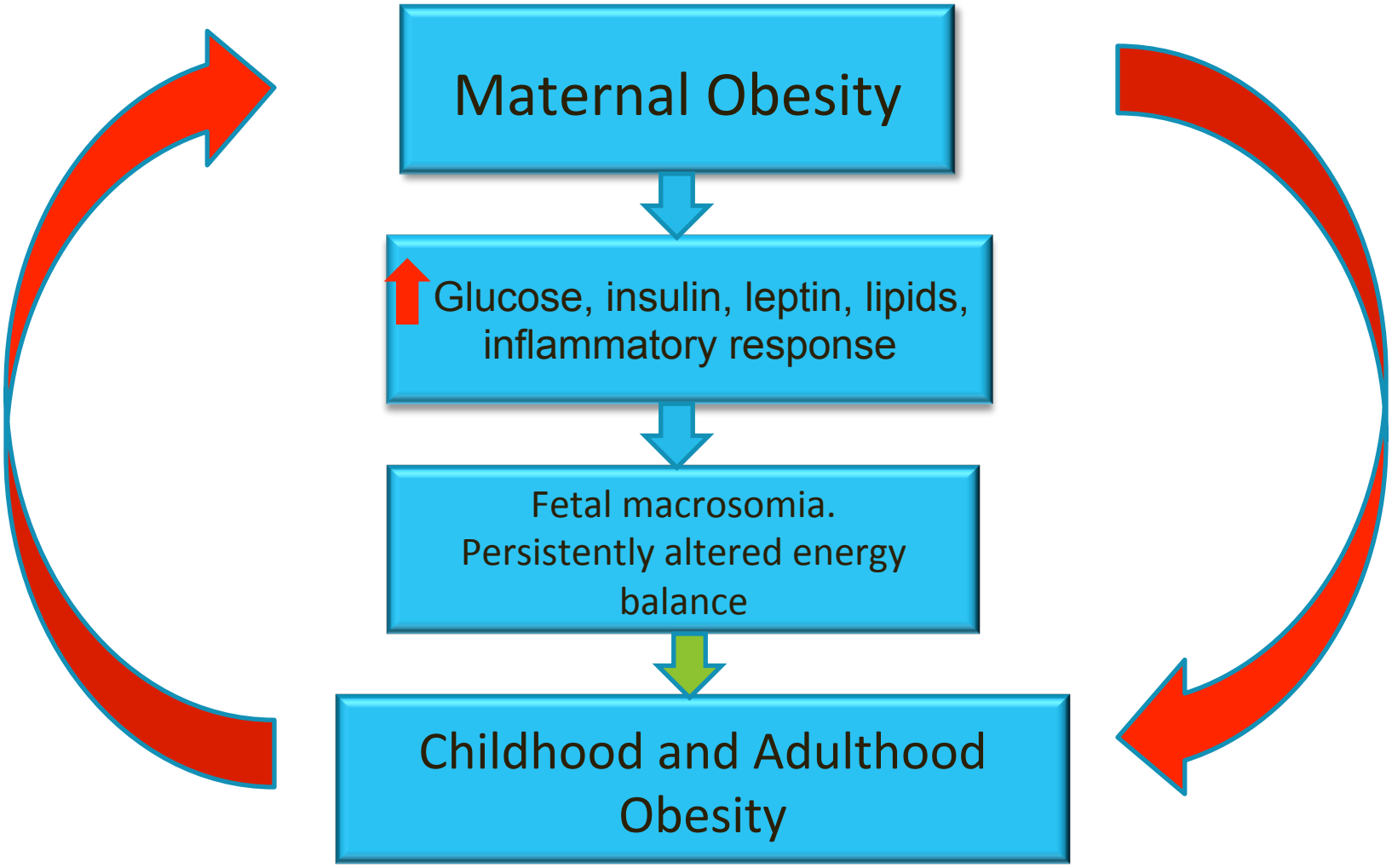
EARLYNUTRITION

Long-term effects of early nutrition on later health

Glycemic Load in Pregnancy

Lucilla Poston

This project receives funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 289346



Transgenerational 'Acceleration ' of Obesity?

High birth weight and obesity-a vicious circle across generations. (Cnattingius S et al 2011)

- 162 676 mothers and first born offspring Swedish Birth Register 1973-2006
- Mothers born large for gestational age (LGA) had increased risk of overweight, obesity Class I, II and III
- Risk of LGA delivery increased with mother's BMI
- Risk of LGA highest in women with high BMI *and* LGA themselves
- Conclusion. Prevention of LGA births may curb the intergenerational vicious cycle of obesity

Glucose homeostasis in pregnancy

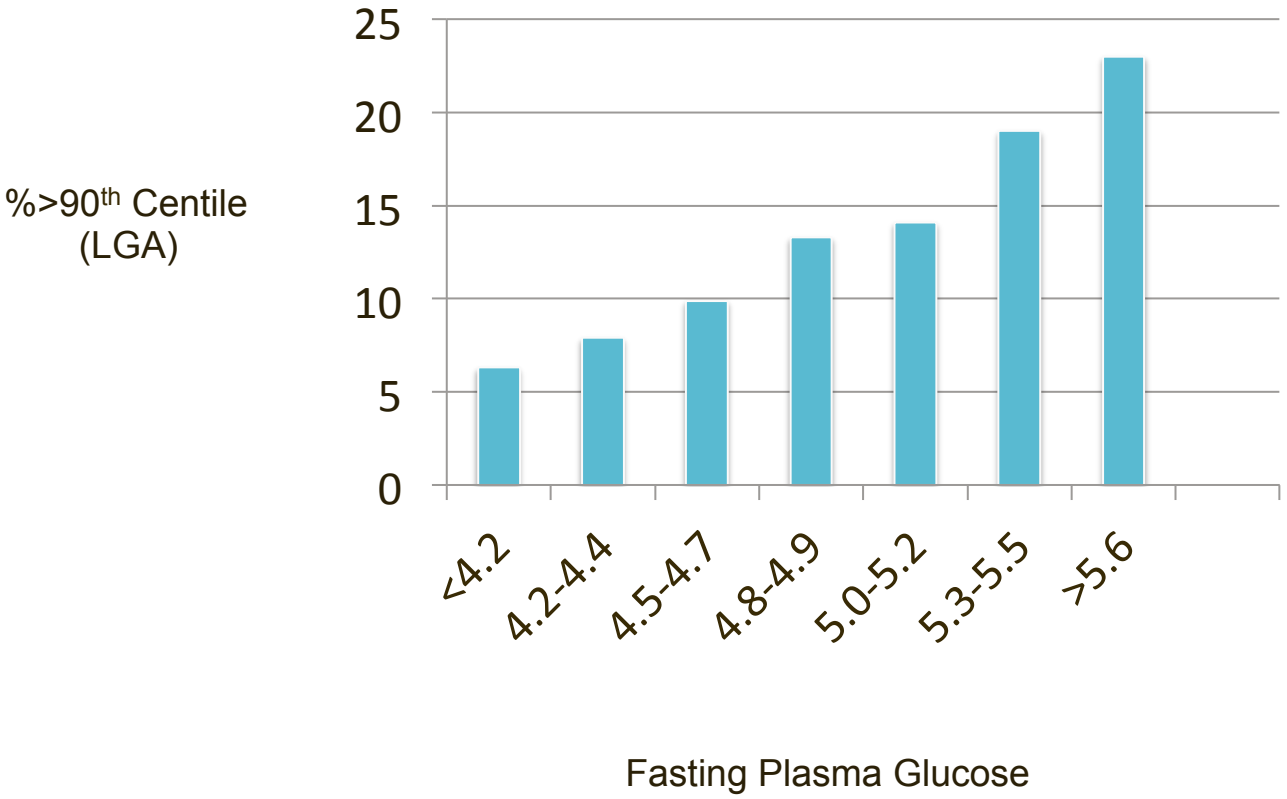
- Insulin resistance increases with gestation in normal pregnancy

- Leads to maternal plasma glucose ↑
  - Fetal insulin ↑
    - Fetal growth ↑

Exacerbated in:

