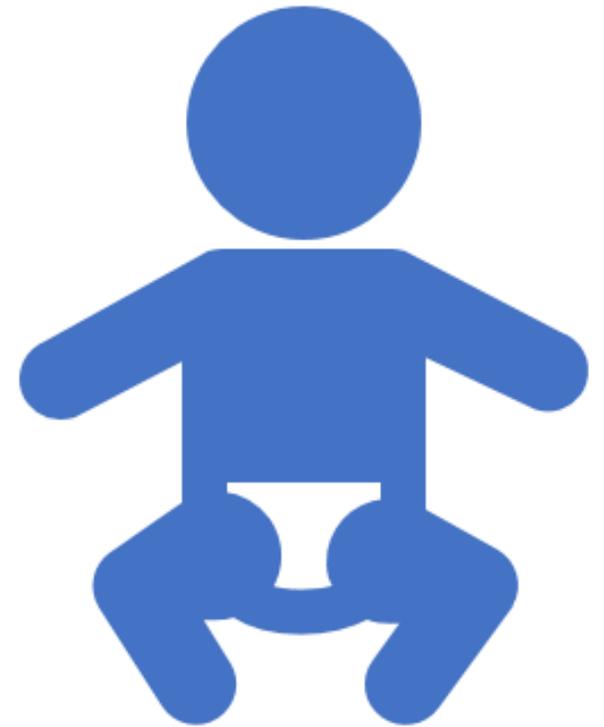


Dud pregnancy= Dud
maternal outcome??



Case study

- 28 year old doctor, speciality trainee.
- Family history
 - Grandparents died of CVD 70's and 80's , all smokers
 - Mother recently diagnosed with hypertension aged 54
- 2 previous spontaneous early miscarriages
- Otherwise fit and well
- BMI 21

First ongoing pregnancy

- Planning to sit exams at 32 weeks gestation
- Initial investigations unremarkable.
- 28/40 visit Fundus smaller than dates- formal scan ordered
 - 30th centile – well baby
- Plan – repeat scan at 32 weeks

Things go awry

- 30 week visit , seen by covering obstetrician– fundus still small, but scan booked for 32 weeks
- Exams 32 weeks- antenatal visit delayed to 33 weeks
- 33.3 weeks
 - 5pm
 - BP 140/90
 - Puffy+++ . Facial oedema. Hadn't been noted by family members.
 - Fundus << dates
 - Urinalysis 2+ protein
 - Plan- fetal monitoring, BP check, bloods next am

33.4 weeks gestation

- Fetal monitoring clinic
 - CTG- unprovoked late decelerations, slow recovery. No variability
 - U/S by midwives- no liquor seen
- Plan made for delivery same day. Celestone given
- C/s 3 hours later
- Baby boy 1.6 kg (< 3rd centile)
- Born in good condition
- Transferred to special care
- Discharged home 2 ½ weeks later weighing 1.9 kg
- Breast fed for 17 months

Next pregnancy

- 30 yo
- Booking BP 100/60
- Thrombophilia screen following last pregnancy NAD
- Initial investigations unremarkable
- Commenced on low dose aspirin

2nd ongoing pregnancy

- 20 weeks morphology scan
- Abnormal uterine artery dopplers on ultrasound
- Increased risk of
 - IUGR
 - Pre-eclampsia
 - Abruptio
- Advised to cease work at 24 weeks
- Modified rest at home

2nd ongoing pregnancy

- 28 weeks presented with reduced fetal movements
- Raised umbilical S/D ratio
- Antenatal steroids given x 2
- Twice weekly fetal monitoring commenced
- 20th centile on ultrasound

2nd ongoing pregnancy

- Growth slowed over following 2/52 scans
- Continued twice weekly fetal surveillance
- 36 weeks- absent end diastolic flow on umbilical artery doppler
- Decision made for delivery same day, emergency LUSCS
- Baby boy 2.342 kg (5th centile)
- Apgars 8¹9⁵
- Spent 1 night in SCN, discharged home day 5
- Breast fed 15 months

3rd ongoing pregnancy

- 33 yo
- Low dose aspirin from 10 weeks
- Initial investigations unremarkable
- 20 week morphology scan – raised uterine artery dopplers
- Work ceased at 24 weeks
- 28, 32, 34 week ultrasounds- slowing growth
- Weekly fetal monitoring

3rd ongoing pregnancy

- 36.2 weeks – oligohydramnios
- Decision made for caesarean section the following day
- Baby girl 2.8kg (25th centile)
- Apgars 8¹ 9⁵
- Went to post-natal ward with mum
- Breast fed 13 months

Long term maternal health

It has become apparent that women with a history of adverse pregnancy outcome are at increased risk of cardiovascular and metabolic diseases later in life

Data increasingly links maternal vascular, metabolic, and inflammatory complications of pregnancy with an increased risk of vascular disease in later life.

