2. Yorkshire and Humber Public Health Observatory (2008). PBS Diabetes Prevalence Model Phase 3: Key Findings. Available at: www.yhpho.org.uk/resource/view.aspx?RI=990. Date accessed: August 2009. 3. International Diabetes Federation. Diabetes and Cardiovascular Disease: Time to Act. Available at: www.cvd.idf.org/Diabetes/The_Extent_of_the_Problem/. Date accessed: August 2009.

Diabetes in Pregnancy

- Type 2 diabetes in pregnancy
 - Increasing rapidly as Type 2 diabetes increases
 - Eg USA 1990-1998
 - Overall increase in Type 2 diabetes: 33%
 - Increase in those 30-39 years: 70%
- Type 1:Type 2 diabetes in pregnancy (US)

• Type 1:Type 2	1980	3:1
•	1995	1:2

(Feig et al. Lancet 2002;359: 1690-1692; Mokdad et al. Diab care 2002;23:1278-83;
Engelgau et al. Diab Care 1995;18:1029-33)

Increasing incidence of Type 2 diabetes in children and adolescents

- **Until recently, most children presenting with diabetes had type 1 diabetes**
- **Type 2 diabetes is now increasingly reported**
 - Case reports in children from many countries, including USA, Canada, Japan, Hong Kong, Australia, New Zealand, Libya and Bangladesh
 - Accounts for up to 45% of recently recognized cases of diabetes among children and adolescents in the US
- **Most cases of type 2 diabetes in children and adolescents are attributable to obesity**

Diabetes is associated with an increase in hospital admissions

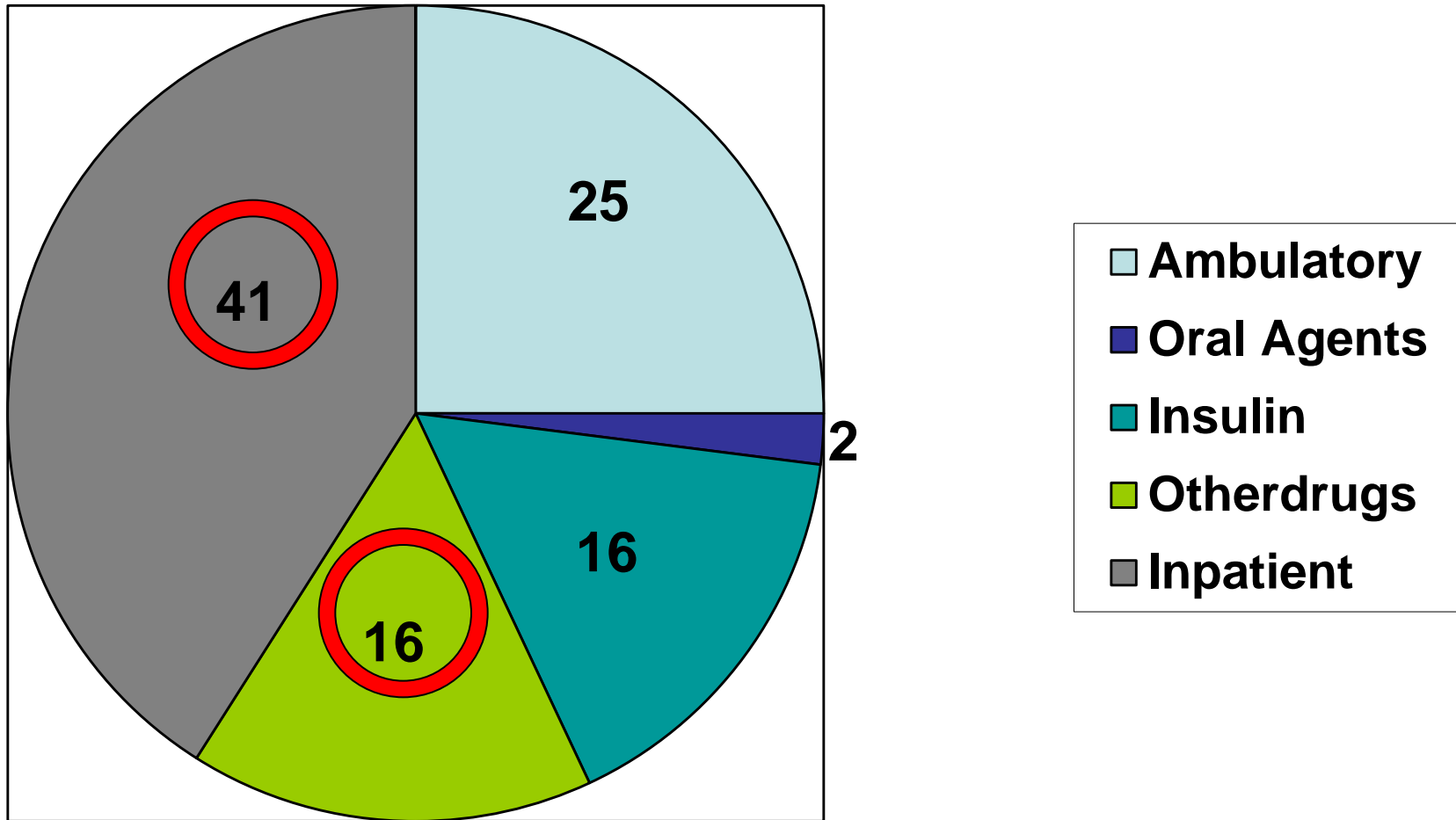
- **People with diabetes are twice as likely to be admitted to hospital¹**
- **60% of inpatients with diabetes have been admitted as emergencies¹**
- **20% of people with diabetes have been admitted in the previous year¹**
- **In the UK, people with diabetes spend 1.1 million days in hospital every year²**
- **Presence of diabetic complications increases NHS costs more than 5-fold**
- **~10% NHS hospital costs**
- **£99m per week; £14m per day**



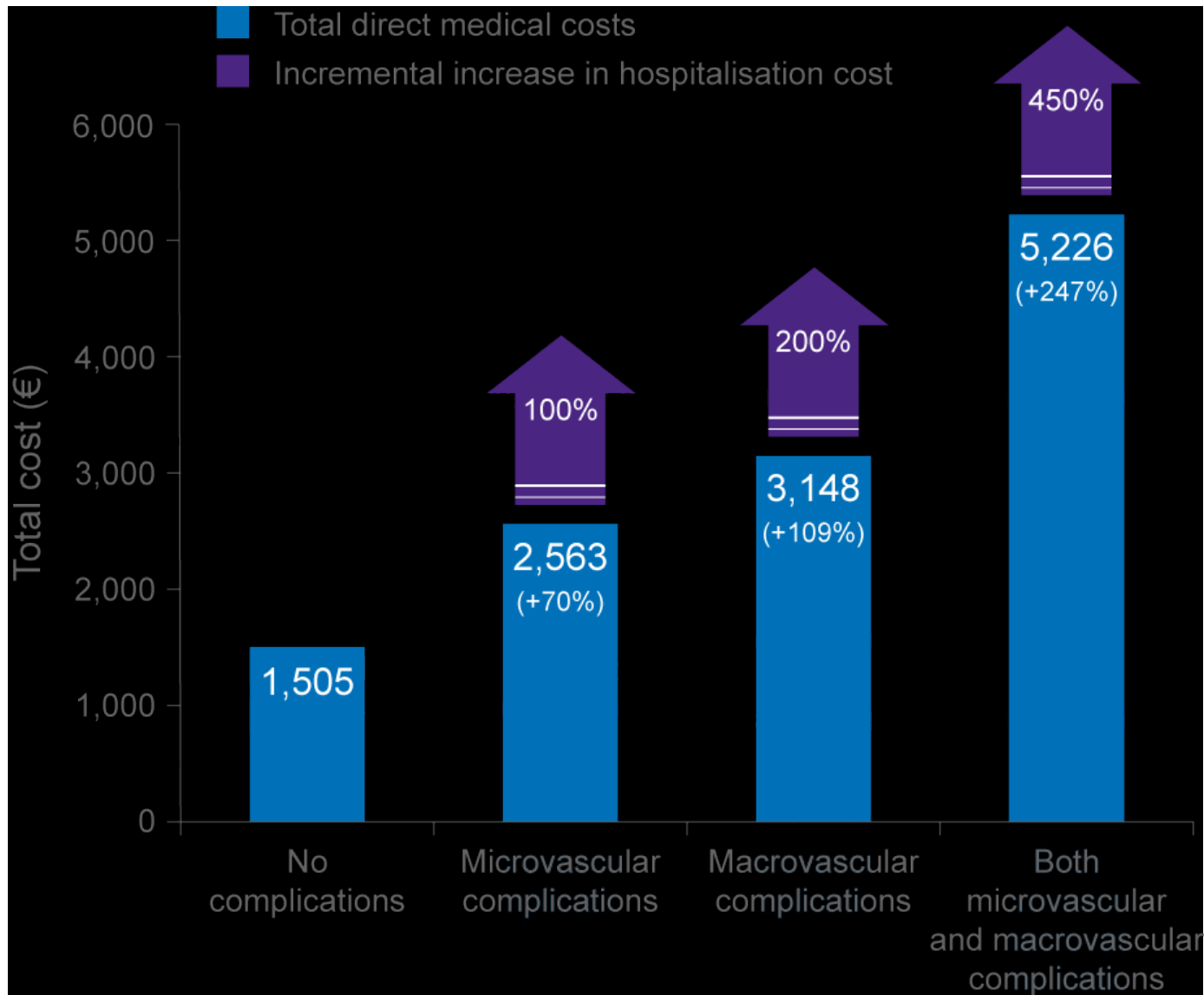
1 in 10 people in a UK hospital bed has diabetes¹

1. National Diabetes Support Team (2008). Improving Emergency and Inpatient Care for People with Diabetes. Available at: www.diabetes.nhs.uk/news-1/Inpatient%20care.pdf/view. Date accessed: August 2009. 2. Diabetes UK (2004). Diabetes in the UK 2004. Available at: www.diabetes.org.uk/Documents/Reports/in_the_UK_2004.doc. Date accessed: August 2009. 3. Department of Health (2006). Turning the Corner: Improving Diabetes Care. Available at: www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4136141. Date accessed: August 2009.

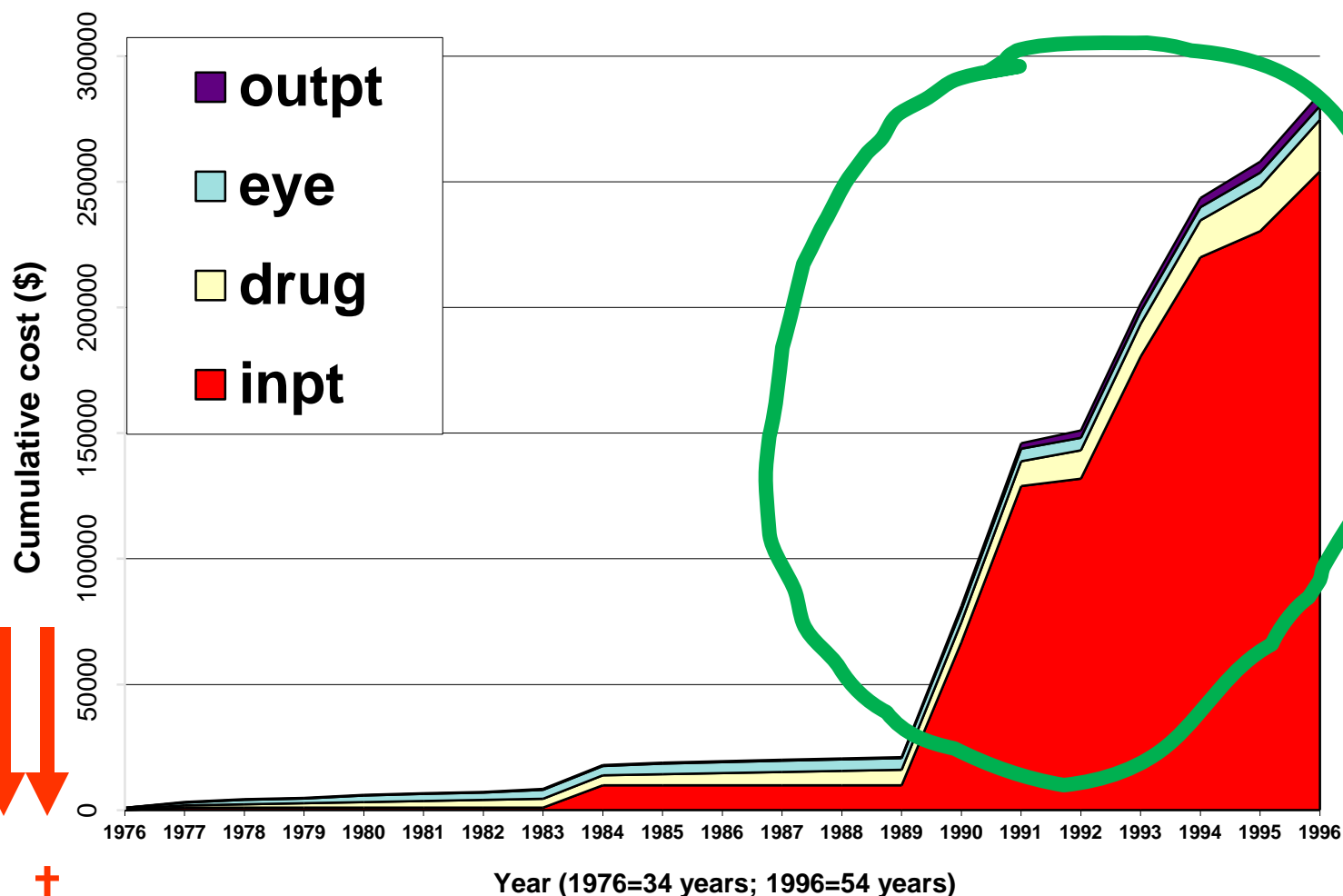
Diabetes Health Costs (%)



