

Management of women at high risk of Preterm birth



GP training day 7/10/21



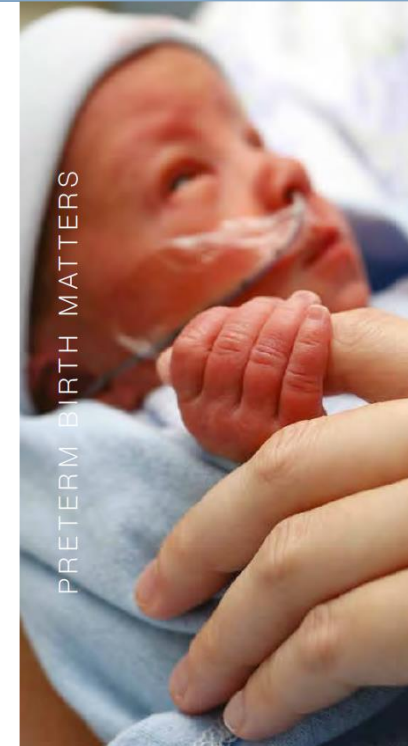
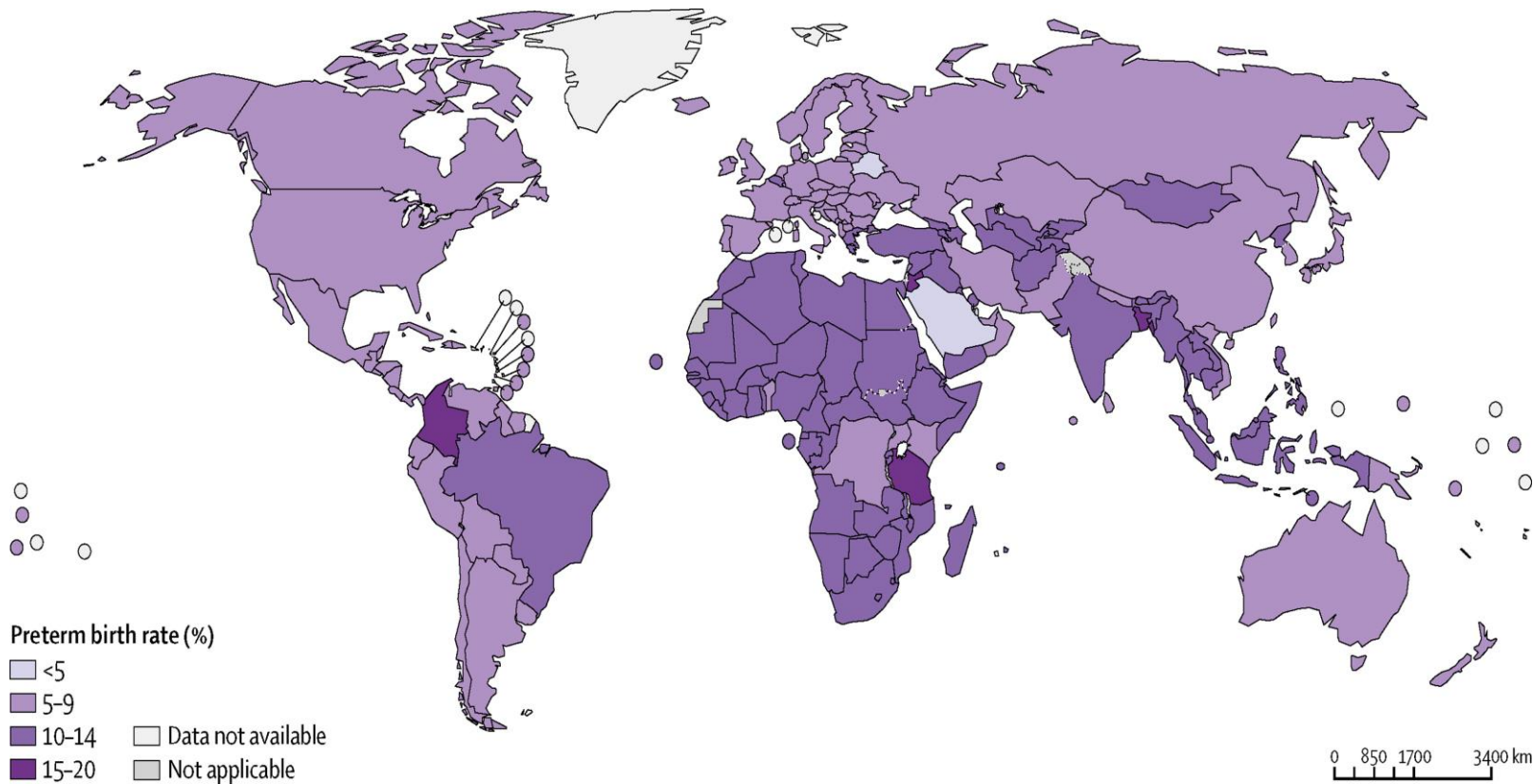
Dr Lynne Sykes BSc MBBS PhD MRCOG
Clinical Senior Lecturer & Consultant Obstetrician, Imperial College London



Content

- Who is at high risk
- Prediction
- Prevention
- Preparation

Who is at risk ?



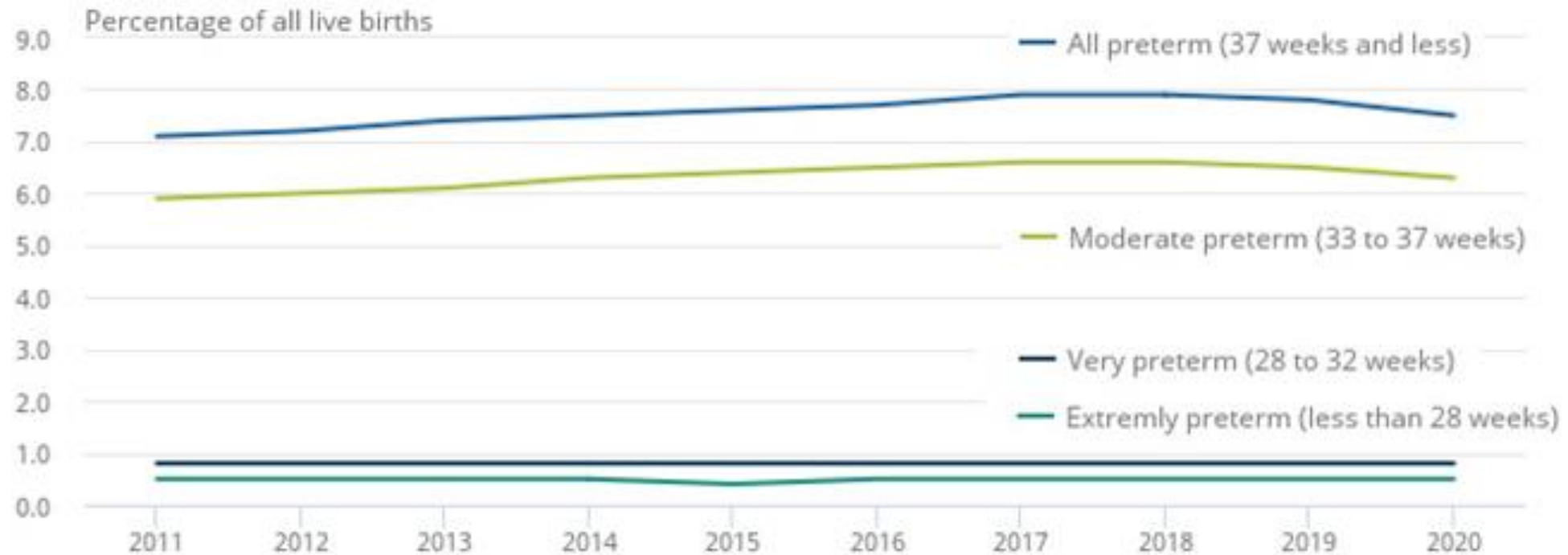
World Health
Organization

Born Too Soon
The Global Action Report
on Preterm Birth

Call to prevent avoidable death:

$\frac{3}{4}$ could be saved with current cost effective interventions such as warmth, breastfeeding, antibiotics, antenatal steroids

Percentage of live births classified as preterm occurring in England and Wales, 2011 to 2020



Source: Office for National Statistics - Provisional births in England and Wales

Classification of PTB

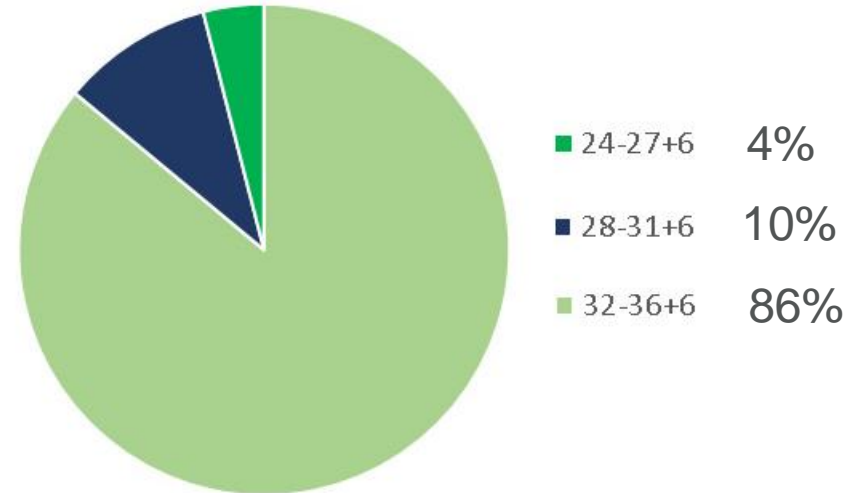


World Health
Organization

2014 Global rate, 11%

- extremely preterm (less than 28 weeks), 5% of PTB
- very preterm (28 to 32 weeks), 10% of PTB
- moderate to late preterm (32 to 37 weeks), 85% of PTB