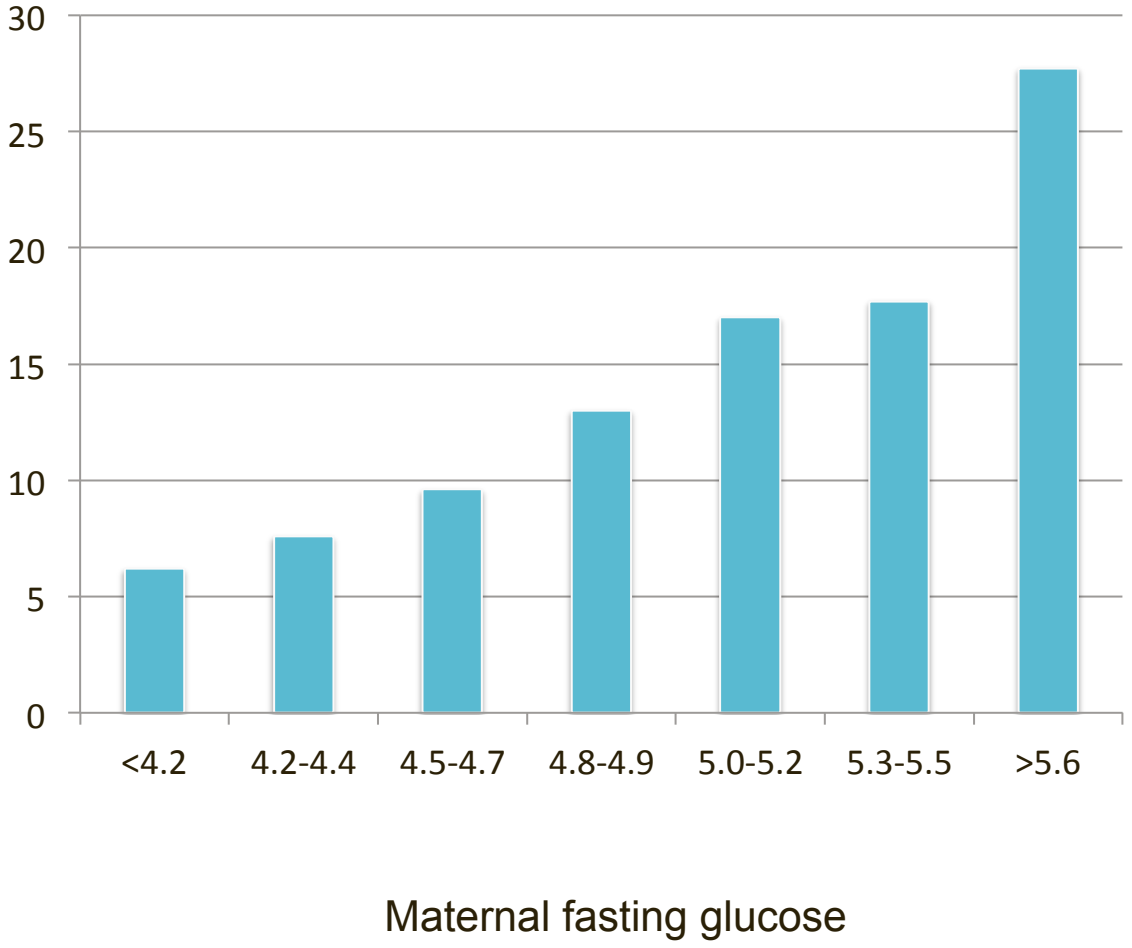
- gestational diabetes mellitus
- obese pregnancies

Association between Maternal Fasting Plasma Glucose and % LGA deliveries (Metzger et al, NEJM 2008). HAPO study



Association between Maternal Fasting Plasma Glcuose and Neonatal Fat >90th centile (Metzger et al, Diabetes Care, 2009)

HAPO study

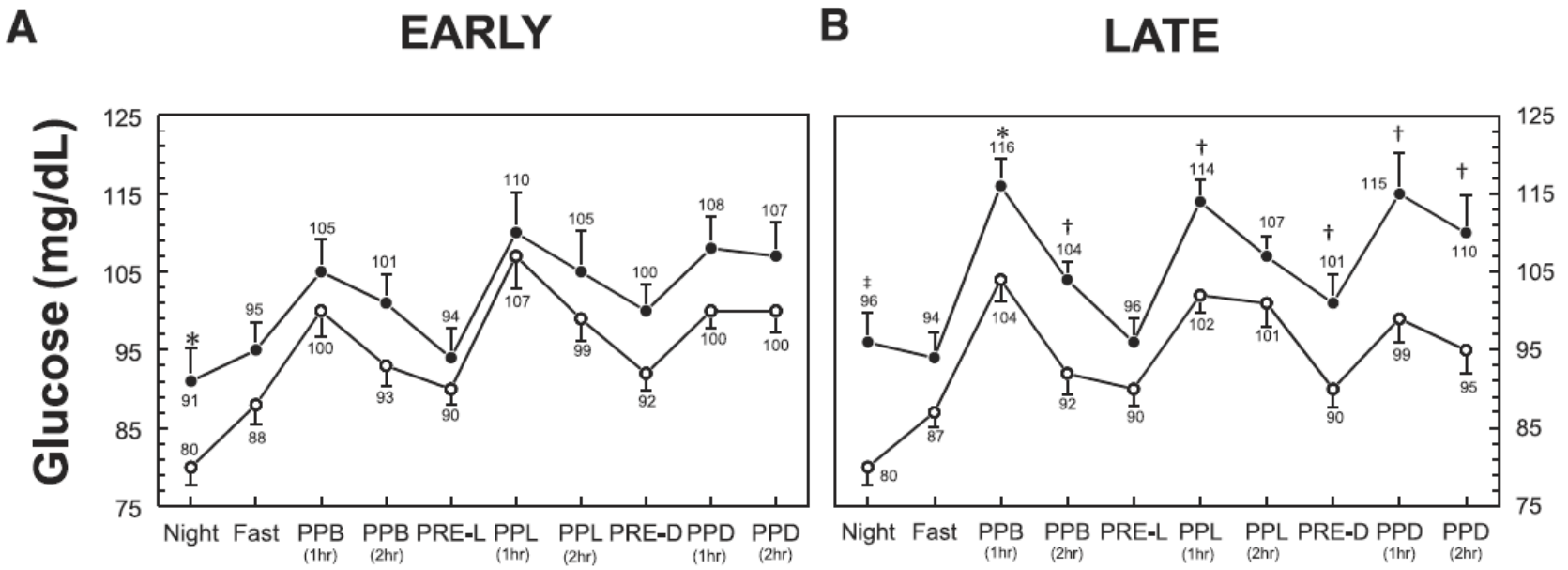


Post-prandial Glucose associated with fetal growth (Parretti et al, 2001)

- Pregnant women; studied every two weeks between 28 and 38 weeks' gestation
- Blood glucose levels recorded post prandially every two hr
- Ultrasound scans 22, 28, 32 and 36 weeks
- Significant association between post prandial glucose 1hr and measures of fetal adiposity

Blood Glucose profile in Obese Pregnant Women in Early and Late Pregnancy (non – diabetic)

