Diabetes and chronic kidney disease during pregnancy

Evelina London

Anita Banerjee
Obstetric Physician
Diabetes and Endocrinologist

@anitawomenshealth

I have no conflicts of interest to disclose

Outline

- Physiology
- Epidemiology
- Evidence
- Guidelines
- Approach
- Case studies

Case studies

46 year old Nigerian
Type 2 DM
PCR 180
BMI 44 kg/m2
IVF pregnancy four embryos placed abroad

34 year old Caucasian Type 1 DM for 15 years
Admitted with preeclampsia and rupture of membranes at 26/40
Creat 101
PCR 850

26 year old Pakistani
Type 1 DM BMI 18kg/m2
P3 Creatinine 95
This pregnancy PCR 90

Physiology of diabetes and chronic kidney disease (DCKD) during pregnancy

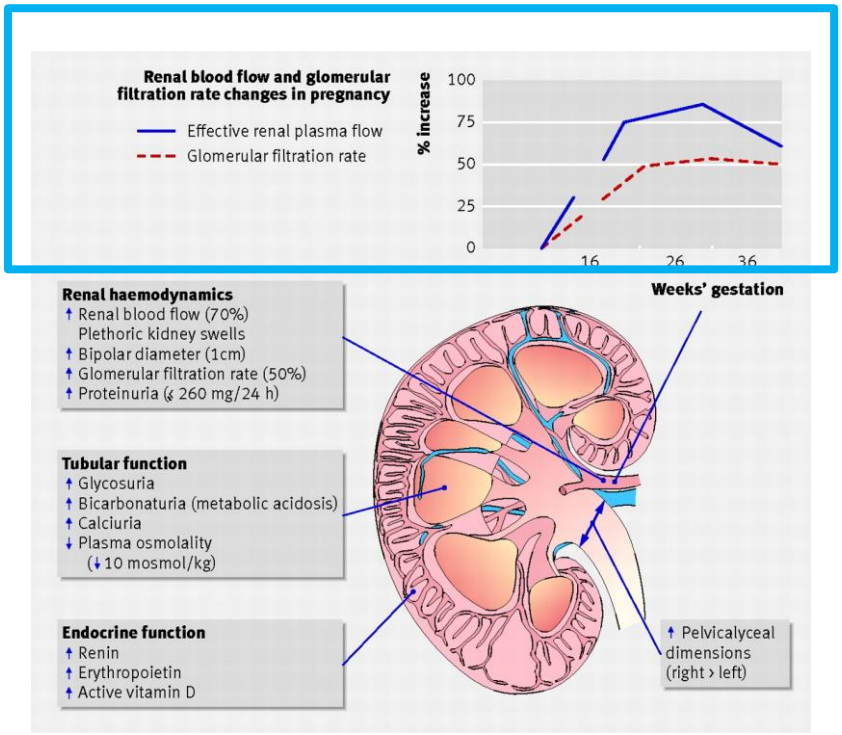
CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE USED BY KDIGO

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. CKD is classified based on Cause, GFR category (G1–G5), and Albuminuria category (A1–A3), abbreviated as CGA.

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red: very high risk.



eGFR validated in pregnancy

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Kidney Disease Improving Global Outcomes (KDIGO)
Clinical Practice Guideline for the evaluation and management of chronic kidney disease.2024..
Williams 2008

(D)CKD in pregnancy: Epidemiology

#4522

PREVALENCE OF CHRONIC KIDNEY DISEASE IN PREGNANCY: A UK POPULATION STUDY

Elizabeth Ralston[1], Yanzhong Wang[1], Steve Childs[2], Chris Farmer[2], Ranjit Akolekar[3] and Kate Bramham[1]

[1]King's College London, School of Life Course and Population Sciences, Great Maze Pond, London, United Kingdom, [2]University of Kent, Centre for Health Services Studies, United Kingdom and [3]Medway NHS Foundation Trust, Medway Fetal and Obstetric Medicine Centre, United Kingdom

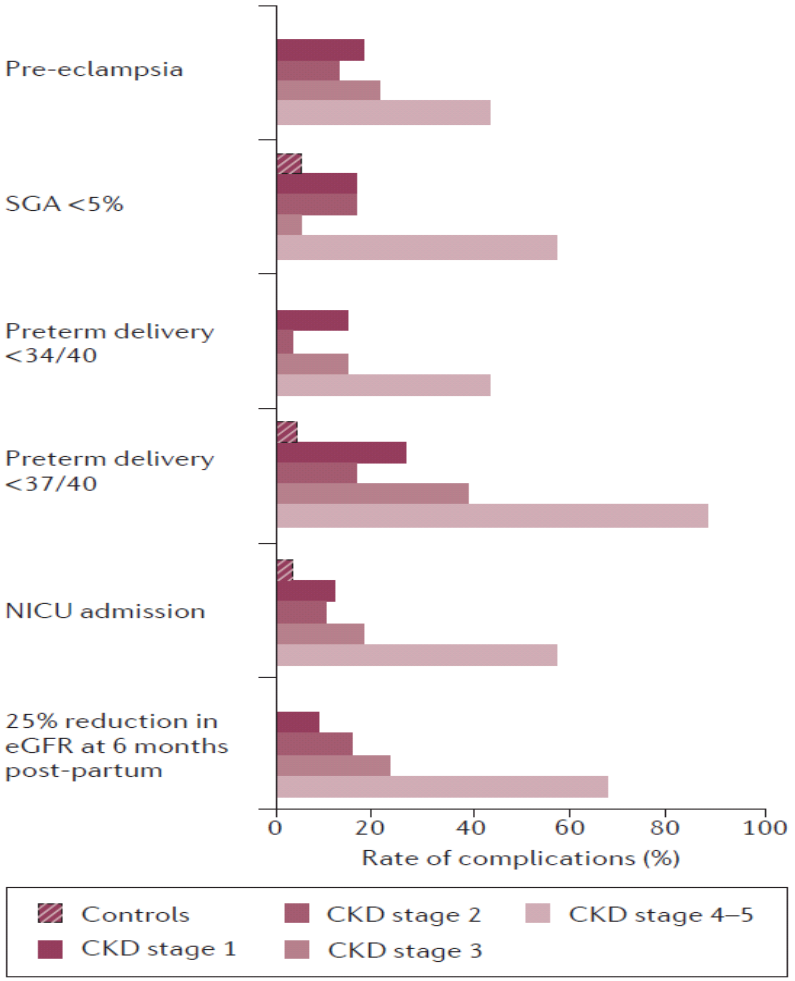
2010-2020
76,766 women
1 in 5 had a pre-pregnancy eGFR
1.5% had CKD