Complications significantly increase the costs of care¹

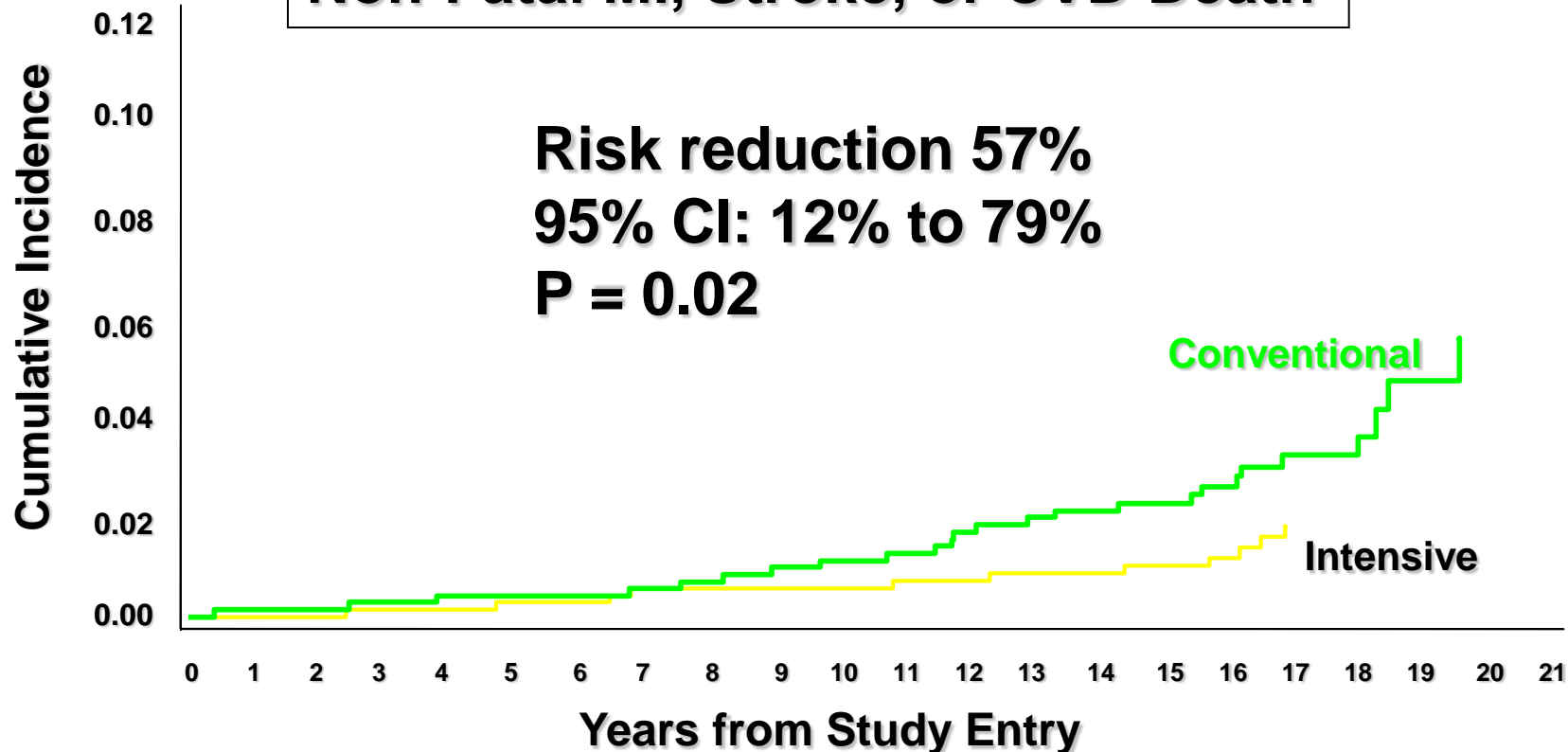


Direct costs of one patient



DCCT/EDIC Findings: Cardiovascular Events-Metabolic memory

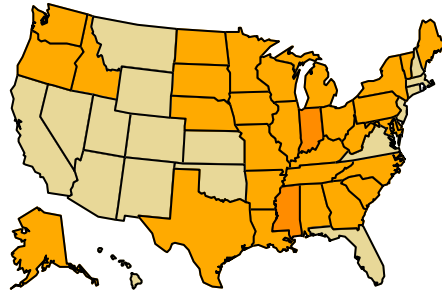
Non-Fatal MI, Stroke, or CVD Death



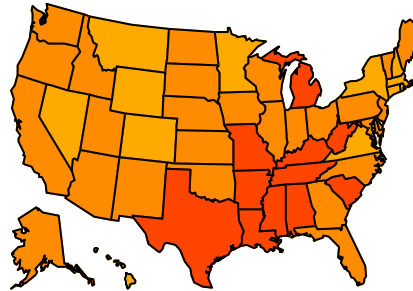
Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among U.S. Adults Aged 18 Years or Older

Obesity (BMI ≥ 30 kg/m²)

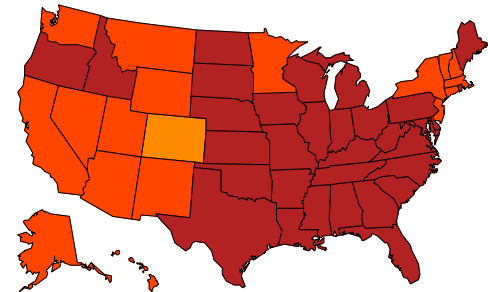
1994



2000



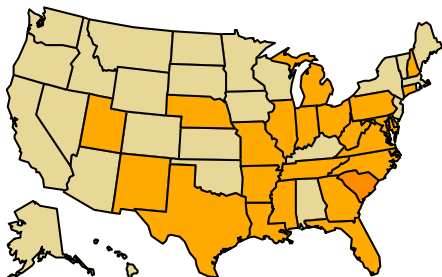
2010



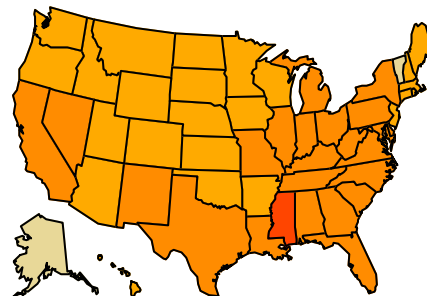
□ No Data □ <14.0% □ 14.0%–17.9% □ 18.0%–21.9% □ 22.0%–25.9% □ 26.0%

Diabetes

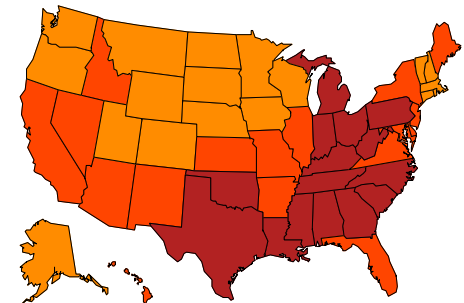
1994



2000



2010



□ No Data □ <4.5% □ 4.5%–5.9% □ 6.0%–7.4% □ 7.5%–8.9% □ $\geq 9.0\%$

CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at <http://www.cdc.gov/diabetes/statistics>

IT'S NOT ALL IN THE GENES

The environment you grow up in is as important as your DNA in determining the person you ultimately become. BY ROBERT SAPOLSKY



1964, the height of the cold war. In an average community surrounding a little-known biological warfare institute, the obesity epidemic is quietly unleashed.

Preventing Type 2 Diabetes:

When and how to intervene....

Insulin secretion/action

- Genetic
- Epigenetic
- Fuel mediated teratogenesis
- Childhood Development
- Multiparity
- Co-morbidities/iatrogenic
- 'toxins'

Demand driven

- Obesity
- Weight gain
- Sedentary life
- Physical activity
- Eating

Preventing Type 2 Diabetes:

When and how to intervene....

- ‘We propose that the whole of patients’ lives need to be considered for effective disease management, and particularly in prevention for reversal of the pandemic.’
- Type 2 diabetes across generations: from pathophysiology to prevention and management
- *Christopher J Nolan, Peter Damm, Marc Prentki*
- www.thelancet.com
Published online June 25, 2011 DOI:10.1016/S0140-6736(11)60614-4

Preventing T2DM-when and how to intervene

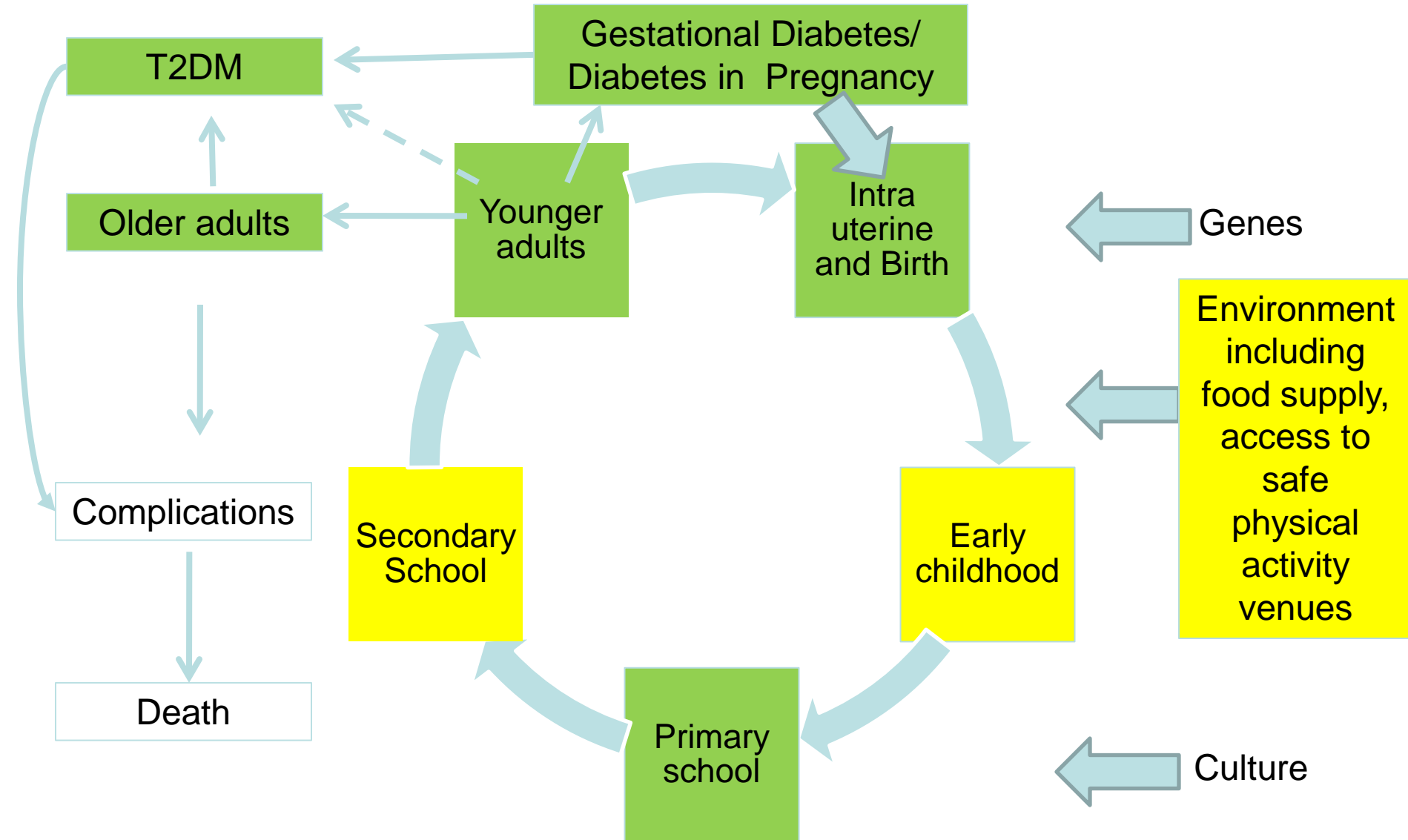
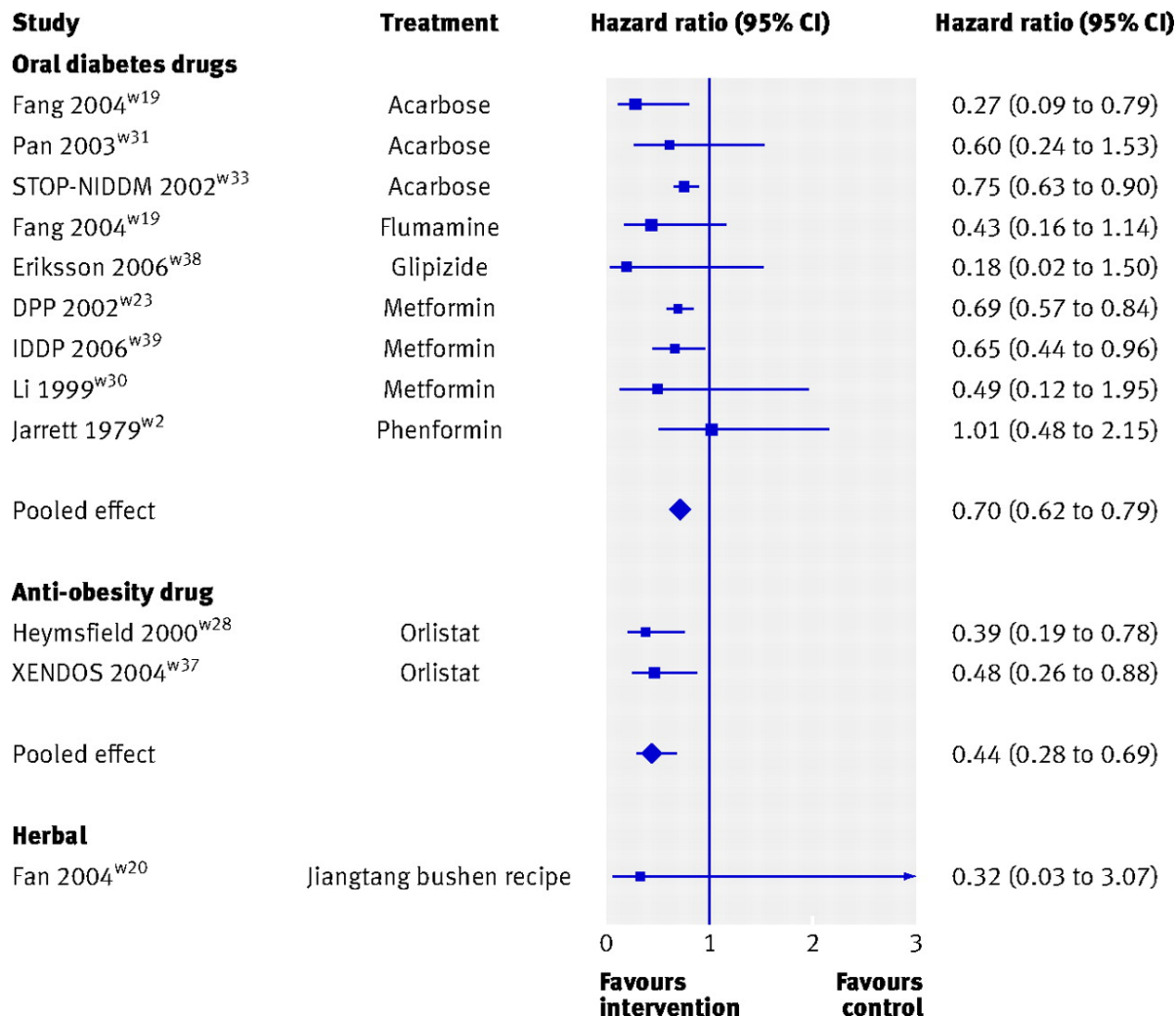


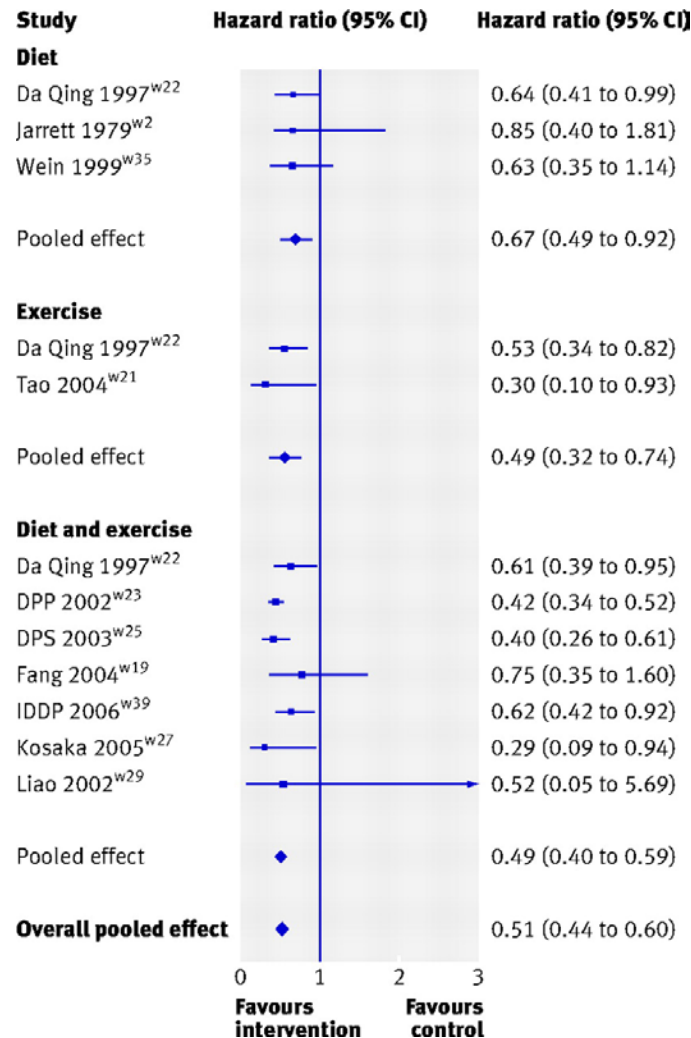
Fig 3 Meta-analyses of effect of pharmacological and herbal interventions on risk of developing type 2 diabetes.