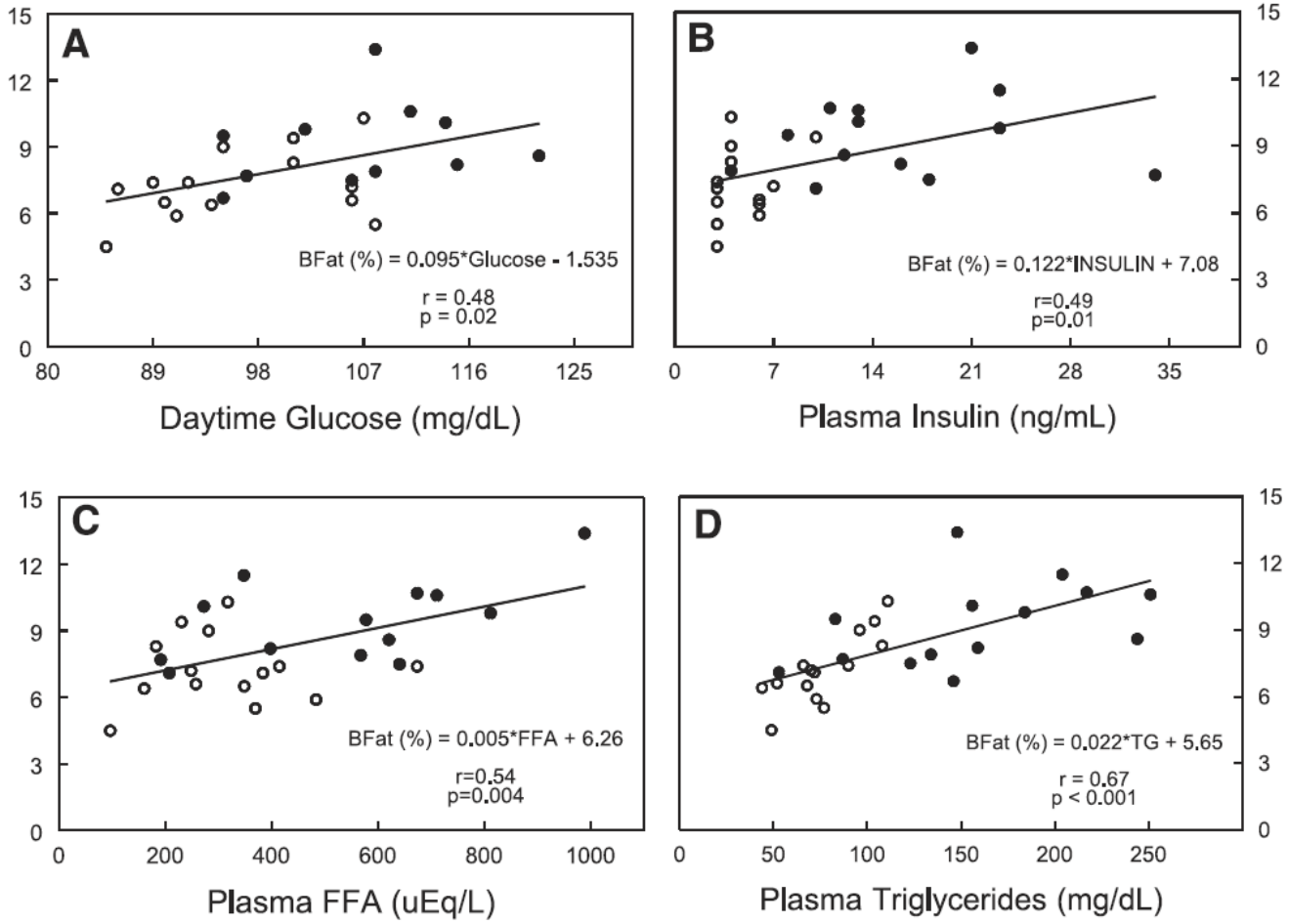
Harmon KA et al, Diabetes Care 2011



PPB –post prandial breakfast; PPL-post prandial lunch; Pre-E; pre-dinner; PPD post prandial dinner

Relationships between maternal variables in obese pregnancies and infant fat mass

Infant Body Fat%



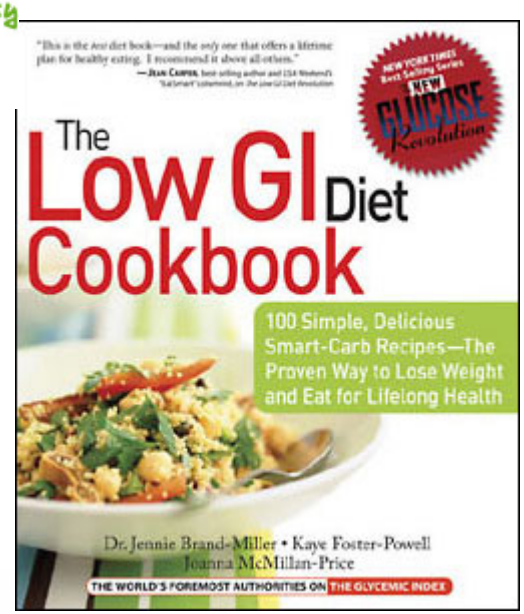
Interventions to reduce plasma glucose and delivery of large for gestational age infants?

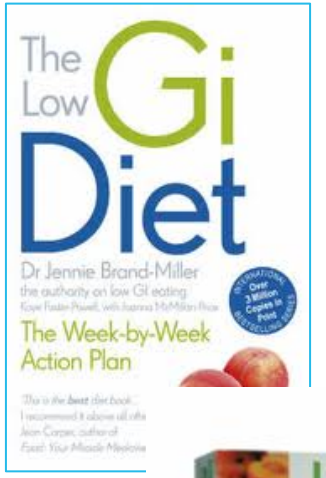
With anti-diabetic drugs?

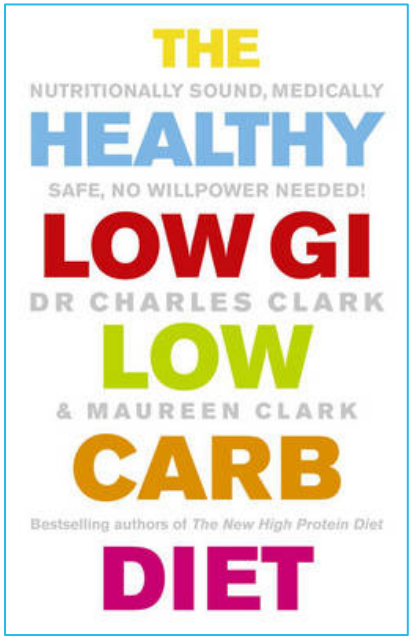
the g.i. Glycemic Index Diet

GLYCEMIC INDEX FOUNDATION LOW GI CERTIFIED

GLYCEMIC INDEX
making healthy choices easy







Understanding the Glycemic Index (GI)

What is it?

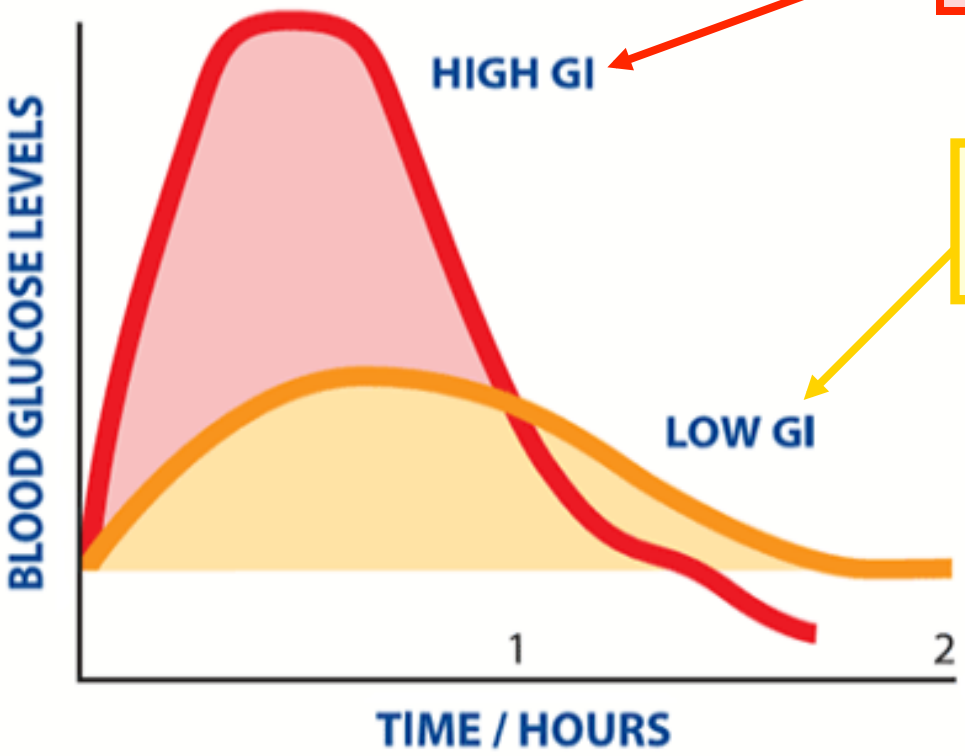
- A way of ranking foods according to the effect they have on blood glucose concentration.

- Foods are ranked from 0 to 100 according to the extent they raise blood sugar levels after eating.

How GI is measured

- Foods that are rapidly digested and absorbed raise blood sugar quickly and are given high GI values.
- Foods that are digested and absorbed slowly raise blood sugar gradually and are given low GI values.