2018 England and Wales, 7.9%



Preterm birth – UK vision



Department
of Health



Safer Maternity Care

Next steps towards the national maternity ambition

2016

Call to reduce stillbirths, neonatal and maternal deaths by 50% by 2030

Safer Maternity Care

The National Maternity Safety Strategy - Progress and Next Steps

2017

Call to reduce PTB rates from 8% to 6% by 2025



England

Saving Babies' Lives
Version Two

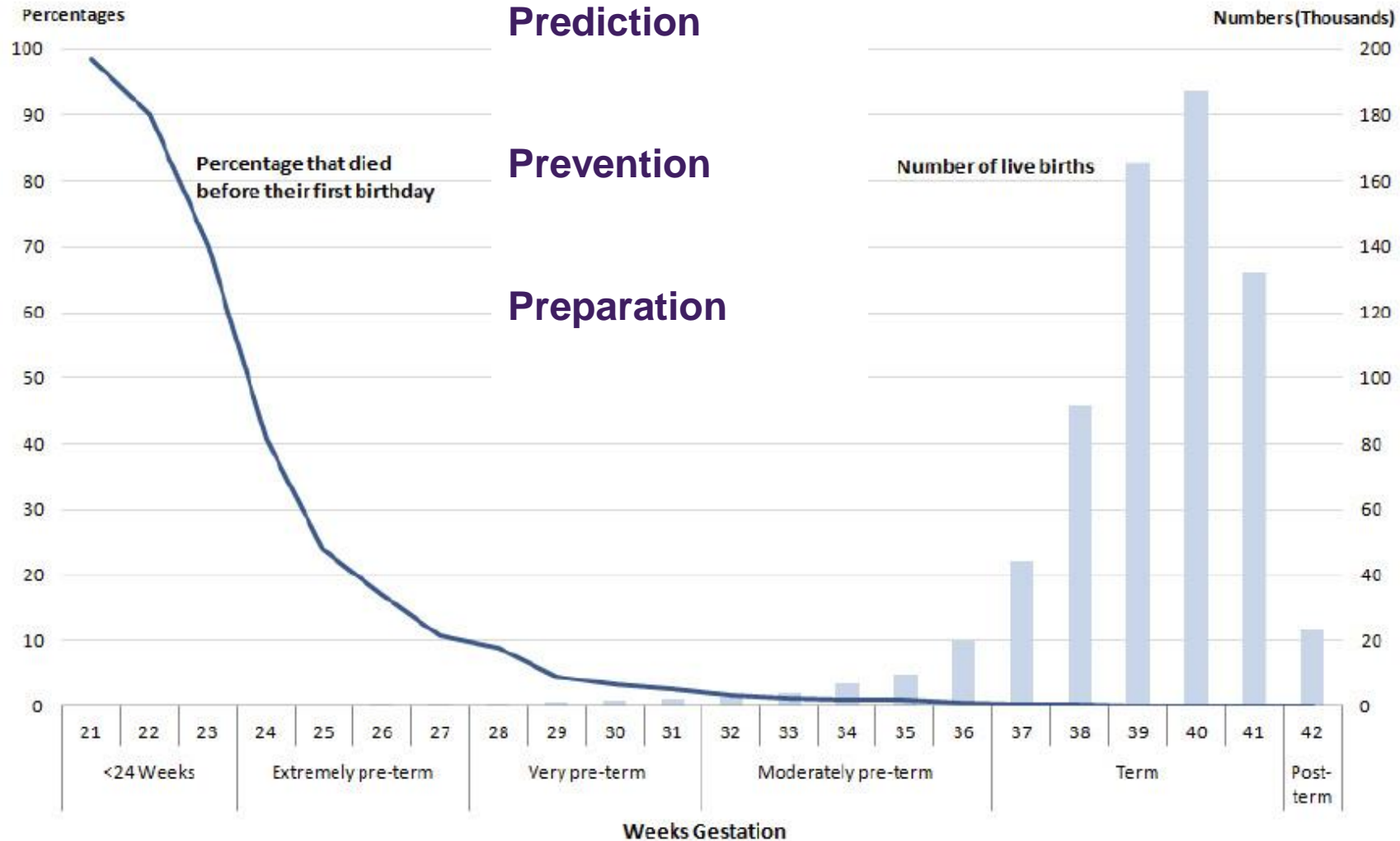
2019

Element 5 is specific to PTB

UK strategy:



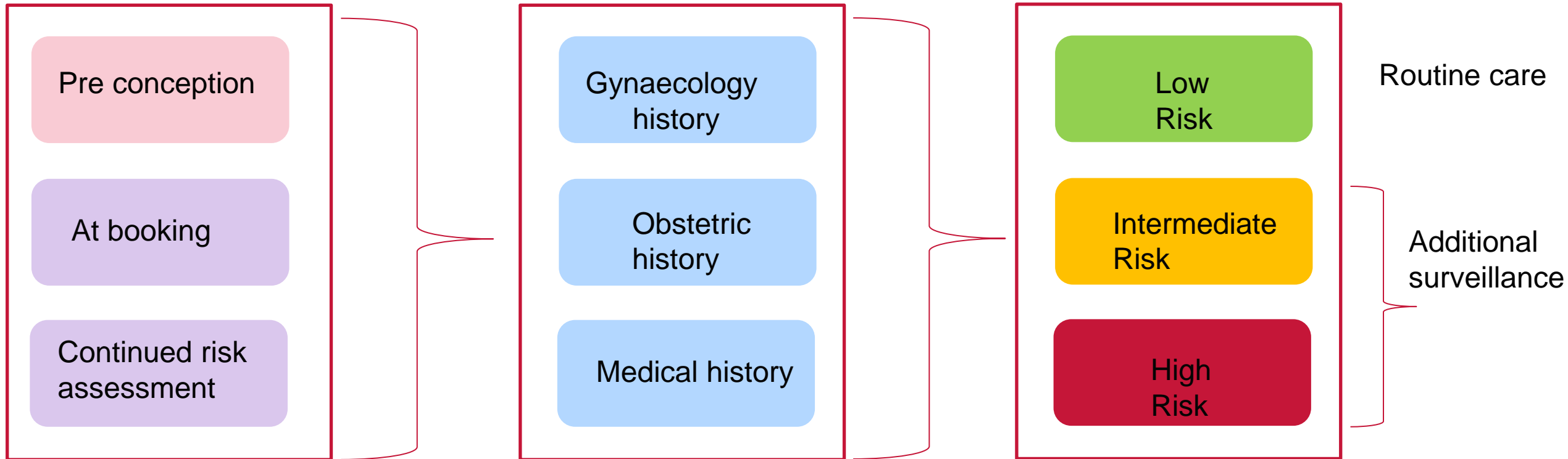
England
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PREDICTION OF PRETERM BIRTH

UK strategy: Prediction

Prediction –when and how do we assess risk ?



*Most women who deliver preterm do not have identifiable risk factors

Precursors of preterm birth

Epidemiology and causes of preterm birth

Robert L. Goldenberg, Jennifer F. Culhane, Jay D. Iams, Roberto Romero

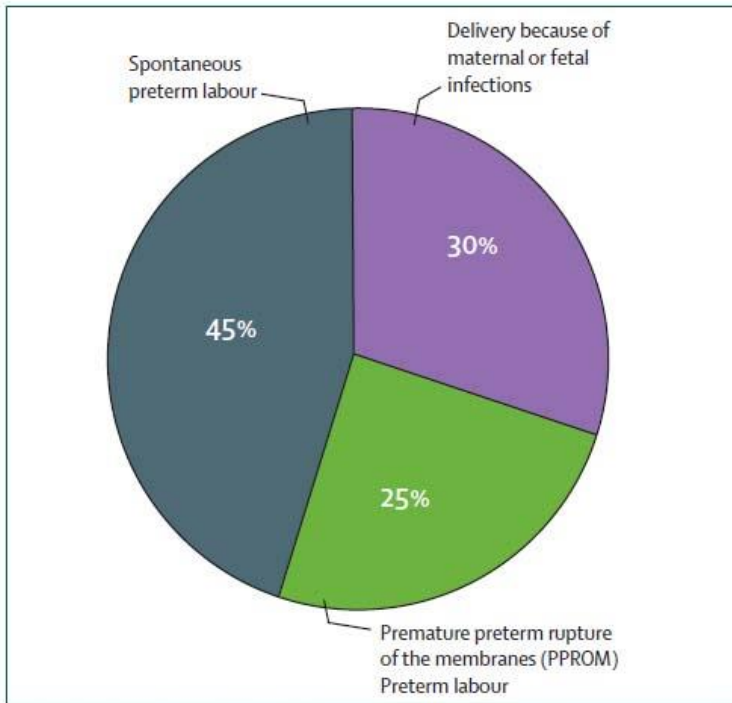


Figure 2: Obstetric precursors of preterm birth

Spontaneous PTL ~45%

PPROM ~25%

Iatrogenic preterm birth ~30%

Prediction – Clinical history

Gynaecological history

Cervical excisional treatment

Trachelectomy

Mid trimester loss

Multiple ERPC/STOPs

History of uterine anomaly

Obstetric history

Previous full dilation
caesarean section

Previous Preterm birth

Previous PPRM

Previous Pre eclampsia

Obstetric Cholestasis

SGA

Current:
PPROM/TPTL/incidental
finding of short/open cervix

Medical history

Chronic hypertension

Diabetes

Inflammatory bowel disease

Connective tissue
disease/SLE

Prediction – Clinical history

Intermediate risk

- Previous delivery by caesarean section at full dilatation.
- History of significant cervical excisional event i.e. LLETZ where >10mm depth removed, or >1 LLETZ procedure carried out or cone biopsy (knife or laser, typically carried out under general anaesthetic).

High risk

- Previous preterm birth or mid-trimester loss (16 to 34 weeks gestation).
- Previous preterm prelabour rupture of membranes <34/40.
- Previous use of cervical cerclage.
- Known uterine variant (i.e. unicornuate, bicornuate uterus or uterine septum).
- Intrauterine adhesions (Ashermann's syndrome).
- History of trachelectomy (for cervical cancer).



England

Saving Babies' Lives
Version Two

Prediction – Cervical excisional treatment

The thickness and volume of LLETZ specimens can predict the relative risk of pregnancy-related morbidity

S Khalid,^a E Dimitriou,^a R Conroy,^b E Paraskevaidis,^c M Kyrgiou,^d C Harrity,^a M Arbyn,^e W Prendiville^a

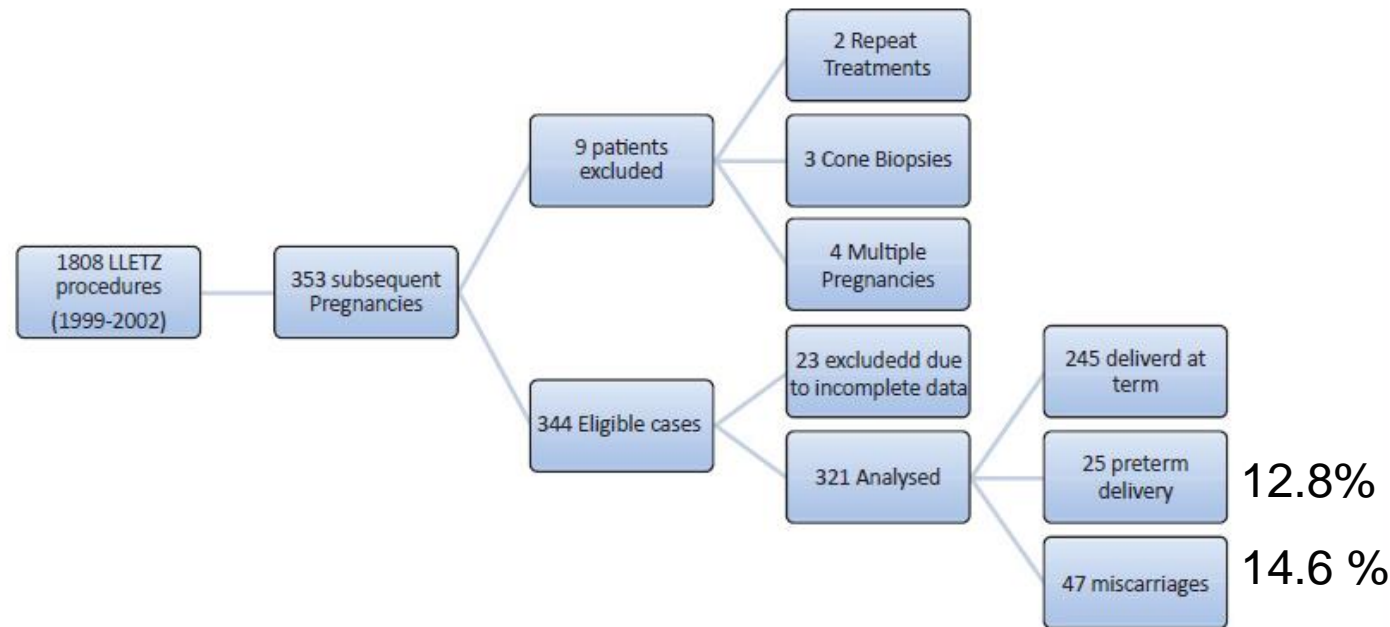


Table 2. Numbers (and percentages) of women delivering at term, at <37 weeks of gestation or with miscarriage at <24 weeks of gestation, based on measurement of LLETZ specimen

