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Saving Babies' Lives

Professor Asma Khalil
St George's Hospital, University of London, UK

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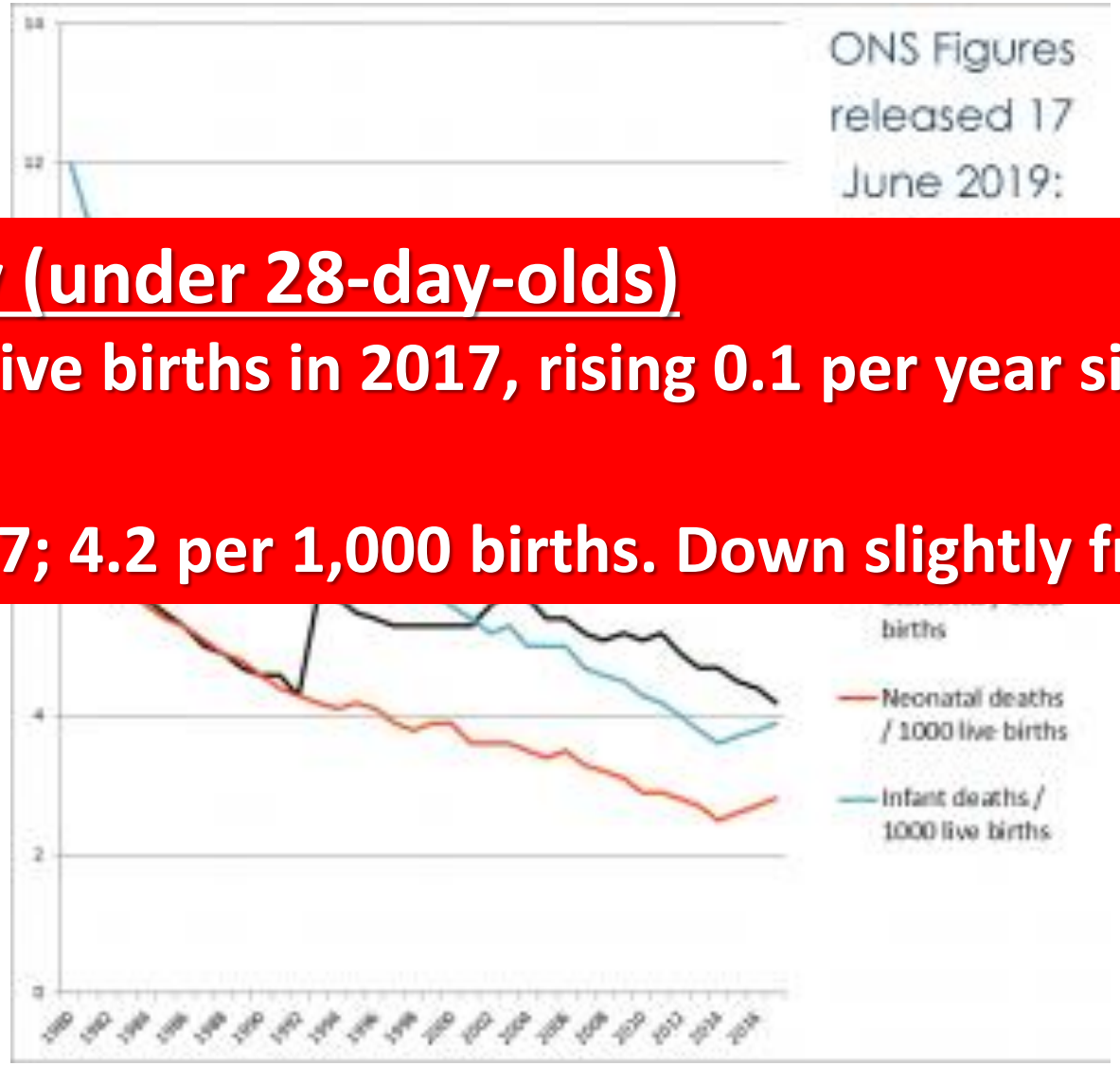

Neonatal mortality (under 28-day-olds)

2.8 deaths per 1,000 live births in 2017, rising 0.1 per year since 2014.

Stillbirth

2873 stillbirths in 2017; 4.2 per 1,000 births. Down slightly from 4.4 in 2016.


9 babies are stillborn
every day in the UK

The UK ranks 24th out of 49 high income countries in terms of stillbirth rates, with around one in 250 pregnancies ending in stillbirth after 24 weeks of pregnancy.

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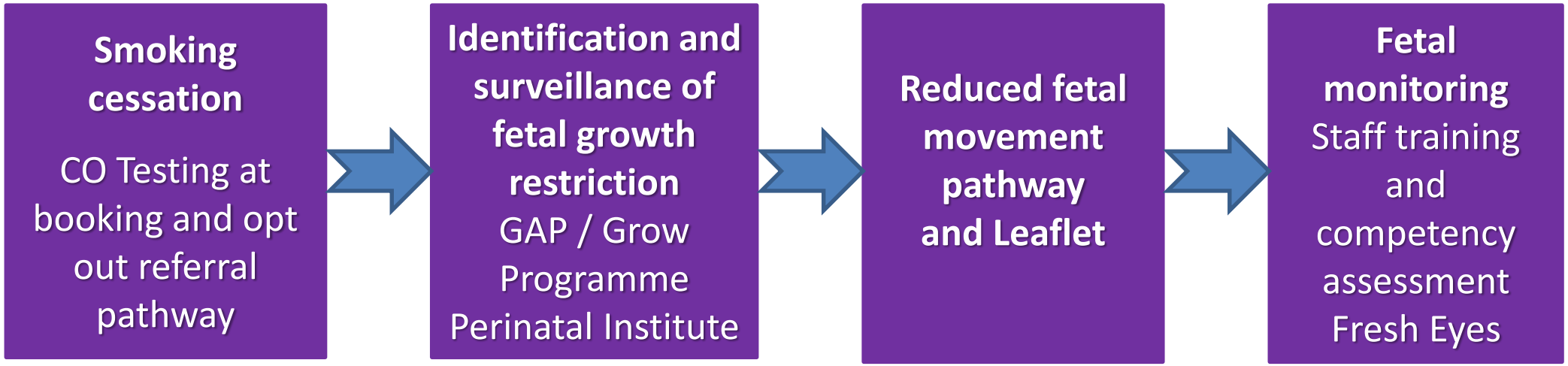
Stillbirth Care Bundle