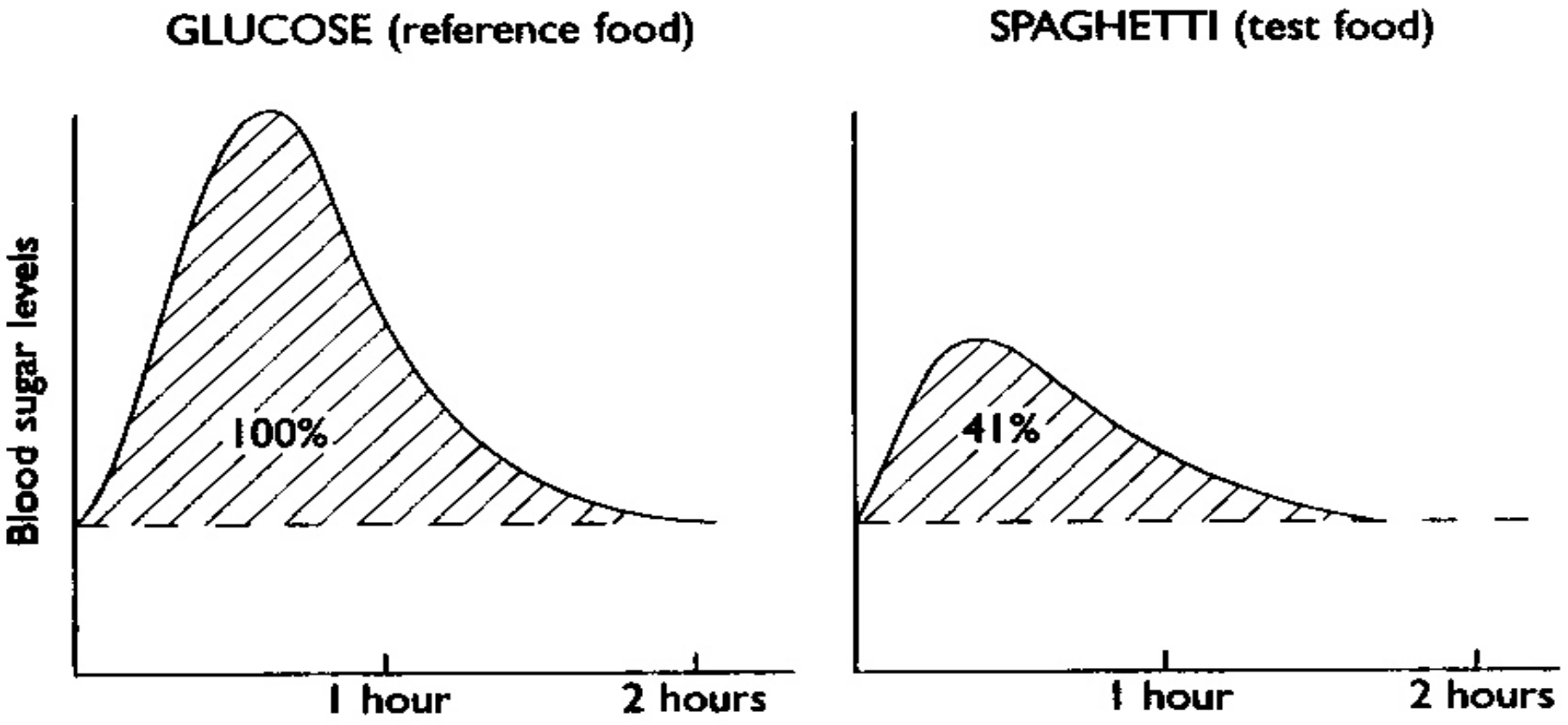
Effect of GI on blood sugar



A high GI food raises blood sugar levels quickly

A low GI food raises blood sugar levels slowly

Glycemic Index integrated area under the curve for blood sugar for a 50g load of available carbohydrate



