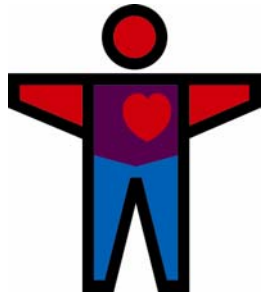


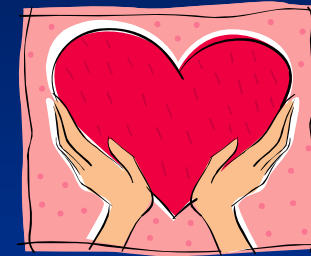
# Celebrating 30 years of the MIDSPAN Studies



**Women, reproduction  
and their hearts**

**Naveed Sattar**

Low birth weight



Poor fetal nutrition



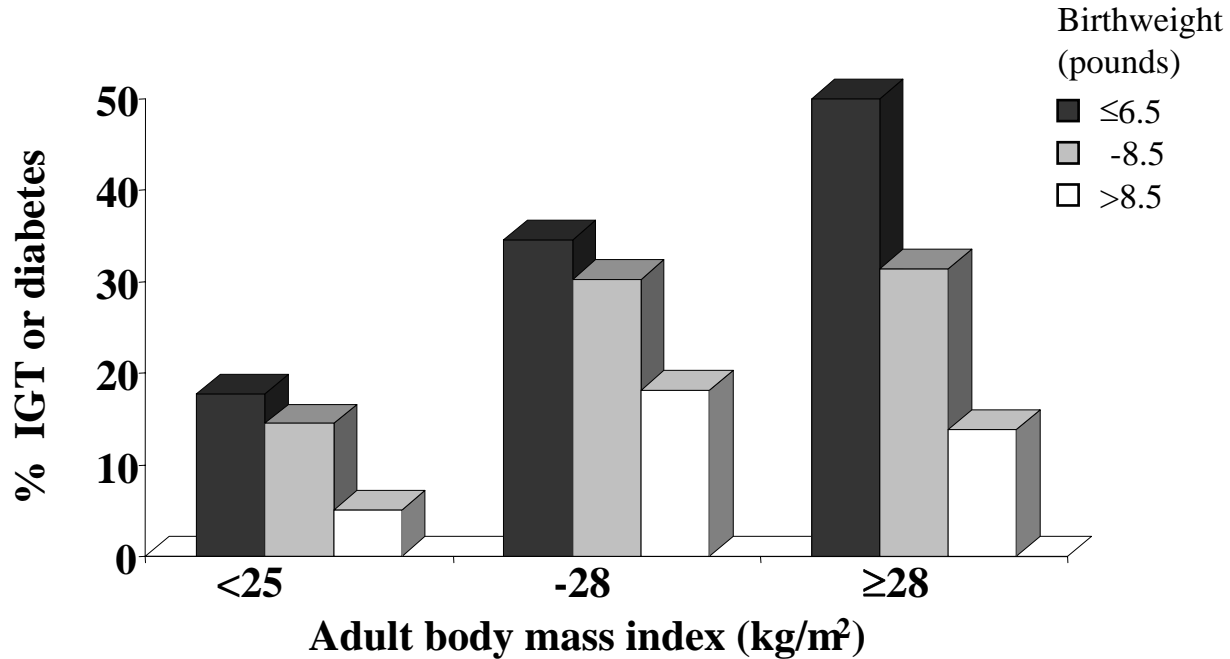
Adaptations

- metabolic
- cardiovascular
- endocrine



Permanent changes  
in structure /  
function

## Birth weight and diabetes in later life



*BMJ 1991;303:1019-1022*

**Prevalence of IGT and Type 2 diabetes (%), Hertfordshire men aged 60-71 (n=370)**

# LBW vs Risk factors

- Blood pressure
- Type 2 diabetes
- Insulin resistance
- Lipids
- Fibrinogen
- Central obesity (waist/hip or subscapular/triceps ratios)
- **INFLAMMATION**

Sattar N, McConnachie A, O'Reilly D, Upton MN, Greer IA, Davey Smith G, Watt G. Inverse association between birth weight and CRP in the MIDSPAN Family Study. *Arterioscler Thromb Vasc Biol.* 2004 Mar;24(3):583-7.