Diabetes	Type 1DM	Type 2 DM
Damm	3%	2%
Relph	5-10%	2-3%

Relph et al 2021
Damm et al 2013
Ralston et al 2023

Effects of CKD on pregnancy outcomes

- ↑ risk of complications
- Worse as ↑renal impairment



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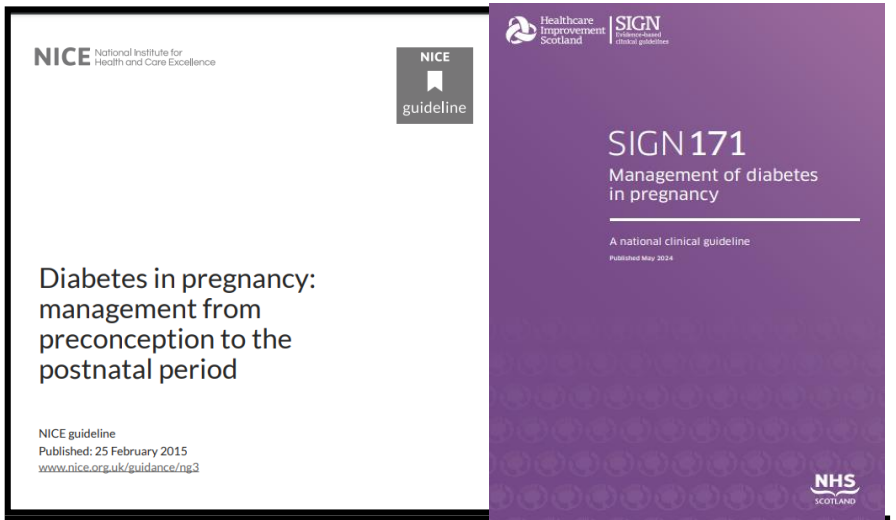
Wiles et al 2018

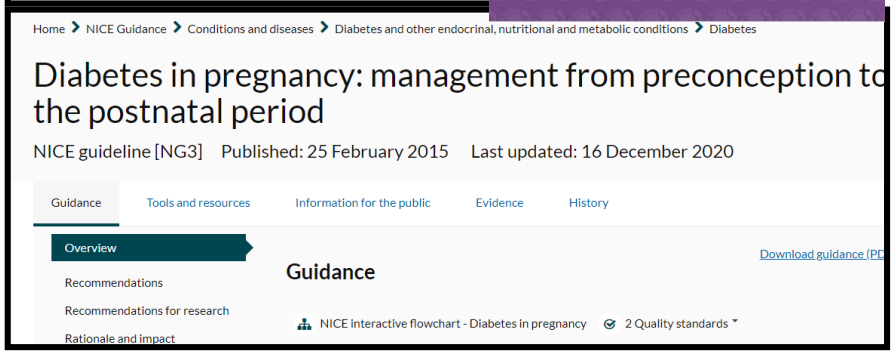
Evidence

	Duration		Pregnancies	Risks
2021 Gleeson	2001-2020	15 studies	874	↑ PET ↑CS
2021 Relph	1990-2021	56 studies	12819	PET OR 10.76 Preterm OR 6.90 CS OR 3.04
2021 Wiles	2003-2017	One study 6 centres	178 9% DCKD	50% preterm 25% severe preterm

CS Caesaren-section

Guidelines Diabetes NICE /SIGN: UK





Key points

- DCKD assessment before pregnancy
- Renal disease at first antenatal review
- Refer to renal team creat > 120µmol/L Or ACR >30
- Consider thromboprophylaxis if ACR>220/PCR 500

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Renal Guidelines; UK

Wiles et al. BMC Nephrology (2019) 20:401
https://doi.org/10.1186/s12882-019-1560-2

BMC Nephrology

THE RENAL ASSOCIATION founded 1950

GUIDELINES Open Access

Clinical practice guideline on pregnancy and renal disease

Kate Wiles[1*], Lucy Chappell[2], Katherine Clark[3], Louise Elman[4], Matt Hall[5], Liz Lightstone[6], Germin Mohamed[4], Durba Mukherjee[4], Catherine Nelson-Piercy[7], Philip Webster[8], Rebecca Whybrow[9] and Kate Bramham[10]

Guideline 5.4.1

We recommend that women with diabetic nephropathy have optimisation of blood glucose, blood pressure and proteinuria prior to conception (1C).

Guideline 5.4.2

Consider thromboprophylaxis if ACR>250/PCR 300

We recommend that women with diabetic nephropathy continue angiotensin converting enzyme inhibitors until conception, with regular pregnancy testing during attempts to conceive (1C).

Guideline 5.4.3

We recommend that the schedule of care, surveillance and management of women with diabetic nephropathy should be untaken according to national guidelines for diabetes in pregnancy, in addition to specialist monitoring of renal disease in pregnancy (1D)

Guidelines: Global





TABLE 2 Key recommendations from international guidelines on diabetic chronic kidney disease and pregnancy.

Guideline	Recommendations					
	Blood pressure management	Proteinuria management	Pre-pregnancy	During pregnancy	Thromboprophylaxis	Diagnostic test for preeclampsia
NICE (diabetes in pregnancy and hypertension in pregnancy) England[18]	Target <135/85 mmHg during pregnancy First-line labetalol, Second-line nifedipine, Third-line methyldopa	Stop ACEi and ARB before conception, or as soon as pregnancy confirmed	Offer renal assessment (including a measure of albuminuria) before stopping contraception Renal referral if serum creatinine is ≥120 µmol/litre or ACR > 30 mg/mmol or eGFR <45 mL/minute/1.73 m^2	Do not use eGFR Renal referral if: creatinine ≥120 µmol/litre or ACR > 30 mg/mmol or total protein excretion >0.5 g/day	If proteinuria > 5 g/day or ACR > 220 mg/mmol	PLGF testing
BMC Clinical Practice Guideline UK[19]	As above	Those taking ACEi should continue until pregnancy confirmed		Do not use eGFR Use ACR or PCR to quantify proteinuria Do not use 24 h urine protein collection	If PCR > 300 mg/mmol or ACR > 250 mg/mmol Consider additionally if any proteinuria and additional risk factors	In proteinuric CKD diagnose preeclampsia if new BP > 140 mmHg and/or diastolic BP > 90 mmHg or maternal organ dysfunction occurs after 20 weeks' gestation In those with hypertension and proteinuria, diagnose preeclampsia if maternal organ dysfunction occurs after 20 weeks' gestation
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Banerjee & Brackenridge 2024

Guidance inside and outside of pregnancy for blood pressure control

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 29, 2015 VOL. 372 NO. 5

Less-Tight versus Tight Control of Hypertension in Pregnancy

Laura A. Magee, M.D., Peter von Dadelszen, M.B., Ch.B., D.Phil., Evelyne Rey, M.D., Susan Ross, M.B.A., Ph.D., Elizabeth Asztalos, M.D., Kellie E. Murphy, M.D., Jennifer Menzies, M.Sc., Johanna Sanchez, M.I.P.H., Joel Singer, Ph.D., Amiram Gafni, D.Sc., Andrée Gruslin, M.D.,* Michael Helewa, M.D., Eileen Hutton, Ph.D., Shoo K. Lee, M.D., Ph.D., Terry Lee, Ph.D., Alexander G. Logan, M.D., Wessel Ganzevoort, M.D., Ph.D., Ross Welch, M.B., B.S., D.A., M.D., Jim G. Thornton, M.B., Ch.B., M.D., and Jean-Marie Moutquin, M.D.

