

**Parental chronic disease history is associated with
polycystic ovary syndrome in daughters**

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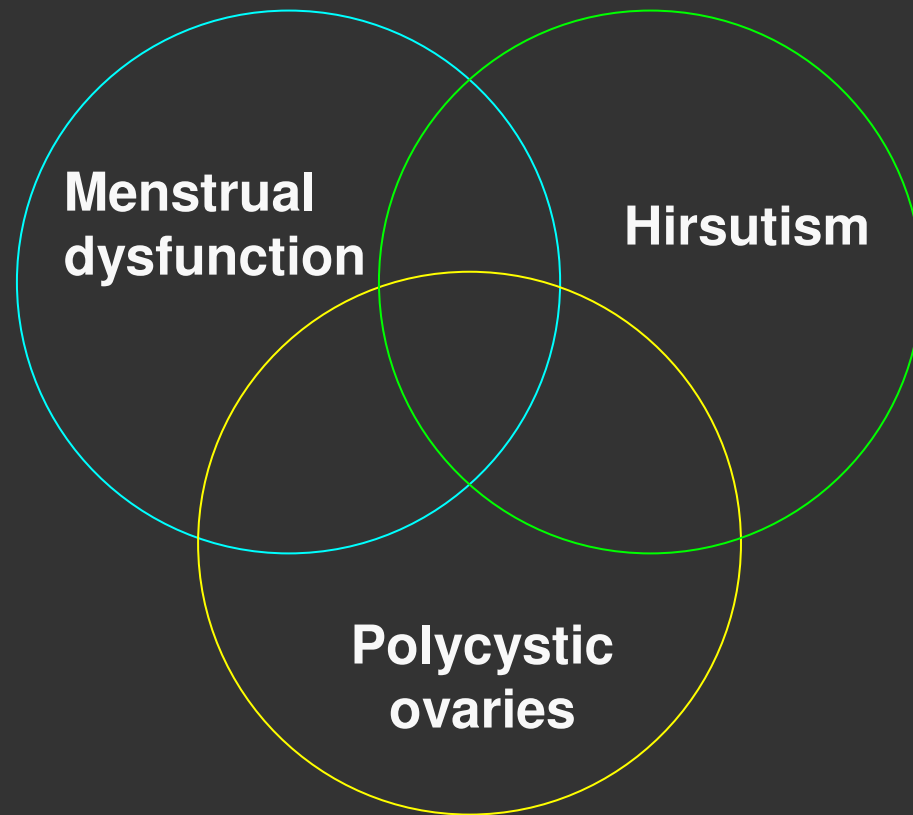
Broad research areas

- Involuntary infertility & assisted conception
- Reproductive careers
- Pregnancy failure
- Optimal conditions for development to birth and beyond
- Intergenerational growth and chronic disease risk



Natural history

- The syndrome classically emerges around puberty, is manifest during the reproductive years and is not readily identified after the onset of menopause.
- Menstrual disorders are frequently associated with anovulation and often require hormonal or surgical intervention.
- Infertility usually requires drug treatment and, in some cases, in vitro fertilization.



**Menstrual
dysfunction**

Hirsutism

**Polycystic
ovaries**

Prevalence of PCOS

- PCOS has been recognised to be a common endocrine condition, depending on diagnostic criteria, afflicting 6 - 12% of the female population of reproductive age.
- Around 20% of women have evidence of polycystic ovaries (PCO) on ultrasound examination with no apparent clinical disorder.
- The heterogenous nature of the syndrome influences diagnostic criteria, prevalence estimates, aetiology **which is unknown.**