Bariatric
Surgery



Gillies C L et al. BMJ 2007;334:299

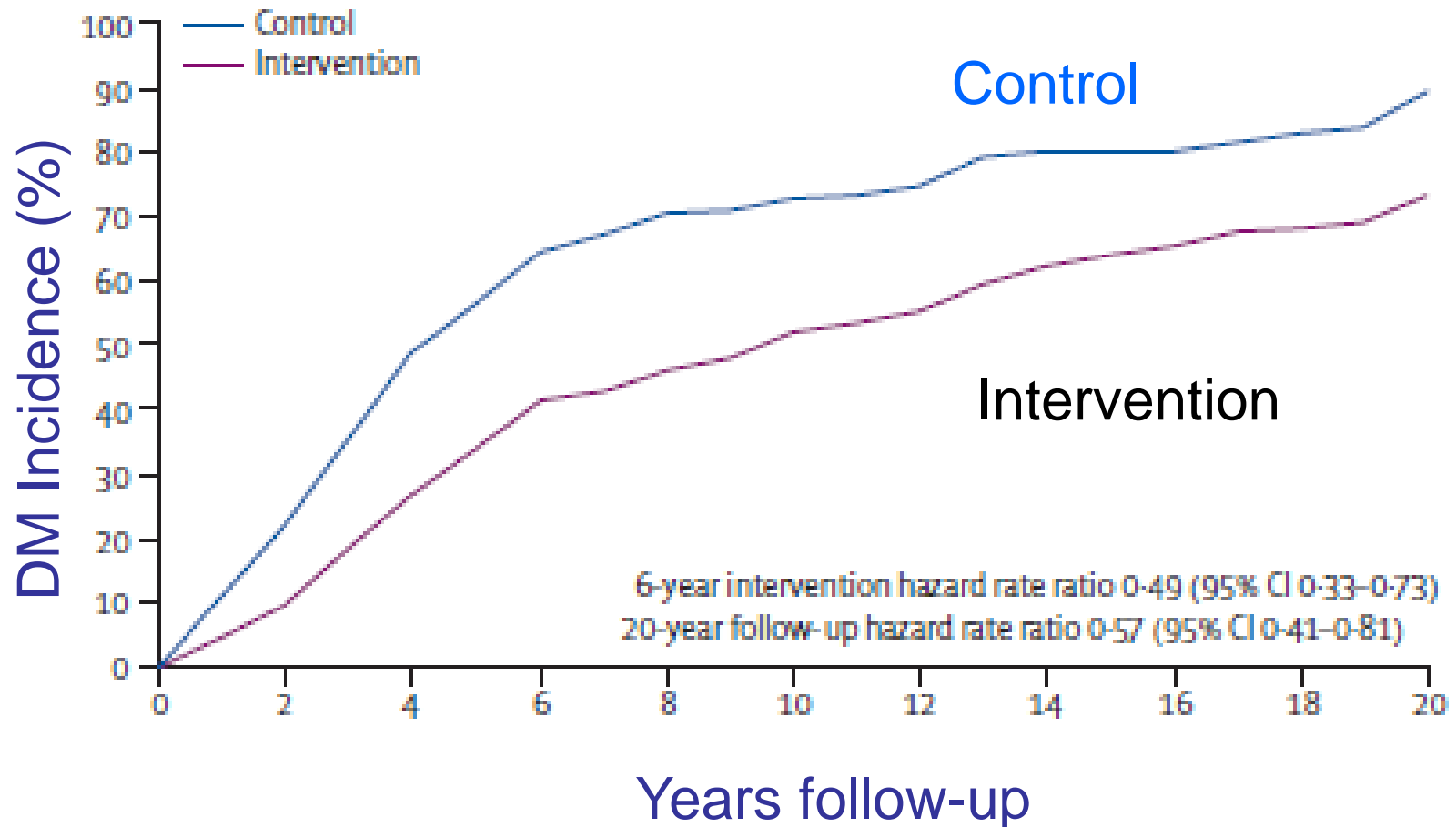
Fig 2 Meta-analysis of effect of lifestyle interventions on risk of developing type 2 diabetes.



Gillies C L et al. BMJ 2007;334:299

Incidence of Diabetes after 20 Years of Follow-up in Da Qing

Li et al www.thelancet.com Vol 371 May 24, 2008



Finnish DPS-similar prevention

Preventing T2DM-when and how to intervene

- How do we implement on a population basis?
- Population based approaches
 - Primary care-Victoria (Life); Finland
 - Change the norm
 - Easy access
 - Cost
- Go upstream



Te Wai o Rona: Diabetes Prevention Strategy

‘Wai hōpuapua e, e mimiti i a koe,
Ko Te Wai a Rona, he manawa a whenua
E kore e mimiti e.’

Preventing Type 2 diabetes by 35%
over 4 years

(2004-2006: No further funding after
3 years)

‘You can cause the waters of a pool to run dry, but the water of Rona is a well spring from the heart of the land which will never run dry.’

Te Wai o Rona: Diabetes Prevention Strategy:

Area covered

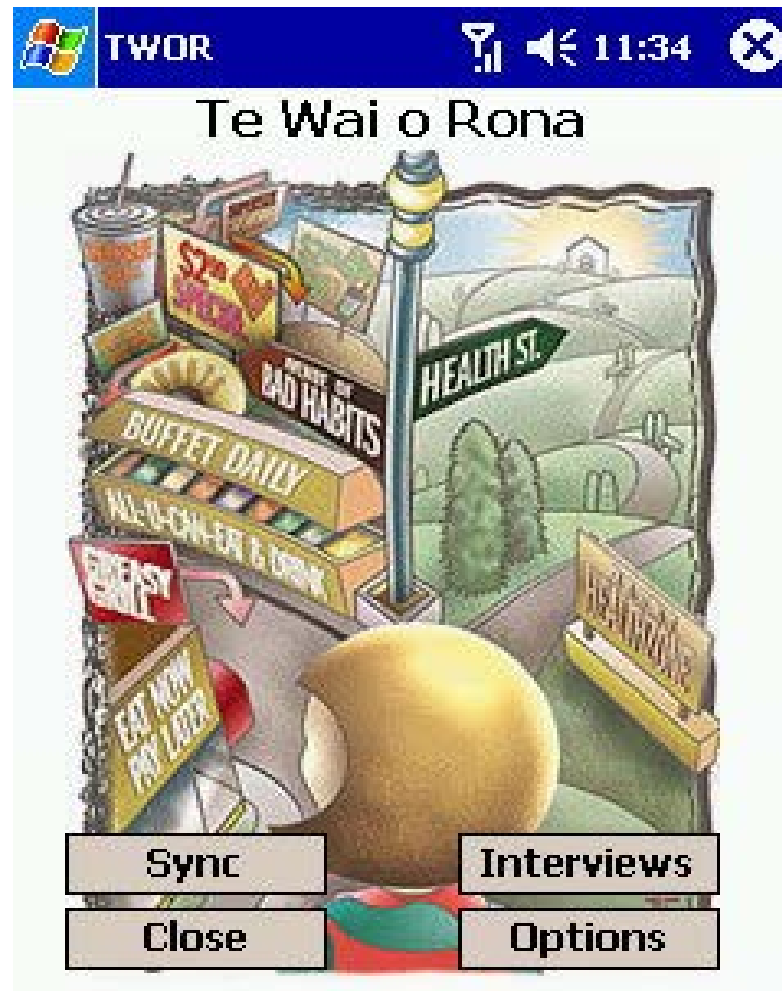


3 key components

- **Coaching**
 - GRx for hi risk
- Access to healthy food
- Community/cultural

Vanguard Study: Intervention

- Intervention
 - MCHW 1:250-Motivational interviewing
 - 12 messages, associated Toolkits, Deskfiles
 - Electronic record and reporting system
- Vanguard
 - Piloted toolkit and messages
 - demonstrated acceptability and utility
 - Piloted Palms and software
 - demonstrated ease of use to MCHWs, record weights
 - demonstrated acceptability to participants
 - identified areas for upgrade
 - Piloted impact on weight-MCHWs carry scales, weigh if participant wishes/every month if agrees



Baseline Characteristics

	Vanguard	Pre-intervention	
N	155	29	
Age	48±14	47±12	.629
IGT/IFG	34	4	.320
Men/Women	48/107	10/19	.708
Fasting Glucose mM	5.3±0.6	5.2±0.5	.245
HbA1c (%)	6.0±0.5	5.8±0.3	.134
Weight (kg)	94.5±23.2	90.0±20.1	.343
BMI (kg/m ²)	34.2±8.0	32.8±7.0	.415

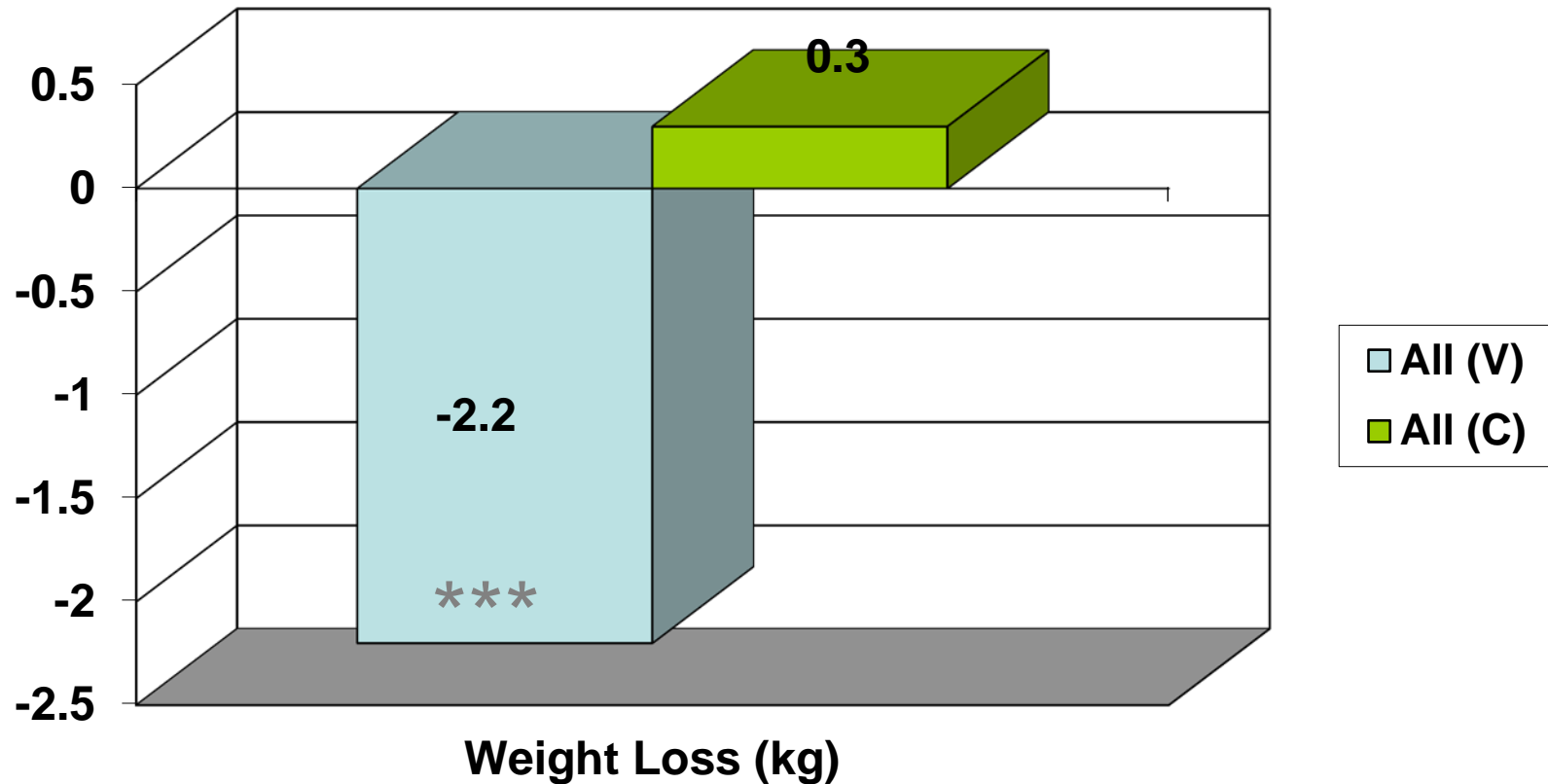
No sig diffs BP, lipids

Visits and Follow up

- Total number seen: 155
- Number of recorded visits:* 3.7 ± 2.2
- Range of visits* 2-17
- Number of days of intervention 168 ± 138

*Excludes initial visit, incidental meetings

Weight loss (kg) in Vanguard

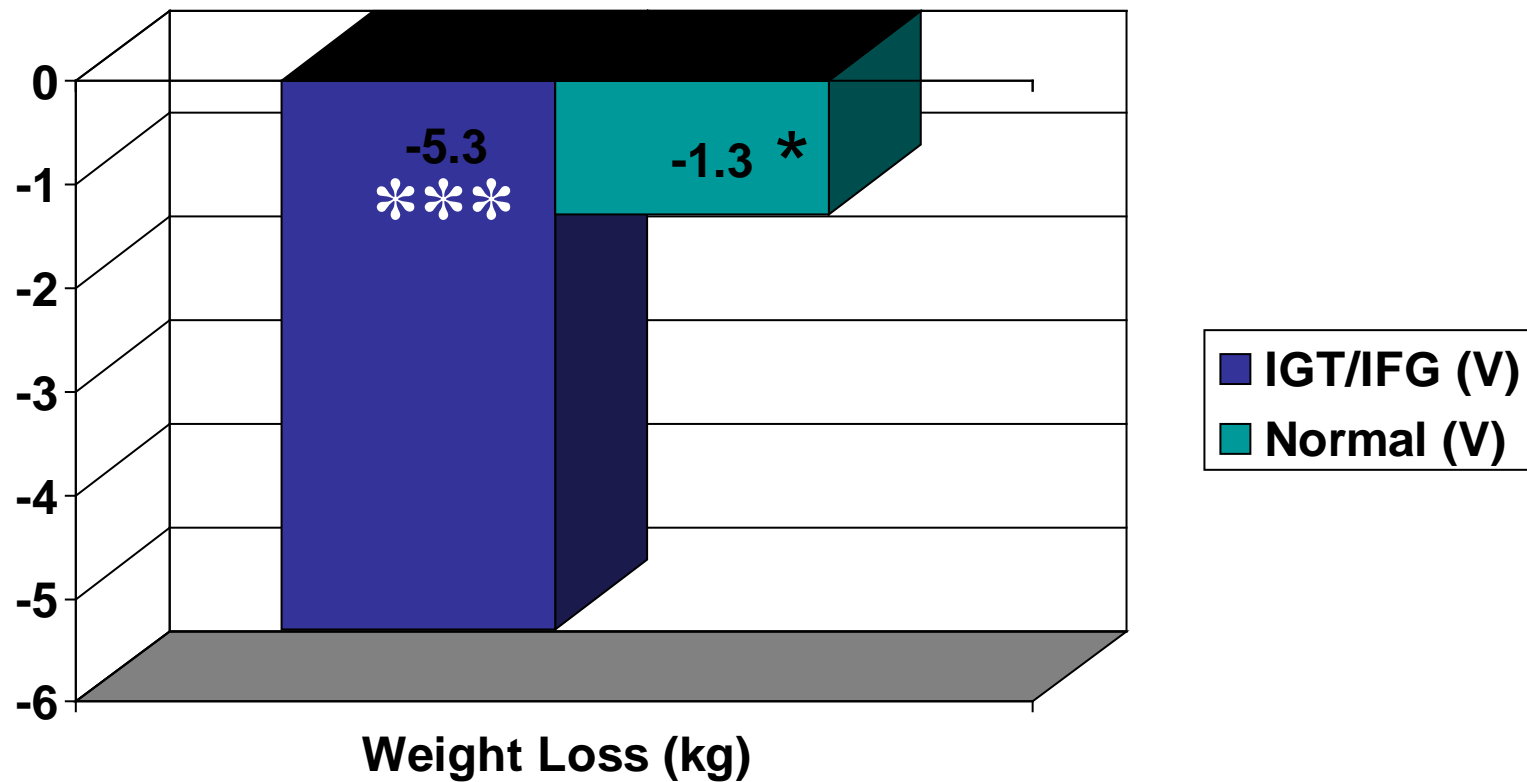


$p < 0.001$ paired t-test vs baseline; M=F

Simmons D, Rush E, Crook N. Development and piloting of a community health worker based intervention for the prevention of diabetes among New Zealand Māori in Te Wai o Rona: Diabetes Prevention Strategy. Public Health Nutrition 2008; 11 : 1318-1325

Weight loss (kg) in Vanguard

$P=0.001$



***, * $p<0.001$, $p<0.05$ paired t-test vs baseline

Preventing diabetes-Primary school interventions

- “It is difficult to create an effective program based only on limited interventions in schools.”
 - Flodmark 2006 on interventions to prevent obesity
- No evidence from intervention studies to indicate that this would prevent development of T2DM
- Expected from epidemiology



Managed by:

Project Director
Stephanie McLennan



Funding:



Medical Leader, Dr David Graham

Evaluation
Funding:



Other
Funding:



Collaborate with:

Academic Leader,
Prof Elaine Rush



Project Consultant,
Prof Bevan Grant



THE UNIVERSITY OF
WAIKATO
Te Whare Wānanga o Waikato

Partners:



Project Overview

A Waikato District Health Board Initiative

Aim: To increase the amount and quality of physical activity and to improve the nutritional status of school age Waikato children.