High/medium GI foods

White bread

Sugary soft drinks

Mashed potatoes

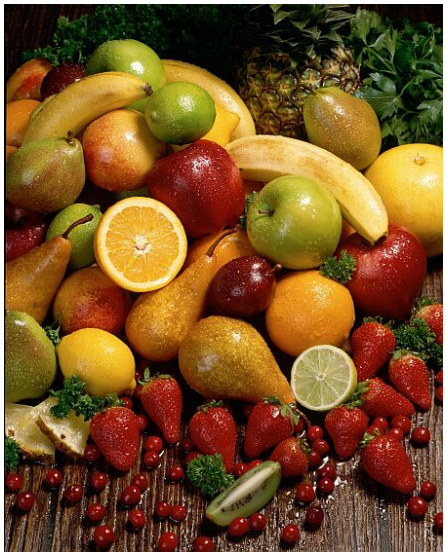
Refined breakfast cereals

Table sugar

White rice

Low GI foods

Most fruit and vegetables



Diet soft drinks

Pasta

Porridge

Nuts and raisins

Basmati rice

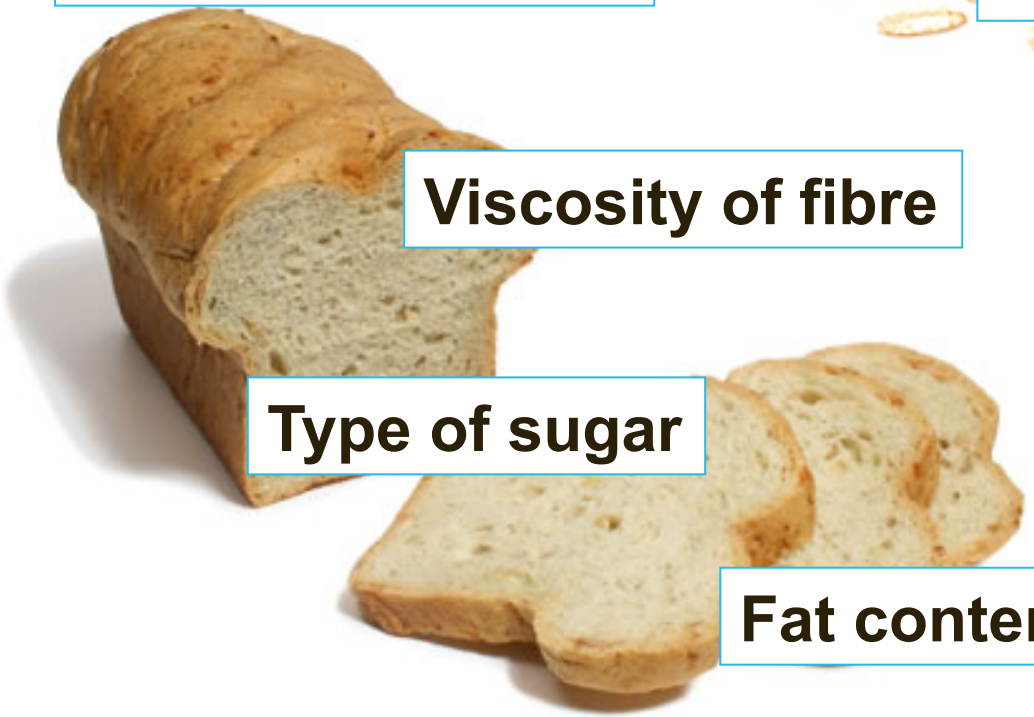
Factors Influencing GI Ranking

Type of starch

Cooking

Physical structure

Food processing



Viscosity of fibre

Acid content

Type of sugar

Protein content

Fat content

Evidence supporting use of Low GI Diets

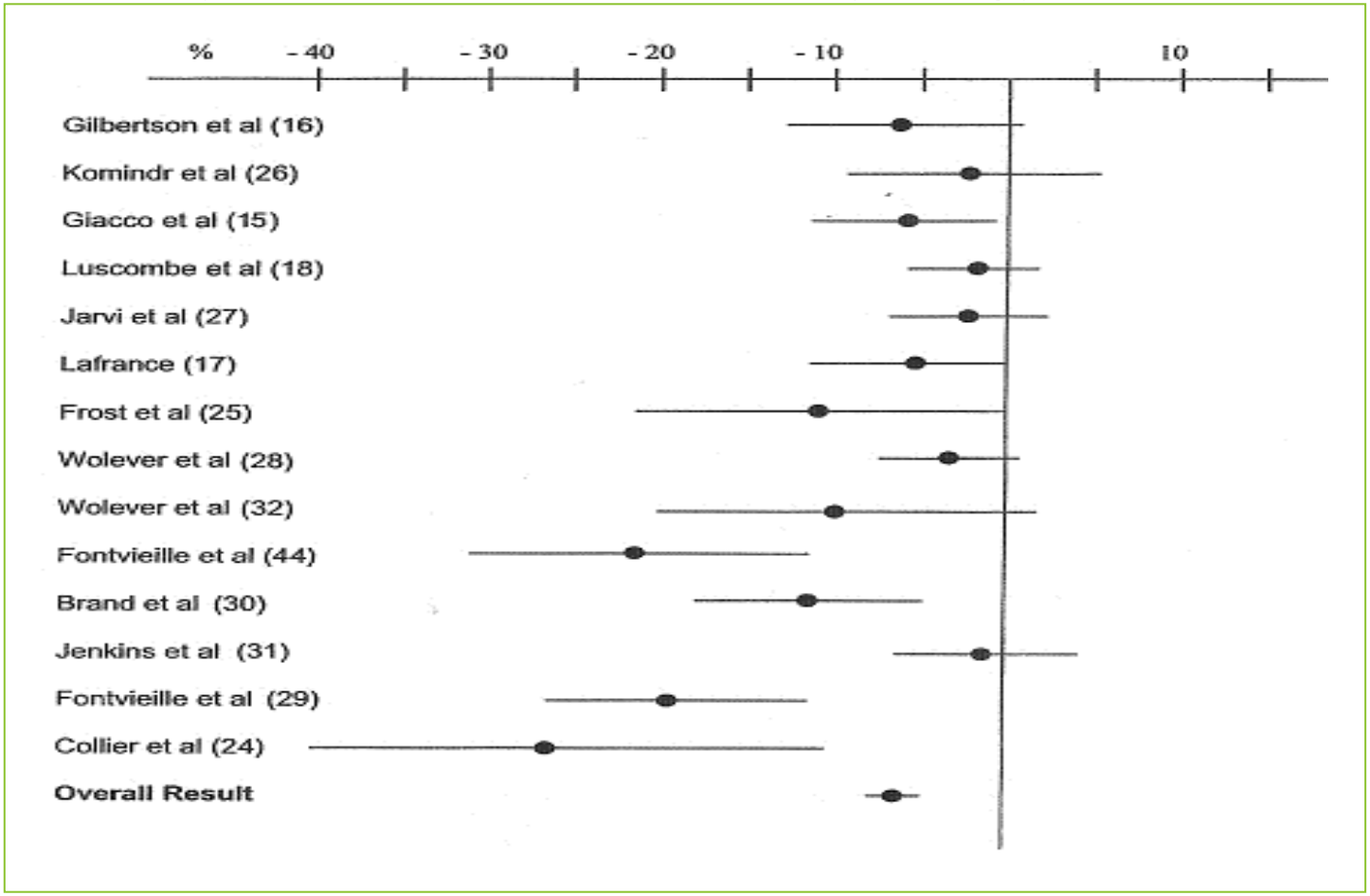
- Meta-analysis (Barclay et al, 2008)
  - Previous findings from observational studies inconsistent.
  - Systematic review of 37 prospective cohort studies
    - Low GI diet reduces T2DM
    - Low GI diet reduces CHD
  - Protection comparable to whole grain/ high fibre evidence.

"There is considerable evidence that a diet with an average GI of approximately 45 will achieve a significant reduction in the risk of chronic disease."

(Barclay et al, 2008 & Brand-Miller et al. 2003)

Low GI Diets and Diabetes Control

Meta-analysis of 14 studies, 356 subjects (types 1 & 2 DM)



Mean difference (Brand-Miller et al, 2003)

- glycated proteins were reduced by 7.4%
- 0.43% points in HbA1c reduction compared with high GI diet

Low GI and weight management

- Cochrane review (Thomas et al., 2007)
- Low glycaemic index or low glycaemic load diets for overweight
- and obesity - 6 RCT eligible
- Low GI versus conventional diet:
  - 1.1kg reduction in weight
  - 0.22 mmol/L reduction in total cholesterol
- No adverse effects reported in any study

"In studies comparing ad libitum low GI diets to conventional restricted energy low-fat diets, participants fared as well or better on the low GI diet, even though they could eat as much as desired"

(Thomas et al., 2007)

Glycemic Load (GL)

- Proposed as a more realistic tool to assess the glycemic response to foods.
- Takes into account carbohydrate content of food and portion size.
- Calculated as:
  - the amount of carbohydrate in a food (g) x its GI / 100

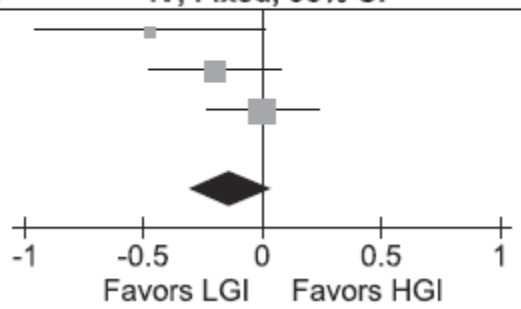
    - Low GL = 10 or less
      Medium GL = 11- 19
      High GL = 20 or more

Intervention studies; low GI diet for Prevention of GDM – influence on fasting glucose and macrosomia

A Outcome maternal fasting blood glucose

Study or subgroup	LGI Mean	LGI SD	LGI Total	HGI Mean	HGI SD	HGI Total	Weight	Mean Difference IV, Fixed, 95% CI
Clapp 1997	3.78	0.348	10	4.25	0.696	10	12.2%	-0.47 [-0.95, 0.01]
Moses 2006	4.1	0.57	32	4.3	0.55	30	36.6%	-0.20 [-0.48, 0.08]
Rhodes 2010	-0.028	0.39	18	-0.028	0.29	14	51.2%	0.00 [-0.24, 0.24]
Total (95% CI)			**60**			**54**	**100.0%**	**-0.13 [-0.30, 0.04]**

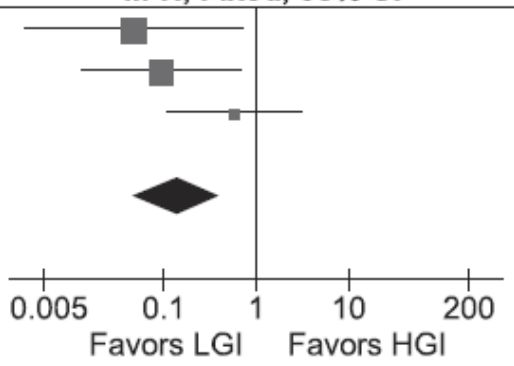
Heterogeneity: Chi² = 3.32, df = 2 (p = 0.19); I² = 40%
Test for overall effect: Z = 1.52 (p = 0.13)