Growth Assessment Protocol (GAP)

- 3 elements:
  - Customised Growth Charts
  - Online training and competency log
  - Rolling audit
- Low-risk pregnancies: fundal height
- High-risk pregnancies: serial scans
  - Obesity
  - Maternal age and parity
  - Smoking
  - Pre-existing diabetes
  - Pre-existing hypertension
  - Antepartum haemorrhage
  - History of SGA or stillbirth

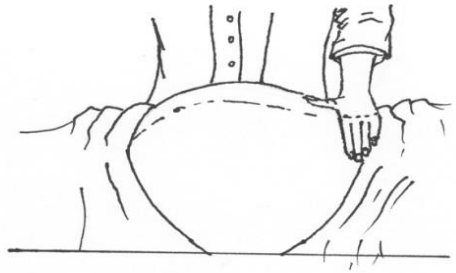
Fetal Growth Competency Assessment

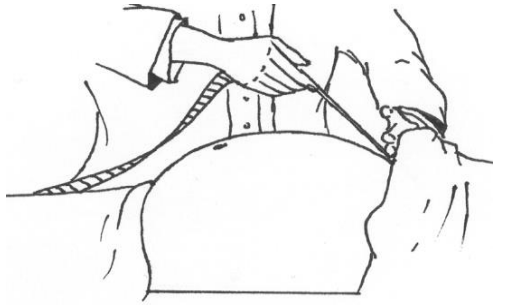
Knowledge of:

- Definitions of IUGR
- Research evidence
- Risk assessment at booking
- Customised growth chart and referral criteria
- Standardised fundal height measurement
- Customised centile at birth and ongoing management

Demonstration of:

- Production of a GROW chart
- Standardised fundal height measurement
- Plotting measurements on a chart
- Post test assessment





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Screening for FGR

BMJ

BMJ 2013;346:f108 doi: 10.1136/bmj.f108 (Published 24 January 2013)

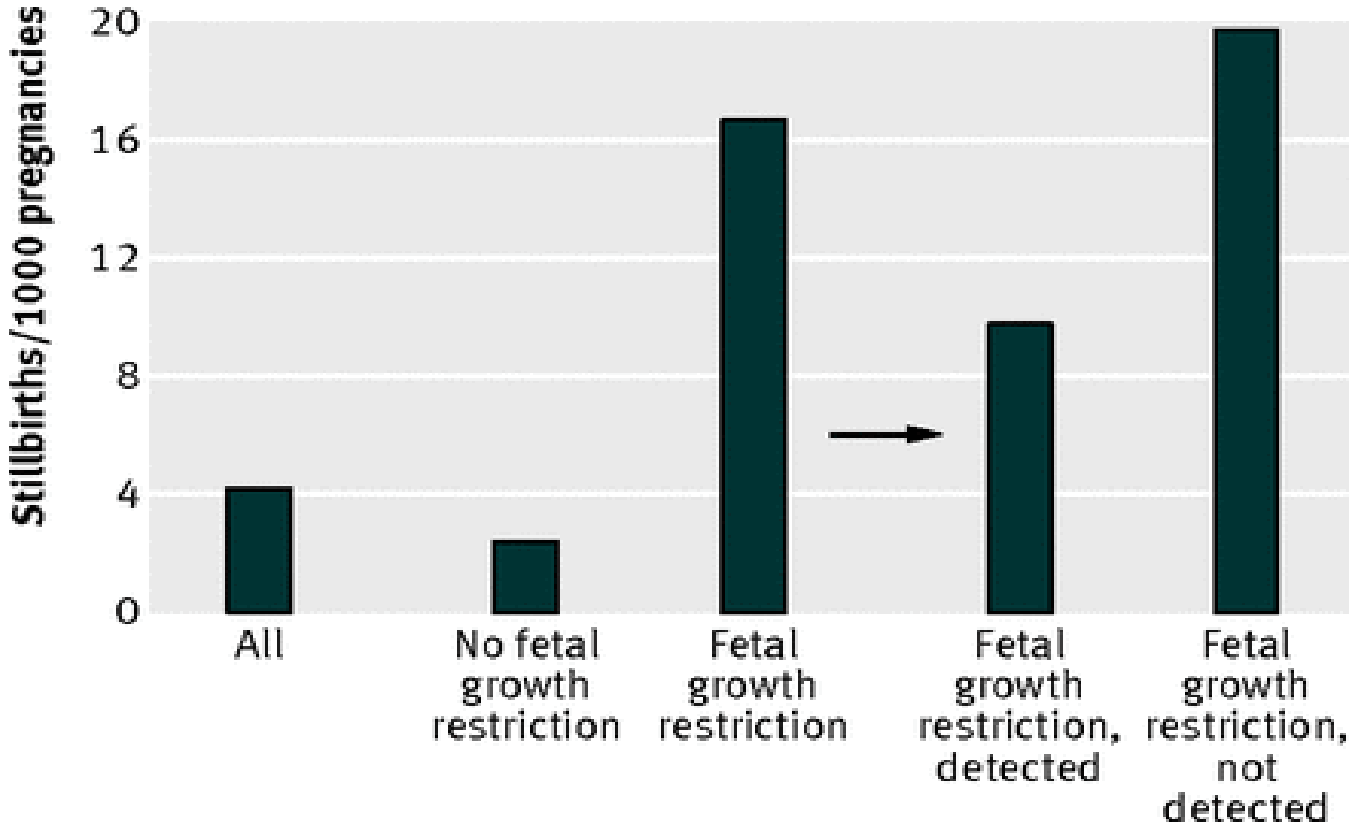
RESEARCH

Maternal and fetal risk factors for stillbirth: population based study

Jason Gardosi *director*[1] *professor of maternal and perinatal health*[2], Vichithranie Madurasinghe *epidemiologist*[1], Mandy Williams *research midwife*[1], Asad Malik *data analyst*[1], André Francis *statistician*[1]

- Early detection of growth problems can substantially reduce the risk of stillbirth
- Cohort study in the West Midlands
- June 2009 and May 2011
- RR of stillbirth halved from 8.0 to 4.0 when FGR is detected antenatally

Growth Assessment Protocol (GAP)



Gardosi J et al BMJ 2013

Growth Assessment Protocol (GAP)