GUIDELINES Open Access

Clinical practice guideline on pregnancy and renal disease

Consultations

Schedule additional antenatal appointments (weekly, or every 2 to 4 weeks) based on individual needs and BP control.

Antihypertensive treatment

- Stop ACE inhibitors or ARBs within 2 working days of notification of pregnancy and offer alternatives.
- Start aspirin[1] 75 mg to 150 mg once daily from 12 weeks.
- Offer antihypertensive treatment to women with sustained blood pressure of ≥140/90 mmHg.
- Use labetalol, nifedipine[2] or methyldopa. Base the choice on any pre-existing treatment, side-effect profiles, risks (including fetal effects) and the woman's preference.
- Aim for target BP ≤135/85 mmHg.

Guidance inside and outside of pregnancy for blood pressure control

Table 1

Blood pressure targets in people with diabetes through stages of kidney function impairment

Type of diabetes	Stage of kidney function impairment				
	Normal kidney function, normoalbuminuria	Normal kidney function, microalbuminuria	CKD stages 1–	CKD stages 4–5 (nondialysis)	CKD stage 5 (dialysis)
Type 1	<140/80–90 (2D) <120/80 (2D)[a] (for <30 yr)	≤130/80 (1B) 120/80 (2D)[a]	≤130/80 (1B) 120/80 (2D)[a]	≤140/90 (1B) ≤130/80 for those with albuminuria (2C)	≤140/90 (2D)[b] (interdialytic BP)
Type 2	<140/90 (1D) <150/90 (2B)[c] (for ≥75 yr)	<130/80 (2D)	<130/80 (2D)	<140/90 (1B)[d] <130/80 for those with albuminuria (2C)	<140/90 (2D)[b] (interdialytic BP)

KI REPORTS
KIReports.org
REVIEW

Management of Hypertension in Patients With Diabetic Kidney Disease: Summary of the Joint Association of British Clinical Diabetologists and UK Kidney Association (ABCD-UKKA) Guideline 2021

Debasish Banerjee[1], Peter Winocour[2], Tahseen A. Chowdhury[3], Parijat De[4], Mona Wahba[5], Rosa Montero[6], Damian Fogarty[7], Andrew Frankel[8], Gabrielle Goldet[8], Janaka Karalliedde[9], Patrick B. Mark[10], Dipesh Patel[11], Ana Pokrajac[12], Adnan Sharif[13], Sagen Zac-Varghese[2], Stephen Bain[14] and Indranil Dasgupta[13]; on behalf of the Association of British Clinical Diabetologists and The UK Kidney Association

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National Pregnancy in Diabetes Audit

Findings

Pregnant women with diabetes in 2021 and 2022

Type 1 — **44%**

Type 2 — **55%***

* 1% of pregnant women with diabetes had other rarer forms of diabetes such as MODY (Maturity Onset Diabetes of the Young) and LADA (Latent Autoimmune Diabetes in Adults) or unspecified diabetes

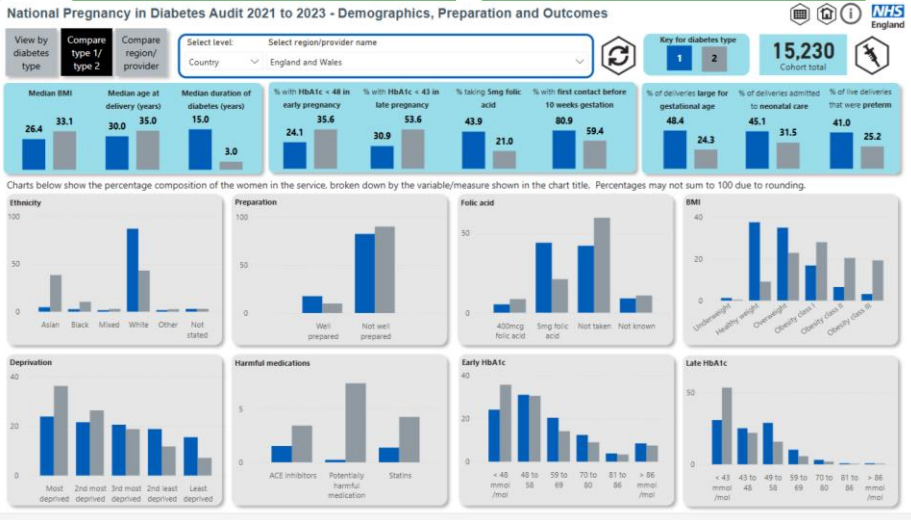
95% of women with type 1 diabetes wore **continuous glucose monitors** in 2022*

improving:

glucose levels for mothers

outcomes for women and babies

* Accurate data on CGM use has only been available since 2022



Findings continued

Pregnant women with **type 2 diabetes** are more likely than those with type 1 to be:

From ethnic minorities

Living in deprived areas

and to experience **health inequalities** before and during pregnancy. This finding is unchanged since 2014.