- 2004-2006 Research Project with two components, Evaluation and Intervention

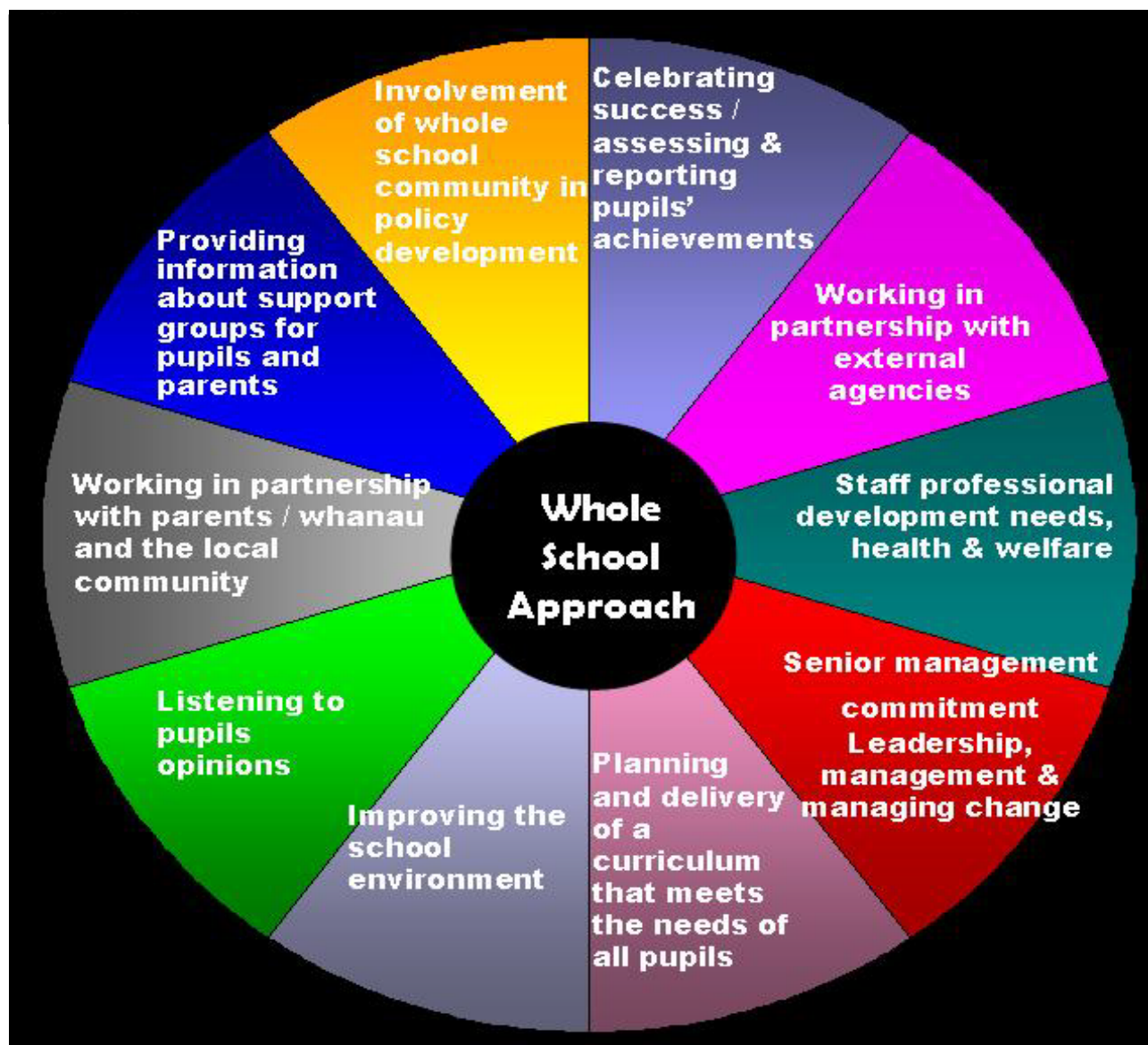
- Evaluation involved a range of physical measures of consenting 5 and 10 year olds; a home questionnaire and school stock take – baseline and end point.

- Intervention involved a facilitator working in programme schools to support them with physical activity and nutrition initiatives.

- End of 2 year RCT suggestion of reduced obesity->extended



Whole School Approach

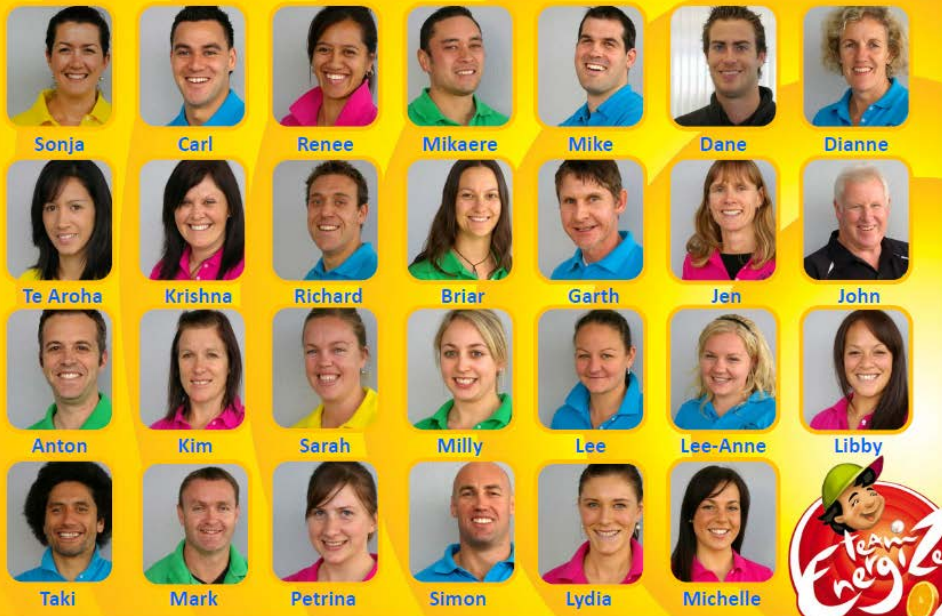


Be active

Have fun

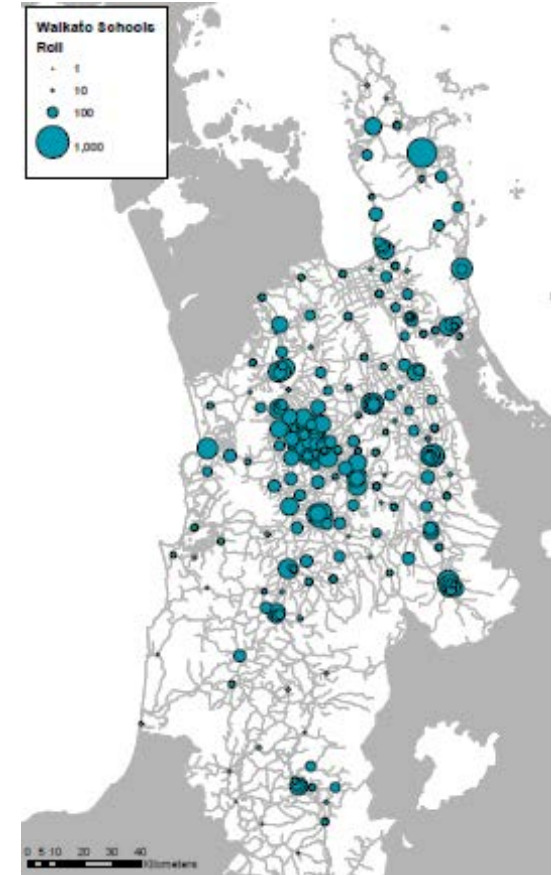


WHO ARE TEAM ENERGIZE?



Project Energize

Addenbrooke's Hospital **NHS**
Cambridge University Hospitals NHS Foundation Trust



Waikato Region

242 schools

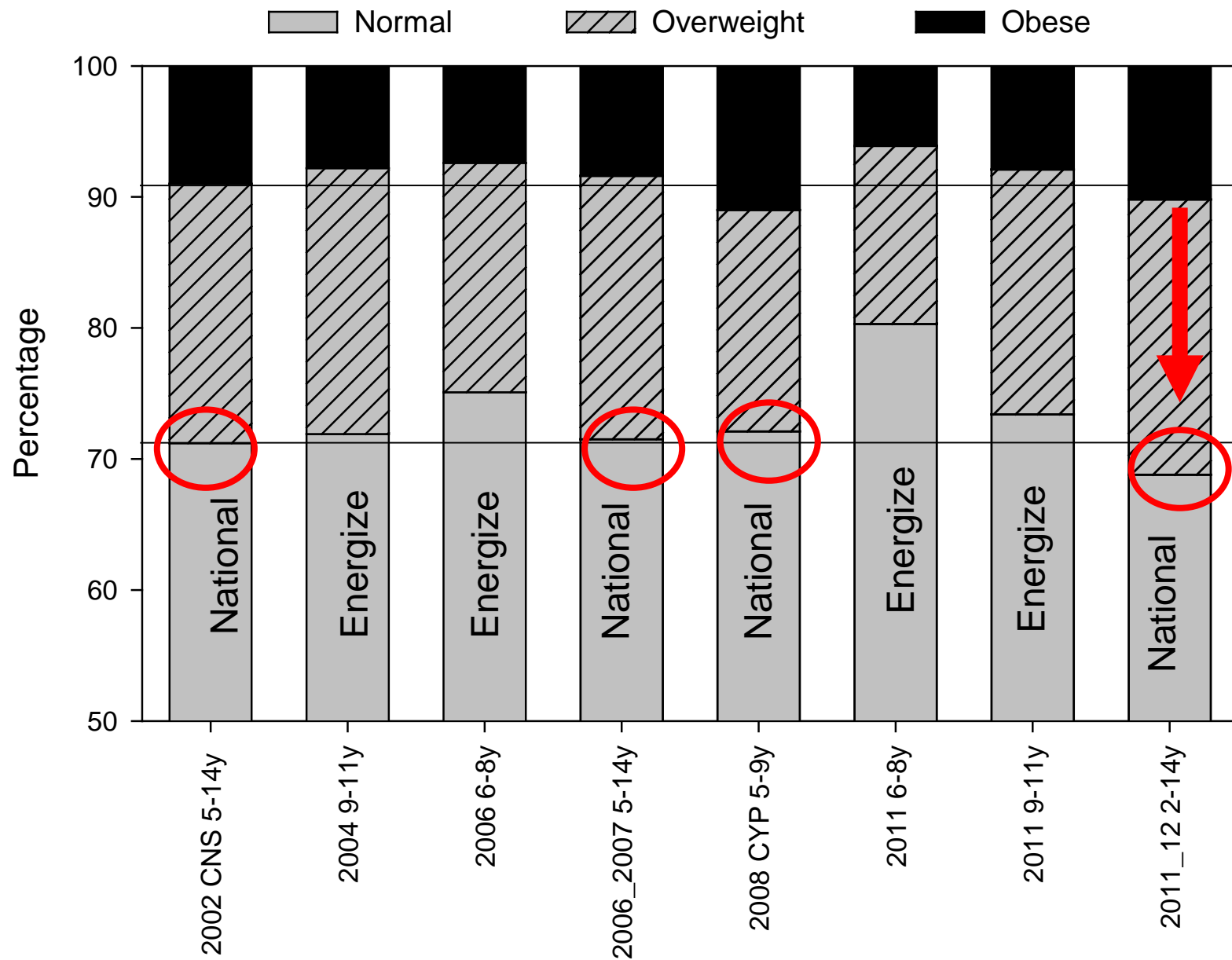
44000 children

\$45/child/year

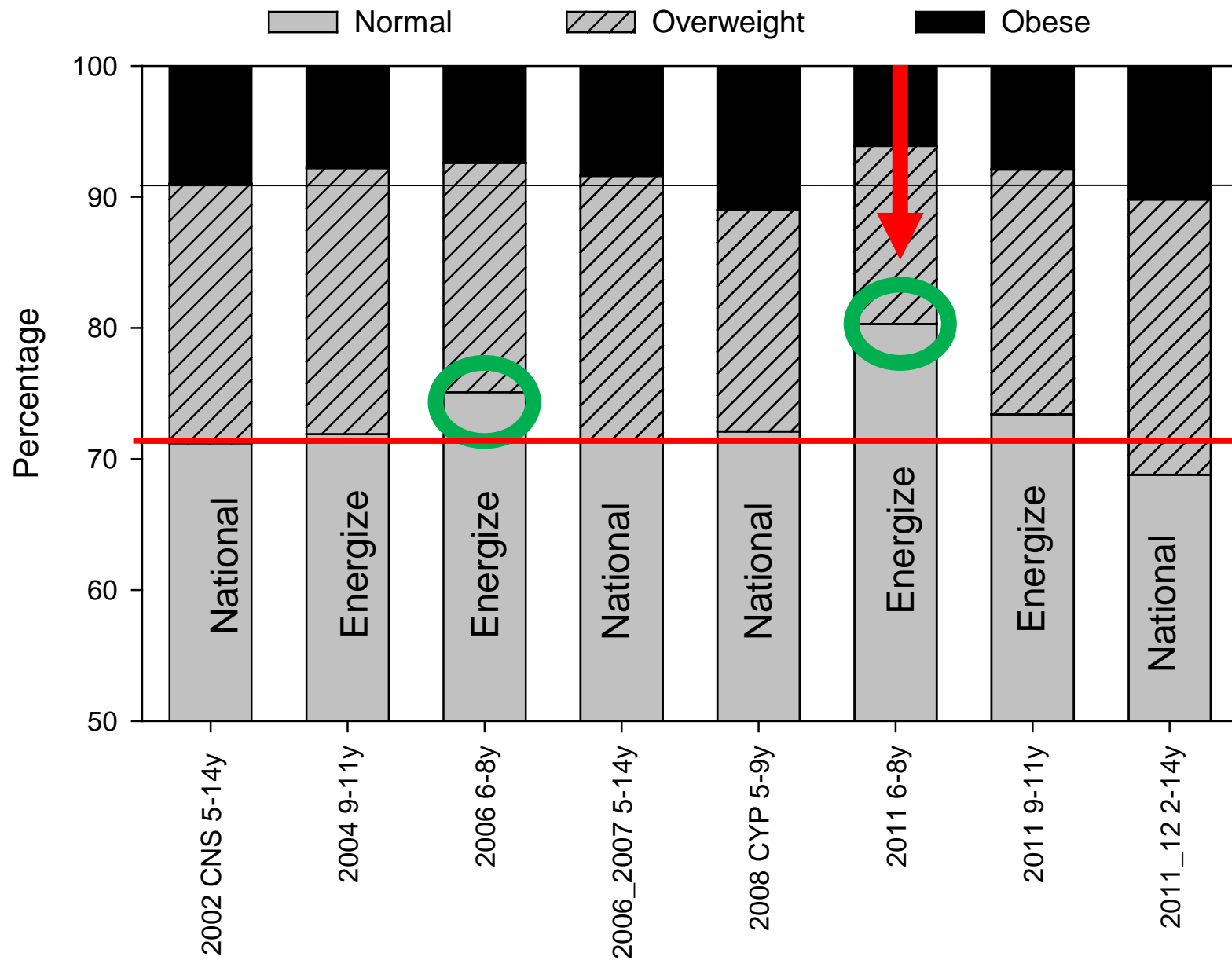
Project Energize Evaluation

- 5110 children aged 6 to 11 years from 192 schools were measured (45% of the 7 and 10 year old children invited)
- Time to run 550m 13% faster vs historical controls
- 2011 Energize vs 2006 Waikato children
 - Waist was 2.3/4.7 cm less (6-8/9-11 yrs)
 - Overweight/obese reduced 4%/1% (6-8/9-11 yrs)