Major Risk Factor	Primips %	Multips %	All %	SGA %
Maternal age >40	1.0	2.6	1.9	17.2
Smokes >10	2.7	5.3	4.2	28.4
BMI >35	6.0	9.1	7.8	16.7
Diabetes (excl GDM)	0.5	0.8	0.7	9.1
Pre-existing Hypertension	1.7	2.9	2.3	18.9
Previous SGA birth	0.0	10.5	5.9	28.2
Previous Stillbirth	0.0	0.6	0.3	17.6
One or more factors	11.9	31.8	**20.6**	**22.0**

Minor Risk Factor	Prevalence %	SGA %
Maternal age 35-40	13.4	14.8
Primipara	42.5	13.8
BMI<20 or 25-35	50.3	14.8
Smokes 1-10	13.7	23.5
Three or more	**4.9**	**21.0**

RCOG Green Top Guidelines
Analysis of West Midlands PEER Database 2
009-11; n=161,936

Growth Assessment Protocol (GAP)

Growth Assessment Protocol (GAP)

- 25% have one major or 3 minor risk factors
  - 3-weekly scans
- 60% of stillbirths had at least one of these risk factors
- Increased rate:
  - SGA births (OR 2.0)
  - Stillbirths (OR 1.6)
- 1100 additional scans / 1000 births
- Increase in IOL

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The DESiGN Trial

DEtection of Small for GestatioNal age fetus (SGA) – a cluster randomised controlled trial to evaluate the effect of the GAP programme

Chief Investigators: Dharmintra Pasupathy

Asma Khalil

Professor Jane Sandall

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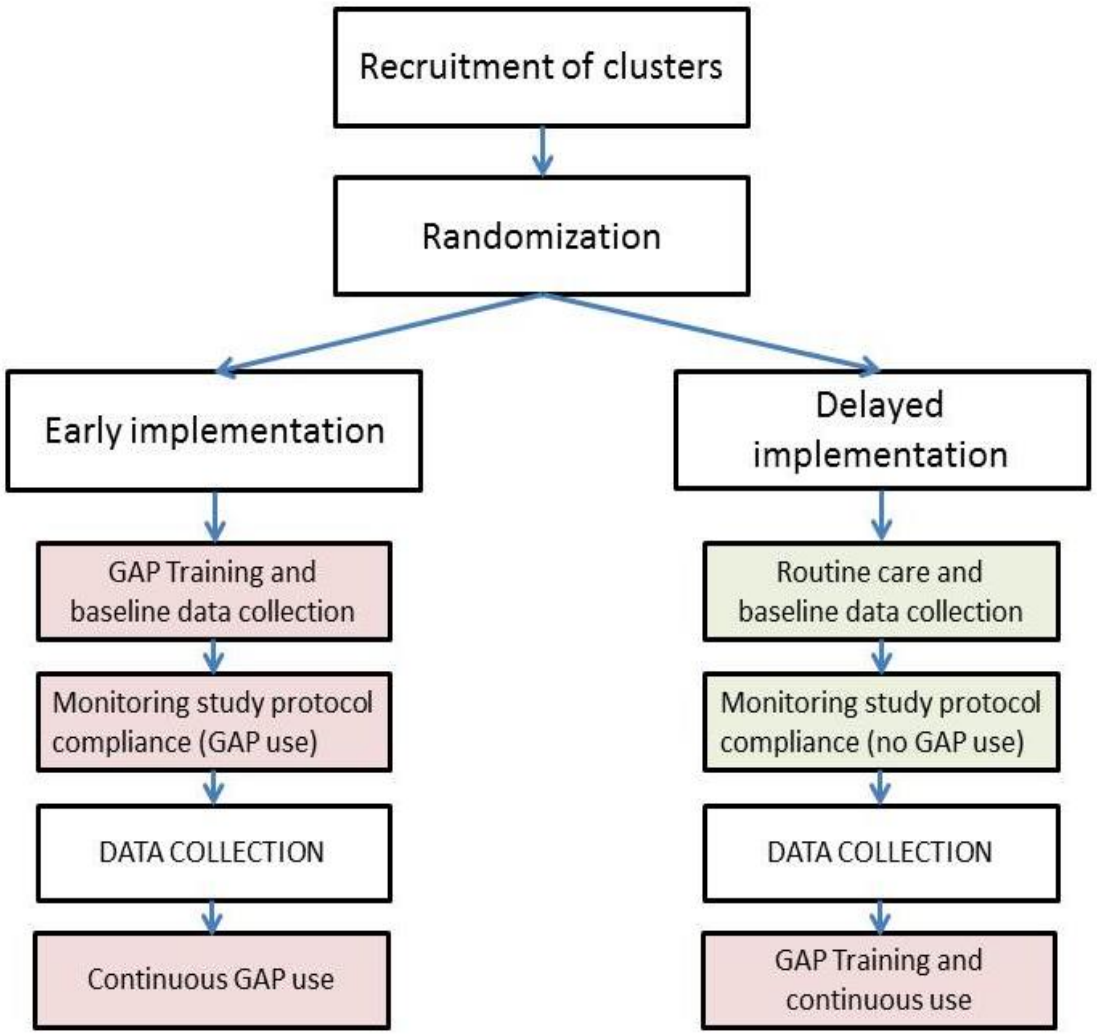

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DESIGN Trial

Primary outcome

Detection of SGA at birth (birthweight <10th centile) that were clinically detected antenatally (by ultrasound scan > 24 weeks)

Secondary outcomes

- **Clinical**
  - Maternal
  - Neonatal
- **Health Economics**
- **Implementation**

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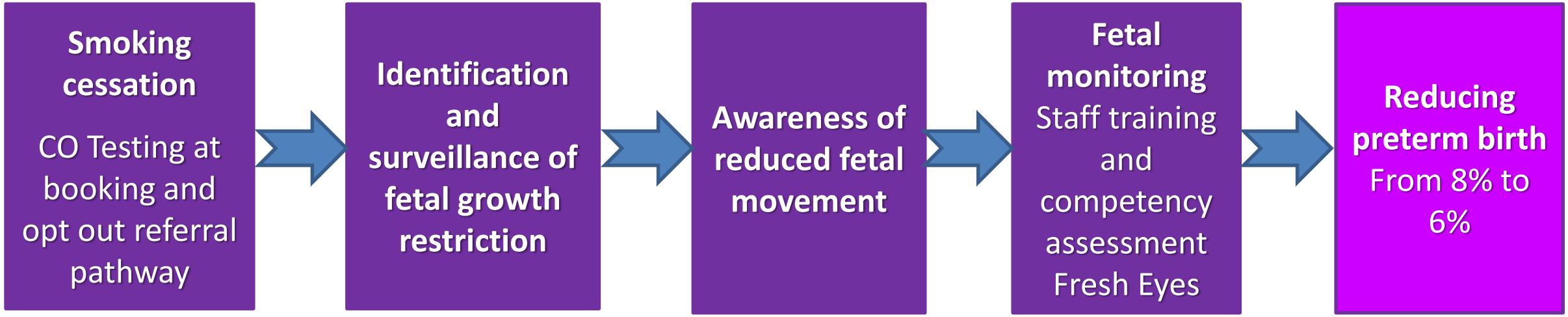
Stillbirth Care Bundle (version 2)