B Outcome large-for-gestational age

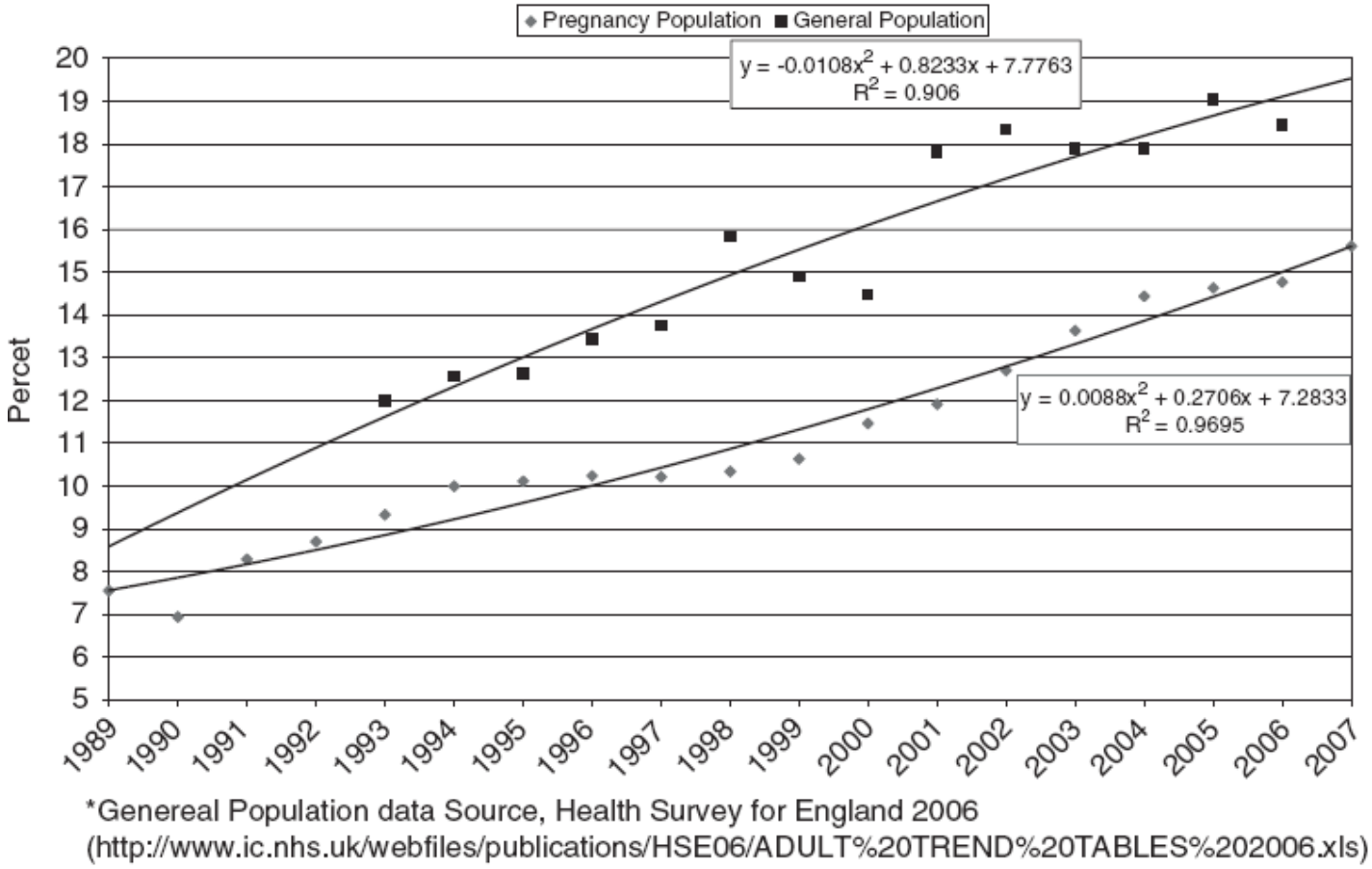
Study or subgroup	LGI Events	LGI Total	HGI Events	HGI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Clapp 1997	0	10	10	10	43.7%	0.05 [0.00, 0.72]
Moses 2006	1	32	10	30	43.0%	0.09 [0.01, 0.69]
Rhodes 2010	2	24	3	21	13.3%	0.58 [0.11, 3.16]
Total (95% CI)		**66**		**61**	**100.0%**	**0.14 [0.05, 0.41]**
Total events	3		23			

Heterogeneity: Chi² = 3.52, df = 2 (p = 0.17); I² = 43%
Test for overall effect: Z = 3.55 (p = 0.0004)



Oostdam et al, Journal of Women's Health 2011

National trend in maternal obesity compared to general population



Heslehurst et al, International Journal of Obesity 2009

Obesity and Pregnancy Outcomes

- Maternal risk
- Gestational diabetes
- Pre-eclampsia
- Venous thromboembolism
- Genital Infection
- Urinary tract infection
- Wound infection
- Postpartum haemorrhage
- Induction of labour

- Fetal/infant risk
- Macrosomia
- Shoulder dystocia
- Brachial Plexus damage
- Intrauterine death
- Spina Bifida
- Heart defects

Work Package 11 (partners UGR, LMU Muenchen, Abbott)

An intervention of diet (low GI) and physical activity in obese pregnant women (n=1562; UPBEAT study KCL, recruitment ongoing 2010-2013)...

In the EarlyNutrition programme, 3 year old children of UPBEAT participants will be studied

The UPBEAT trial

NHS National Institute for Health Research

Complex intervention of low GI diet and physical activity in1562 obese women

- Pilot RCT- 110 women completed;
  - does intervention lead to change in dietary and physical activity behaviour?
  - barriers to behavioural change?
  - acceptability

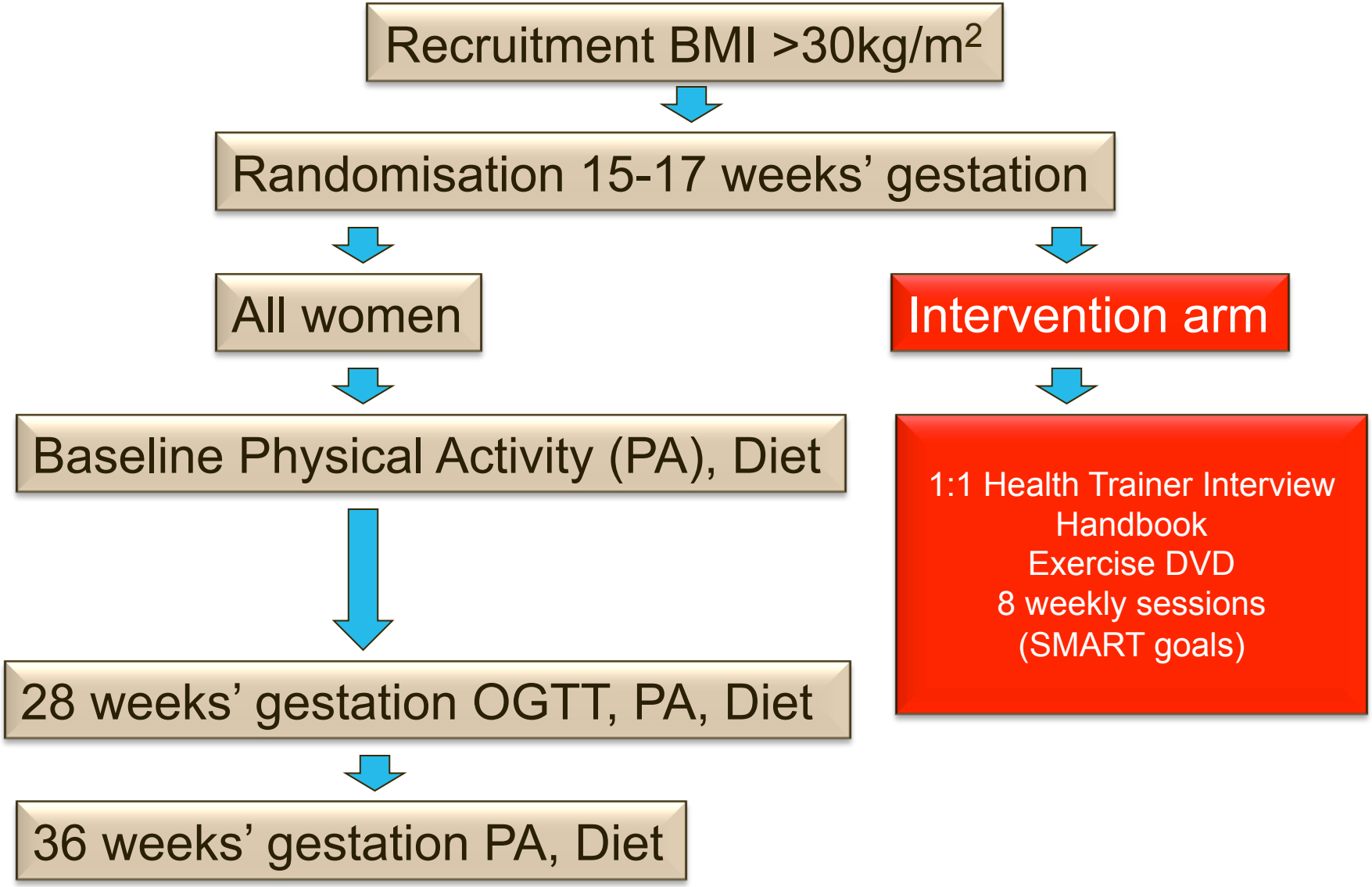
- Multicentre RCT

  Primary Outcome:
  - Maternal: OGTT at 28weeks
  - Neonatal: macrosomia

  Secondary outcomes
  - Neonatal, 6mth and 3 yr adiposity

The Rationale for Combining Physical Activity and Low Glycemic Index Diet Intervention in Obese Pregnancy

- Regular physical activity lowers insulin resistance in pregnancy (*Clapp 2006*)
- Physical activity improves control of GDM *(Brankston et al, 2004)*
- Physical activity prior to and in pregnancy reduces risk of GDM *(Dempsey et al, 2004)*
- Two trials; exercise training more effective than standard care in prevention of macrosomia (RR 0.36 95%CI0.13-0.99) *(Barakat et al 2009; Hopkins et al 2010)*
- Systemic review suggests reduction in macrosomia in non-diabetic women on low GI diet (*Oostdam et al, 2011*).