	Miscarriage no. (%)	Pre-term labour no. (%)	Term delivery no. (%)
Volume (cm³)			
<3	33 (17.1)	14 (7.3)	145 (75.6)
3–6	8 (9.9)	5 (6.2)	68 (83.9)
>6	6 (12.5)	10 (20.8)	32 (66.7)
Thickness (mm)			
<4	14 (21.3)	3 (4.5)	49 (74.2)
4–8	20 (12.4)	14 (8.7)	127 (78.9)
8–12	10 (13.7)	7 (9.6)	56 (76.7)
>12	3 (14.3)	5 (23.8)	13 (61.9)
Length (cm)			
<1	5 (19.2)	2 (7.7)	19 (73.1)
1–2	33 (15.6)	17 (8.0)	162 (76.4)
>2	9 (10.8)	10 (12.1)	64 (77.1)

Prediction – Trachelectomy

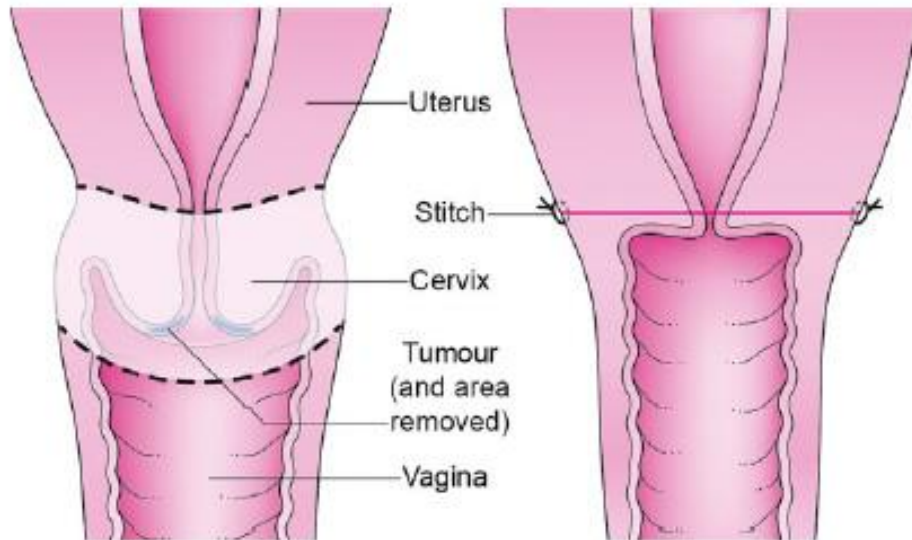
DOI: 10.1111/tog.12415
The Obstetrician & Gynaecologist
<http://onlinetog.org>

2017;19:299–305

Review

The management of pregnancy after trachelectomy for early cervical cancer

Anushka Tirlapur MRCOG MD,^a Fredric Willmott MRCOG,^b Philippa Lloyd BSc MSc,^c Elly Brockbank MD MRCOG,^d
Arjun Jeyarajah MA FRCOG,^d Kalpana Rao MD FRCOG^{e,*}



© Jo's Cervical Cancer Trust

Figure 1. A diagram showing trachelectomy surgery and the position of a permanent suture. Reproduced with permission from Jo's Cervical Cancer Trust (<https://www.jostrust.org.uk/>).

1st trimester loss 16%
2nd trimester loss 7%
PTB 45%
PPROM usually in third trimester

Prediction – Uterine anomaly

OBSTETRICS

Cervical length and quantitative fetal fibronectin in the prediction of spontaneous preterm birth in asymptomatic women with congenital uterine anomaly



Alexandra E. Ridout, MBBS; Linda A. Ibeto, PhD; Georgia N Ross, MBBS; Joanna R. Cook, PhD; Lynne Sykes, PhD; Anna L. David, PhD; Paul T. Seed, MSc; Rachel M. Tribe, PhD; Phillip R. Bennett, PhD; Vasso Terzidou, PhD; Andrew H. Shennan, MD; Manju Chandiramani, PhD; and collaborators: Richard G. Brown, PhD; Susan Chatfield, MBBS; Dana Sadeh, MBBS

TABLE 1

Spontaneous preterm birth in women with congenital uterine anomalies

Fusion

Resorption

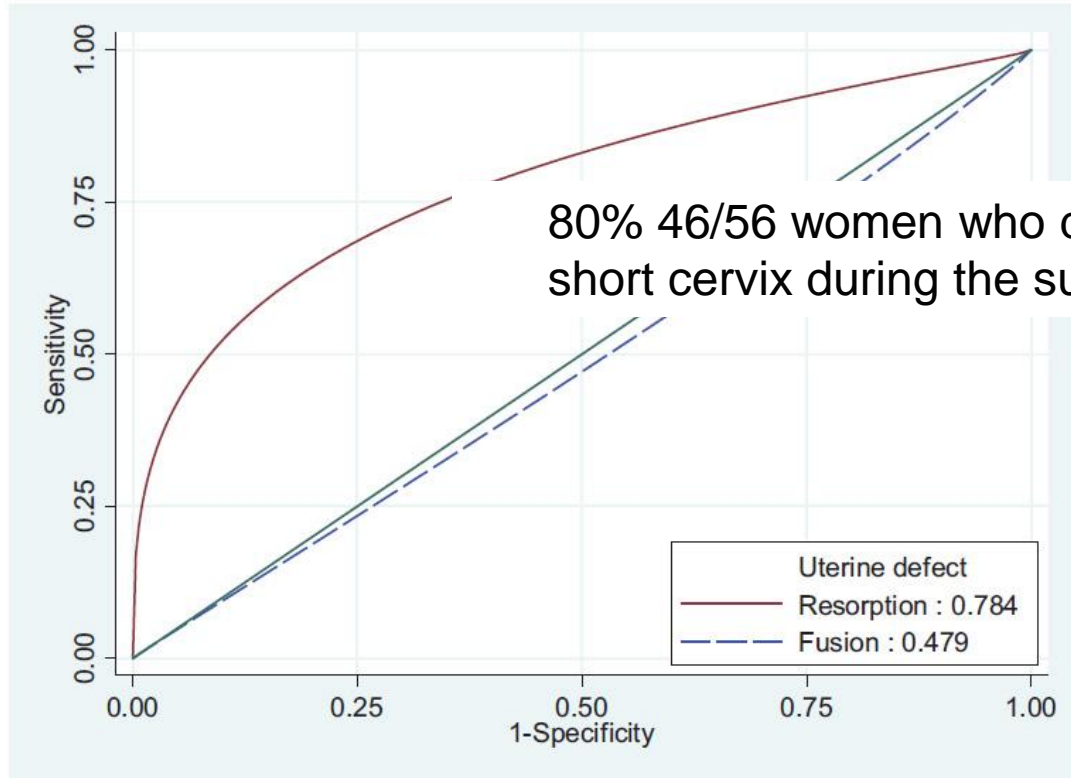
Pregnancy outcome	Cohort (n = 319)	Unicornuate (n = 27)	Didelphys (n = 34)	Bicornuate (n = 189)	Septate (n = 56)	Arcuate (n = 13)
sPTB at <37 wk	17.6% (56)	25.9% (7)	20.6% (7)	16.4% (31)	12.5% (7)	30.8% (4)
sPTB at <34 wk	7.2% (23)	3.7% (1)	8.8% (3)	6.3% (12)	5.4% (3)	30.8% (4)
sPTB at <37 wk when CUA is the sole risk factor	12.8% (33/257)	26.9% (7/26)	20.0% (6/30)	9.1% (13/143)	12.5% (6/48)	10% (1/10)

CUA, congenital uterine anomaly; sPTB, spontaneous preterm birth.

Ridout et al. Preterm birth prediction by cervical length and quantitative fetal fibronectin in congenital uterine anomalies. *Am J Obstet Gynecol* 2019.

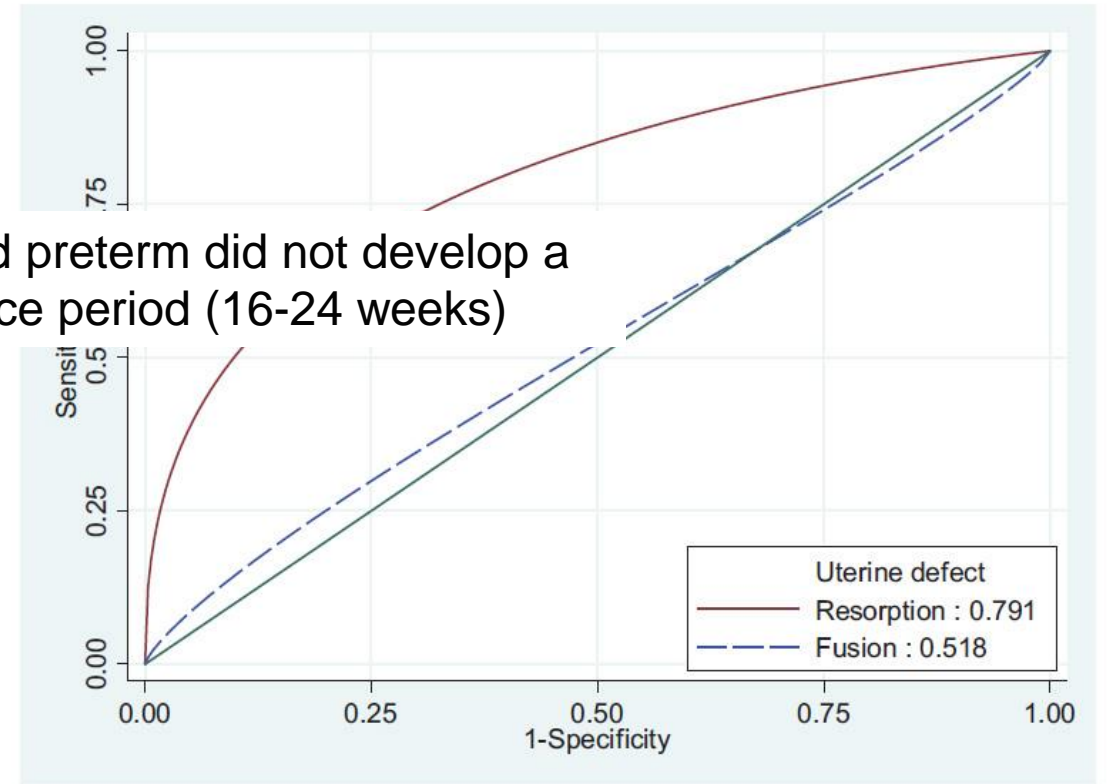
Prediction – Uterine anomaly

FIGURE 1
Transvaginal ultrasound cervical length to predict spontaneous preterm birth at <34 weeks in women with congenital uterine anomalies, grouped by fusion or resorption defect



Ridout et al. Preterm birth prediction by cervical length and quantitative fetal fibronectin in congenital uterine anomalies. Am J Obstet Gynecol 2019.

FIGURE 3
Quantitative fetal fibronectin to predict spontaneous preterm birth at <37 weeks, grouped by fusion or resorption defect



Ridout et al. Preterm birth prediction by cervical length and quantitative fetal fibronectin in congenital uterine anomalies. Am J Obstet Gynecol 2019.

Prediction – Previous fully dilated c-section

Published in final edited form as:

Am J Obstet Gynecol. 2015 March ; 212(3): 360.e1–360.e7. doi:10.1016/j.ajog.2014.09.035.

Does stage of labor at time of cesarean affect risk of subsequent preterm birth?