Rates of **serious outcomes** for women with **type 2** diabetes and their babies increased in 2022*

2014-2020: 5.5%

2021: 4.9%

2022: 6.6%

* Serious outcomes include miscarriage, stillbirth or neonatal death, or birth defect. It's important to remember that these outcomes are rare and there are many things you can do to reduce the risk

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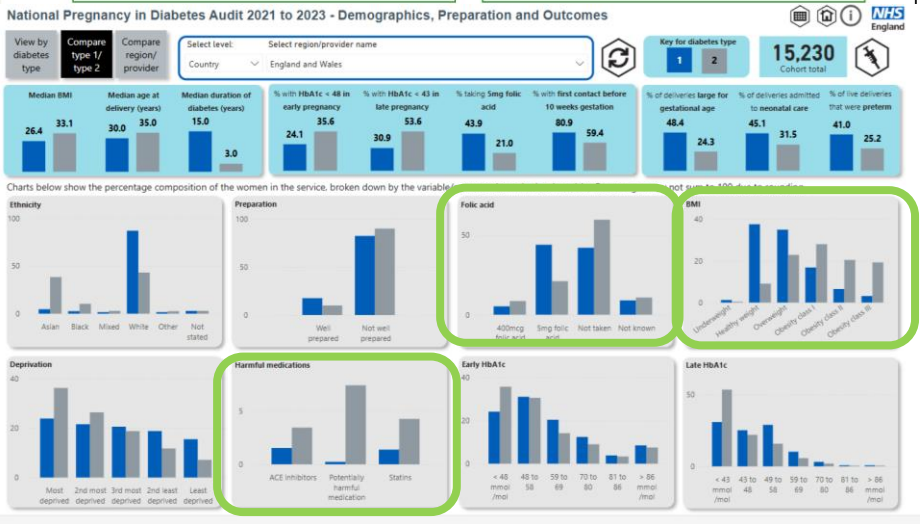

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National Pregnancy in Diabetes Audit

NHS England

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Saving babies' lives version three: a care bundle for reducing perinatal mortality

Document first published: 31 May 2023
Page updated: 29 September 2023
Topic: Maternity, Nursing, midwifery and

The Saving babies' lives care bundle provides evidence-based best practice for providers and commissioners of maternity care across England to reduce perinatal mortality.

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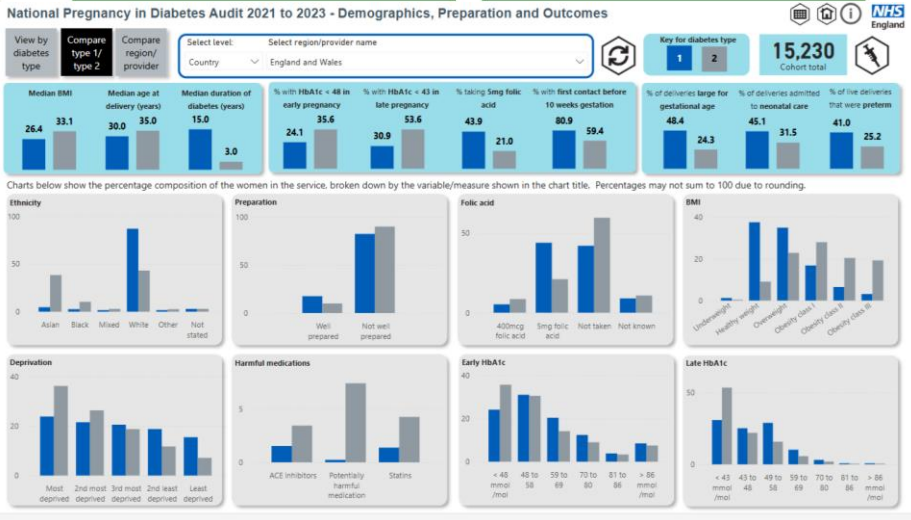

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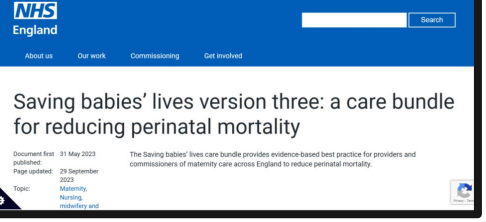
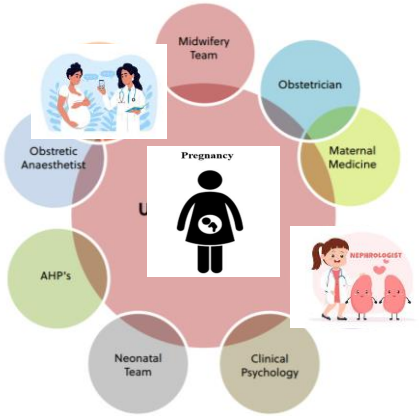
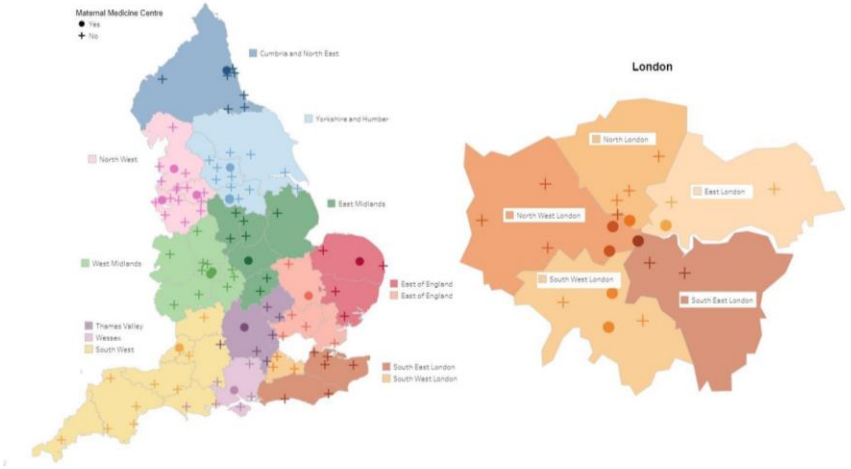


Saving Babies lives Bundle Version 3

6.5 Women with diabetes and retinopathy requiring treatment during pregnancy and/or kidney impairment (CKD 2 with significant proteinuria i.e. PCR>30; or CKD 3 or more) should be managed in a regional maternal medicine centre where care can be delivered in a single MDT clinic. In circumstances where regular travel to a tertiary clinic is not possible, ongoing care should be planned via regular (4-6 weekly) MDT discussion with the MMC centre throughout the pregnancy'





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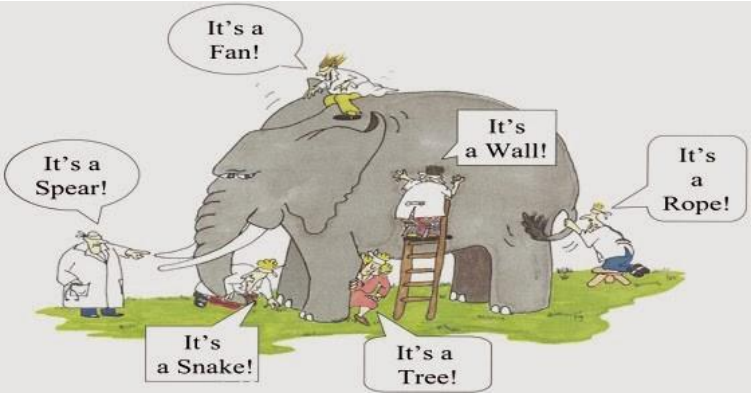
How would you approach DCKD during pregnancy?