Recruitment BMI >30kg/m2
Randomisation 15-17 weeks' gestation
All women
Intervention arm
Baseline Physical Activity (PA), Diet
1:1 Health Trainer Interview
Handbook
Exercise DVD
8 weekly sessions
(SMART goals)
28 weeks' gestation OGTT, PA, Diet
36 weeks' gestation PA, Diet

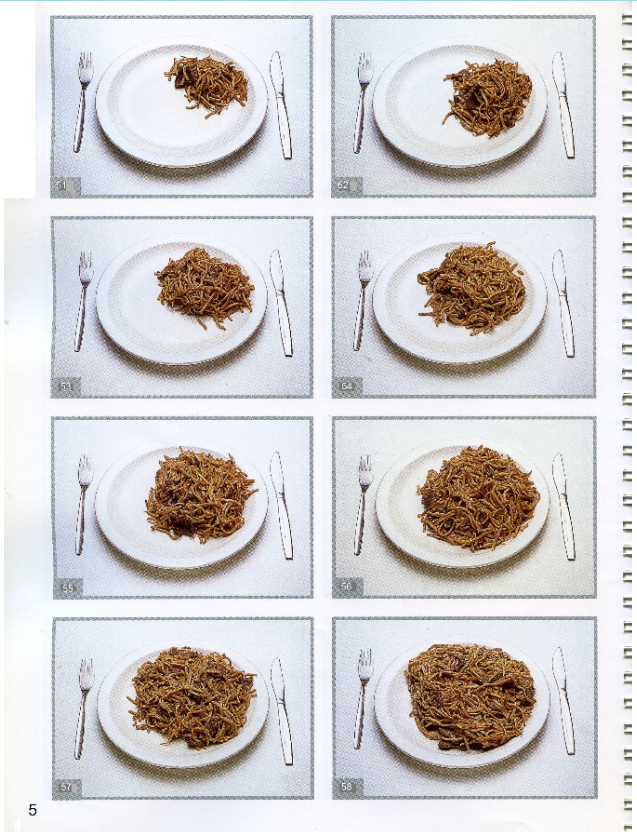
Diet 24-hour recall

'Triple Pass' method

1) Quick list

2) Detailed information (portion size & prompting)

3) Review



SPECIFIC FOOD DESCRIPTION PROMPT SHEET

Food	Description
Biscuits	Name and type Chocolate covered, iced, sandwich (cream, jam)
Bread	Name and type White, High fibre white, Brown, Brown with added bran, Granary, Multigrain, Wholemeal, Wheatgerm, Soda, French Was it toasted? Thin or medium or thick sliced? Large or small loaf? If rolls: soft, crusty, hamburger, hot dog, iced or plain **PROMPT:** Ask about spreads
Breakfast cereals (including porridge)	Name and type Added fruit and/or nuts? Muesli – added sugar/fruit? Porridge – made with oats or cornmeal? Instant? Made with milk or water or both? Type of milk on cereal/porridge. **PROMPT:** *Amount of milk = damp/normal/drowned* Sugar/sweetener added?
Butter, margarine and spreads	Full product name /brand Butter? Spreadable butter? Spreads - Is it polyunsaturated? Is it with olive oil? % fat if known (grams of fat per 100g)
Cakes	Type e.g. Sponge or fruit? If fruit: rich fruit cake? Flavour e.g. chocolate. Icing, fresh cream, jam filling, buttercream filling?
Cheese	Name of product and type Standard/half fat/reduced fat
Chocolates	Type e.g. milk, plain, white Any filling and, if so, what type e.g. wafer, caramel etc? Any additions e.g. raisins, nuts etc?
Chips	If made at home: frozen, oven, microwave, fresh cut. If take-away, where from i.e. fish & chip shop, Chinese, McDonalds Cut: thick/thin/crinkle/French fries
Cream	Single, double, whipping, aerosol Imitation cream e.g. Elmlea Coconut cream – normal or reduced fat?
Crisps	Name of product and type Standard/low fat/low salt Potato, corn, wheat, maize, vegetable, plantain etc Flavour **PROMPT:** from a multipack?
Fruit, vegetables, pulses - canned	Name and type Fruit - canned in water/unsweetened juice/syrup Vegetables/pulses - standard, reduced sugar, reduced salt or both e.g. reduced sugar and salt baked beans
Meat	Type of meat (name of animal, cut of meat, preparation e.g. minced) Standard or lean e.g. very lean mince beef

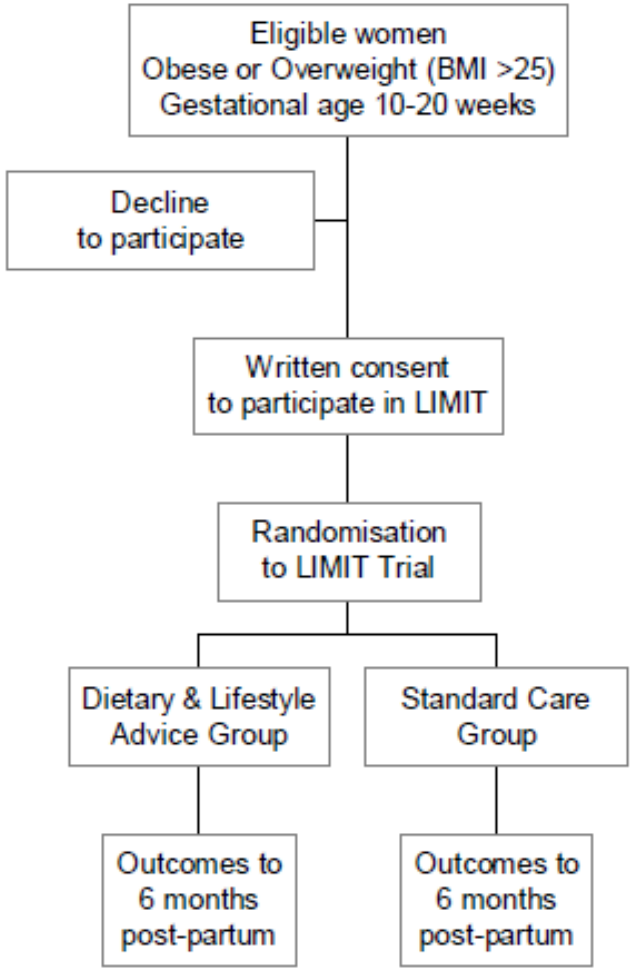
Pilot Study Results; Glycaemic Load

Triple pass 24hr recall before and after intervention

		Control	Intervention	Difference (95% CI)	P-value
Subjects*		n=59, 50	n=58, 45		
Energy					
Total Energy intake (kcal)	Baseline	1875 (569)	1753 (553)		
	28 weeks	1864 (564)	1646 (690)	-189 (-434 to 56)	0.129
Global GI	Baseline	57.6 (6.2)	58.3 (5.7)		
	28 weeks	67.8 (36.3)	52.4 (13.2)	-15.5 (-26.4 to -4.6)	0.006
Dietary GL	Baseline	137(50)	128 (43)		
	28 weeks	150 (58)	110 (42)	-34 (-51 to -17)	<0.001

Global GI; GL/ carbohydrate intake

The LIMIT trial; J Dodd et al



Primary endpoint:
Infant large for gestational age
Birthweight >90th centile
Target 25% reduction (14.4 to 10.8%)
N= 2,832

ROLO Study (Dublin, Ireland)

Hypothesis.