Main Objectives

- Investigate the combinations of factors that can predict perinatal death
- Evaluate the interventions that will help prevent perinatal deaths

Proposed research projects

IPPIC IPD meta-analysis for predicting stillbirth/perinatal death

Meta-analysis of interventions to prevent stillbirth/perinatal deaths

Developing a core outcome set for interventions to prevent stillbirth

Outputs

1. The prognostic value of individual clinical, biochemical and ultrasound markers , individually and in combination for predicting stillbirth/ perinatal death

2. Prediction models for preterm, term and all stillbirths/ perinatal deaths

3. The differential performance of the models in various predefined subgroups based on population characteristics (unselected; selected) and timing of model use (first trimester; second trimester; third trimester)

4. The potential additional value of novel biomarkers on the accuracy of these models

1. Tables outlining the data extracted from individual studies
2. Relative risk of the effect of each intervention investigated as part of the met-analysis (Forest plots)
3. Assessment of the quality of the included studies

1. a core outcome set which has been agreed by the stakeholders using Delphi consensus
2. Validated tools for measuring outcomes

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Why is the identification of pregnancies at high-risk of stillbirth important?

- Closer surveillance or early delivery.
- Currently recognised risk factors are extremely poor at predicting stillbirth; in the Stillbirth Collaborative Research Network study 81% of stillbirths occurred in women without established risk factors in early pregnancy.
- Enable further stratification of care pathways, allowing antenatal surveillance and intervention to be tailored to those at high risk.
- Investigating promising preventative therapies, such as low-dose aspirin and early delivery.
- Reassure the majority of pregnant women who are at low risk of an adverse perinatal outcome, and possibly avoid unnecessary medical intervention or earlier delivery.
- Abandon surveillance tests found to be ineffective (savings in time, effort and money).

Research priorities for stillbirth

1. How can the structure and function of the placenta be assessed during pregnancy to detect potential problems and reduce the risk of stillbirth?
2. Does ultrasound assessment of fetal growth in the third trimester reduce stillbirth?
3. **Do modifiable 'lifestyle' factors (e.g. diet, vitamin deficiency, sleep position, sleep apnea, lifting and bending) cause or contribute to stillbirth risk?**
4. Which investigations identify a fetus at risk of stillbirth after a mother believes she has experienced reduced fetal movements?
5. **Can the wider use of existing tests and monitoring procedures, especially in later pregnancy, and the development and implementation of novel tests (biomarkers) in the mother or in early pregnancy, help prevent stillbirth?**
6. What causes stillbirth in normally grown babies?
7. What is the most appropriate bereavement and postnatal care for both parents following a stillbirth?
8. **Which antenatal care interventions are associated with a reduction in the number of stillbirths?**
9. Would more accessible evidence-based information on signs and symptoms of stillbirth risk, designed to empower women to raise concerns with healthcare professionals, reduce the incidence of stillbirth?
10. How can staff support women and their partners in subsequent pregnancies, using a holistic approach to reduce anxiety, stress and any associated increased visits to healthcare settings?
11. Why is the incidence of stillbirth in the UK higher than in other similar high-income countries, and what lessons can we learn from this?

Accuracy of clinical characteristics, biochemical and ultrasound markers in the prediction of pre-eclampsia: an Individual Participant Data (IPD) Meta-analysis

International Prediction of Pre-eclampsia IPD Collaborative Network (IPPIC)

Queen Mary University of London

UCC Coláiste na hOllscoile Corcaigh, Éire University College Cork, Ireland

MANCHESTER 1824 The University of Manchester

THE UNIVERSITY of ADELAIDE

St George's University of London

NHS National Institute for Health Research

ACTION ON PRE-ECLAMPSIA PROMOTING SAFER PREGNANCY

UNIVERSITY OF EXETER

Aston University Birmingham

KING'S College LONDON

St George's Healthcare NHS NHS Trust

UMC Utrecht

Keele University

PCTU

IPD meta-analysis

Central collection, checking and analysis of individual patient data

All published and unpublished work

Observational studies, registry data and cohorts nested within randomised trials

Collaborators

Global support Networks

PRE-EMPT

Pre-eclampsia and eclampsia monitoring, prevention & treatment

GONet

Global Obstetrics Network

SCOPE

HOME DISEASES RESEARCH YOUR PARTICIPATION NEWS CONTACT

Through the collaboration of women and scientists across the globe, our vision is to predict and prevent the major diseases of late pregnancy. With the valued participation of women around the world, the SCOPE study has established a unique pregnancy biobank for scientific discovery to develop tests that predict these conditions.

Learn how you can help us make pregnancy safer...