Associated risks of PCOS

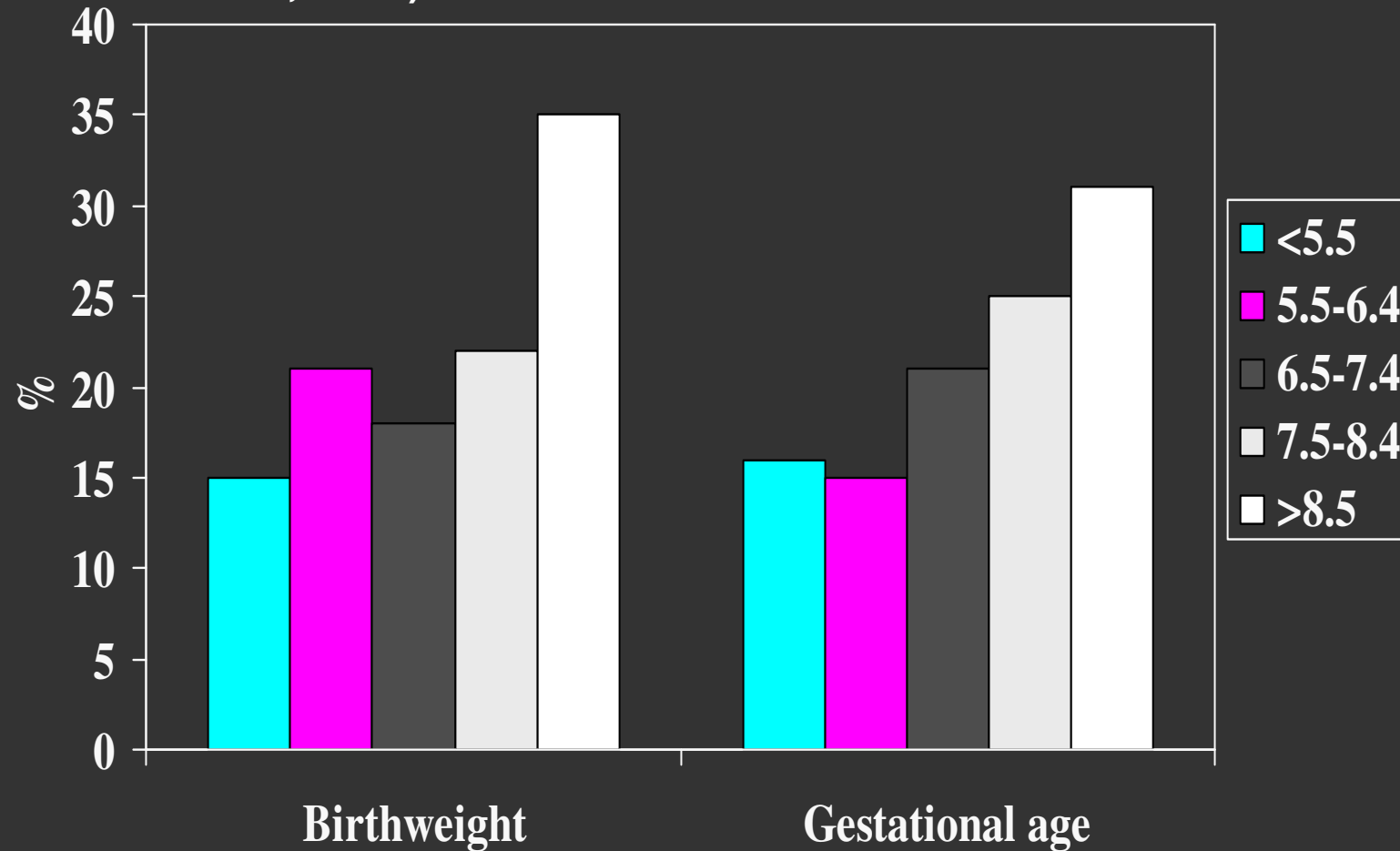
PCOS is associated with high lifetime risks of

- infertility
- menstrual disorders
- abnormal lipid profiles
- diabetes mellitus
- endometrial cancer
- Cosmetic effects of hyperandrogenism include acne, hirsutism, temporal hair loss and lack of self-esteem.