Long term maternal health

Pre-eclampsia, gestational
diabetes, preterm labour- what
do they mean for long term
maternal health

Pregnancy as a stress test??

Is it the pregnancy that has this
long-term effect on maternal
health?

Is it the result of predisposing
maternal conditions which are
expressed during pregnancy?

Pregnancy disease	Sample (n)	Literature (Reference number/year)	Definition of health risk in later maternal life	Association of health risk HR/OR/RR (95% CI)
Cardiovascular				
>1 miscarriage	129,200	(27)2003	Ischemic heart disease (IHD)	HR 1.52 (1.13–2.06)
2 miscarriages	129,200	(27)2003	IHD	HR 1.25 (1.04–1.49)
≥3 miscarriages prior to first birth	129,200	(27)2003	IHD	HR 1.56 (1.14–2.15)
Child with FGR (general)	923,586	(28)2011	CAD, CVD, cerebrovascular disease	HR 1.39 (1.22–1.58)
Term FGR	923,586	(28)2011	CAD, CVD, cerebrovascular disease	HR 1.38 (1.15–1.65)
Preterm FGR	923,586	(28)2011	CAD, CVD, cerebrovascular disease	HR 3.4 (2.26–5.11)
Birthweight	783,814	(29)2010	Maternal CVD mortality	0.74/kg (0.56–0.99)—inverse relationship
Birthweight	783,814	(29)2010	Maternal grandfather CVD mortality	1.05 (1.01–1.09)
Birthweight (inverse relationship)	783,814	(29)2010	Paternal Grandmother CVD mortality	0.93/kg (0.85–1.00)—inverse relationship
Low birthweight <2,500 g	119,668	(30)2004	Cerebrovascular disease	aHR 2.51 (1.71–3.70)
Multiparity	2,533	(31)1993	CVD	RR 1.5 (1.1–1.9)
1 birth	1,332,062	(31)1993	CVD	1.09 (95% CI 1.03–1.15)
>5 births	1,332,062	(31)1993	CVD	1.47 (95% CI 1.37–1.57)
>2 children	4,286	(32)2003	Maternal CVD	OR 1.30 (1.17–1.44)
>2 children	4,252	(32)2003	Paternal CVD	OR 1.12 (1.02–1.22)
Preeclampsia (general)	1,985	(33)2016	Death at coronary revascularization	HR 1.61 (1.00–2.58)
Maternal placental disease	1,130,764	(34)2012	Premature heart failure or dysrhythmia	HR 1.51 (1.26–1.80)
Maternal placental disease + FGR	1,130,764	(34)2012	Premature heart failure or dysrhythmia	HR 2.42 (1.25–4.67)
Maternal placental syndrome	1,030,000	(35)2005	CVD	HR 2.0 (1.7–2.2)
Maternal placental syndrome + FGR	1,030,000	(35)2005	CVD	HR 3.1, 2.2–4.5
Maternal placental syndrome + FD	1,030,000	(35)2005	CVD	HR 4.4, 2.4–7.9
Preterm birth 32–37 weeks	923,686	(28)2011	CVD	HR 1.39 (1.22–1.58)
Preterm birth 28–31 weeks	923,686	(28)2011	CVD	HR 2.57 (1.97–3.34)
Spontaneous preterm birth (SPB)	750,350	(36)2015	Death from IHD	HR 2.26 (1.88–2.71)
SPB	750,350	(36)2015	Total IHD	HR 1.58 (1.47–1.71)
Preterm birth 32–36 weeks	782,287	(36)2015	Thromboembolism	aOR 1.42 (1.24–1.62)
Metabolic				
(No) Breastfeeding	23,701	(37)2014	Increased maternal weight after 7 years	$\beta = 0.003$ (0.01, 0.003) path analysis, inverse relationship
Breastfeeding (with formula) in patients with GDM	1,010	(38)2015	Incidence of type 2 DM after 2 years	aHR 0.64 <i>p</i> trend = 0.016 (formula = 1)
Breastfeeding (mostly) in patients with GDM	1,010	(38)2015	Incidence of type 2 DM after 2 years	aHR 0.54 <i>p</i> trend = 0.016
Breastfeeding (exclusive) in patients with GDM	1,010	(38)2015	Incidence of type 2 DM after 2 years	aHR 0.46 <i>p</i> trend = 0.016
Pregnancy weight gain > IOM limits	65,000	(39)2011	3 years postpartum weight gain	3.06 (1.50–4.63) kg, <i>p</i> < 0.001
Pregnancy weight gain > IOL limits	65,000	(39)2011	15 years postpartum weight gain	Mean increase of 4.72 (2.94–6.50) kg
Gestational diabetes	675,455	(40)2009	Manifest type 2 DM	RR 7.43 (4.79–11.51)
Maternal obesity	46,688	(41)2016	Hospitalization for CV events	HR 2.6 (2.0–3.4)
Pre-pregnancy BMI > 30 kg/m ²				
Premature ovarian insufficiency	190,588	(42)2016	IHD	HR 1.69 (1.29–2.21)
Premature ovarian insufficiency	190,588	(42)2016	Total CVD	HR 1.61 (1.22–2.12)