Predict to Prevent:
Creating Safer Pregnancies
for Lifelong Health

PRE-EMPT COLAB

Global Pregnancy CoLaboratory

News | Agenda | Participating authors

Protocol | Contact | Results

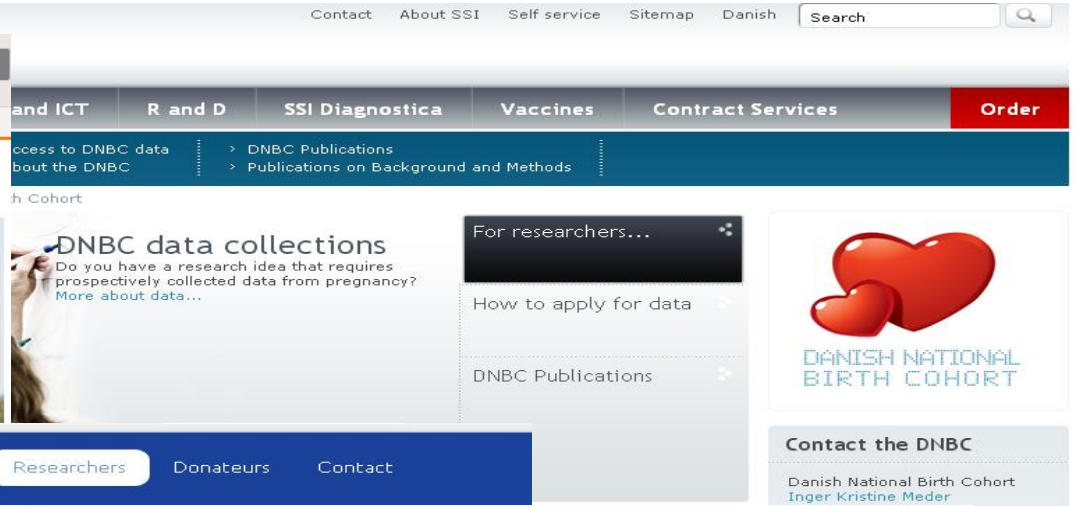
IPD-PREPARE

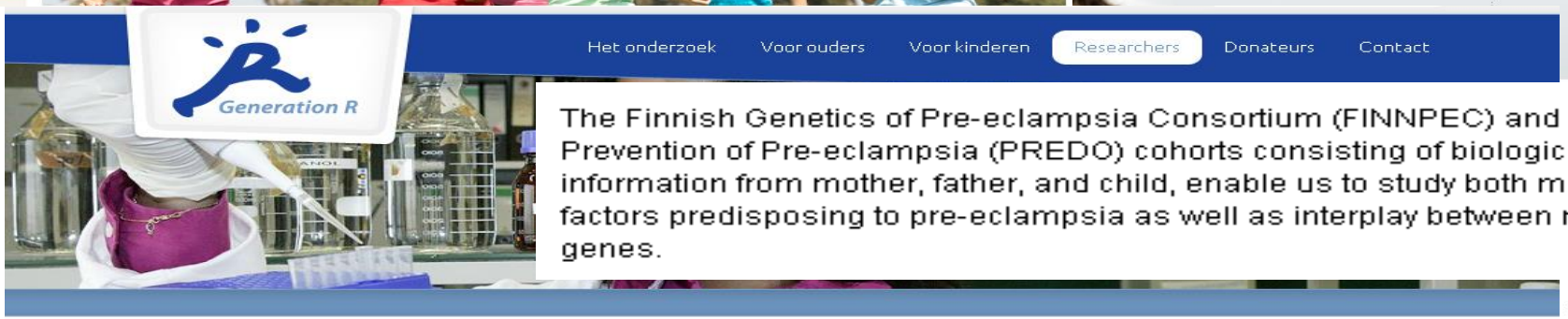
Back to IPD homepage

Welkom To the IPD-PREPARe page

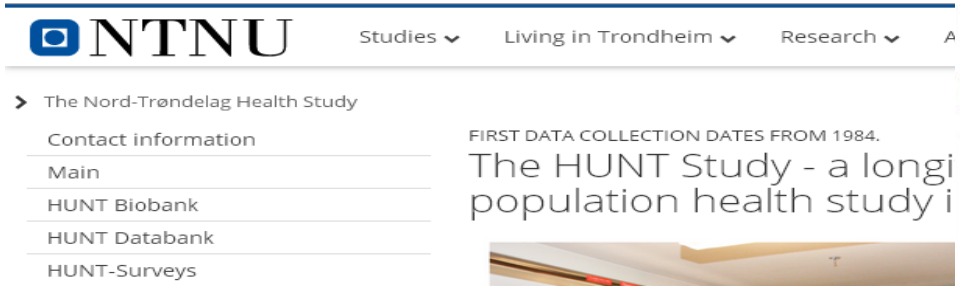
Prediction of REcurrent hypertensive disorders using Previous pregnancy data, Anthropometric parameters and maternal Risk factors, PREPARe

Birth Cohorts





The Finnish Genetics of Pre-eclampsia Consortium (FINNPEC) and the Prediction and Prevention of Pre-eclampsia (PREDO) cohorts consisting of biological samples and medical information from mother, father, and child, enable us to study both maternal and foetal genetic factors predisposing to pre-eclampsia as well as interplay between maternal and foetal genes.