- Personalised care
- Identify early
- Consider risk factors
- Clinical assessment
- Surveillance
- Psychological aspect
- Social aspect
- Family engagement

Case Study

37 yr old
P0
Type 1 diabetes mellitus
Poor glycaemic control
Premature rupture of membranes & superimposed pre-eclampsia

Delivered at $27^{+3}/40$

Son born
Died 3 months later

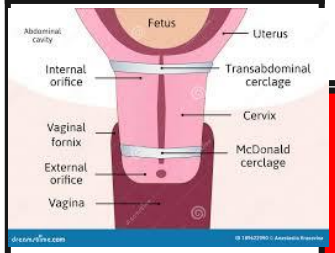
38 yr old

Improved glycaemic control
Premature rupture of membranes at 17/40

A baby boy

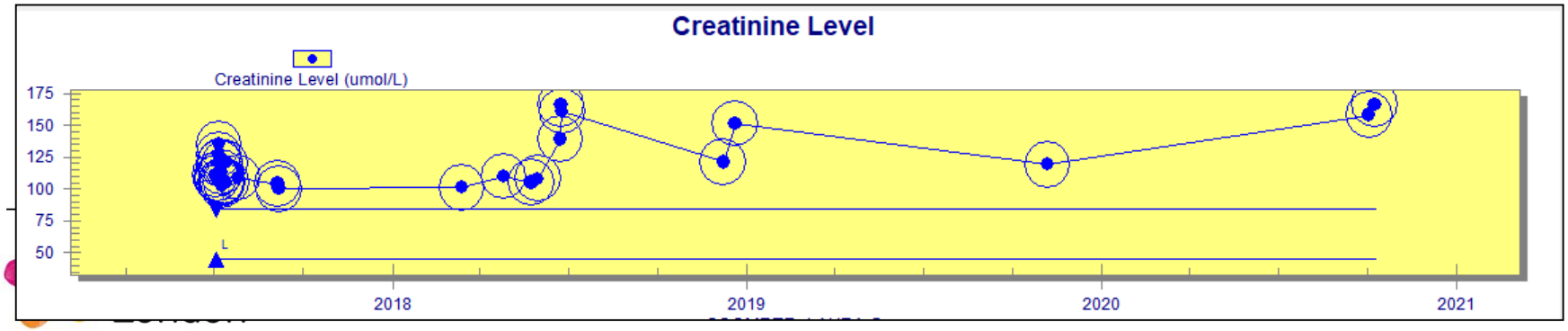
39 yr old
1st trimester miscarriage

39 yr old
Abdominal cerclage placed



40 yr old
Pregnant
creatinine 166µmol/L
urea 20mmol/L
dialysis commenced

Miscarriage at 14 weeks gestation



Definitions – Pre-Eclampsia

International Society for the Study of Hypertension in Pregnancy

Pre-eclampsia is gestational hypertension accompanied by *one or more* of the following new-onset conditions at or after 20 weeks' gestation:

Proteinuria*

Significant proteinuria is > 300mg protein in a 24-hr urine collection
OR
>30mg/ml in a spot urinary PCR

*NOT needed for the diagnosis of pre-eclampsia

Other maternal organ dysfunction, including:

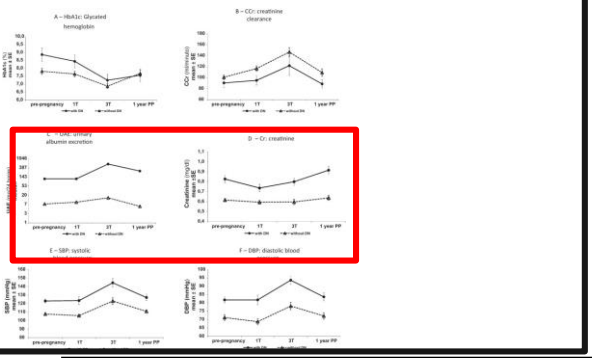
- Acute Kidney Injury (creatinine ≥90 µmol/L, or doubling of serum creatinine in absence of renal disease)
- Liver involvement (elevated transaminases with or without right upper quadrant or epigastric abdominal pain)
- Neurological complications (examples include eclampsia, altered mental status, visual disturbance, stroke, clonus, headaches)
- Haematological complications (thrombocytopenia – platelet count below 150,000/µL, disseminated intravascular coagulation, haemolysis)

Uteroplacental dysfunction (such as fetal growth restriction, abnormal umbilical artery doppler wave form analysis, or stillbirth)

Brown, M. *et al.* (2018) "187. the hypertensive disorders of pregnancy: ISSHP classification, Diagnosis & Management Recommendations for International Practice," *Pregnancy Hypertension*, 13.

Dilemma : is there progression of disease or superimposed preeclampsia

Studies examining in pregnant women with DCKD:
X2 uPCR from 1st trimester
2.1–5.3 fold 3rd trimester
42–73% of these pregnancies went on to develop PET



Young et al 2011
Morton et al 2020
Bertoni & Williams 2024

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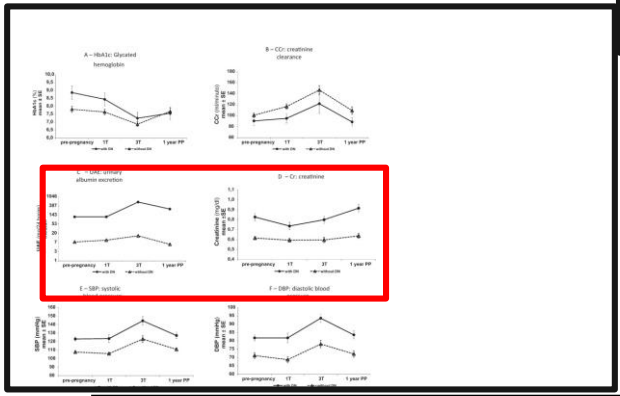

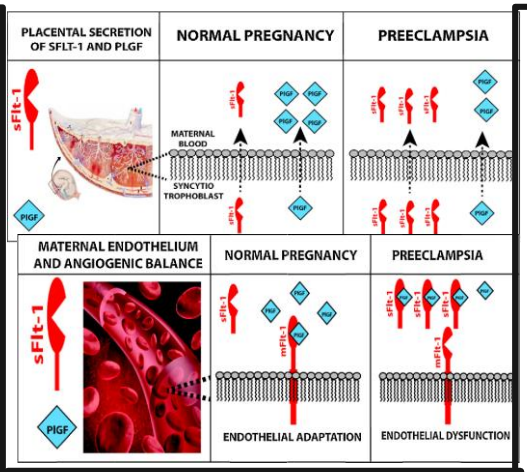

Predictive / Diagnostic tests

Recommended cut-offs for PlGF testing PlGF levels, National Institute for Health and Care Excellence (NICE). Levels vary by gestational age, with the lower limit of normal ranging from 141 pg/mL at 30 weeks' gestation to 23 pg/mL at term.[10]