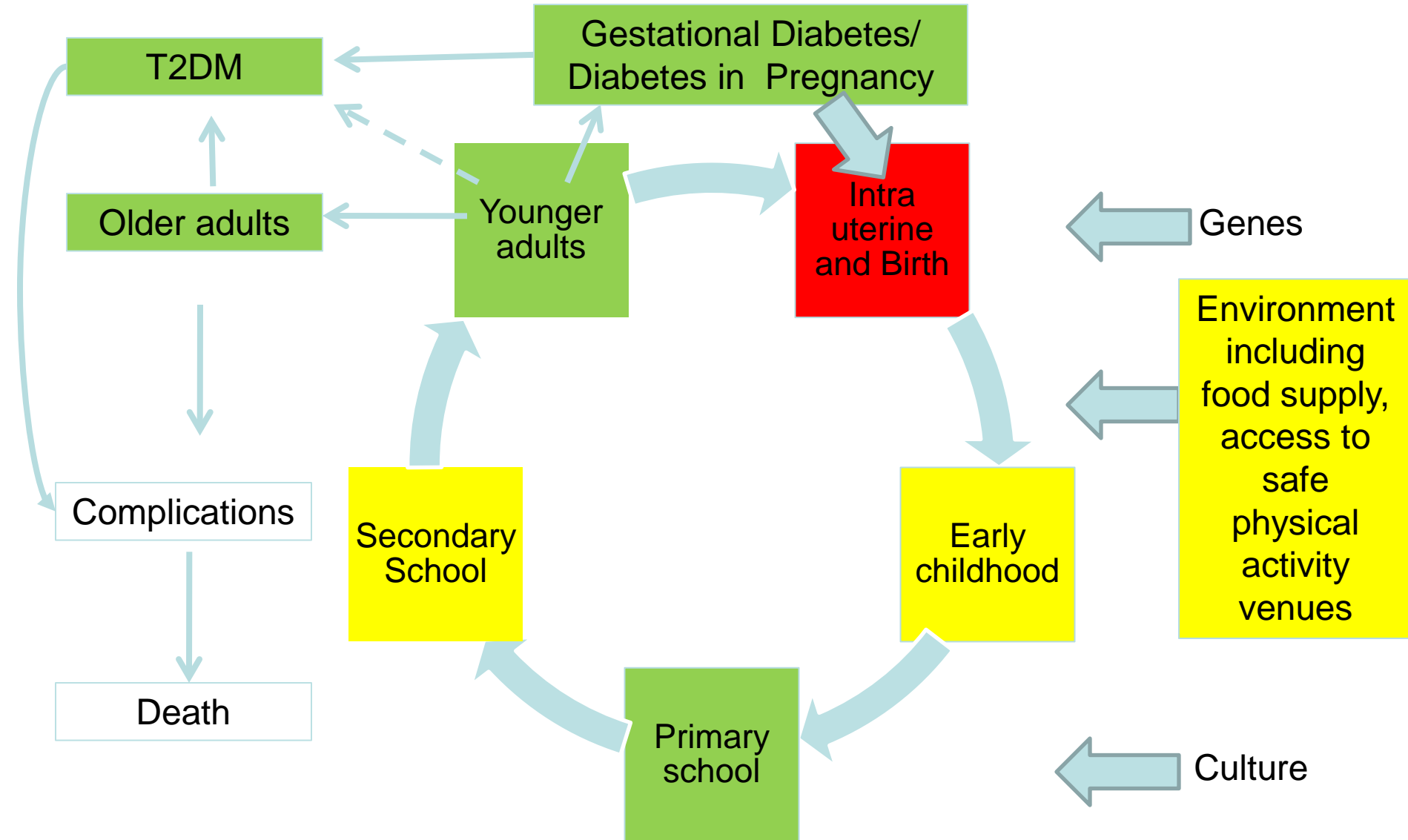
All children, obesity and overweight scale expanded



All children, obesity and overweight scale expanded



Preventing T2DM-when and how to intervene



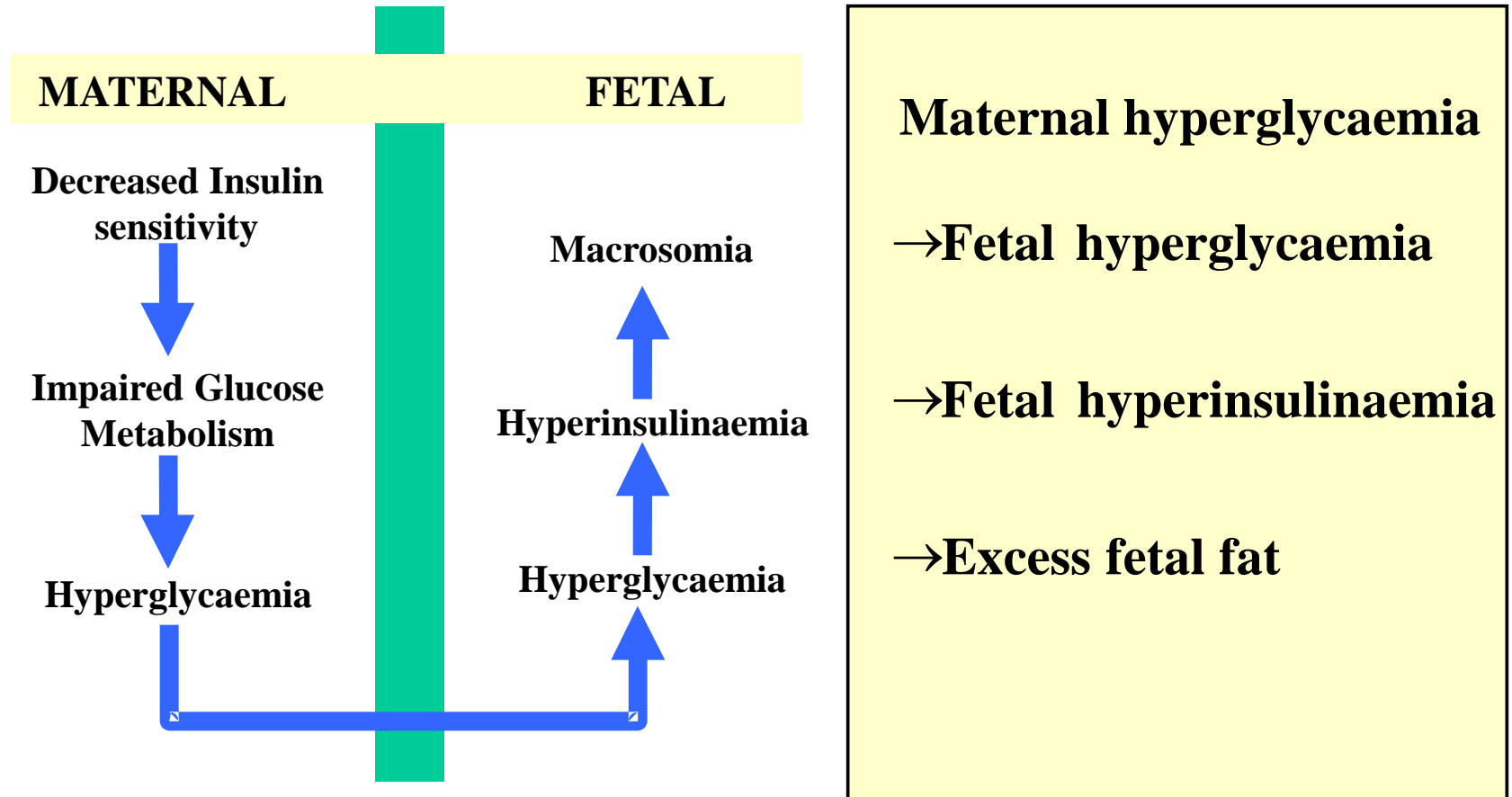
Culture of rat embryos from the early head-fold stage to the 26-to-29-somite stage (Days 9-1/2 through 11-1 of gestation).

*The addition to culture mediums of METABOLIC INDUCERS
caused growth retardation
somite reduction
and
faulty neural-tube closure*



***Mannose
Glucose
Myoinositol***

Pedersen- Freinkel Hypothesis



Fuel mediated teratogenesis (Freinkel)

Aerts and Van Assche: Evidence

Induce diabetes (STZ) in mother rat (F0)



Diabetes in pregnancy



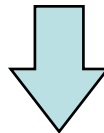
Diabetes in F1



Diabetes in pregnancy

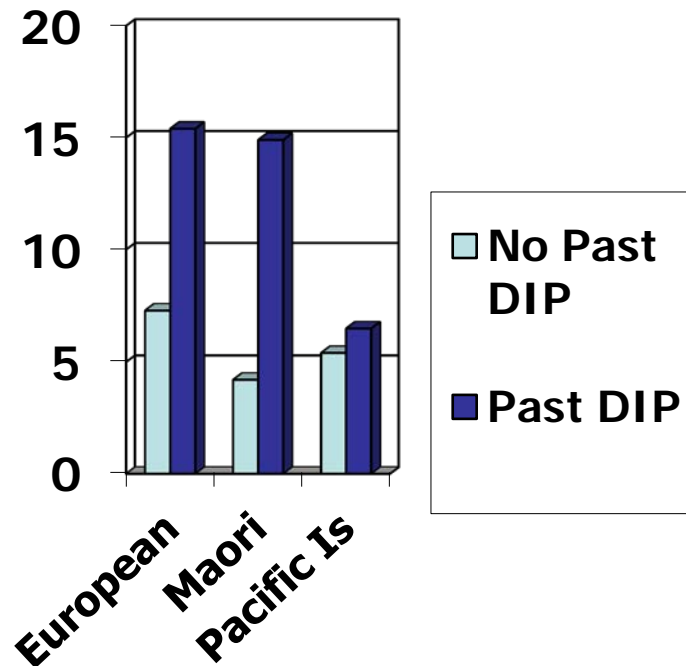


diabetes in F2



All generations to F3 (expt terminated)

Diabetes in the offspring of Women with and without Past known Diabetes in Pregnancy



Odds Ratio

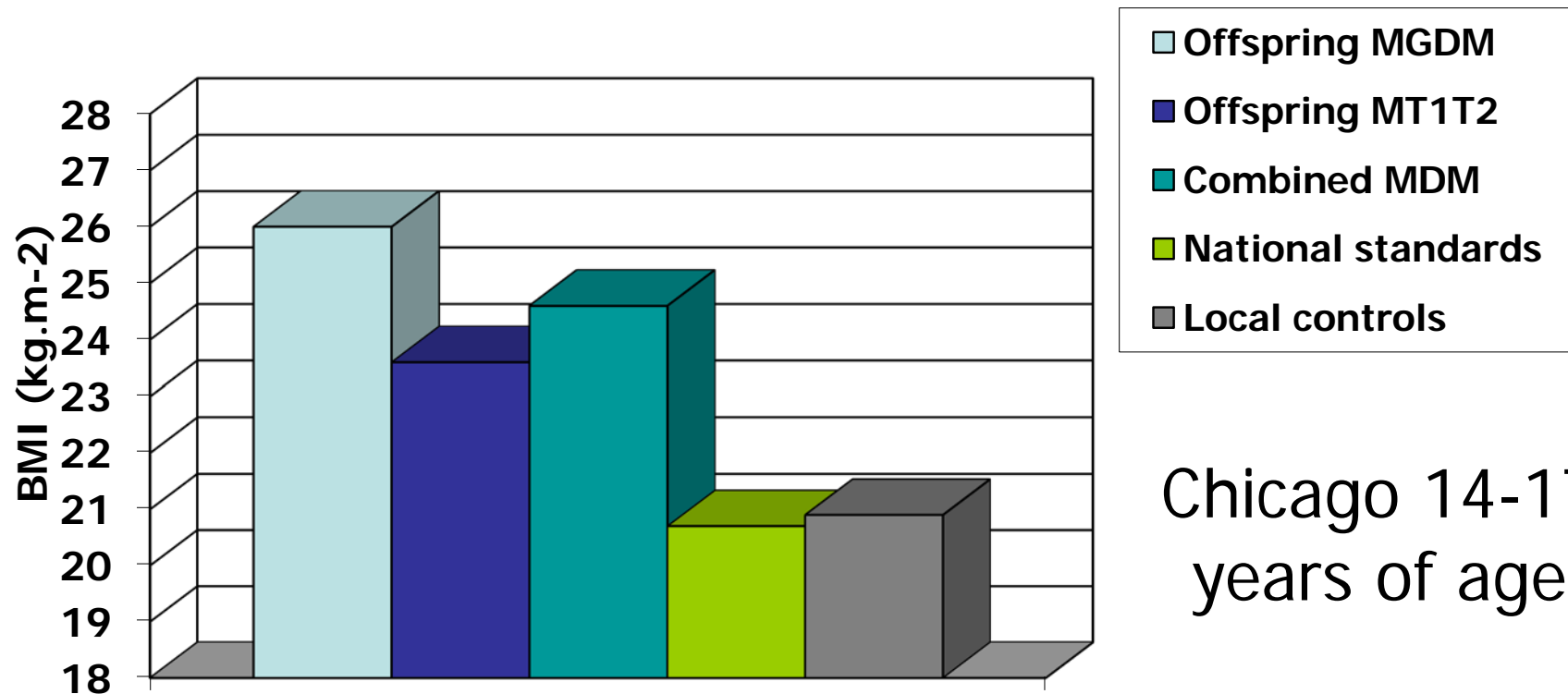
Past DIP: No Past DIP

Overall

2.05 (1.01-4.15)

Simmons et al J Intern Med
1995;237:315-321

And its not just IGT/Diabetes-Obesity in the offspring



Chicago 14-17
years of age

DOES INTERVENTION MAKE A DIFFERENCE?

**Solid lines
appropriate for
gestational age
children**

**Dashed
lines large
for
gestational
age children**

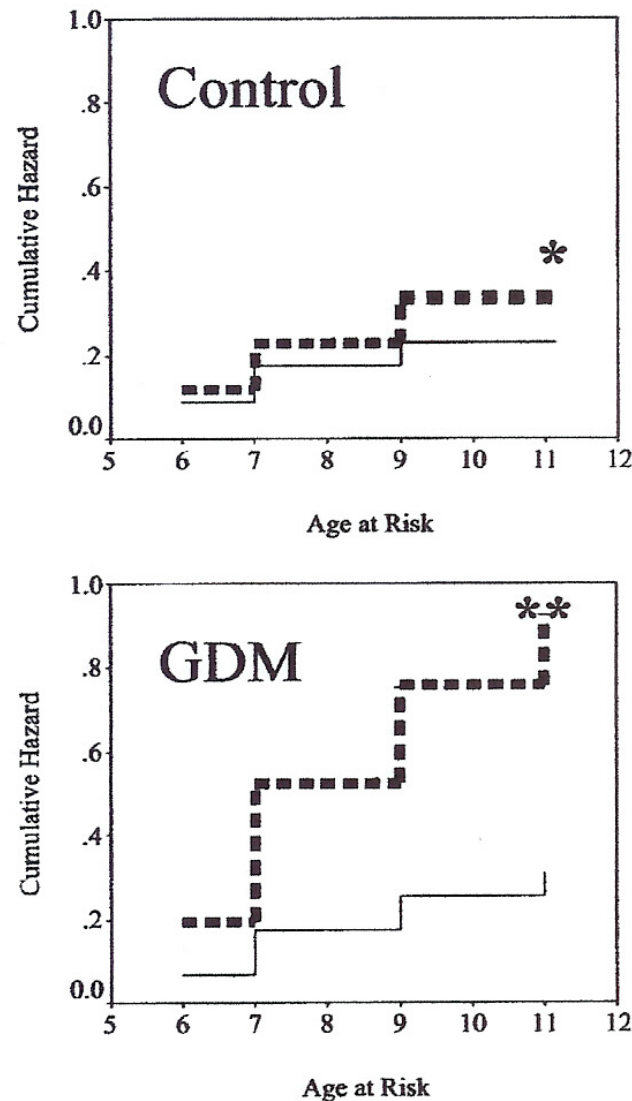


Fig 2. Cumulative hazard (risk) function for development of MS according to birth weight. Children were divided into control ($n = 83$) ($*P = .56$) and GDM ($n = 92$) ($**P = .004$) groups. The cumulative risk of MS was stratified according to birth weight; solid lines represent AGA children, and dashed lines represent LGA children.