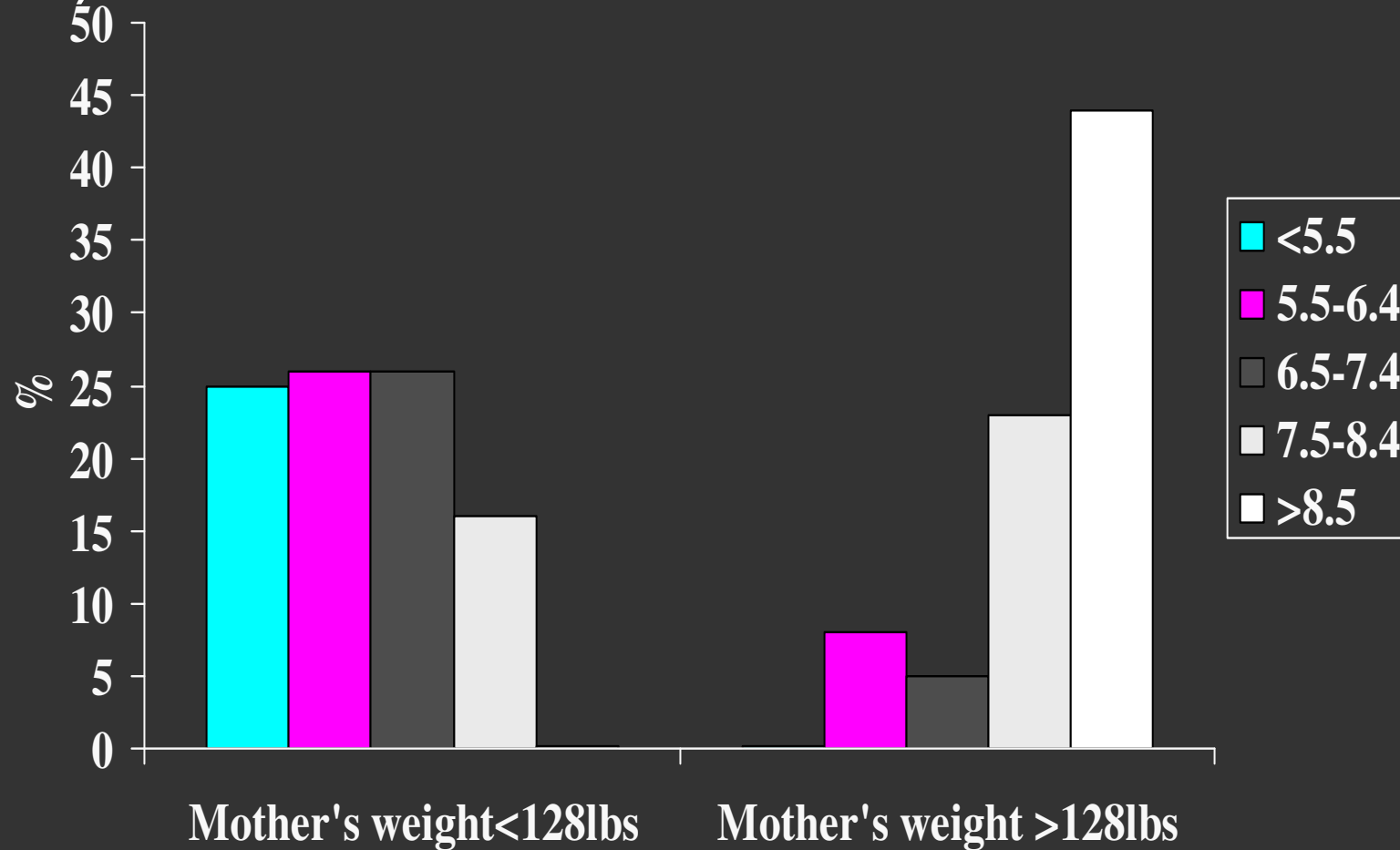
- What is the prevalence of PCOS symptoms?
- What are the aetiological pathways to PCOS?
- Which fetal growth parameters are linked to PCOS phenotypes and obesity in adult life?
- What is the prognostic value of poor pregnancy outcomes for future metabolic disease in the mother?

Per cent of women with polycystic ovaries by birth weight and gestational age.