PlGF level (pg/mL)	Interpretation
<12	Highly abnormal – suggestive of severe placental dysfunction and increased risk of pre-term delivery
12–100	Abnormal – suggestive of placental dysfunction and increased risk of pre-term delivery
≥100	Normal – suggestive of no placental dysfunction and unlikely to progress to delivery within 14 days

PLGF can be measured as a free concentration in blood :

- In PET a significant↓ free concentration of PLGF
- sFLT-1 increases binds to growth factors (VEGF, PLGF) thus creating a deficiency

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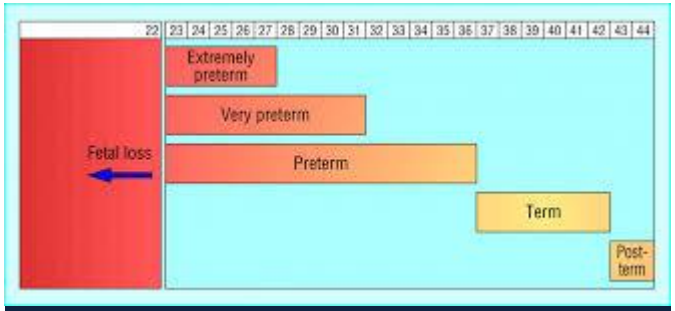
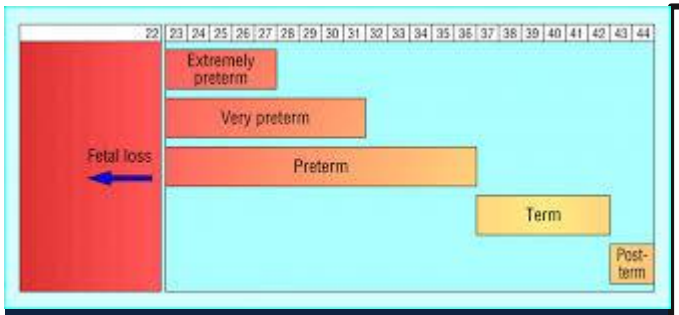
Young et al 2011
Morton et al 2020
Bertoni & Williams 2024

The consequences of preterm delivery



The consequences of preterm delivery



Neurological

- Cerebral palsy
- Neurodevelopmental delay

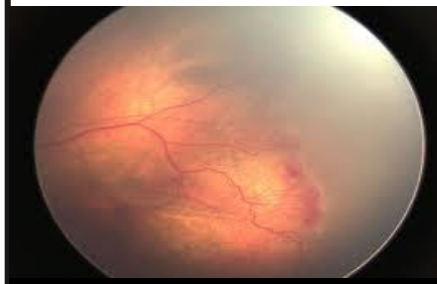
Retinopathy of Prematurity

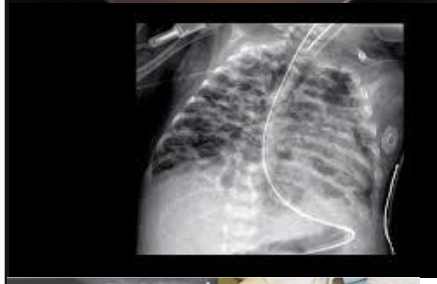
Respiratory

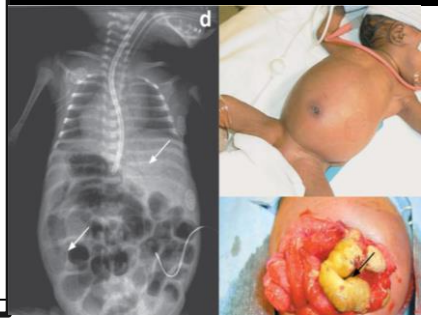
- Bronchopulmonary dysplasia
- Asthma

Gastrointestinal

- Necrotising enterocolitis







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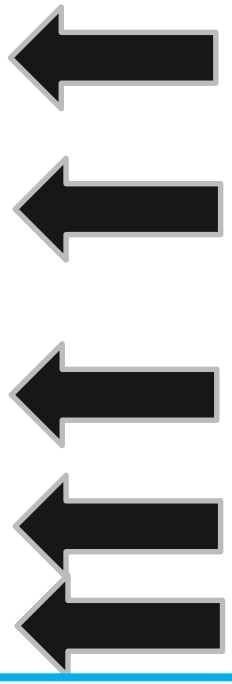
Antenatal diabetes care pathway

Gestation in weeks:	Diabetes team	Scans	Obstetric team	Diabetes midwifery team
FIRST TRIMESTER				
Positive preg test	Diabetes team review within 1 week			
7	**Diabetes team review every 1-2 weeks**	Viability scan		
8				MW booking
12-13		Dating scan / CST	Post scan obstetric review	
SECOND TRIMESTER				
16	**Diabetes team review every 1-2 weeks**			MW review
20		Anomaly scan, uterine A Doppler, echo	Post scan obstetric review	
24				MW review
THIRD TRIMESTER				
28	**Diabetes team review every 1-2 weeks**	Growth scan	Post scan obstetric review and give IOL / CS leaflet	
30				MW review
32		Growth scan	Post scan obstetric review, date and consent if CS	
34				MW review and discuss colostrum
36	Diabetes team review and confirm birth plan	Growth scan	Post scan obstetric review and confirm birth plan	
37	Diabetes team review			MW review
38-39 (may be 37 if complex)	Spontaneous labour or Induction of Labour / CS, and birth			

How often is a renal assessment required?