a, adjusted; BMI, body mass index; CAD, coronary artery disease; CVD, cardiovascular disease; DM, diabetes mellitus; FGR, fetal growth restriction; FD, fetal death; HR, hazard



Maternal placental syndrome

- Term coined by researchers to look at maternal outcomes
- Defective deep placentation associated with a spectrum of pregnancy complications including
 - preeclampsia,
 - intrauterine growth restriction
 - preterm labour
 - preterm premature rupture of membranes
 - late spontaneous abortion
 - abruptio placentae.
- suggestion that the major obstetric syndromes may be caused by impaired placental bed spiral artery remodeling



Maternal placental syndrome

- Short term (5 years) risk demonstrated in a study population of 302,686 women.
- Even after adjusting for sociodemographic factors, preexisting conditions and clinical and behavioral conditions associated with the current pregnancy,
 - women with any placental syndrome experienced a 19% increased risk of cardiovascular disease.
 - Women with >1 placental syndrome had the highest cardiovascular disease risk
 - When placental syndrome was combined with preterm birth and/or small for gestational age, the adjusted risk of cardiovascular disease increased 45%.

Gestational Diabetes Mellitus

Women who had prior GDM have a 36–70% risk of developing type 2 DM later in life, depending on risk factors and length of follow-up

Gestational diabetes mellitus (GDM) is an independent risk factor for future

- type 2 diabetes mellitus
- metabolic syndrome, cardiovascular morbidity
- vascular endothelial dysfunction
- renal and ophthalmic disease.

The risk of these conditions may be decreased with proper prevention and interventions.

Pre-eclampsia

New onset of a multisystem pregnancy-related disorder that includes hypertension and either proteinuria or end-organ dysfunction, identified after 20 weeks gestation.

Pre-eclampsia causes multi-system damages due to micro-angiopathy that lead to maternal morbidity that may include

- cardiac and renal failure,
- liver damage,
- cerebrovascular bleeding,
- pulmonary edema,
- disseminated intravascular coagulopathy (DIC),
- placental ischemia, etc.

Pre-eclampsia

The American Heart Association considers a history of preeclampsia or pregnancy-induced hypertension a major risk factor for development of CVD

The future risk CVD is related to the

- severity of preeclampsia
- the gestational age at delivery
- and the number of disease recurrences

Women with early-onset/severe preeclampsia with preterm delivery are at highest risk of CVD later in life, including during the premenopausal period

Deaths from cardiovascular causes

Population	Relative hazard rate (95% CI)
No preeclampsia, term delivery	1
No preeclampsia, preterm delivery	2.95 (2.12-4.11)
Preeclampsia, term delivery	1.65 (1.01-2.70)
Preeclampsia, preterm delivery	8.12 (4.31-15.33)

Data from: Irgens HU, Reisaeter L, Irgens LM, Lie RT. Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. BMJ 2001; 323:1213.

Pre-eclampsia

2017 systematic review, 22 studies . 6.4 million women > 258,000 had pre-eclampsia.

Compared with women with no history , women with pre-eclampsia were at risk for future CVD

- Heart failure (RR 4.19, 95% CI 2.09-8.38)
- Coronary heart disease (RR 2.50, 95% CI 1.43-4.37)
- Death from CVD (RR 2.21, 95% CI 1.83-2.66)
- Stroke (RR 1.81, 95% CI 1.29-2.55)

Persisted after adjustment for age, BMI and DM

Pre-eclampsia

Women who had preeclampsia had a significantly higher incidence of long-term ophthalmic morbidity such as diabetic retinopathy and retinal detachment.