Boney C et al
2005:
Pediatrics
115:290-296

Neonatal Diabetes Study

Mothers: E, M/PI GDM:OGTT @ 30w



Fasting venesection 36/40



Delivery: Venous cord sampling

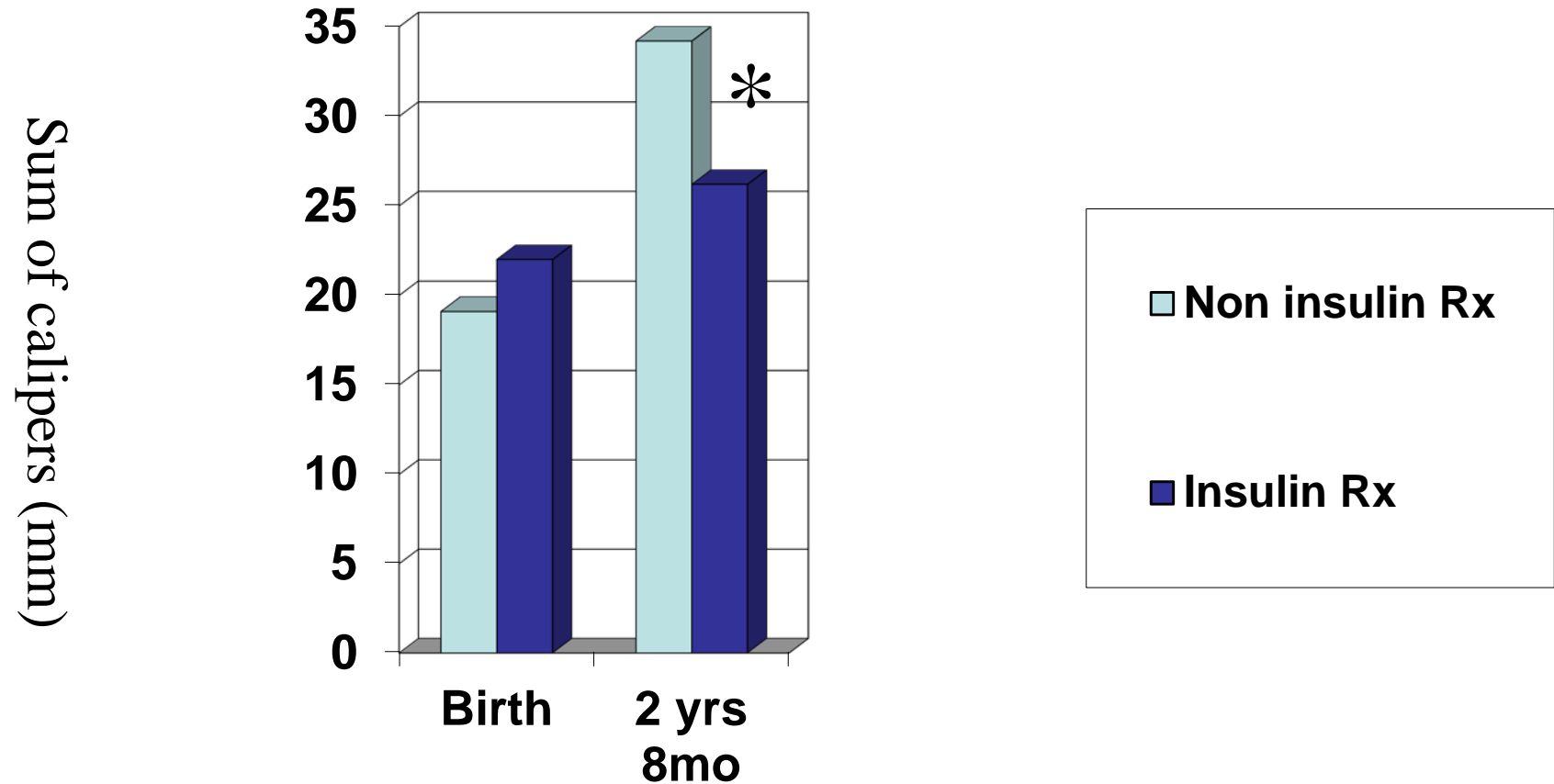


24 hrs post delivery:anthropometry



Follow up at 2.8 years

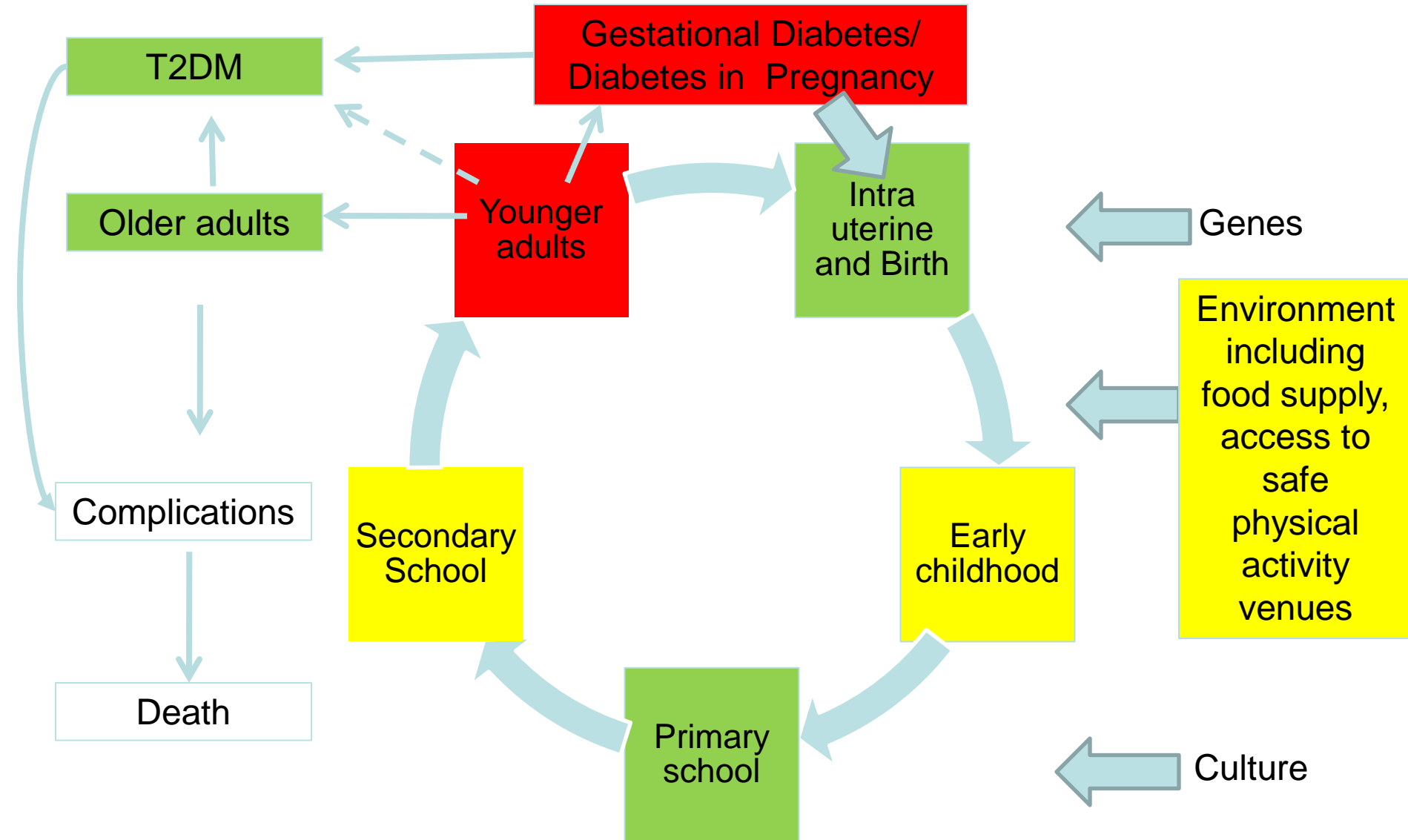
2.8 year follow up of infants from diabetic mothers



Diab Med 1997;14:762-765

HOW CAN WE REDUCE FUEL MEDIATED TERATOGENESIS?

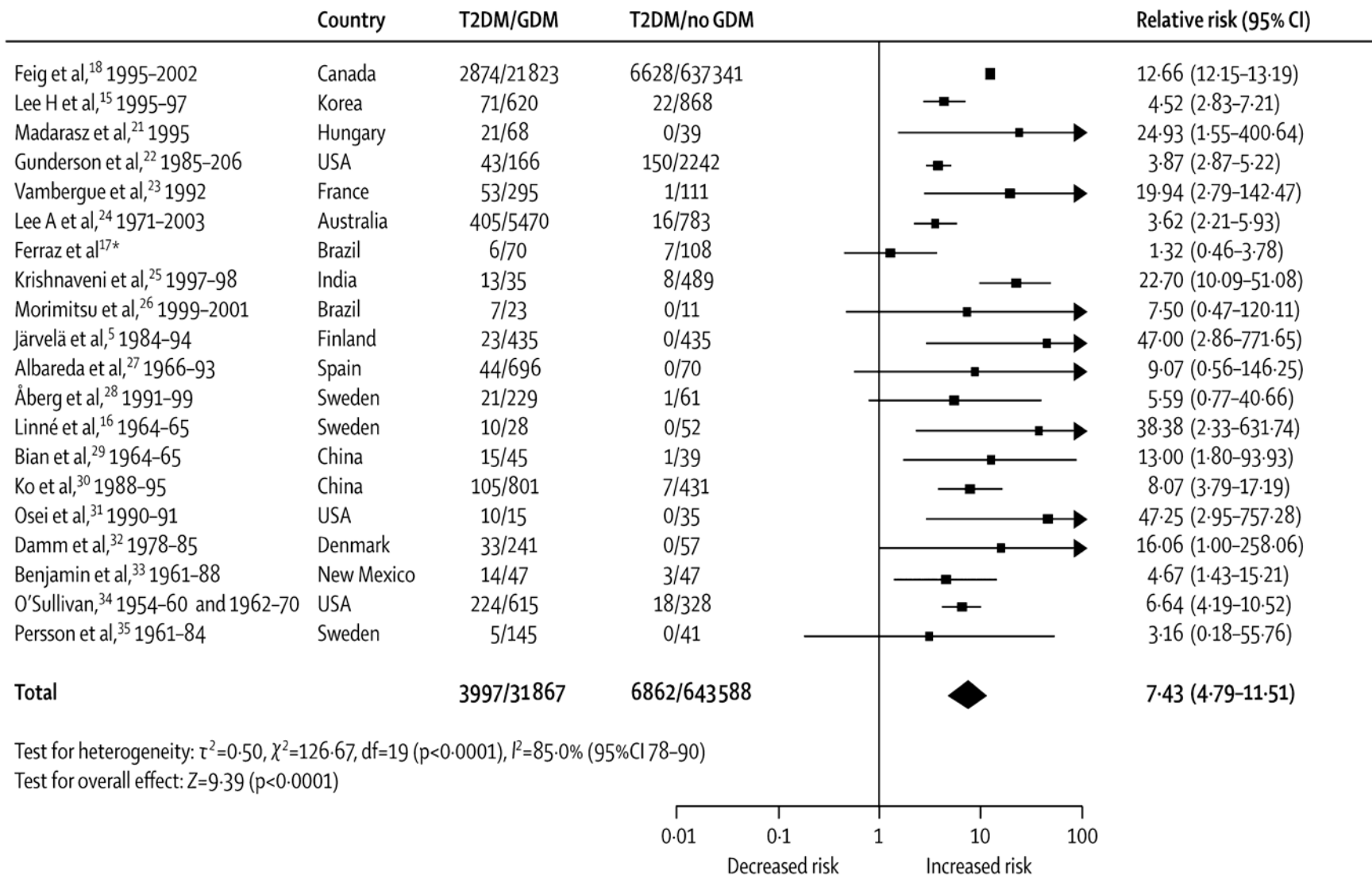
Preventing T2DM-when and how to intervene



HOW CAN WE REDUCE FUEL MEDIATED TERATOGENESIS?

- Reduce the potential for women to enter pregnancy obese/overweight/with diabetes eg intervene pre-pregnancy eg Te Wai o Rona: Diabetes Prevention Strategy, DPP, women with past GDM
- Minimise hyperglycaemia among women with diabetes entering pregnancy/early pregnancy
- Find hyperglycaemia in pregnancy early and intervene effectively
- Prevent GDM occurring within pregnancy

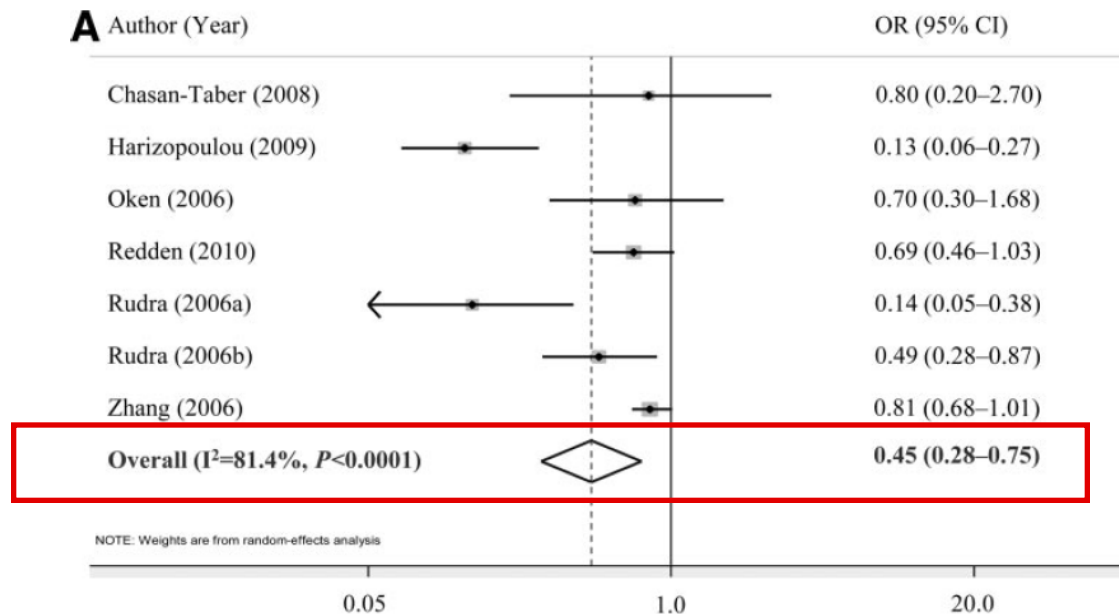
Risk of progression (% pa) from GDM to diabetes



Bellamy et al. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009;373:1773-9