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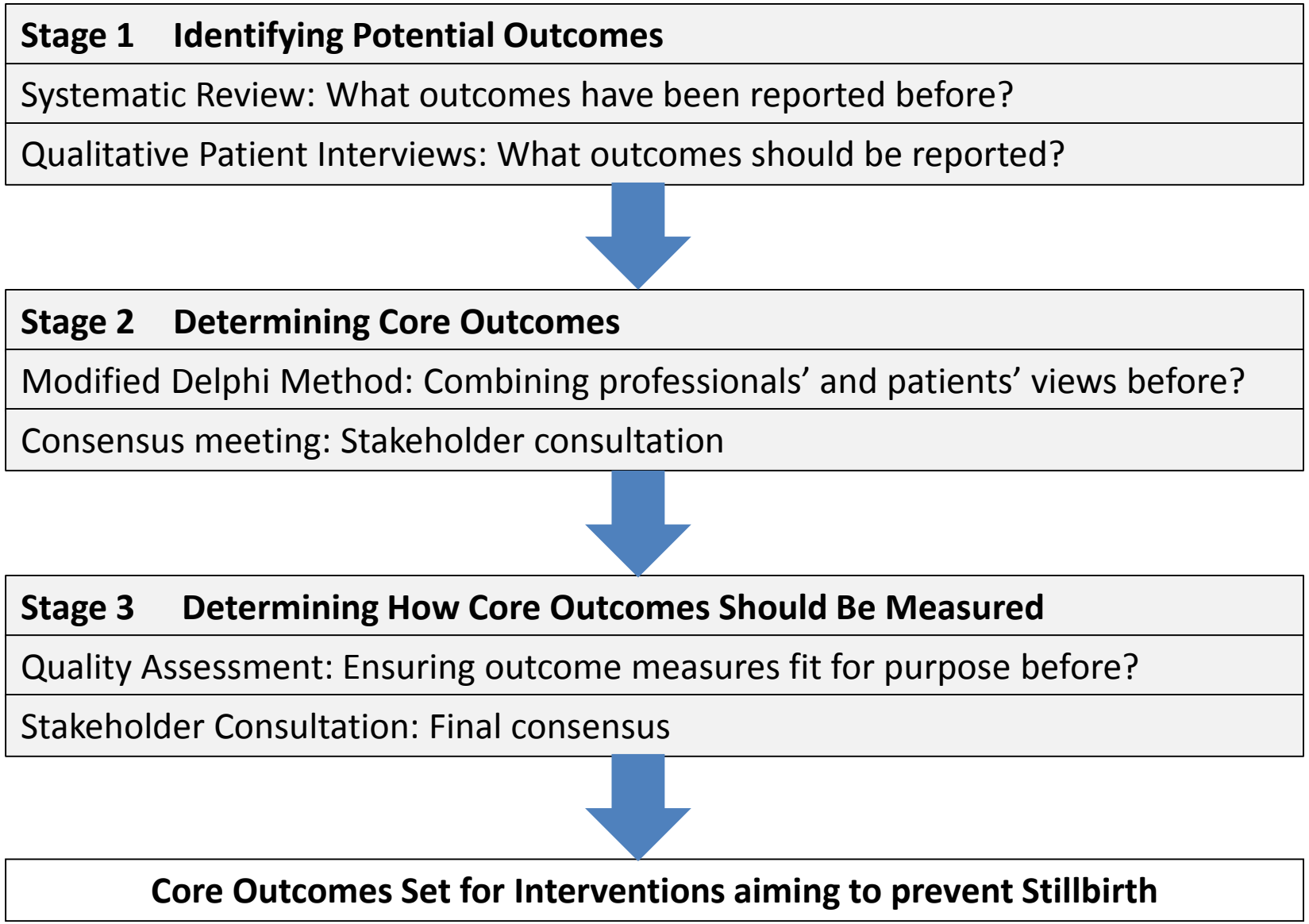
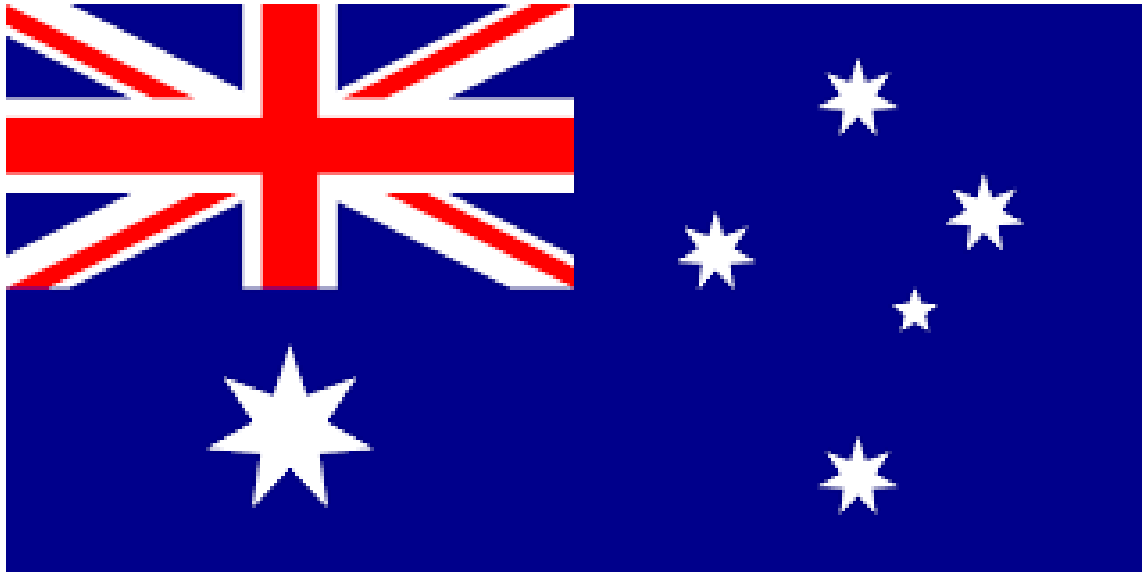
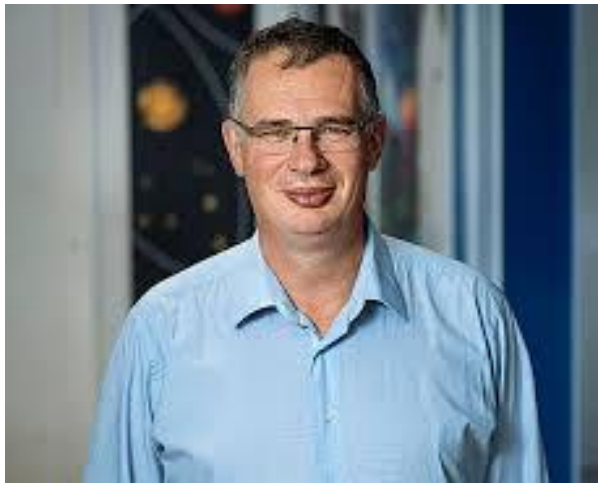
Stillbirth Core outcome set


Stage 1 Identifying Potential Outcomes
Systematic Review: What outcomes have been reported before?
Qualitative Patient Interviews: What outcomes should be reported?
Stage 2 Determining Core Outcomes
Modified Delphi Method: Combining professionals' and patients' views before?
Consensus meeting: Stakeholder consultation
Stage 3 Determining How Core Outcomes Should Be Measured
Quality Assessment: Ensuring outcome measures fit for purpose before?
Stakeholder Consultation: Final consensus
Core Outcomes Set for Interventions aiming to prevent Stillbirth



Sands
Stillbirth & neonatal death charity

Stillbirth Foundation
AUSTRALIA



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Outcomes for the mother	Outcomes for the offspring
Fetal loss (to include both miscarriage and stillbirth)	Timing of stillbirth - antepartum/intrapartum
Mode of delivery (to include induced/spontaneous and instrumental/vaginal/CS)	Neonatal mortality
Maternal mortality or near miss (according to WHO definition)	Gestational age at delivery
Psychological and social impact on the mother (assessed using a validated tool appropriate to context)	Birthweight
Women's knowledge	Congenital anomaly
	NICU/SCBU/KMC or other higher level neonatal care length of stay (days)

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Induction of labour at 41 weeks versus expectant management and induction of labour at 42 weeks (SWEdish Post-term Induction Study, SWEPIS): multicentre, open label, randomised, superiority trial