Women with preterm preeclampsia more often had cerebral white matter lesions (WML) on follow-up

Associated with an increased risk of chronic end stage renal disease

Women with pre-eclampsia twice as likely to develop subclinical hypothyroidism during pregnancy and remote from delivery

Children of pre-eclamptic pregnancies

more prone to hypertension, insulin resistance, and diabetes mellitus, neurological problems, stroke, and mental disorders during their lifetime.

Another study demonstrated offspring born to women with preeclampsia were also more likely to have a higher blood pressure from childhood and stroke in later life

Pre-term deliveries

Women who delivered prematurely are also at increased risk of long-term cardiovascular disease (CVD) and additional morbidities

Four of five studies that examined death showed that women with a history of PTB have twice the risk of CVD death compared with women who had term births.

Preterm birth

- Australian study 1994-2011 NSW
- 59,563 women (7.5%) had at least one preterm birth.
- Adjusted for CVD risk factors other than smoking
 - adjusted hazard ratios (AHR) of CVD was 1.78 [1.61–1.96].
- Associations were greater for extreme (AHR = 1.98 [1.63–2.42]) and moderate (AHR = 2.06 [1.69–2.51])

Pre-term birth

- 2015 systematic review and meta-analysis of 10 cohort studies of women with spontaneous pre-term birth compared with women who delivered at term. Followed for 12-35 years
 - Fatal and nonfatal ischemic heart disease (hazard ratio [HR] 1.38, 95% CI 1.22-1.57)
 - Fatal and nonfatal stroke (HR 1.71, 95% CI 1.53-1.91)
 - Fatal and nonfatal overall cardiovascular disease (HR 2.01, 95% CI 1.52-2.65)



Pre-term birth

- 99,338 women who delivered over a period of 25 years, of whom 16,364 (16.4%) had at least one PTD, over a mean follow-up duration of 11.2 years.
- significant dose response between the number of previous PTDs and the gestational age at birth of the PTDs and future risk of renal-related hospitalizations.

Small for gestational age

Risk factor for subsequent long-term maternal cardiovascular morbidity

47,612 deliveries that met the inclusion criteria, 4411 (9.3%) women delivered SGA neonates.

Delivery of an SGA neonate was a risk factor for long-term complex cardiovascular events

Small for Gestational Age

99,342 deliveries; 10,701 (10.7%) women who had at least one previous delivery of an SGA neonate,

Delivery of an SGA neonate was an independent risk factor for long-term maternal renal disease

Small for gestational age

Delivering an FGR infant is associated with maternal coronary artery disease, cerebrovascular disease, or cardiac insufficiency with HRs ranging from 1.35 to 3.4 for severe early-onset FGR

Birth weight has an inverse linear association with maternal CVD mortality and is also related to grandparental CVD and CVD mortality

These BW associations across generations are independent of socioeconomic, environmental, or behavioral factors, body mass index (BMI), age, or smoking status.

Maternal obesity

Associated with an increased risk of various long-term maternal morbidity.

High BMI at the beginning of pregnancy significantly increased the risk of several diseases later in life.

A high weight gain during pregnancy was only significant for future overweight and obesity

Even short-term weight loss decreases the risk of cardiovascular disease (CVD).

What happened next?

- 1st child- now 16yo
 - 180cm, 50kg
 - On autism spectrum, diagnosed at the age of 4
- Mother of patient aged 65
 - Fit, well. Non drinker. BMI 25.
 - Rode “Around the Bay in a Day” the previous year
 - Developed chest pain, AMI. Quadruple bypass 2 days later.

Can we make a difference?

Berks et al. assessed whether offering lifestyle intervention after a complicated pregnancy significantly reduced weight and/or other cardiovascular and metabolic risk factors

Between six and 13 months postpartum, weight was significantly reduced in cases compared to controls by 2.1 kg (95% >CI 0.4–3.7), resulting in lower BMI.

Systolic blood pressure (5.0 mmHg), waist circumference and waist-to-hip ratio were significantly improved compared to controls.

However Heart rate, hip circumference, and total cholesterol were not improved compared to controls. Diastolic blood pressure and fasting glucose were not improved.

Dancing

“Dancing is an enjoyable activity that was also reported to have a risk-reducing effect”

Moderate-intensity dancing was associated with reduced risk of cardiovascular disease mortality to a greater extent than walking.

The association between dance and cardiovascular disease mortality may be explained by high-intensity bouts during dancing, lifelong adherence, or psychosocial benefits.