(Cresswell et al, 1997)



Per cent of women with polycystic ovaries by birth weight and mother's weight in early pregnancy. (Cresswell et al, 1997)



Birth weight Z scores of control girls and postmenarcheal girls with a history of precocious pubarche

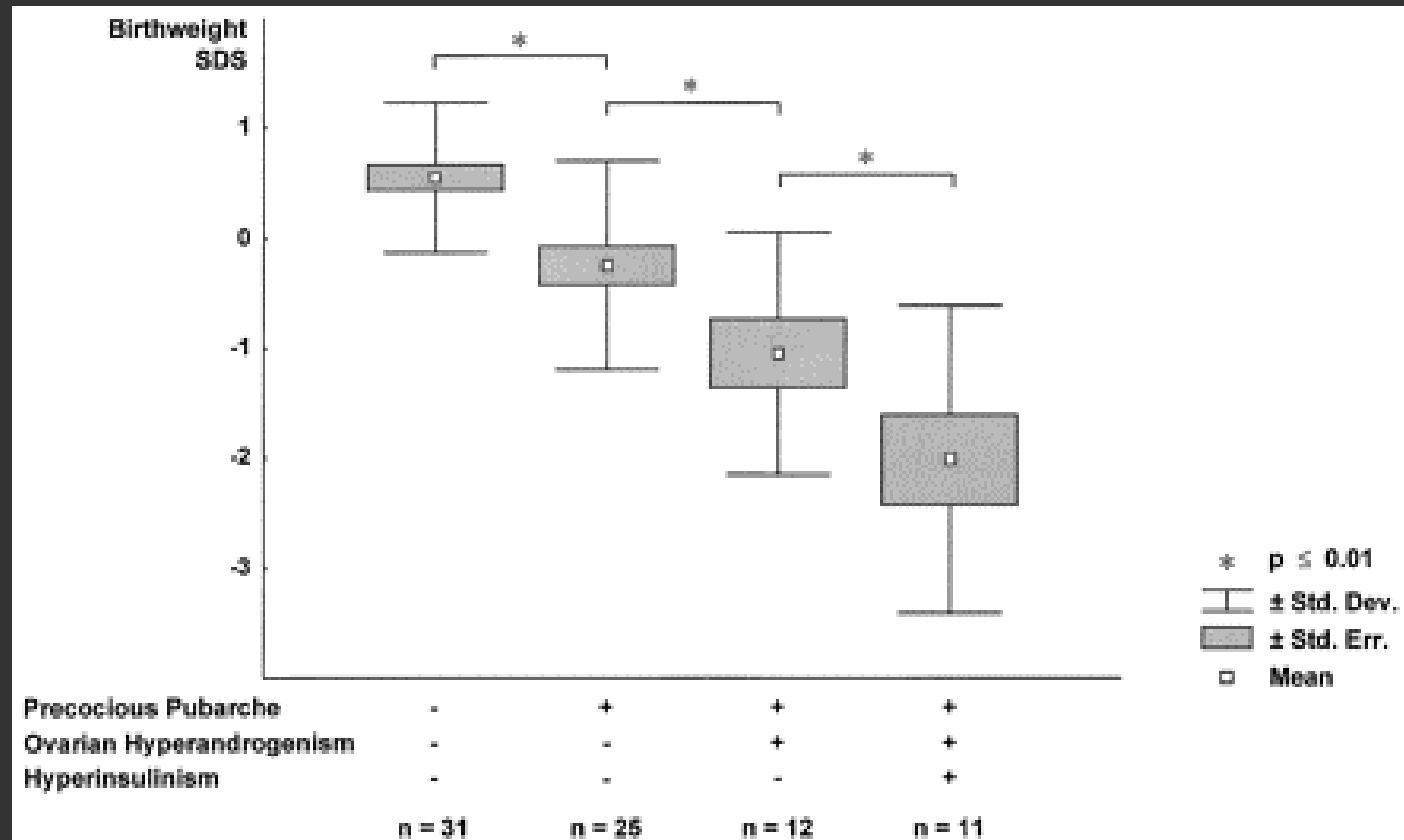
Groups

1 control

2 precocious pubarche

3 = 2 plus ovarian hyperandrogenism

4 = 3 plus hyperinsulinemia



Groups 1 2 3 4

Theoretical possibilities

- **These findings suggest that exposure to different conditions in intrauterine life could predispose individuals to different forms of PCOS.**
- **This may occur by setting patterns of hormone release and tissue sensitivity.**
- **Similarly, the effects of the intrauterine environment may interact with genetic factors to determine the complex clinical and biochemical heterogeneity of PCOS.**

Lucina

“she who brings children into the light“



- A cohort study of young women
- Based on a census of female births surviving to discharge for 1973-75 from the Queen Elizabeth Hospital, Adelaide
- Focus on intergenerational reproductive health