Aspirin EC 150mg nocte, early viability scan



DCKD women more likely to need EPO

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Rate of DCKD progression postpartum

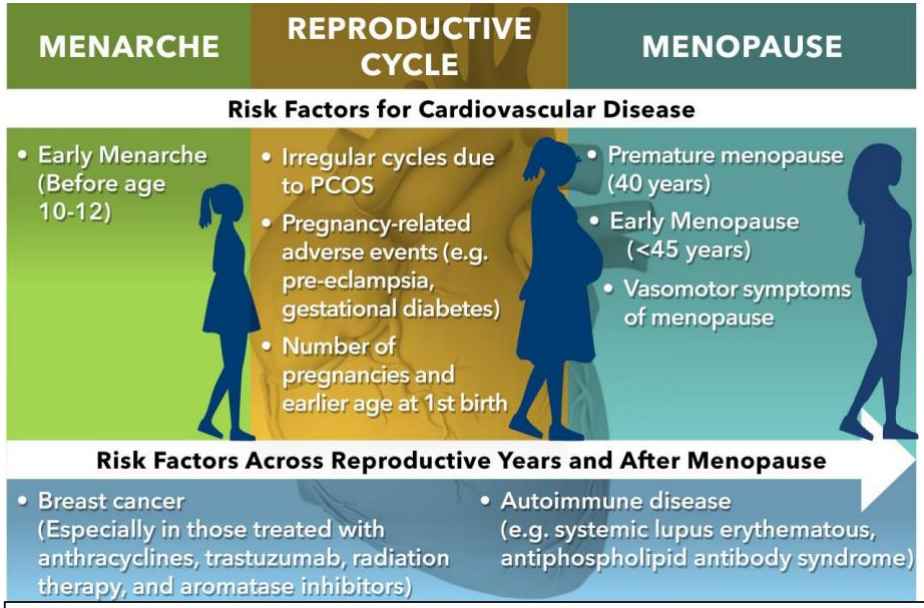
Older literature……

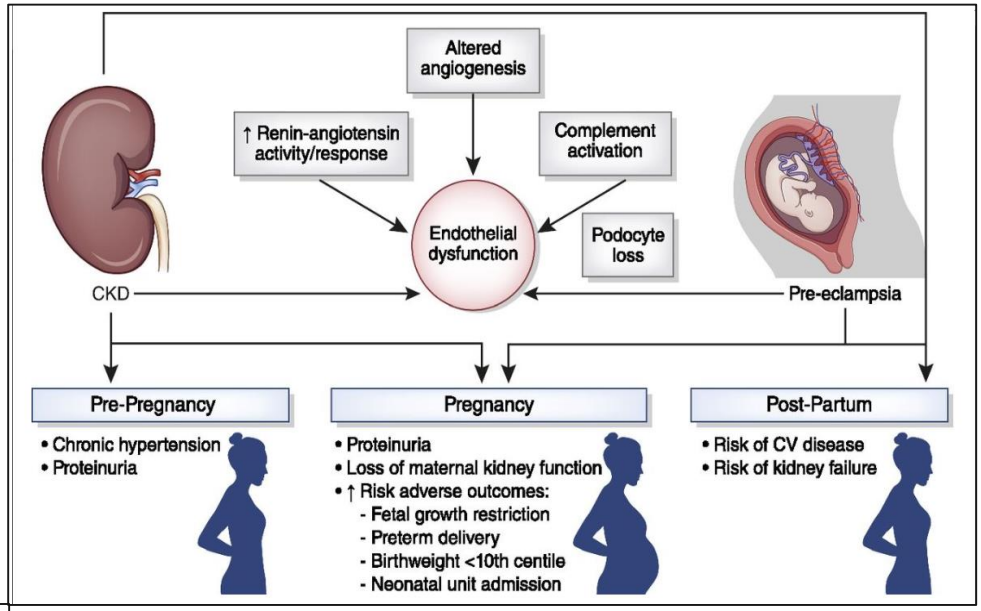
- Kitzmiller 23 women followed up 9-35 months
- Reece 11 women followed up prepregnancy to 4 years post
- Kimmerle 29 women
- Gordon 29 women 2.8 years pregnancy may accelerate loss
- Biesenback decline in renal function may be related to increasing hypertension during pregnancy

2 cases
Type 1 DM in their 30s
Hypertensive and poor glycaemic control throughout pregnancy
Superimposed PET
ESRD within 2 years postpartum

Attique et al 2021
Kitzmiller et al 1981
Reece et al 1988
Kimmerle et ai 1995 Gordon et 1995
Bissenbach et al 1992

Female specific risk factors





Women with diabetes
↑risk of CVD compared to men
female-specific risk factors

- reproductive life cycle factors
- pregnancy
- breast cancer
- ↑ autoimmune diseases

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Le Blanc et al 2024
Wiles et al 2020

Local Data

In the last 6 months (July-December 2024), 477 deliveries in women

445 with gestational diabetes mellitus

32 with pre-existing diabetes mellitus

Diabetes (gestational and pre-existing) – ethnicity breakdown:

White	139	29.1%
Black or Black British	129	27.0%
Asian or Asian British	125	26.0%
Any other ethnic group	37	7.8 %
Mixed	27	5.7%
Not stated/undefined	14	2.9%
Any other ethnic group		15.9 %
Mixed		12.9 %
South American		1.3 %

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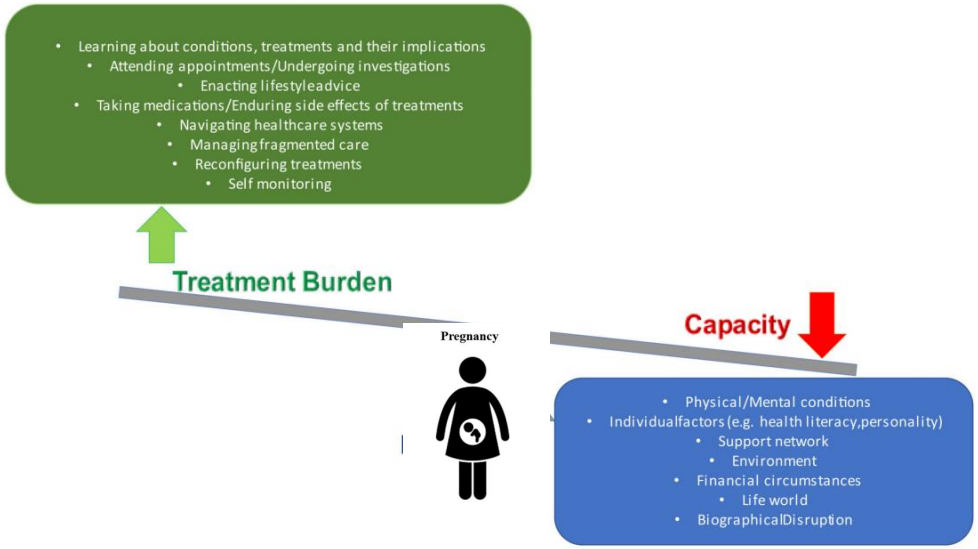
Acknowledgement to Dr Chandramani

Treatment burden & social determinants of health



Antihypertensives used more frequently in the type 1 DM cohort

Role and access to modern diabetes technology

Type 2 DM:
Multimorbidity
Obesity
Advanced maternal age

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Modified from Skou et al 2022
Homles et al 2011