Alteration of the source of maternal dietary carbohydrate would prove valuable in the prevention of fetal macrosomia in at risk women (with previous LGA delivery)

HEALTH RESEARCH BOARD IRELAND
NATIONAL MATERNITY HOSPITAL MEDICAL FUND

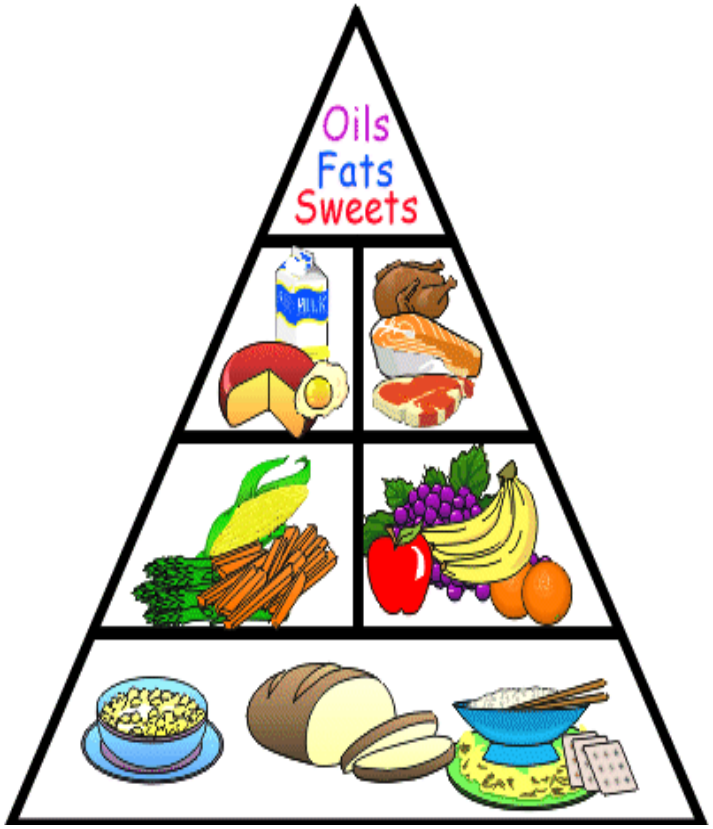
ROLO

Intervention arm:

- Single dietary education session
- Small groups of 2 – 6 people
- Lasted 2 hours
- Gestation 15.7+/-3.0 weeks

Dietary Intervention

- Women were first given advice on healthy eating guidelines for pregnancy
- Focused on the glycemic index
- No advice on gestational weight



Results – GI Index

	Intervention Group Low GI diet	Control Group
Early pregnancy	57.3 ± 4.2	57.7 ± 4.0
Second trimester	56.1 ± 4.0	57.8 ± 3.7 *
Third trimester	56.0 ± 3.8	57.7 ± 3.9 *

Results - Compliance

Compliance Scale	%
Followed the diet ‘all of the time’	3.8
Followed the diet ‘most of the time’	76.4
Followed the diet ‘some of the time’	17.0
Followed the diet ‘none of the time’	2.8

Work Package 11 (partners UGR, LMU Muenchen, Abbott)

A new trial in 720 obese pregnant women randomised to a low GI dietary substitute form 16-18 week's gestation until delivery (partner Abbott) or to standard care.

Primary outcome; neonatal fat mass

PILOT STUDY about to start

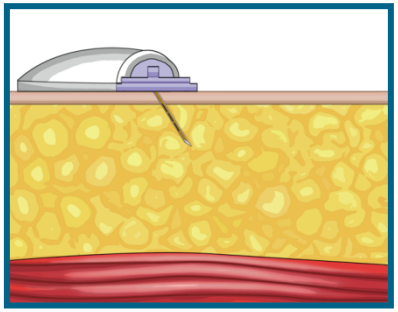
Aim of Pilot study

- To evaluate relative efficacy of 3 low GI supplements versus a control on post-test glycemic response; capillary blood glucose sampling

- With the most promising supplement, evaluate effect on post prandial glycemic response; Cotinuous glucose monitoring

Continuous Glucose Monitoring Sensors
Abbott FreeStyle® Navigator

- subcutaneous electrochemical enzymatic sensor inserted under the skin to a depth of ~5mm
- Connect via blue-tooth technology to receiver
- measures glucose concentration of interstitial fluid
- Lag time: physiological delay 10-15 min between change in blood & interstitial glucose
- In-built glucometer
- Can be worn for 5 days



Efficacy of dietary supplement to reduce Post Prandial Glycemic Response

- The prototype with the most superior glucose lowering effect demonstrated in stage 1 will be taken to stage 2
- A CHO and calorie controlled diet will be provided for the 48hr period following ingestion of the control/ prototype
- 15 min interval venous sampling will be performed up to 210min following ingestion of prototype or control
- CGMS will be inserted to asses longer impact of the low GI supplement v control over 48 hrs
- Sample analysis; glucose, insulin, c-peptide, TAG and NEFA

EARLYNUTRITION

The UPBEAT team

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www.project-earlynutrition.eu

This project receives funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 289346

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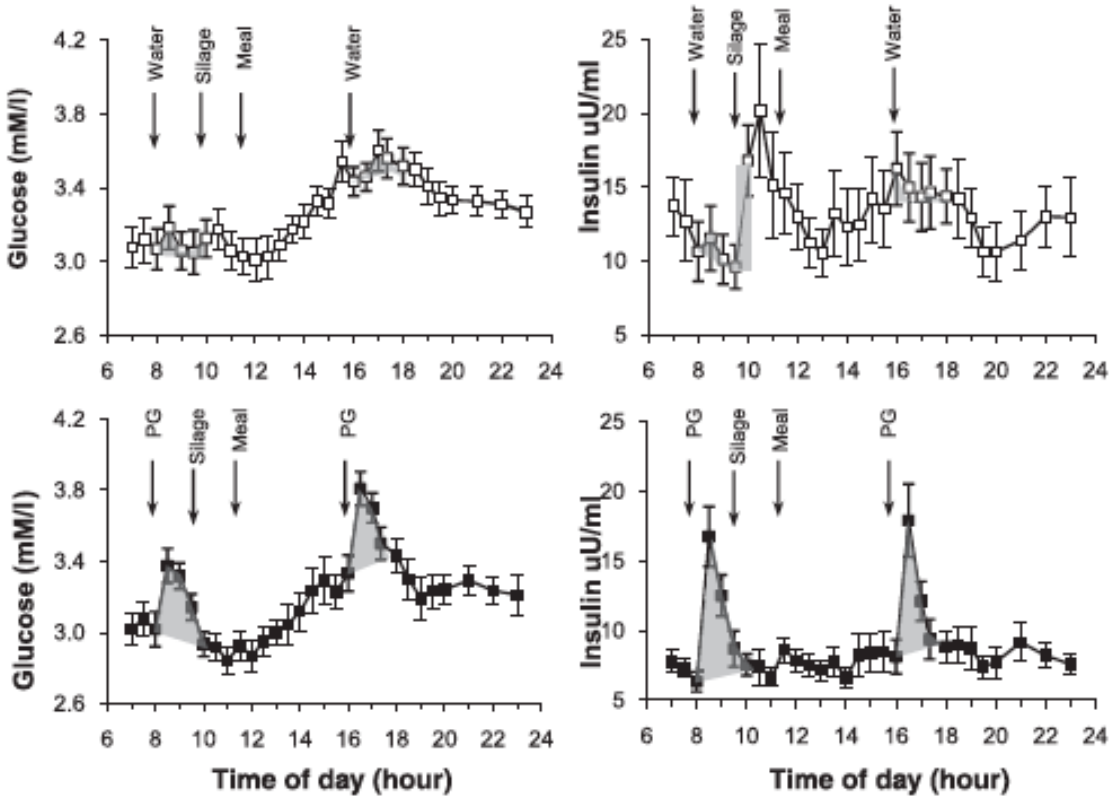
Postprandial maternal hyperglycemia in sheep leads to increased fetal growth (Smith et al, BJOG 2009)



Fetal birthweight (p-0.032) and fetal glucose (p<0.001) increased in sheep exposed to maternal post prandial hyperglycaemia induced by propylene glycol.