Sampling

- Records for 2,410 consecutive female births surviving to discharge from 1973-75, plus all sibling records,
- We first traced the mother as the name of the child is unknown from the maternity record and the birth record is unavailable to us for this purpose
- Through the mother (occasionally father) we contacted the daughter

Data sources and variables

Routine obstetric record

- Date of delivery

- Maternal age

- Maternal weight in pregnancy

- Birth weight, placental weight

Interview with young women

- History of reproduction

- Menstrual cycles

- Ferriman-Gallwey score

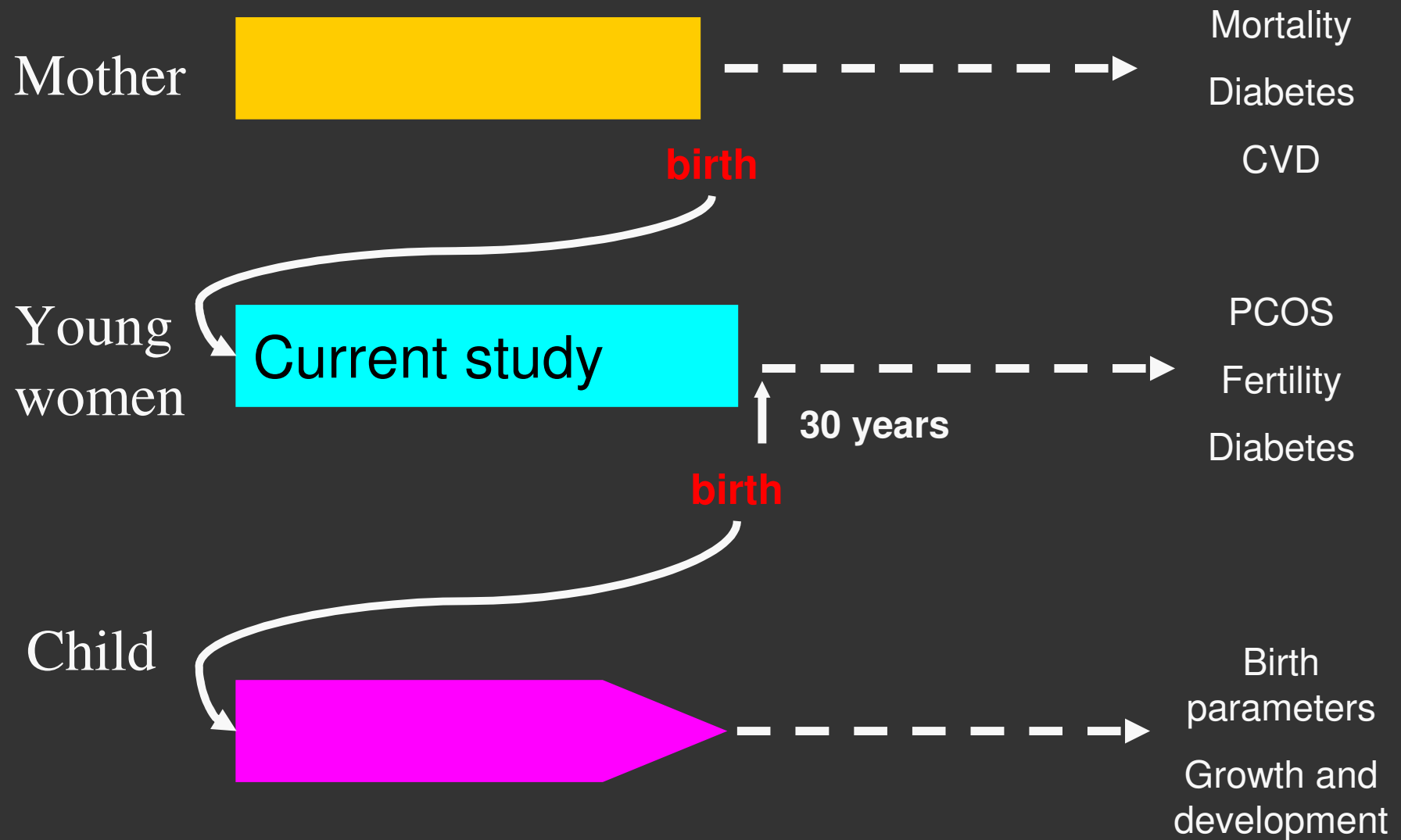
- Anthropometry

- + bloods, ultrasound data

Status

- Over 1,000 women have now been interviewed, of whom approximately 800 live in Adelaide
- A further 200 interviews will be conducted in 2008
- Expansion studies are being designed in detail

Lucina Study



Preliminary findings

- Of 998 women, 62 (6.2%) had a pre-existing diagnosis of PCOS by a physician.
- Are there distinguishing features in the histories of these women?