Lisa D. LEVINE, MD, MSCE^{1,*}, Mary D. SAMMEL, ScD², Adi HIRSHBERG, MD¹, Michal A. ELOVITZ, MD¹, and Sindhu K. SRINIVAS, MD, MSCE¹

887 women	PTB rate <37 w	
721 Vaginal deliveries	7.8%	
129 1 st stage CS	2.3% ¹	
37 2 nd stage CS	13.5 %	
	P= 0.003	OR 2.4 (NS)

Prediction – Previous fully dilated c-section

OBSTETRICS

Cesarean delivery in the second stage of labor and the risk of subsequent premature birth

Stephen L. Wood, MD; Selphee Tang, BSc; Susan Crawford, MSc

189,021 paired 1st and second births
(Canadian perinatal database)

RR of PTB <37w 1.57 (1.43-1.73 95% CI)
RR PTB <32 w 2.12 (1.67-2.68 95% CI)

TABLE 1

Rates of premature birth and perinatal outcome in second birth by type of delivery in first birth, n (%)

Second birth	Delivery method, first birth					
	Cesarean delivery before labor, n = 6346	Cesarean delivery in first stage, n = 23,072	Cesarean delivery in second stage, n = 8607	Cesarean delivery unknown stage, n = 6049	Operative vaginal delivery, n = 44,991	Spontaneous vaginal delivery, n = 99,956
Gestational age at delivery, wk						
<32	54 (0.9%)	185 (0.8%)	117 (1.4%)	48 (0.8%)	311 (0.7%)	763 (0.8%)
32–36	269 (4.2%)	1023 (4.4%)	482 (5.6%)	268 (4.4%)	1665 (3.7%)	3732 (3.7%)
37–42	6023 (94.9%)	21,864 (94.8%)	8008 (93.0%)	5733 (94.8%)	43,015 (95.6%)	95,461 (95.5%)
Delivery >32 wk	6292 (99.2%)	22,887 (99.2%)	8490 (98.6%)	6001 (99.2%)	44,680 (99.3%)	99,193 (99.2%)
Spontaneous premature birth <32 wk	24 (0.4%)	99 (0.4%)	80 (0.9%)	23 (0.4%)	187 (0.4%)	439 (0.4%)
Indicated premature birth <32 wk	30 (0.5%)	86 (0.4%)	37 (0.4%)	25 (0.4%)	124 (0.3%)	324 (0.3%)
Delivery >37 wk	6023 (94.9%)	21,864 (94.8%)	8008 (93.0%)	5733 (94.8%)	43,015 (95.6%)	95,461 (95.5%)
Spontaneous premature birth <37 wk	171 (2.7%)	728 (3.2%)	457 (5.3%)	185 (3.1%)	1470 (3.3%)	3373 (3.4%)
Indicated premature birth <37 wk	152 (2.4%)	480 (2.1%)	142 (1.7%)	131 (2.2%)	506 (1.1%)	1122 (1.1%)
Spontaneous premature birth <32 wk, RR (95% CI)	0.86 (0.57–1.30)	0.98 (0.79–1.21)	2.12 (1.67–2.68)	0.87 (0.57–1.32)	0.95 (0.80–1.12)	Reference
Spontaneous premature birth <37 wk, RR (95% CI)	0.80 (0.69–0.93)	0.94 (0.86–1.01)	1.57 (1.43–1.73)	0.91 (0.78–1.05)	0.97 (0.91–1.03)	Reference
Live birth, no neonatal death	6260 (99.59%)	22,705 (99.54%)	8470 (99.48%)	5940 (99.53%)	44,411 (99.64%)	98,485 (99.64%)
Antepartum stillbirth	21 (0.33%)	67 (0.29%)	11 (0.13%)	17 (0.28%)	94 (0.21%)	205 (0.21%)
Intrapartum stillbirth	0 (0.00%)	13 (0.06%)	9 (0.11%)	2 (0.03%)	18 (0.04%)	42 (0.04%)
Neonatal death, excluding congenital anomalies	5 (0.08%)	26 (0.11%)	24 (0.28%)	9 (0.15%)	48 (0.11%)	109 (0.11%)
Stillbirth or neonatal death, RR (95% CI)	1.15 (0.77, 1.71)	1.29 (1.04, 1.60)	1.44 (1.05, 1.96)	1.30 (0.89, 1.91)	1.00 (0.83, 1.20)	Reference

CI, confidence interval; RR, relative risk.

Wood et al. Cesarean delivery in second stage of labor and subsequent premature birth. Am J Obstet Gynecol 2017.

Prediction – Previous Mid trimester loss and Preterm birth

[



Prediction tools- Cervical Length

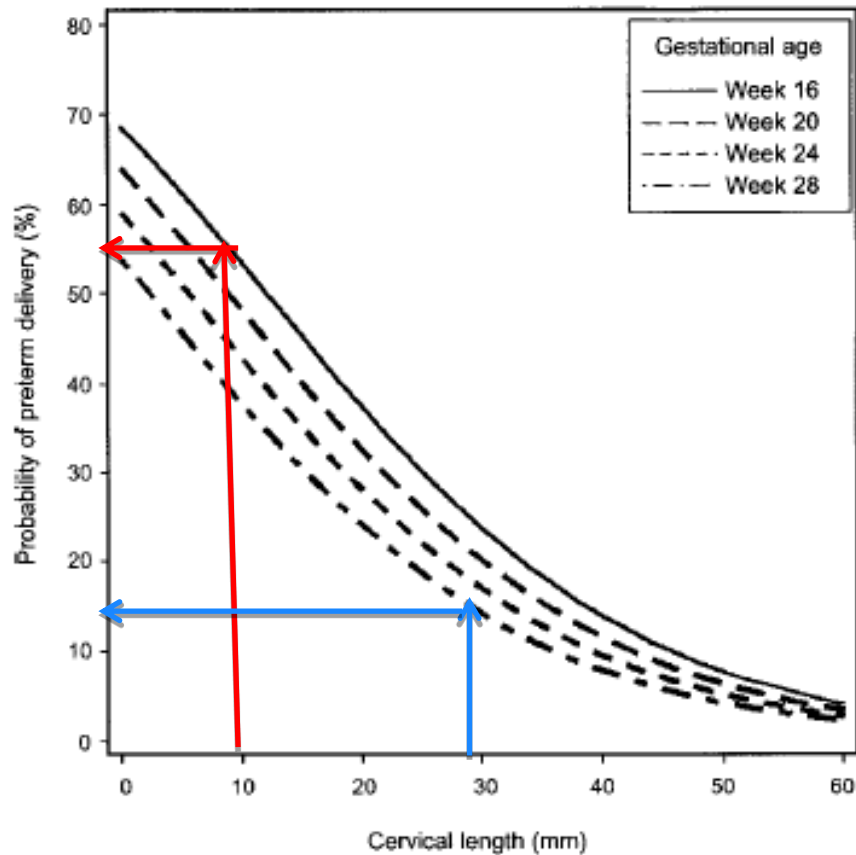
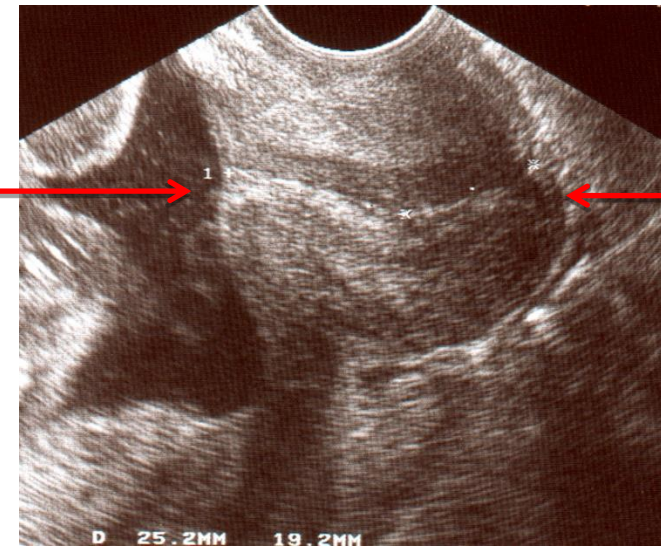


Fig. 2. Predicted probability of delivery before week 35, by cervical length (mm) and time of measurement (week of pregnancy).

Berghella. Effect of Gestational Age at Short Cervix. Obstet Gynecol 2007.

Figure 1.

Internal os



External os

Figure 2.

Short cervix



Prediction tools- Fetal fibronectin

Adhesive glycoprotein

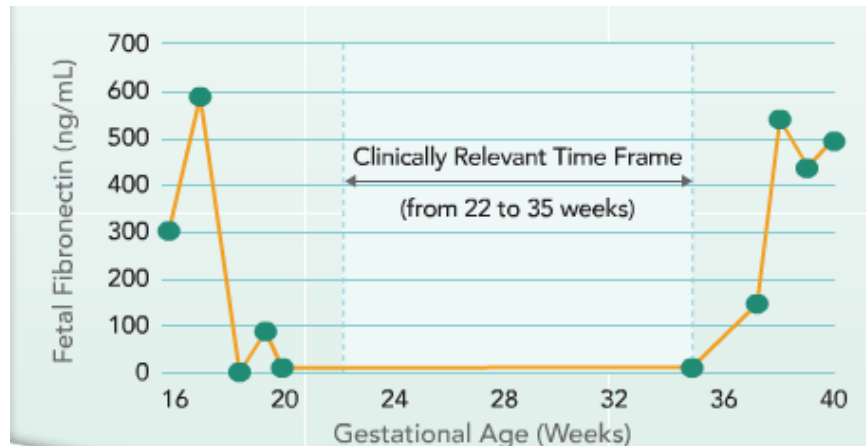
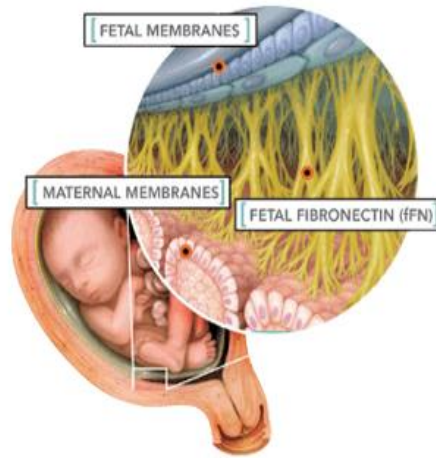
Positive if $> 50\text{ng/ml}$

NPV 97-99%

PPV 25-50%

LR of del $<34/40$

- 3.99 for + result
 - 0.38 for – result
- (H Honest BMJ 2002)



EQUIPP

Evaluation of Fetal Fibronectin with a Quantitative Instrument for the Prediction of Preterm birth

Overview The Science of fFN FullTerm™ Test The fFN Experience FAQ & Resources Contact FullTerm The Fetal Fibronectin Test

PRENATAL HEALTH

The Consultant Experience
by Prof. P Bennett

- An introduction to Professor Phillip Bennett
- What level of neonatal care does your hospital offer?
- Why do you use FullTerm™ The Fetal Fibronectin Test?
- How do you use the test on symptomatic and asymptomatic patients?
- Can the test help with targeted use of steroids?
- How do you manage patients who have had the test?
- What is your opinion on cervical length measurement and Fetal Fibronectin Testing?
- What are the financial benefits of using fFN?
- What are the benefits of the test for the patient?
- Where do you perform the test?
- Do you find it easy to perform the test?
- Are you satisfied with the available clinical data for FullTerm™, The Fetal Fibronectin Test?

HOLOGIC WWW.FULLTERM.NET

QUIPP
A tool to predict spontaneous preterm birth

21

QUIPP Home

Symptomatic
Previous PPROM or Previous Preterm Birth $\leq 34+6$
 Yes No Unknown

Gestation of test

24w	0d
25w	0d
26w	1d
27w	1d
28w	2d

fFN result (ng/ml):

*Cervical length data currently not utilized for symptomatic patients.