Ulla-Britt Wennerholm,[1] Sissel Saltvedt,[2] Anna Wessberg,[3] Mårten Alkmark,[1] Christina Bergh,[1] Sophia Brismar Wendel,[4] Helena Fadl,[5] Maria Jonsson,[6] Lars Ladfors,[1] Verena Sengpiel,[1] Jan Wesström,[7] Göran Wennergren,[8] Anna-Karin Wikström,[6] Helen Elden,[3] Olof Stephansson,[9] Henrik Hagberg[1]

Pregnancy

Post-term pregnancy research cancelled after six babies die

Swedish researchers say proceeding with induction trial would have been unethical

David Crouch
Gothenburg

Mon 28 Oct 2019
07.00 GMT

▲ A newborn baby with his mother moments after birth. Photograph: Lionel Wotton/Alamy

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The Question Time leaders' special: our panel's verdicts
Owen Jones, Polly Toynbee, Martin Kettle and Katy Balls

BBC Question Time leaders special: who came out on top?

Raab and McDonald in

RCOG response to study on induction of labour

News **21 November 2019**

Inducing labour at 41 weeks in low risk pregnancies is associated with a lower risk of newborn death compared with expectant management (a "wait and see" approach) until 42 weeks, suggests a trial published by The BMJ.

Although the overall risk of death at 42 weeks is low, the team of researchers say induction of labour should be offered to women no later than 41 full weeks.

The trial involved 2,760 women, with an average age of 31 years, and an uncomplicated, single pregnancy. Participants were recruited from 14 Swedish hospitals between 2016 and 2018. Women were randomly assigned to induction of labour at 41 weeks (1,381) or expectant management (1,379) until induction at 42 weeks if necessary.

The main outcome was a combined measure of babies' health, including stillbirth or death in the first few days of life (known as perinatal death), Apgar score less than 7 at five minutes, low oxygen levels, and breathing problems. But there was no difference between the groups - 2.4% of women in the induction group had an adverse perinatal outcome compared with 2.2% in the expectant management group.

However, six babies in the expectant management group died compared with none in the induction group, and the trial was stopped early. The researchers estimate that, for every 230 women induced at 41 weeks, one perinatal death would be prevented.

PLOS | MEDICINE

RESEARCH ARTICLE

Risks of stillbirth and neonatal death with advancing gestation at term: A systematic review and meta-analysis of cohort studies of 15 million pregnancies

Javaid Muglu[1], Henna Rather[2], David Arroyo-Manzano[3], Sohinee Bhattacharya[4], Imelda Balchin[5], Asma Khalil[6], Basky Thilaganathan[6,7], Khalid S. Khan[8], Javier Zamora[3,8], Shakila Thangaratinam[8,9]*

Significant additional risk of stillbirth, with no corresponding reduction in neonatal mortality, when term pregnancies continue to 41 weeks compared to delivery at 40 weeks.

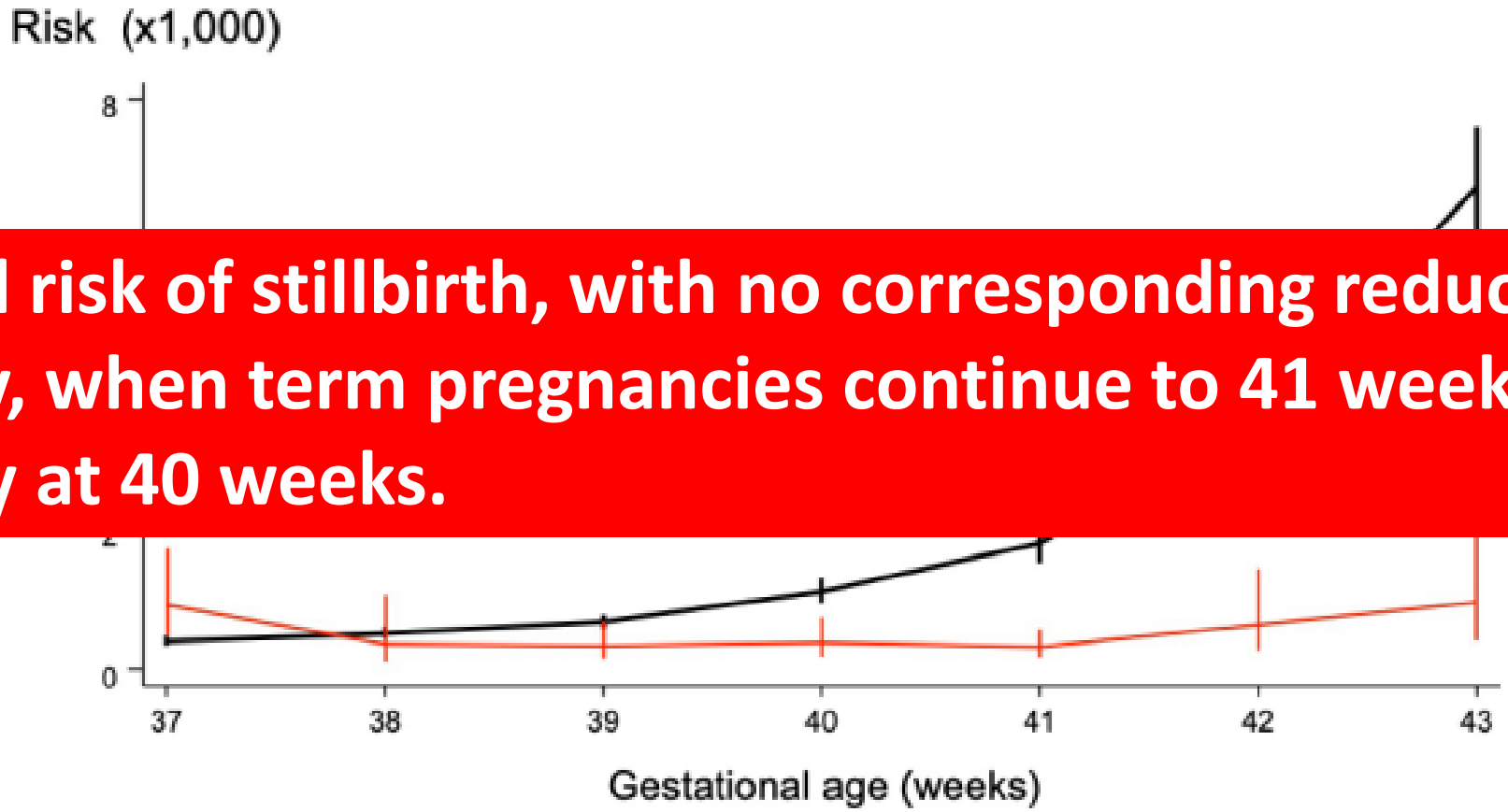

Fig 3. Prospective risk of stillbirth per 1,000 pregnancies and risk of neonatal death per 1,000 deliveries by gestational age in pregnancies continued to term. Stillbirth risk (solid back line); neonatal death risk (solid red line).