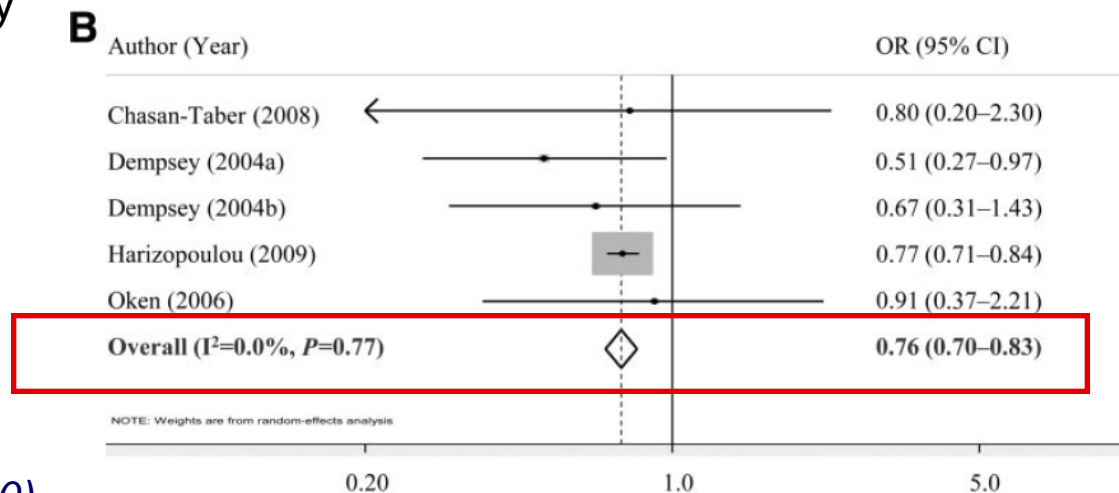
PA and GDM prevention

Prepregnancy



OR 0.45

Early pregnancy



OR 0.76

Threshold glucose concentrations and proportion of HAPO cohort identified

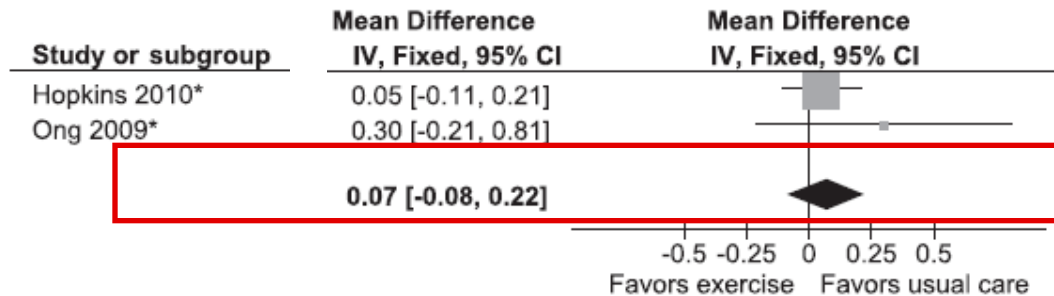
Glucose Measure	Glucose Concentratn	Threshold	Percent => Threshold
	mmol/l	mg/dl	Cumulative
FPG	5.1 (C=5.3)	92	8.3
1-hr PG	10.0	180	14.0
2-hr	8.5	153	16.1 *

In addition, 1.7% of participants in the initial cohort were unblinded because of a FPG >5.8 mmol/l (105 mg/dl) or 2-hr OGTT values >11.1 mmol/l (200 mg/dl).

PA and GDM prevention

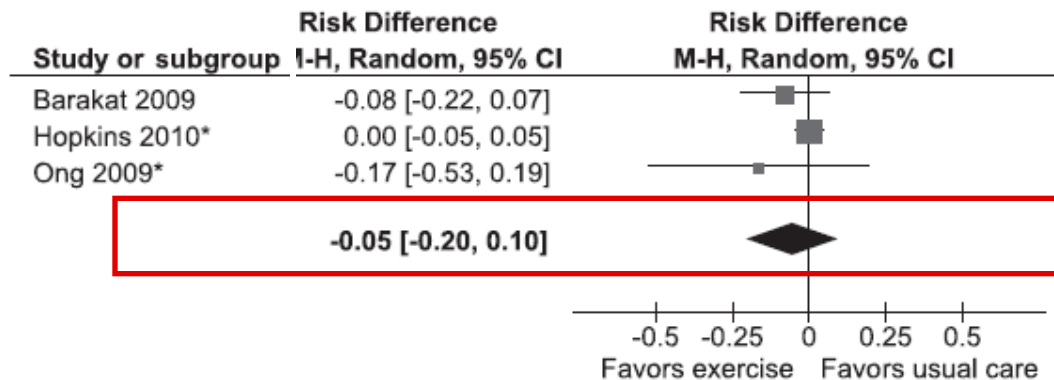
PA interventions in 2nd and 3rd trimester

Fasting blood glucose



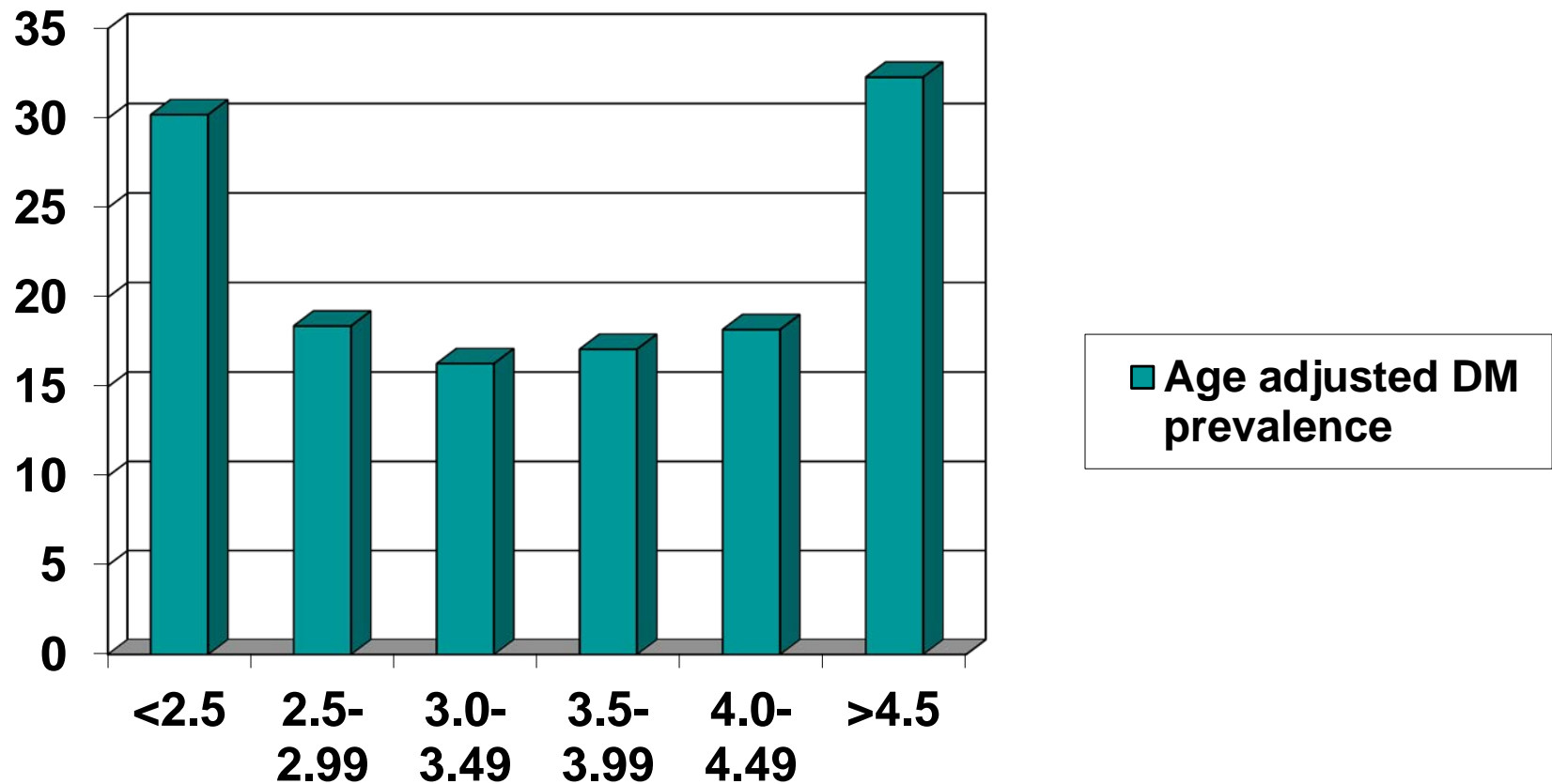
Δ 0.07 mmol/l

GDM



Δ -0.05%

Age adjusted prevalence of diabetes according to birth weight in 1179 Pima Indians



McCance DR et al BMJ 1994;308: 942-5

Background

- ❑ **Guidelines** for adequate **gestational weight gain** (GWG) in obese pregnant women were developed by Institute of Medicine (IOM) in order to reduce perinatal complications (IOM, 2009)
- ❑ Obese women have **low compliance** for adequate GWG(28%) (Bogaerts et al., 2012)
- ❑ **Existing intervention studies** aimed at reducing GWG
 - ➔ **inconsistent and contradictory results** (Campbell et al., 2012)
 - ➔ **psychological factors understudied** (Skouteris et al., 2010; Claesson et al., 2008)

FitFor2: effects of an exercise training program on the incidence of gestational diabetes



MNM van Poppel,¹ N Oostdam,¹ MGAJ Wouters,² EMW Eekhoff,³ W van Mechelen¹

¹*Dept of Public and Occupational Health; EMGO Institute;*

²*Dept of Obstetrics and Gynaecology; ³Dept of Internal Medicine;*

VU University Medical Centre, Amsterdam, the Netherlands

DOI: 10.1111/j.1471-0528.2012.03366.x
www.bjog.org

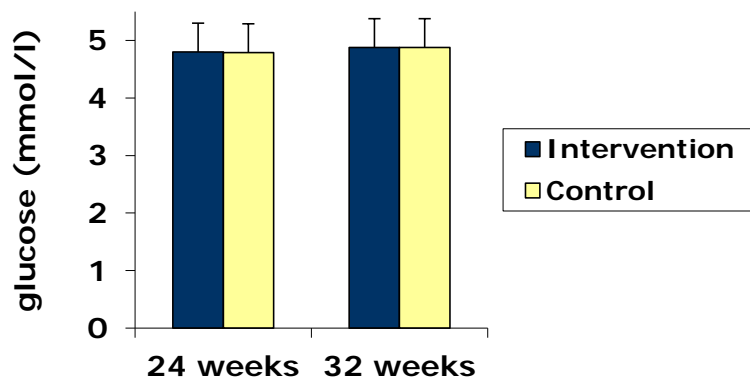
Epidemiology

No effect of the FitFor2 exercise programme on blood glucose, insulin sensitivity, and birthweight in pregnant women who were overweight and at risk for gestational diabetes: results of a randomised controlled trial

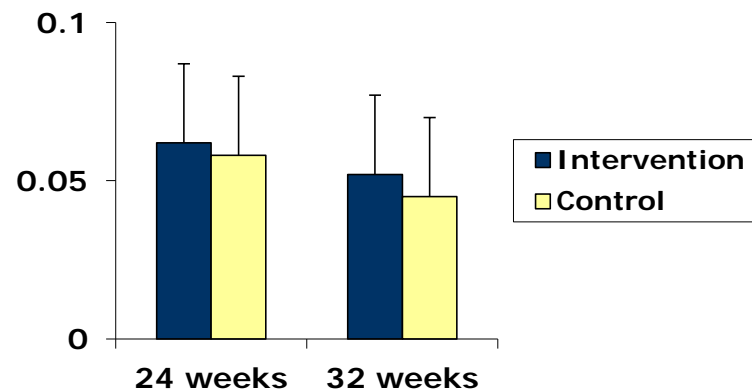
N Oostdam,^a MNM van Poppel,^{a,b} MGAJ Wouters,^c EMW Eekhoff,^d DJ Bekedam,^e WKH Kuchenbecker,^f HWP Quatero,^g MHB Heres,^h W van Mechelen^{a,b}

Results

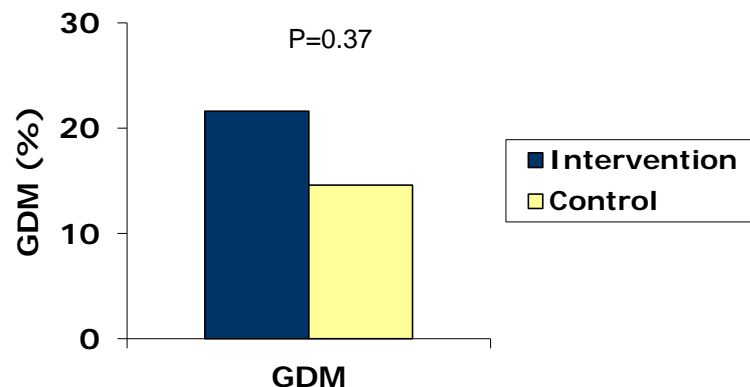
Fasting glucose



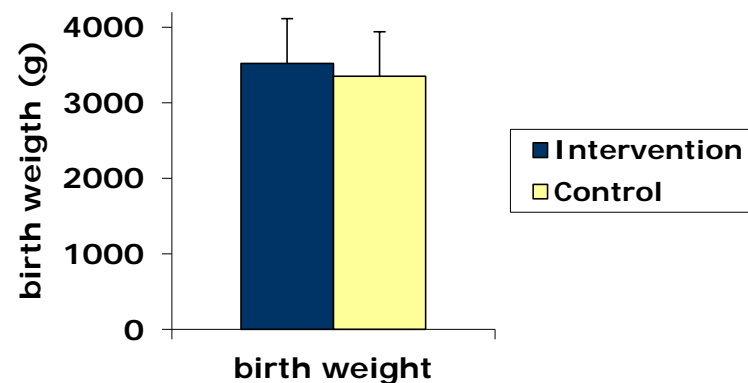
Insulin sensitivity (HOMA)



GDM



Birth weight



Results

- Compliance very low!
 - 1/3 in first half of intervention period
 - 1/8 overall
 - Explanation for lack of effect
- Extremely difficult group to recruit and even more to get active (training, appointments, wearing accelerometer etc)

Psycho-education Reduces Gestational Weight Gain in Obese Pregnant Women: a Randomized Controlled Trial

Bogaerts A., Devlieger R., Nuyts, E., Witters I., Gyselaers, W. & Van den Bergh, B

KHLim – PHL, Hasselt (BELGIUM)
KULeuven (B) - UvTilburg (NL)

Aim

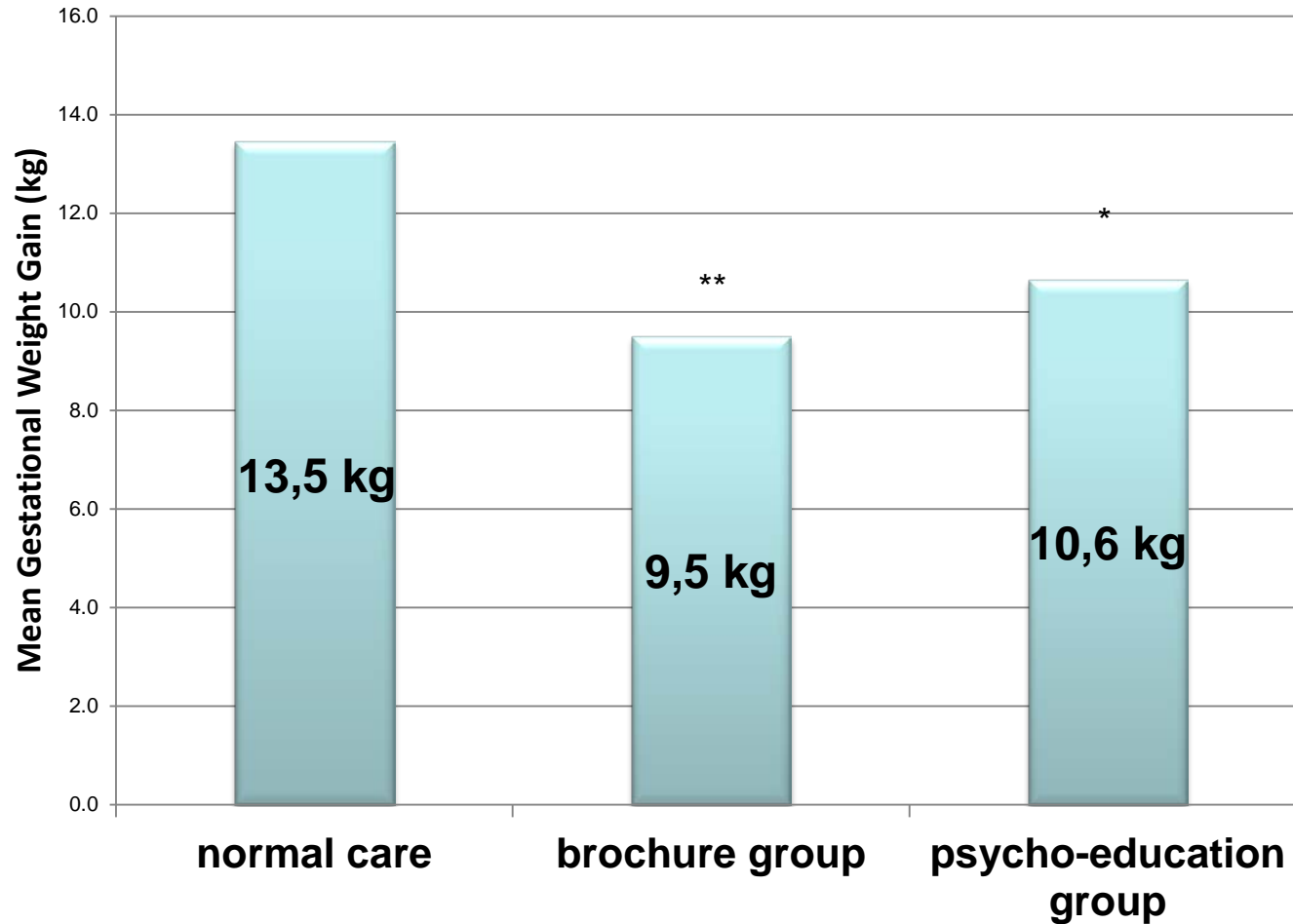
To evaluate whether a **prenatal psycho-educational program affects GWG**