Get Results

KING'S College LONDON
PARTNERS IN HEALTH
PLANNING BETTER HEALTH FOR ALL

Risk of sPTB:

- < 30 weeks = 4.2%
- < 34 weeks = 13.5%
- < 37 weeks = 23.9%

Tommy's
Healthy pregnancies = Healthy babies

developed by
appatta

Within 1 week = 0.7%
Within 2 weeks = 1.6%
Within 4 weeks = 4.2%

Prediction – Medical history

*Chronic hypertension – 5 fold higher risk
25% risk of developing PET*

Diabetes 3.5 fold higher risk

Inflammatory bowel disease – 2 fold increased risk

Prediction – Medical history

National Pregnancy in Diabetes (NPID) Audit Report 2018

- Early preterm births between 2014 and 2018 9% for Type 1 diabetes and around 5% for Type 2 diabetes
- The percentage of preterm births to women with Type 1 diabetes (including early preterm) has increased significantly between 2014 and 2018 – from 40% to 45%.
- This has not been mirrored in births to women with Type 2 diabetes

Figure 23: Percentage of live singleton births which are before 34 weeks' gestation, England and Wales, 2014-2018

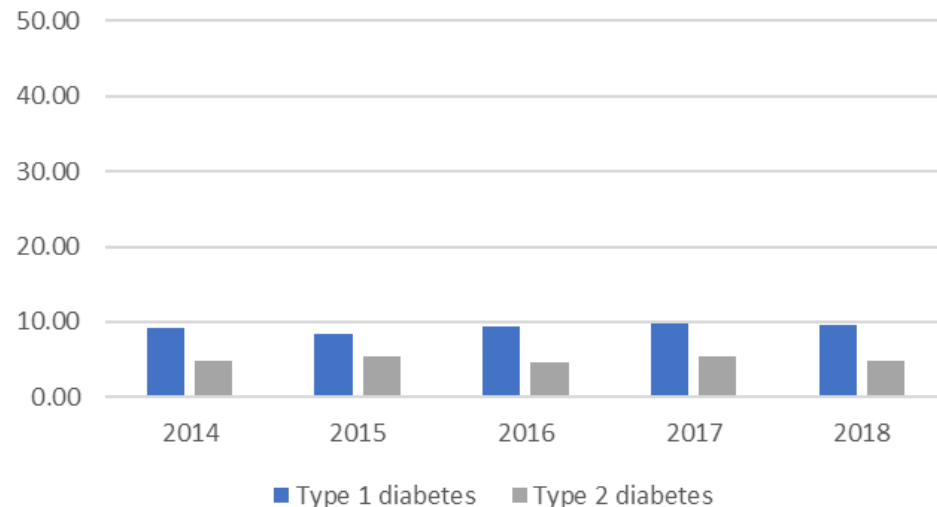
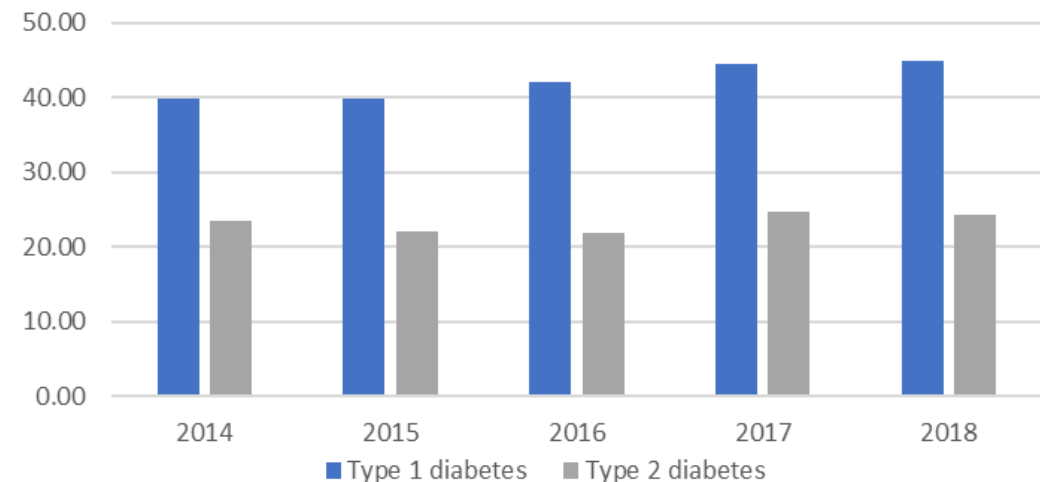


Figure 24: Percentage of live singleton births which are before 37 weeks' gestation, England and Wales, 2014-2018



PREVENTION OF PRETERM BIRTH

UK strategy: Prevention

Saving Babies' Lives Version Two

A care bundle for reducing perinatal mortality

- Stop smoking pre conception, at least by 16 weeks
- Aspirin prophylaxis if at risk of preeclampsia/ SGA
- Offer testing for asymptomatic bacteria, treat a positive culture
- Preconception clinics for medical disorders (e.g diabetes, hypertension)
- Assess need and refer to preterm birth prevention clinic if at risk of sPTB



Prevention: Smoking

BMJ

RESEARCH

Spontaneous preterm birth and small for gestational age infants in women who stop smoking early in pregnancy: prospective cohort study

Lesley M E McCowan, associate professor of obstetrics and gynaecology,¹ Gustaaf A Dekker, professor of obstetrics and gynaecology,⁶ Eliza Chan, research fellow,¹ Alistair Stewart, statistician,² Lucy C Chappell, senior lecturer in maternal and fetal medicine,⁴ Misty Hunter, medical student,¹ Rona Moss-Morris, professor of health psychology,⁵ Robyn A North, professor in obstetric medicine³ On behalf of the SCOPE consortium

Local target to reduce proportion of women who smoke from 4 to 3 %

	Non smokers N=1992	Stopped smokers N=261	Current smokers n=251
sPTB	88 (4.4%)	10 (3.8%)	25 (10%)
SGA	195 (9.8%)	27 (10%)	42 (16.7%)

Prevention: Aspirin

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

AUGUST 17, 2017

VOL. 377 NO. 7

Aspirin versus Placebo in Pregnancies at High Risk
for Preterm Preeclampsia

- Double blind, placebo controlled randomised
- 1776 women with singleton pregnancies at high risk of PET 150mg aspirin or placebo from 11-14 weeks till 36 weeks
- Primary outcome PET <37 weeks
- Aspirin n= 798 PET 1.6%
- Placebo n= 822 PET 4.3%

Prevention: Aspirin

Table 1: Clinical risk assessment for preeclampsia as indications for aspirin in pregnancy

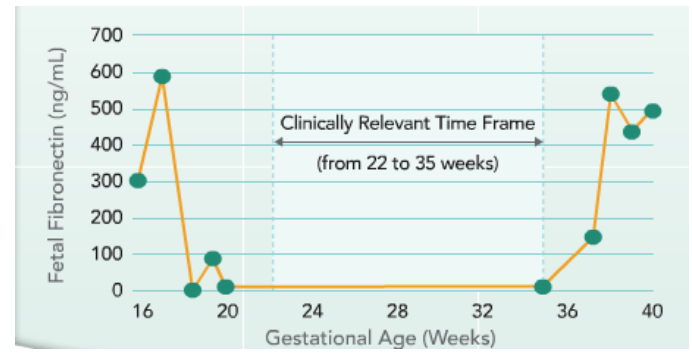
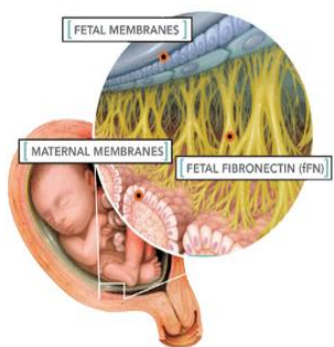
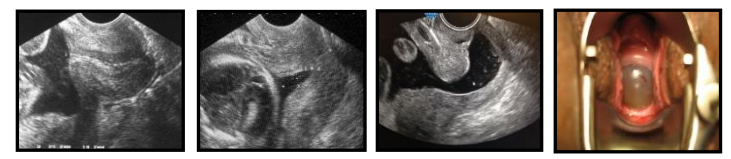
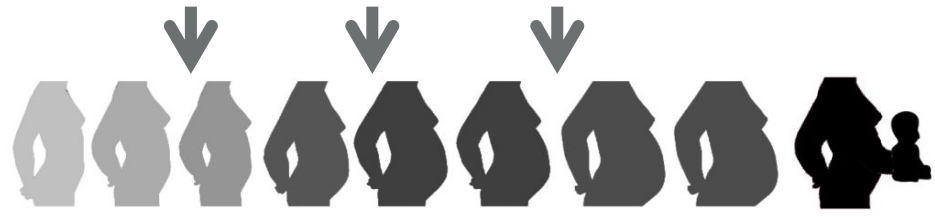
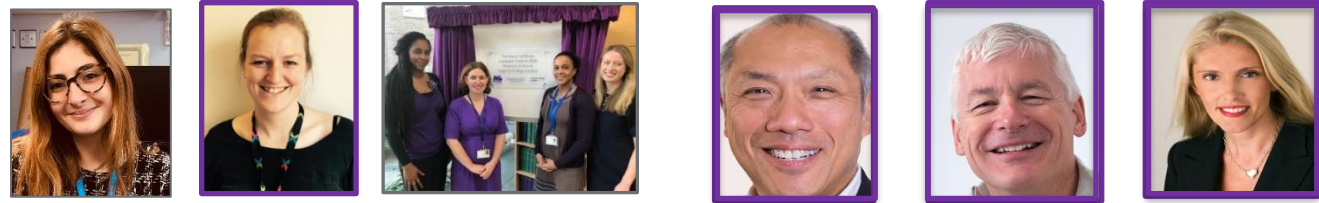
Risk level	Risk factors	Recommendation
High	<ul style="list-style-type: none"> • Hypertensive disease during a previous pregnancy • Chronic kidney disease • Autoimmune disease such as systemic lupus erythematosus or antiphospholipid syndrome • Type 1 or type 2 diabetes • Chronic hypertension • Placental histology confirming placental dysfunction in a previous pregnancy 	Recommend low dosage aspirin if the woman has ≥ 1 of these high risk factors
Moderate	<ul style="list-style-type: none"> • First pregnancy • Are 40 years or older at booking • Pregnancy interval of more than 10 years • Body mass index (BMI) of 35kg/m^2 or more at first visit • Family history of preeclampsia in a first degree relative • Multiple pregnancy 	Consider aspirin if the woman has two or more