# But does pregnancy outcome tell us about mums future risk?



Subtle CHD risk factors / genetic make-up MUM



Defective implantation  
↓ Fetal nutrition

**IUGR**  
**PE pregnancies**



## Mothers vascular risk according to pregnancy outcome?

Pregnancy outcome	Incidence in pregnancy	Association with CHD mortality morbidity [Hazard Ratios (95% CI)]
<b>Pre-eclampsia</b>	2-4%	1.9 (1.0-3.5) vs PIH alone 1.7 (1.3-2.2) vs no PE 2.0 (1.5-2.5) vs no PE
<b>Low birth weight (&lt;2500g)</b>	5%	11.3 (3.5-36.1) vs $\geq 3500g$ 7.1 (2.6-18.7) vs $\geq 3500g$
<b>Pre-term delivery (&lt;37 weeks)</b>	5-6%	1.8 (1.3-2.5) vs term delivery 2.1 (1.2-3.5) vs term delivery
<b>Gestational diabetes</b>	1.9-5%	↑ risk of type 2 diabetes, especially if recurrence of gestational diabetes in a subsequent pregnancy.

# YES!

Mothers  
CHD risk

Offspring  
risk – in part  
reflected by:  
low birth weight

3<sup>rd</sup> generation  
offspring  
risk

# MIDSPAN

More than 1000 mothers  
already characterized for several pathways  
blood pressure, adiposity, lipids, clotting, inflammation, oxidation

We have collected their pregnancy outcome  
data

Power sufficient to examine interaction of  
LBW vs mothers phenotype



# Indirect benefit of Midspan

- IUGR follow-up
- Mothers – 70% smoking rate vs 30% controls
  - Major reason for risk factor profile
  - ICAM-1, CRP, trigs, vascular dysfunction



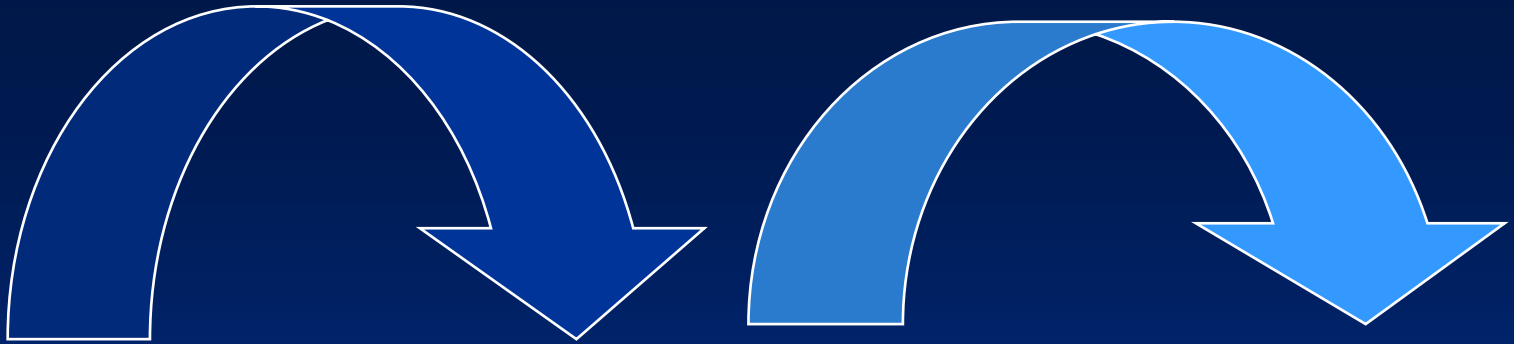
# Obesity rising – at risk larger babies?

	1990	02/04
Number in study	203	312
Maternal age (yrs)	28.0	27.8
Obese %	9.4%	18.9%



## Obesity

Overweight women may 'overfeed'  
their developing offspring –  
glucose, FFAs, etc with excess fat  
deposition



Original cohort

Offspring  
**Daughters** &  
Sons (1996)

3<sup>rd</sup> generation:  
birth details for offspring  
for Daughters

Mortality data for  
Maternal  
grandparents

**Daughters** CHD risk  
measures in 1996  
Hospitalisations for CHD  
1996-2005(?) SMR data

# Immediate goal

- Women with a history of adverse pregnancy outcome are at increased risk of metabolic and vascular diseases in later life
- These associations suggest common disease mechanisms for pregnancy complications and CHD that may be explained through common genotypes or phenotypes