Secondly, to evaluate the **effect on perinatal outcome.**

Inclusion

- Between march 2008 – april 2011 in 3 regional hospitals
- **Inclusion criteria:**
 - BMI ≥ 29 kg/m² (IOM,1990)
 - Before 15 weeks pregnancy
 - Sufficient knowledge of Dutch
 - No multiple preg., no DM T1, no primary need for nutritional advice

Results: Gestational Weight Gain



* P=0.06; ** P=0.008

Thanks to Roland Devlieger, Leuven

Primary Prevention of Gestational Diabetes Mellitus and Large-for-Gestational-Age Newborns by Lifestyle Counseling: A Cluster-Randomized Controlled Trial

Riitta Luoto et al, Finland

PLoS Med 8(5): e1001036.
doi:10.1371/journal.pmed.1001036

Finnish Study

- 2,271 women-OGTT at 8–12 wk gestation
- Euglycemic ($n = 399$) women with at least one GDM risk factor (body mass index [BMI] ≥ 25 kg/m², glucose intolerance or newborn's macrosomia ($\geq 4,500$ g) in any earlier pregnancy, family history of diabetes, age ≥ 40 y were included

➤ ****Heterogeneity in
GDM-slim women are
different to obese

Finnish study-Intervention

- Physical activity+nutrition together
- Physical activity comparable to DALI
- Nutrition:
- “The aim of the dietary counseling was to help the participants to achieve a diet containing saturated fat $\leq 10\%$, polyunsaturated fat 5-10% and total fat 25-30% (includes saturated, monounsaturated, polyunsaturated and trans fatty acids) of total energy intake and fiber 25 to 35 g/day.”
- ***BUT the key issue in GDM is carbohydrate metabolism-this intervention focused on fat reduction
- Weight management is also important
- 5 antenatal contacts-?enough

Counseling on gestational weight gain

- The recommendations for total gestational weight gain were
 - 12.0-18.0 kg for women
 - pre-pregnancy BMI 18.5-19.9 kg/m²
 - 11.5-16.0 kg for women
 - pre-pregnancy BMI 20.0-26.0 kg/m²
 - 7.0-11.5 kg for women
 - pre-pregnancy BMI ≥ 26.0 kg/m²

Finnish study

- 15.8% (34/216) of women in the intervention group and 12.4% (22/179) in the usual care group developed GDM (absolute effect size 1.36, 95% confidence interval [CI] 0.71–2.62, $p=0.36$)
- Gestational weight gain 13.8 vs 14.2 kg
Intervention vs control (mean BMI 26)



DALI



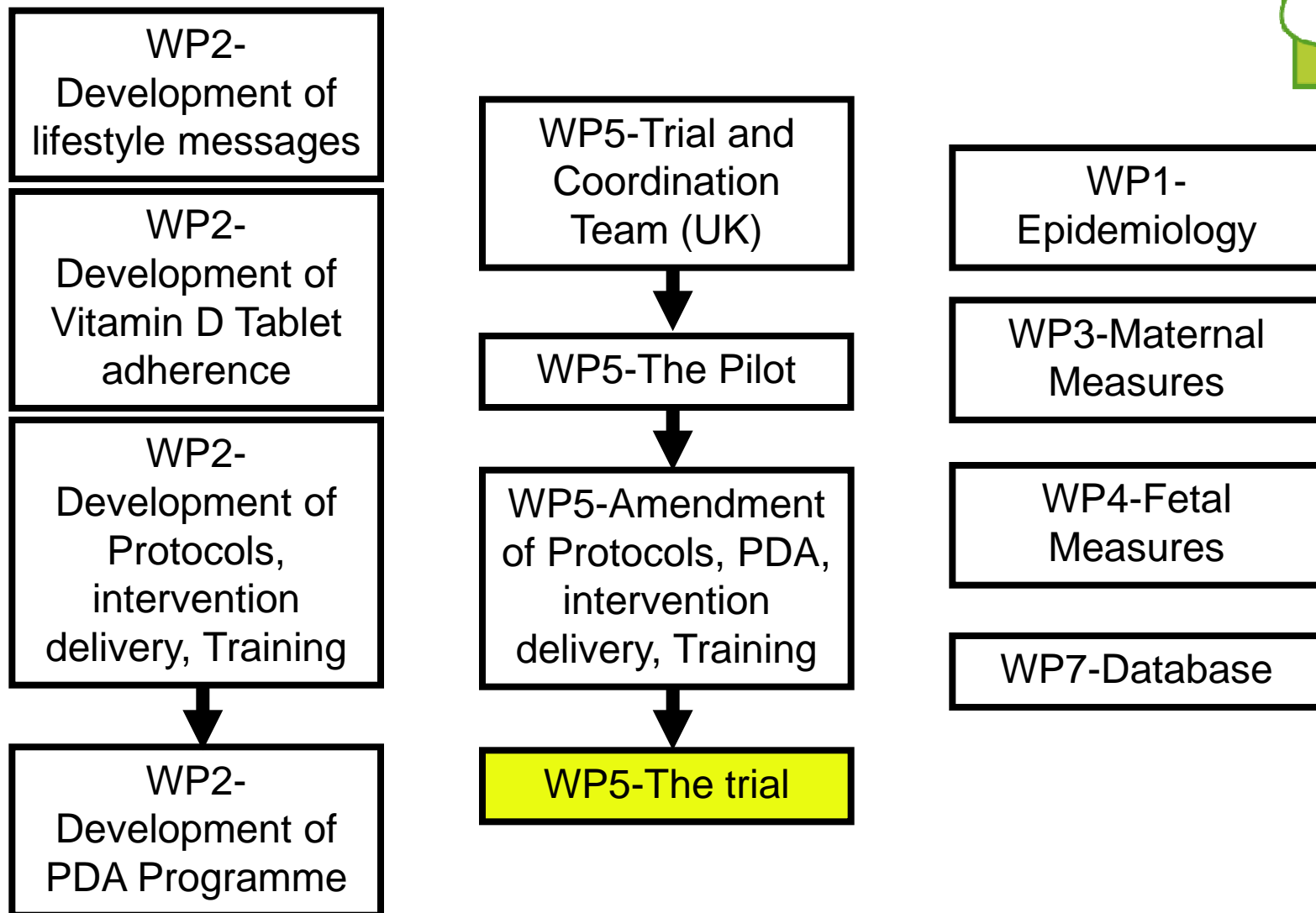
Vitamin D And Lifestyle Intervention to prevent gestational diabetes mellitus



Study design

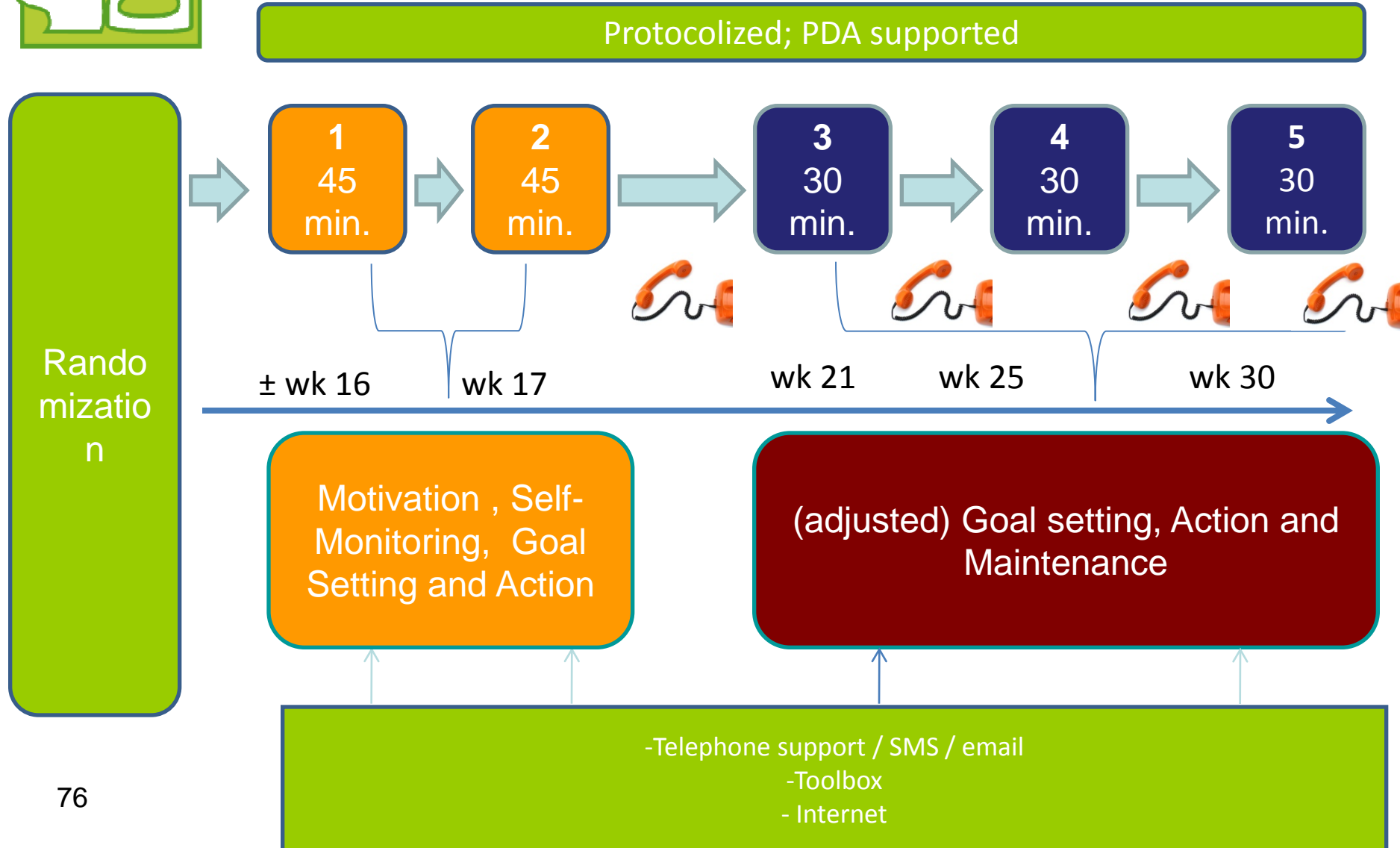


- 2*2*2 RCT
 - Healthy eating vs PA vs both vs neither
 - Vit D vs Vit D +both vs both vs placebo
- BMI 29+
- GDM by IADPSG criteria
- Outcomes=FBG, GWG, Si
- 10 countries across Europe-n=880
- Database in Switzerland;Economics Spain



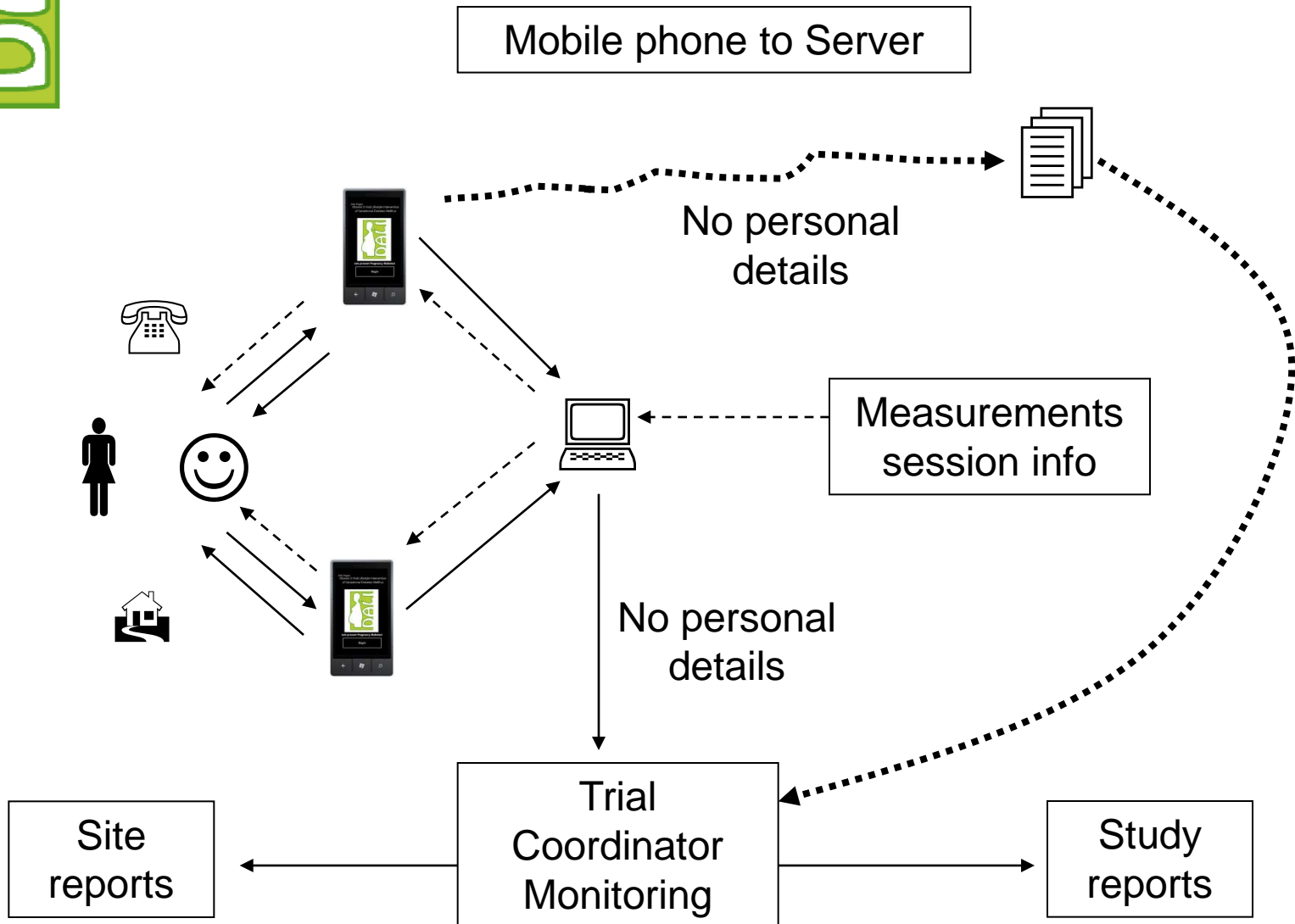


Intervention process





Use of the PDA



Conclusions

- Pandemic of diabetes
- Prevention shown to be possible-now a balance of cost and how to implement
- Requires a smorgasbord of interventions
 - Environmental/population, high risk adults, childhood, pregnancy
- Lifestyle preferred-simple messages behavioural delivery, monitoring
- Upstream is intra-uterine milieu-complicated by potential for risk-approaches being developed

Thanks to

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Questions?