England

Saving Babies' Lives
Version Two

Prevention- Preterm birth prevention clinics



Women's Health - Information for patients
Preterm birth prevention clinic



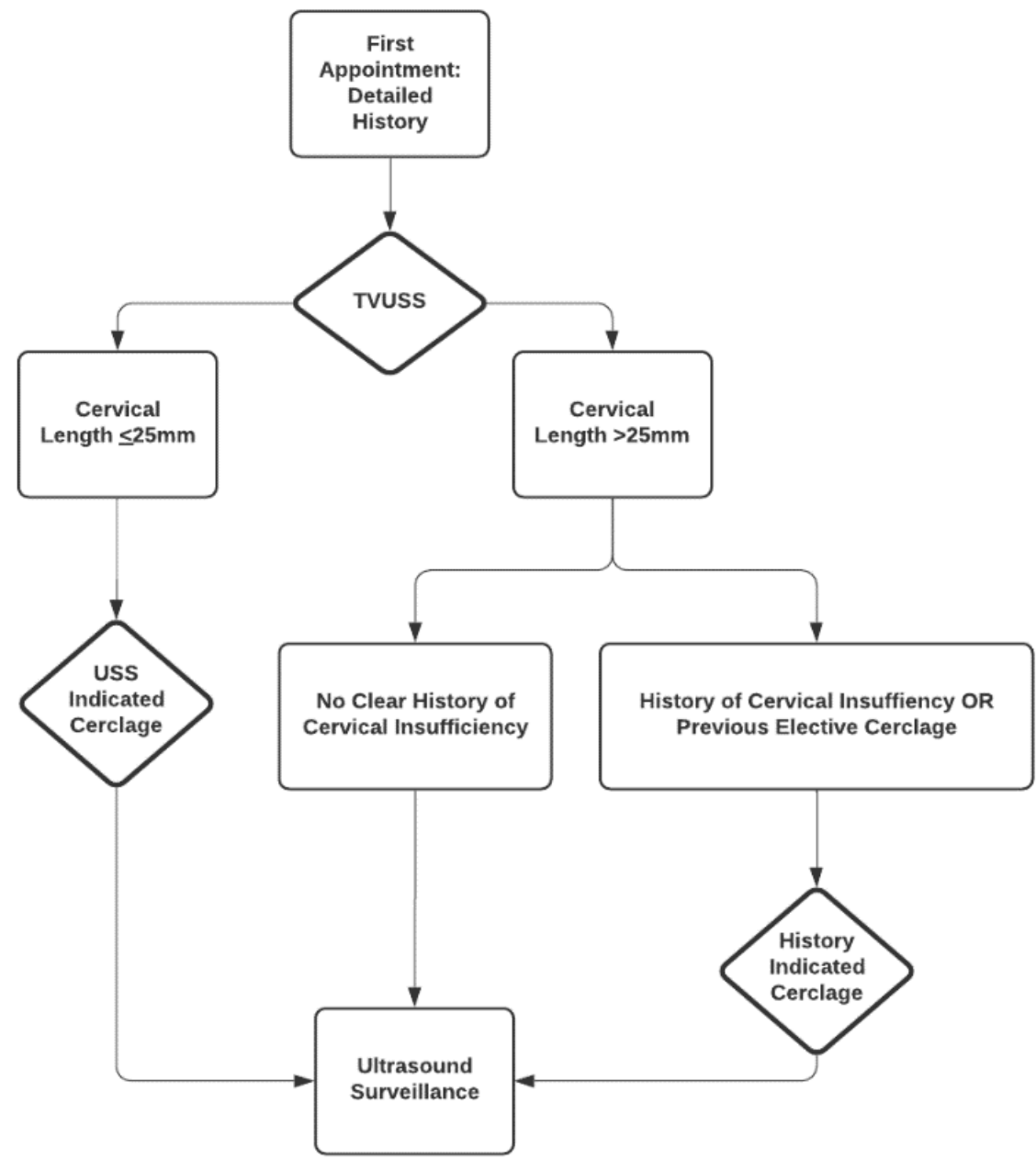
Prediction: Ultrasound surveillance, FN
Prevention: Medical/surgical Interventions,
Continuity of care
Preparation: Admit/Steroids/Mg SO4

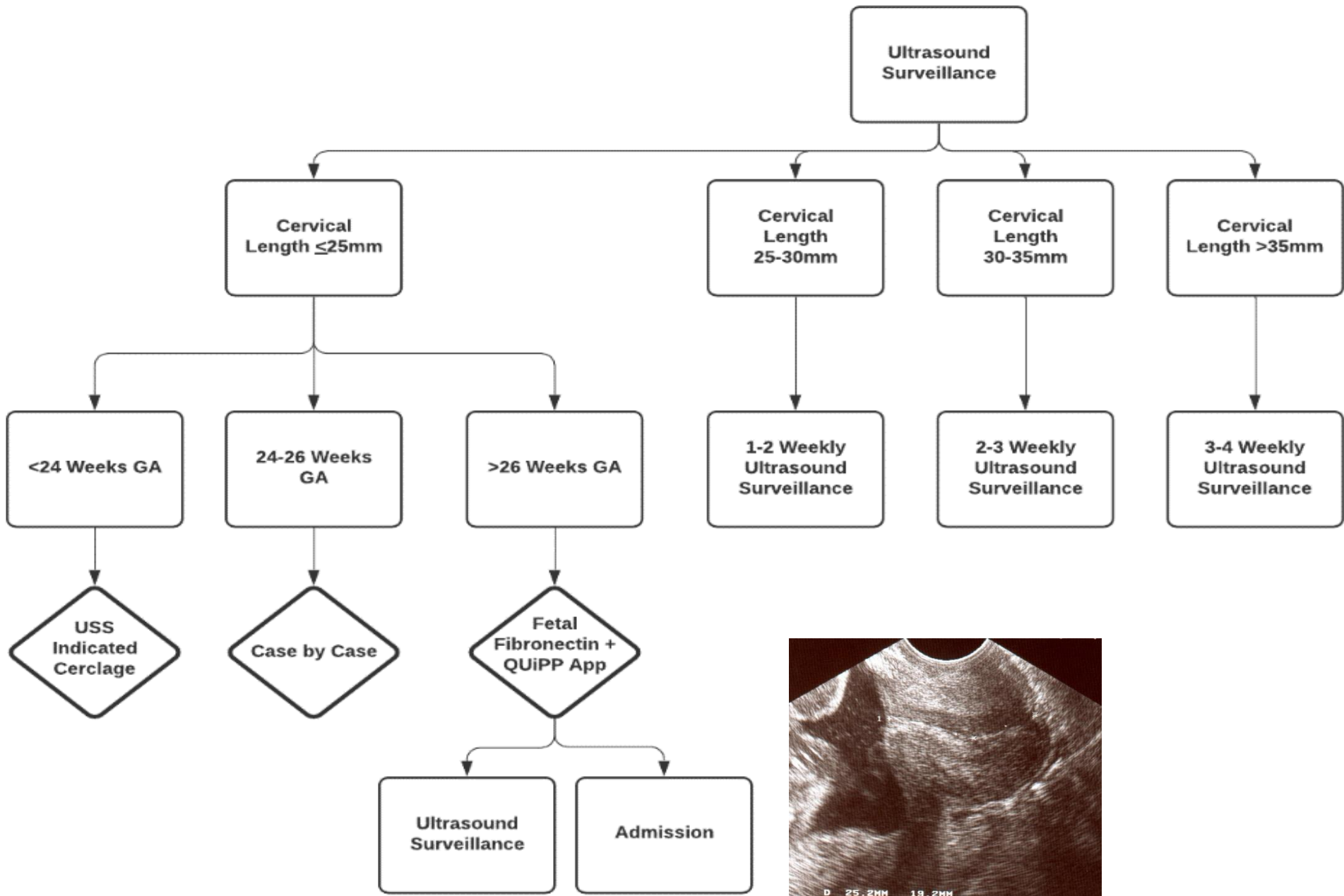
Prediction – Specialist care/ services

Risk Factor	2013	2014	2015	2016	2017	2018	2019	2020*
Previous spontaneous delivery < 37+ 0 weeks						✓	✓	
Previous spontaneous delivery < 34 + 0 weeks	✓	✓	✓	✓	✓	✓	✓	✓
Spontaneous mid-trimester loss (16+0-23+6 weeks)	✓	✓	✓	✓	✓	✓	✓	✓
Cervical cerclage in previous pregnancy	✓	✓	✓	✓	✓	✓	✓	✓
Single LLETZ procedure of >10mm depth, or more than one LLETZ procedure	✓	✓	✓	✓	✓	✓	✓	✓
Knife cone biopsy of the cervix	✓	✓	✓	✓	✓	✓	✓	✓
Radical trachelectomy for locally invasive carcinoma of the cervix	✓	✓	✓	✓	✓	✓	✓	
Surgical termination and surgical management of miscarriage beyond 16 weeks	✓	✓	✓	✓	✓	✓	✓	
Previous Full Dilation Caesarean Section					✓	✓	✓	✓
Known Congenital Uterine Abnormality	✓	✓	✓	✓	✓	✓	✓	✓
Diagnosis of Mixed Connective Tissue Disorders	✓	✓	✓	✓	✓	✓	✓	✓

*Referral criteria was modified and reduced in 2020 due to the effects of the COVID-19 Pandemic

Women's Health - Information for patients
Preterm birth prevention clinic





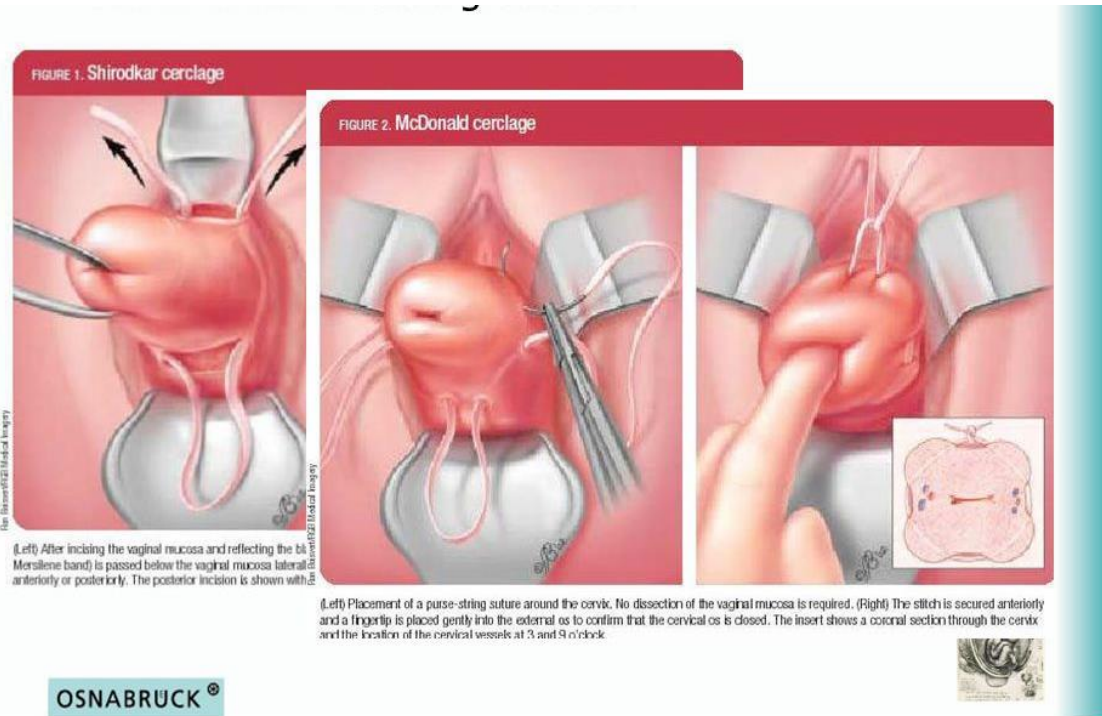
Cervical Length and risk of adverse outcome



Sykes et al, unpublished work



Intervention: Cervical cerclage

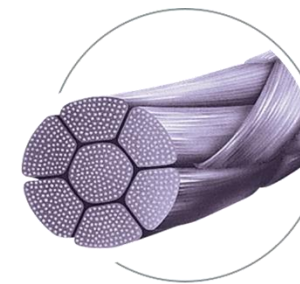


- Suture material
Monofilament vs braided
Nylon vs Mersilene

80% of surgeons use
mersilene (braided)
NOT evidence based



Monofilament suture
(Nylon)



Braided Multifilament suture
(Mersilene™)





Intervention: Cervical cerclage – Does it work?

a Elective Cerclage

b Emergency Cerclage

Sykes et al, unpublished work

CT

weakness in those with previous CT.