*Sattar & Greer BMJ (2003)*

*Programme grant to BHF  
In submission*

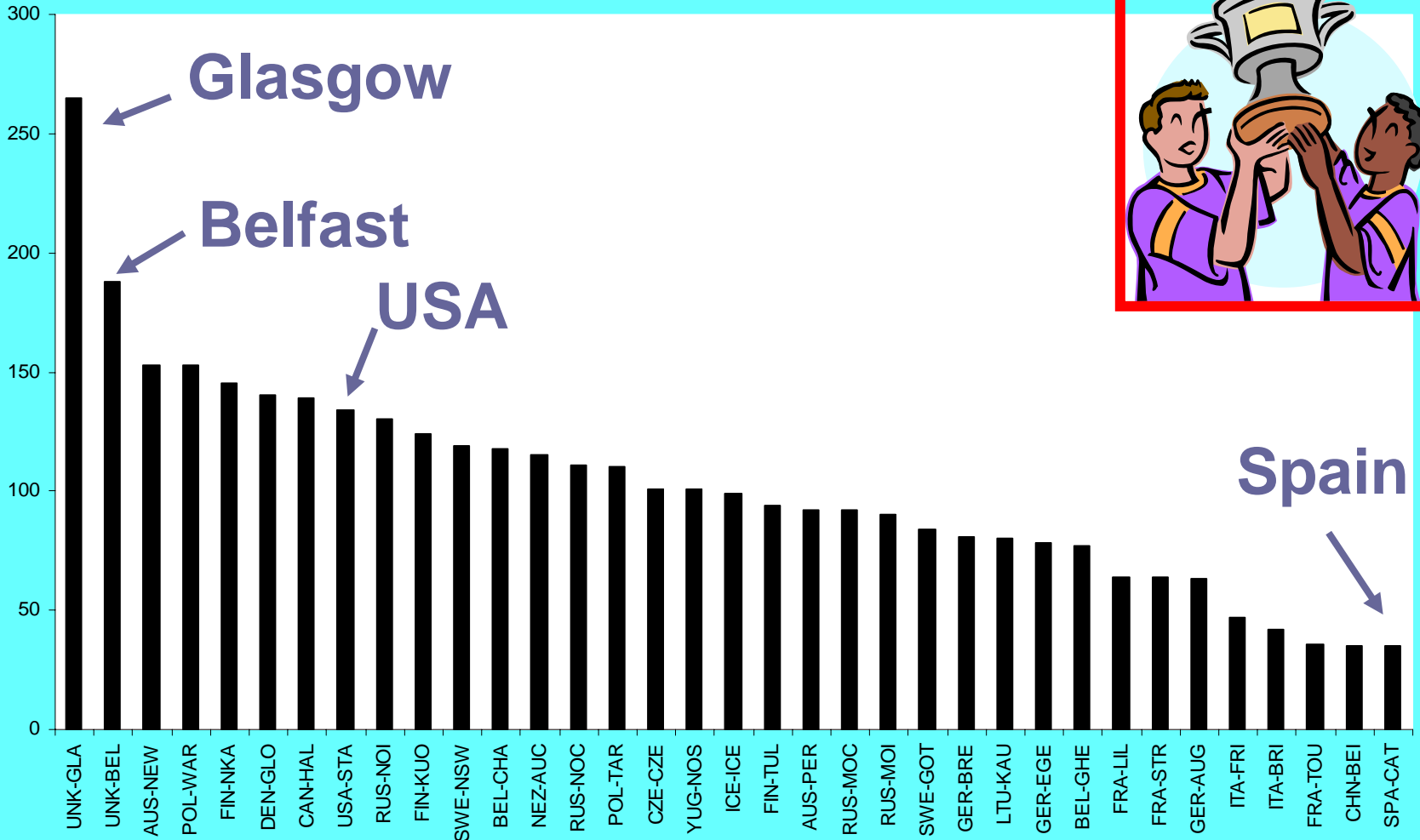
# Eventual goal

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“The possibility that maternal vascular risk factors, potentially ‘modifiable’ prior to pregnancy, correlate with increased risk of pre-eclampsia, pre-term delivery and low birth weight, and thus also fetal programming, requires further investigation”

# CHD Incidence in Women

Annual rate per 100,000



Population

# Acknowledgements

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Dilys Freeman

Gordon Lowe

Anne Rumley

George Davey Smith

Debbie Lawlor



Trophoblast