Case studies

46 year old Nigerian
Type 2 DM
PCR 180
BMI 44 kg/m2
IVF pregnancy four embryos placed abroad
This pregnancy one embryo remained. BP difficult to control. PCR peaked 890 before PET confirmed
EMCS at 33 weeks

34 year old Caucasian Type1 DM for 15 years
Admitted with preeclampsia and rupture of membranes at 26/40
Creat 101
PCR 850

26 year old Pakistani
Type 1 DM BMI 18kg/m2
2 children. Creatinine 95
This pregnancy PCR 90
Had a PPH and abruption at 35/40 required dialysis for a week postpartum. Baseline creatinine now 155

Areas of uncertainty in DCKD in pregnancy

- *BP target in pregnancy. Should we be aiming lower than 135/85mmHg for women with DCKD?*
- *When to use low molecular weight heparin for thromboprophylaxis and what dose*
- *Distinguishing progression of DCKD from superimposed preeclampsia*
- *Optimum use of PLGF and value of serial measurements*
- *Effect of gestational weight gain on DCKD in pregnancy*
- *Effect of glycaemic control on DCKD in pregnancy*
- *Optimum timing of delivery for women with progression of underlying DCKD, balancing risks of potentially irreversible maternal organ dysfunction against foetal prematurity*
- *When and how to treat anaemia in pregnancy in women with DCKD*
- *Differences between DCKD in women with type 1 and type 2 diabetes, and implications for management*

Take home messages

- Multidisciplinary team working is key
- Personalised care

My own reflections on the cases:

- *engagement*
- *improved glycaemic & blood pressure control*
- *consequences of a preterm delivery*

- ↑morbidity burden among women of reproductive age attention from a policy point of view

Prevention is better than treatment

Meet the Team and Thank you

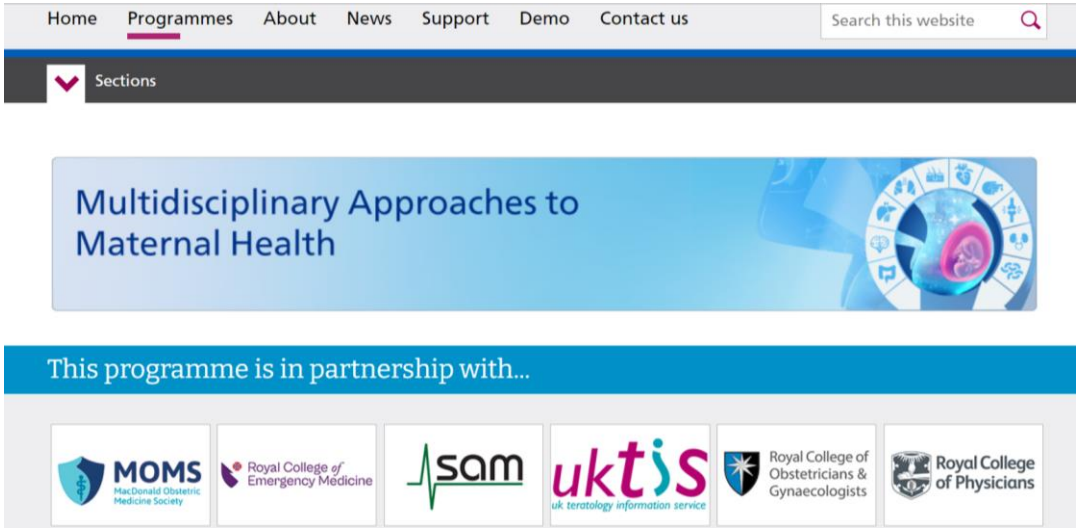
Anna Brackenridge
Sara White
Caroline Ovadia
Caroline Knight
Manju Chandramani
Sarah Hopkin
Rebecca Hyslop
Julia Kidd
Emma Hall
Scarlet Plaster
Jade Deacon Cummings

Taryn Pile

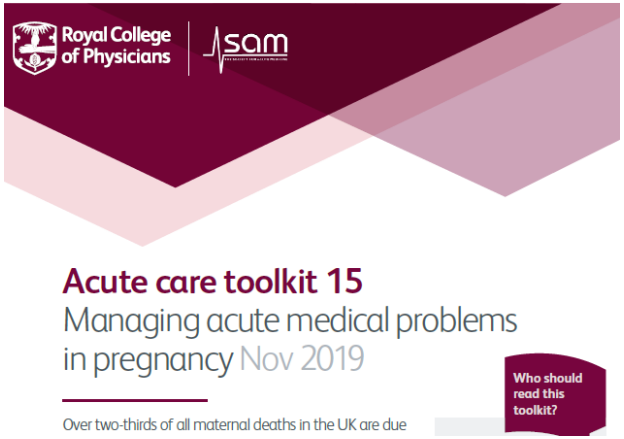
Angus Forbes
Rita Forde
Mark Chamley

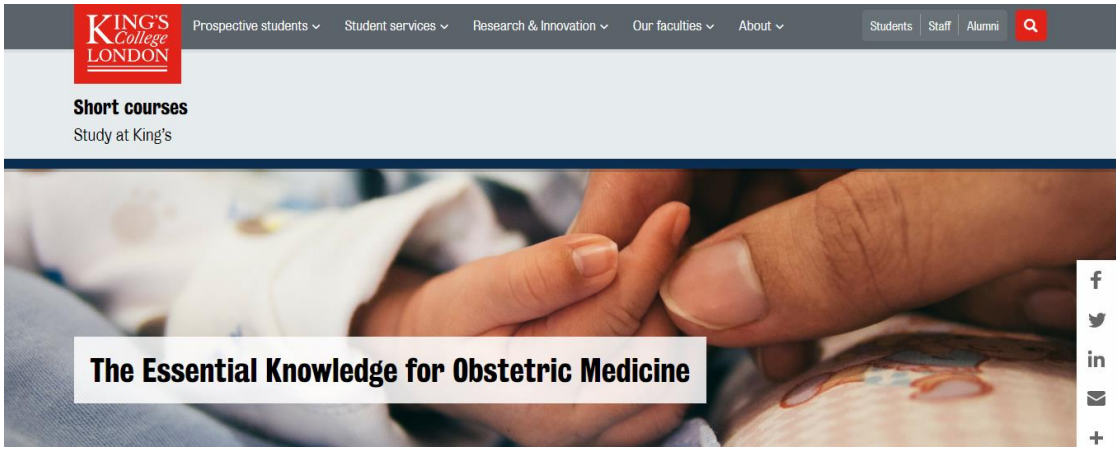
Our women and staff

Q & A
Thank you for listening



eLfH package





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