Maternal characteristics in pregnancy by PCOS in daughters

Existing PCOS, Y/N		Mean	Std. Dev	95% Confidence Interval for Mean	
				Lower Bound	Upper Bound
Age	No	24.60	5.20	24.26	24.93
	Yes	23.47	5.18	22.15	24.78
	Total	24.53	5.21	24.20	24.85
Height	No	159.55	6.28	159.01	160.09
	Yes	160.79	7.08	158.53	163.05
	Total	159.64	6.34	159.12	160.16
First weight	No	63.90	11.45	62.93	64.88
	Yes	65.31	12.90	61.34	69.28
	Total	64.01	11.56	63.06	64.95
Weight 26 weeks	No	67.67	10.95	66.50	68.84
	Yes	68.59	13.31	63.33	73.86
	Total	67.74	11.12	66.60	68.88

Birth characteristics by PCOS in daughters

Existing PCOS, Y/N		Mean	Std. Deviation	95% Confidence Interval for Mean	
				Lower Bound	Upper Bound
Birthweight	No	3290.90	531.75	3256.79	3325.01
	Yes	3206.37	448.26	3092.53	3320.21
Chest	No	32.93	2.25	32.78	33.07
	Yes	32.56	1.79	32.10	33.01
Head	No	34.02	1.66	33.92	34.13
	Yes	33.85	1.43	33.49	34.21
Length	No	50.53	3.17	50.32	50.73
	Yes	50.40	3.07	49.62	51.18
Placental weight	No	577.29	118.82	569.57	585.02
	Yes	549.14	102.72	522.37	575.90

Daughters at age 30-32		by PCOS			
		Mean		95% CI	Sig
Height	0. No	163.97	163.53	164.42	0.98
	1. Yes	163.99	161.85	166.13	
Weight	0. No	72.86	71.63	74.09	0.01
	1. Yes	81.10	75.11	87.09	
Waist	0. No	83.09	82.13	84.04	0.01
	1. Yes	91.10	86.80	95.41	
Hips	0. No	106.57	105.60	107.54	0.04
	1. Yes	110.65	106.82	114.47	
% fat	0. No	35.58	34.89	36.26	0.01
	1. Yes	38.91	36.43	41.40	
BMI	0. No	27.08	26.63	27.52	0.01
	1. Yes	29.93	28.15	31.71	

Maternal history and PCOS in daughter

	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
			Lower	Upper
Blood pressure	0.02	1.86	1.10	3.16
Cholesterol	0.95	0.98	0.51	1.88
Heart disease	0.14	1.94	0.80	4.72
Stroke	0.87	0.88	0.21	3.77
Diabetes	0.56	1.27	0.56	2.89
Gest diabetes	0.88	1.07	0.47	2.40
Mother PCOS	0.00	7.88	1.92	32.30
Mother smoked	0.01	1.12	1.03	1.22

Unadjusted OR

Paternal history and PCOS in daughter

	Sig.	Exp(B)	95.0% C.I. for EXP(B)	
			Lower	Upper
Blood pressure	0.89	0.96	0.53	1.74
Cholesterol	0.26	1.37	0.79	2.36
Heart disease	0.01	2.14	1.18	3.89
Stroke	0.01	3.61	1.43	9.10
Diabetes	0.23	1.51	0.76	2.97

Unadjusted OR

Conclusion

- **The association of PCOS with a family history of hypertension heart disease and stroke in either mother or father imply a possible genetic contribution to the aetiology of PCOS for at least a sub-group of women.**
- **This does not preclude other pathways for the various phenotypes that need to be systematically investigated**