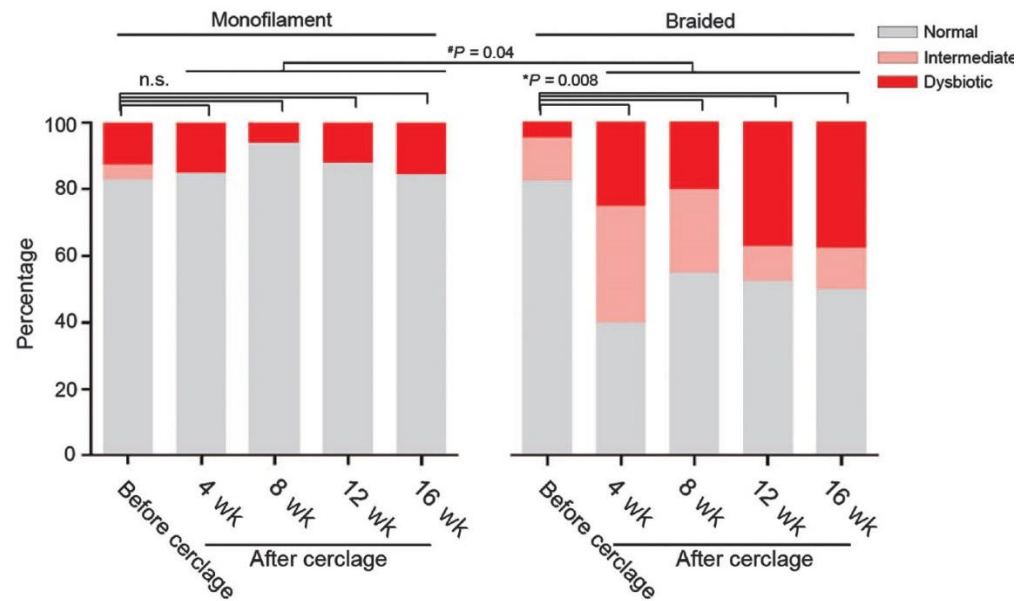
Intervention: Cervical cerclage – Does it matter which stitch material?

RESEARCH ARTICLE

PREGNANCY

Relationship between vaginal microbial dysbiosis, inflammation, and pregnancy outcomes in cervical cerclage

Lindsay M. Kindinger,^{1,2,3} David A. MacIntyre,^{1*} Yun S. Lee,¹ Julian R. Marchesi,^{4,5} Ann Smith,⁵ Julie A. K. McDonald,⁴ Vasso Terzidou,^{1,6} Joanna R. Cook,¹ Christoph Lees,^{1,2,7} Fidan Israfil-Bayli,⁸ Yazmin Faiza,⁹ Philip Toozs-Hobson,⁸ Mark Slack,⁹ Stefano Cacciatore,¹ Elaine Holmes,^{4,10} Jeremy K. Nicholson,^{4,10} T. G. Teoh,³ Phillip R. Bennett^{1,2*}



a

Mediators of microbial recognition

C

Cytokines

GM-
TI

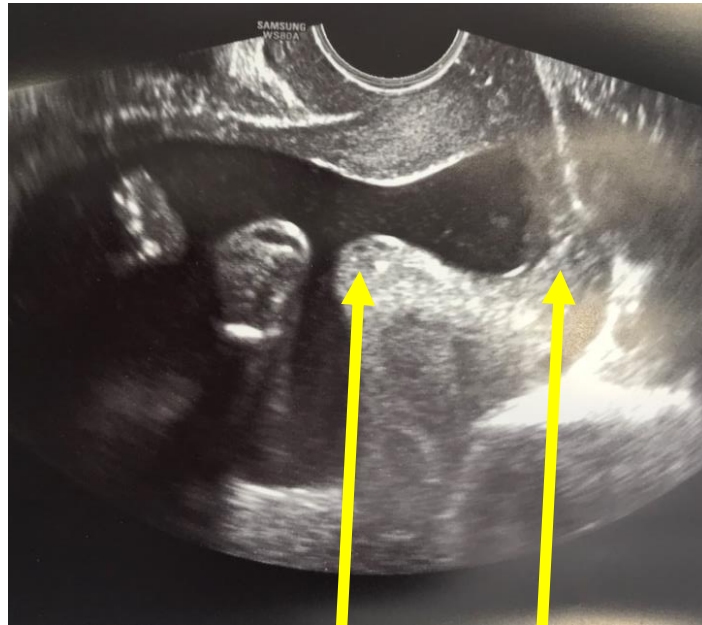
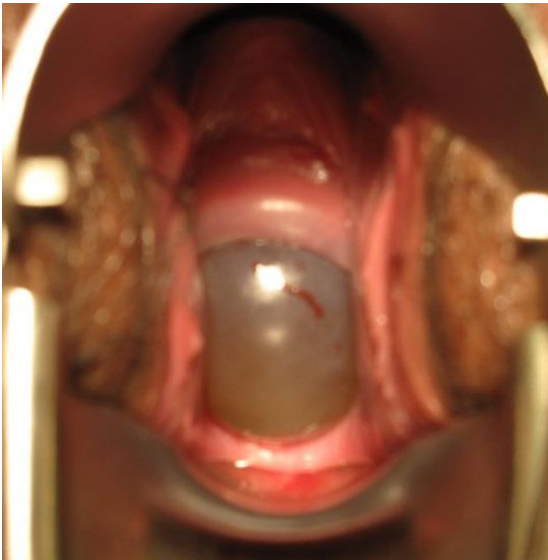
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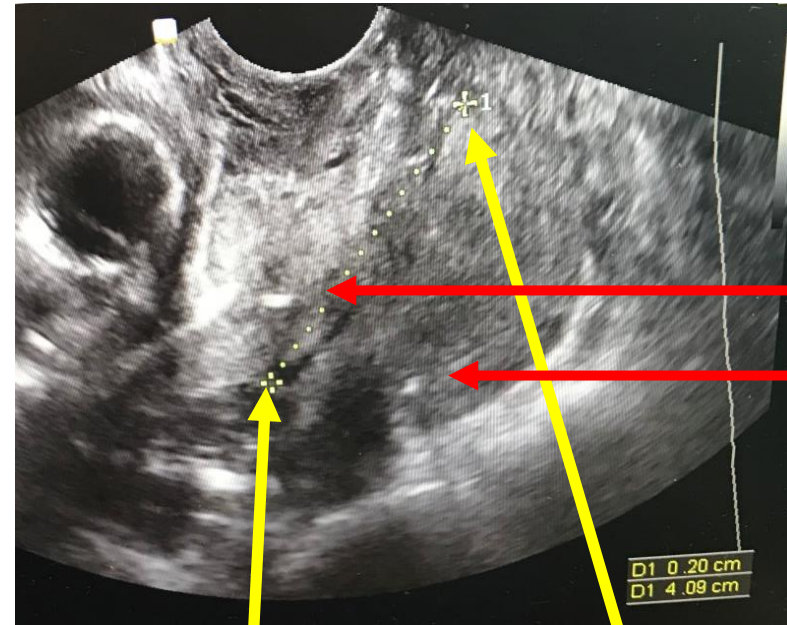
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Mono

Intervention: Rescue cervical cerclage

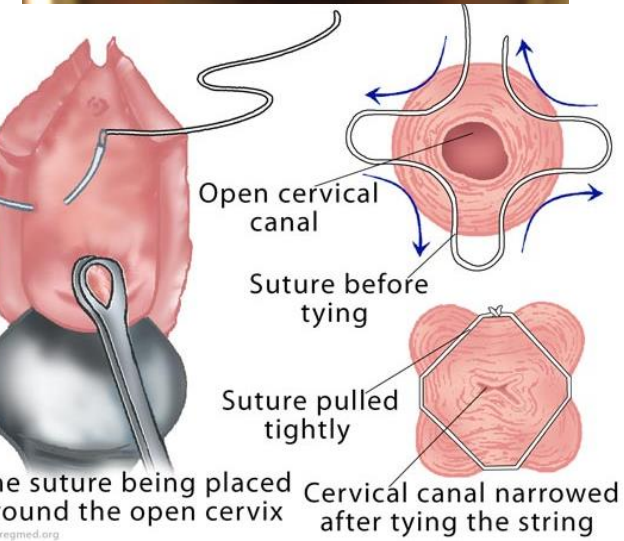


Internal os External os



Suture

Internal os External os





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Progesterone and the Risk of Preterm Birth among Women with a Short Cervix

Eduardo B. Fonseca, M.D., Ebru Celik, M.D., Mauro Parra, M.D.,
Mandeep Singh, M.D., and Kypros H. Nicolaides, M.D.,
for the Fetal Medicine Foundation Second Trimester Screening Group*

24,620 pregnant women
Cervical <15 mm 413 women (1.7%)
250 (60.5%) randomised

Delivery < 34 weeks
35% vs 19%

200mg nocte

Ultrasound Obstet Gynecol 2011; 38: 18–31
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.9017



Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial

S. S. HASSAN^{1,2}, R. ROMERO^{1,3,4}, D. VIDYADHARI⁵, S. FUSEY⁶, J. K. BAXTER⁷,
M. KHANDELWAL⁸, J. VIJAYARAGHAVAN⁹, Y. TRIVEDI¹⁰, P. SOMA-PILLAY¹¹,
P. SAMBAREY¹², A. DAYAL¹³, V. POTAPOV¹⁴, J. O'BRIEN^{15,16}, V. ASTAKHOV¹⁷, O. YUZKO¹⁸,
W. KINZLER¹⁹, B. DATTEL²⁰, H. SEHDEV²¹, L. MAZHEIKA²², D. MANCHULENKO²³,
M. T. GERVASI²⁴, L. SULLIVAN²⁵, A. CONDE-AGUDELO¹, J. A. PHILLIPS²⁶ and G. W. CREASY²⁷,
for the PREGNANT Trial

32,091 pregnant women
Short cervix 10-20 mm
458 randomised

Preterm birth

≤ 35 weeks **23% v 14%**
≤ 33 weeks **16% v 9%**
≤ 28 weeks **10% v 5%**

RDS reduced 7.6% vs 3% p=0.03
Neonatal morbidity and mortality
13.5% vs 7.7% p=0.04



ELSEVIER



Vaginal progesterone prophylaxis for preterm birth (the OPPTIMUM study): a multicentre, randomised, double-blind trial

Jane Elizabeth Norman, Neil Marlow, Claudia-Martina Messow, Andrew Shennan, Phillip R Bennett, Steven Thornton, Stephen C Robson, Alex McConnachie, Stavros Petrou, Neil J Sebire, Tina Lavender, Sonia Whyte, John Norrie, for the OPPTIMUM study group

Fibronectin positive (>50ng/ml) 22-24 weeks

Previous preterm birth <34 weeks
Cervical length <25mm



Obstetric Outcome:
Fetal death or delivery <34 weeks

Neonatal Outcome:
Death, BPD, ultrasound brain injury

Childhood Outcome:
Bayley III at 22 to 26 months

No significant benefit in any primary outcome

No benefit in short cervix

No long term harm

11

Efficacy of progesterone for prevention of preterm birth

Lynne Sykes*, Phillip R. Bennett

Parturition Research Group, Institute of Reproductive and Developmental Biology, Du Cane Road, London, W12 0NN UK



Evaluating Progestogens for Preventing Preterm birth International Collaborative (EPPPIC): meta-analysis of individual participant data from randomised controlled trials



The EPPPIC Group*

Summary

Background Preterm birth is a global health priority. Using a progestogen during high-risk pregnancy could reduce preterm birth and adverse neonatal outcomes.

Lancet 2021; 397: 1183-94
This online publication has been corrected. The corrected version

Preterm birth prevention clinic – continuity of care



Cochrane Database of Systematic Reviews

Midwife-led continuity models versus other models of care for childbearing women (Review)

Sandall J, Soltani H, Gates S, Shennan A, Devane D

Continuity of career model improves outcome:
19% less likely to have a miscarriage/mid trimester loss
24% less likely to experience preterm birth

Implementing Better Births: Continuity of Carer

Five Year Forward View

December 2017

Publications Gateway
Ref No. 07342

Consistency of midwife /clinical team to look after:
Pregnancy
Labour
Postnatal period

National target of 75% by 2024 for Black/minority ethnic groups/those living in deprived areas

PREPARATION FOR PRETERM BIRTH

Preparation – optimise outcome



1. Optimise timing of delivery
2. Optimise place of delivery with neonatal team and cot
3. Optimise use of corticosteroids and magnesium sulphate

Preparation – optimise timing of delivery



- Women whose pregnancy is complicated by PPRM after 24⁺⁰ weeks' gestation and who have no contraindications to continuing the pregnancy should be offered expectant management until 37⁺⁰ weeks; timing of birth should be discussed with each woman on an individual basis with careful consideration of patient preference and ongoing clinical assessment. [Grade A]

Care of Women Presenting with Suspected
Preterm Prelabour Rupture of Membranes
from 24⁺⁰ Weeks of Gestation

Green-top Guideline No. 73
June 2019

Recommendation comes from the Cochrane review of 3617
Conclusions influenced by late PPRM trials 34-36 weeks

No difference in neonatal sepsis with expectant management
Increased RDS and CS with earlier delivery

It is less clear if expectant management to 37+0 is appropriate
for women who experience PPRM at earlier gestations

Median latency from PPRM 7 days



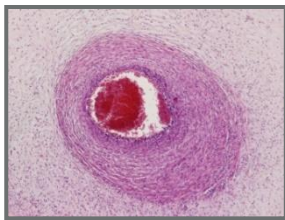
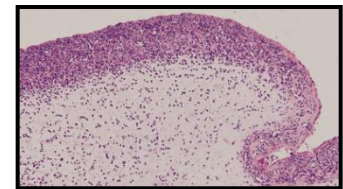
Clinical Chorioamnionitis:

Uterine tenderness,
offensive discharge
Tachycardia, Pyrexia
Leukocytosis, High CRP

GA at (weel medi
GA at (weel medi

Histological Chorioamnionitis:

Neutrophil invasion of the
Fetal membranes
and umbilical cord



Using
predic

ositive

Preparation – optimise place of delivery



Perinatal Management of Extreme Preterm
Birth before 27 weeks of gestation
A Framework for Practice
October 2019



Perinatal outcomes for extremely preterm babies in relation to place of birth in England: the EPICure 2 study

N Marlow,¹ C Bennett,¹ E S Draper,² E M Hennessy,³ A S Morgan,¹ K L Costeloe^{4,5}

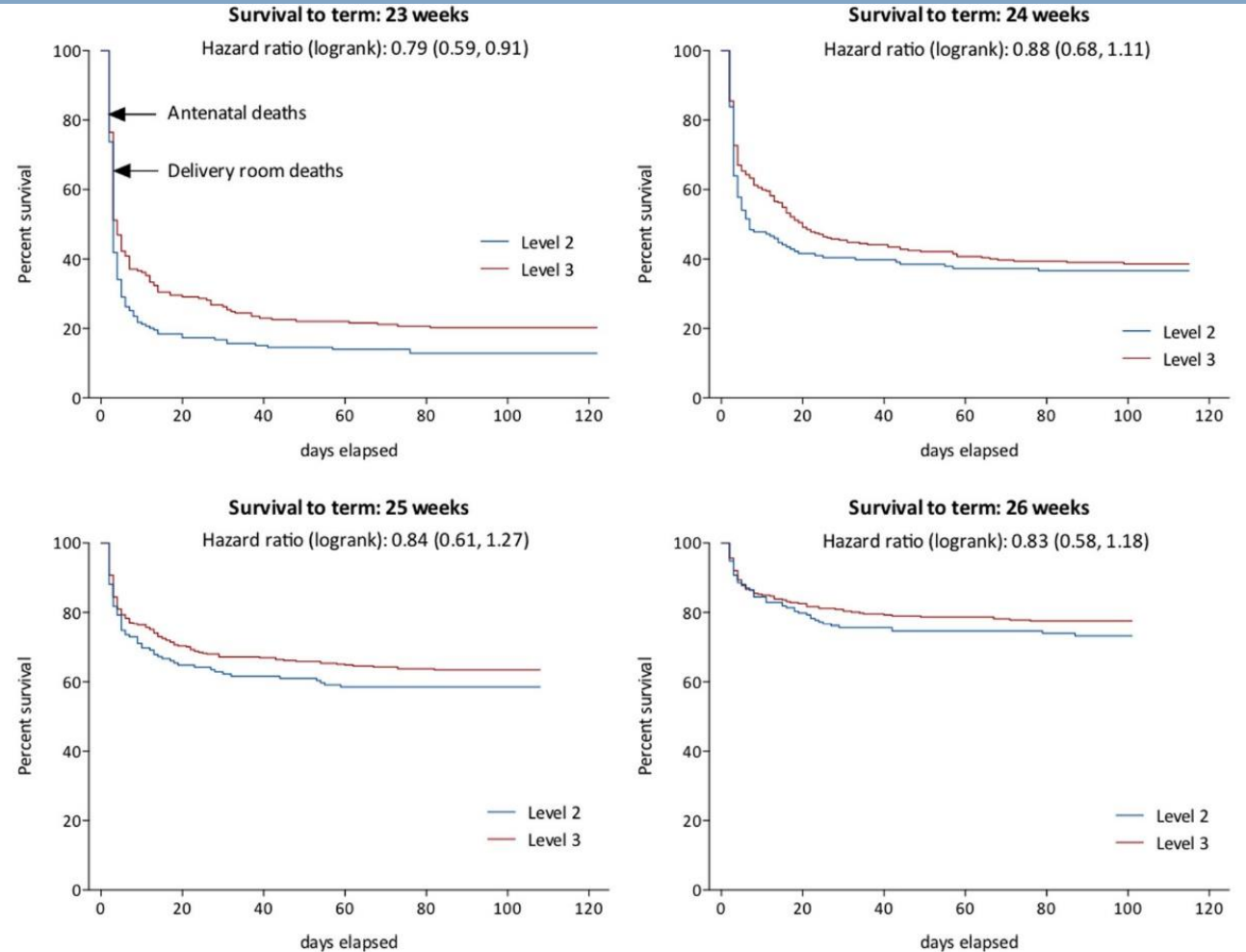


Figure 3 Kaplan–Meier plots of survival by gestational week for babies born at 23–26 weeks of gestation in level 3 and level 2 centres in England in 2006. Antenatal deaths are plotted as t=1 and delivery room outcomes care as t=2, with admission to neonatal unit as t=3 and subsequently postnatal age in days to 40 weeks postmenstrual age.

Corticosteroids –



Nice guideline 2015

23-23+6 – consider – MDT approach

24-25+6 consider

26+0- 33+6 offer

34+0- 35+6 consider

Betamethasone 12mg 12 hrs apart

Care with diabetics – sliding scale

Interval	Death	RDS	CVS haemorrhage
<24 hr	RR 0.6 (0.39-0.94)	RR 0.87 (0.66-1.15) NS	
<48 hr	RR 0.59 (0.41-0.86)	RR 0.67 (0.49-0.93)	RR 0.26 (0.09-0.75)
1-7 days	RR 0.81 (0.6-1.09) NS	0.46 (0.35-0.6)	
>7 days	RR 1.42 (0.91-2.23) NS	0.82 (0.53-1.28) NS	

Magnesium sulphate for neuroprotection – NICE guideline 2015

Magnesium sulphate:
For every 37 mothers who receive treatment 1 case of Cerebral Palsy is prevented (Crowther, 2018)
Cost: £1

24+0- 29+6 in established labour or having planned delivery within 24 hours

*consider in women 30-33+6

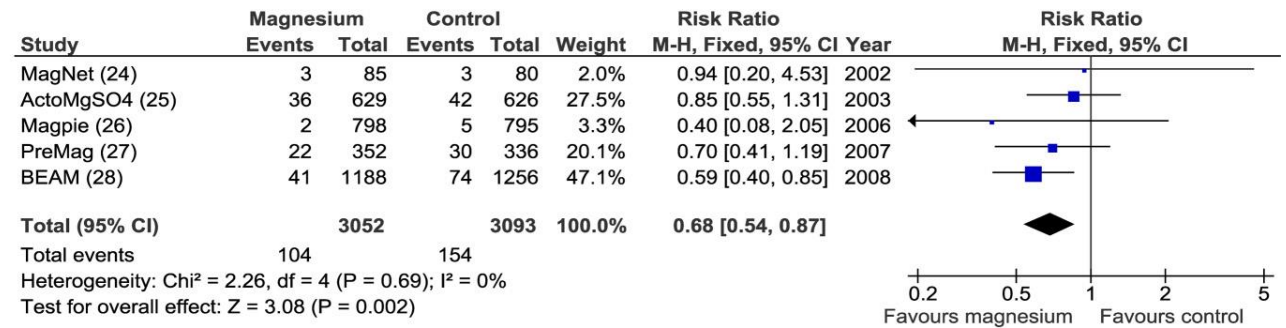
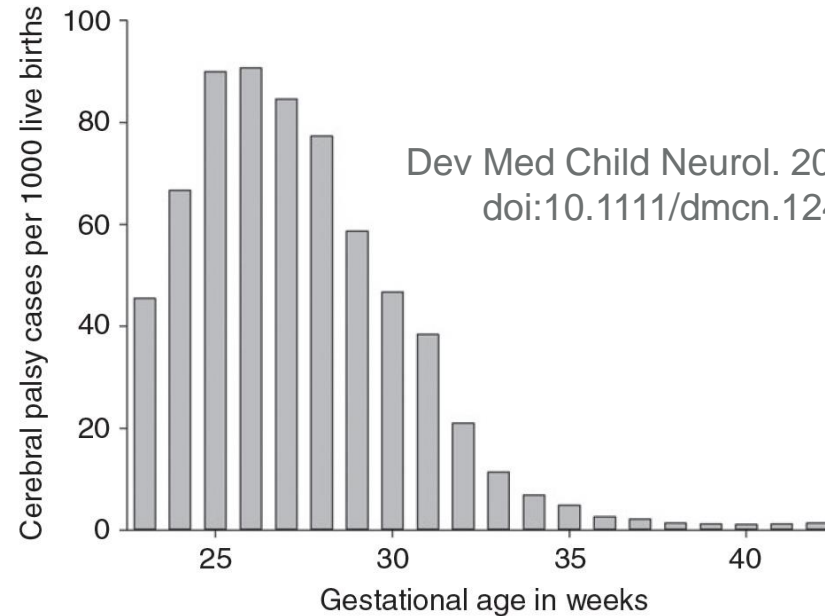
4g loading dose over 15 mins

1g/hr till birth or for 24 hours, minimum of 4-6 hours prior to delivery

Monitor mother of magnesium toxicity :
 UO/RR/Reflexes

CI: Myasthenia gravis/urgent del

Warn of flushing!



Tocolytics – NICE guideline 2015

Indication:

- Suspected or diagnosed labour
- To obtain benefit from steroids
- To obtain time to transfer to tertiary unit

CI: fetal or maternal compromise, bleeding, infection

1st line: Nifedipine (Cochrane review 2014 more effective at delaying PTB<48hrs compared to no tocolytic)

20mg SR to start

10-20mg every 6 hours for 48 hrs

Max dose 60mg/day

SE: HTN/ tachycardia/palpitations/flushing/headaches

2nd line: Atosiban (if hypotension, cardiac disease, hepatic dysfunction, multiple pregnancies)

Loading dose 6.75mg over 1 min, 18mg/hr for 3 hours, 6mg/hr for 21 hrs

IN SUMMARY

Prediction

Clinical history

Cervical length

Fetal fibronectin

Prevention

Medical:
Progesterone
Aspirin

Surgical:
Cerclage

Continuity of care

Preparation

Timing

Location

Steroids
Magnesium

THANK YOU !

Thank you !

Preterm Prevention Team



Prof Phil Bennett



Dr Vasso Terzidou



Prof TG Teoh



Rachel, Maria, Malko



Dr Erna Bayar



Dr Katie Mountain



Sara