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Induction of labour in low-risk nulliparous

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IOL in low risk nulliparous

Published in final edited form as:

N Engl J Med. 2018 August 09; 379(6): 513–523. doi:10.1056/NEJMoa1800566.

Labor Induction versus Expectant Management in Low-Risk Nulliparous Women

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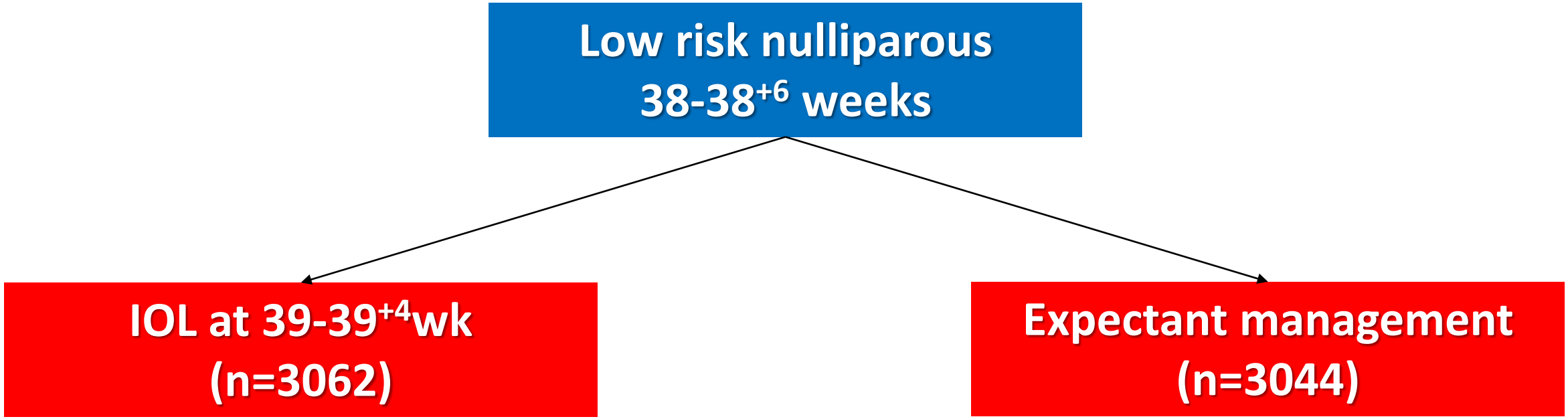
IOL in low risk nulliparous



- Primary outcome: composite of perinatal death or severe neonatal complications
- Principal secondary outcome: CS

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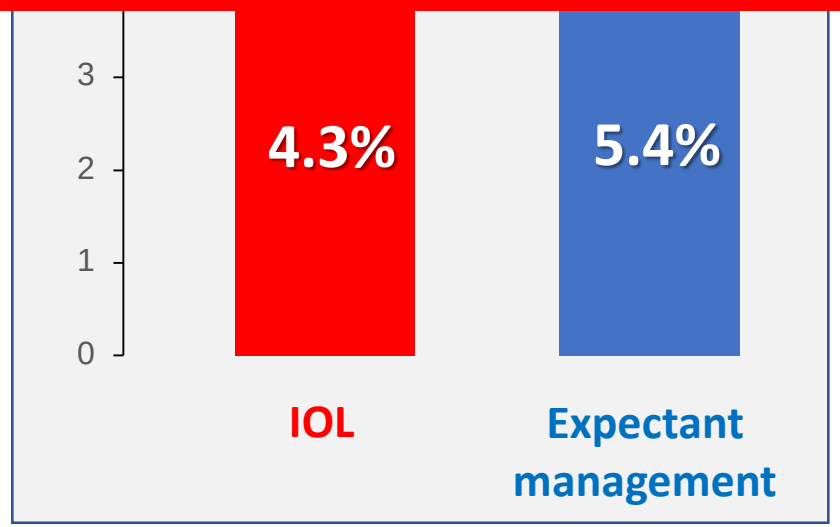
IOL in low risk nulliparous

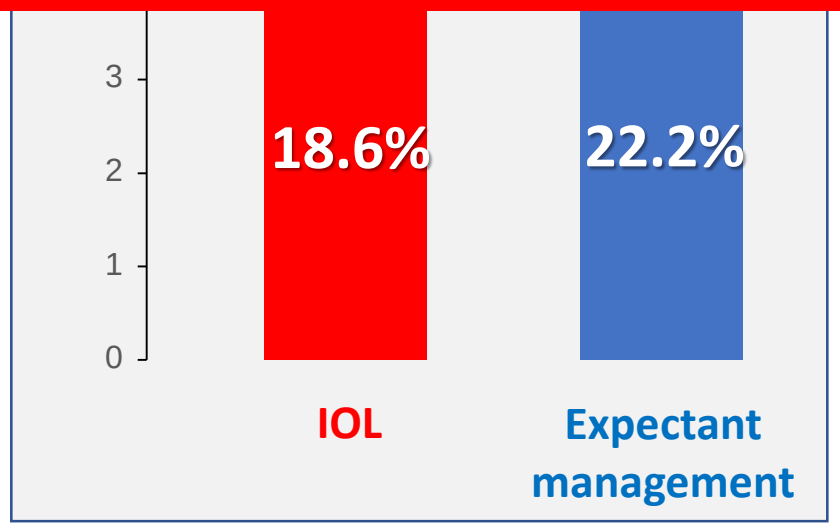
Perinatal outcome

RR 0·8 (0.64-1.00)



CS

RR 0.84 (0.76-0.93)



IOL at 39 weeks in low-risk nulliparous women:

- ↓ CS
- did not result in ↓ adverse perinatal outcome

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Induction of labour in older women

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IOL in older women

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Labor Induction in Women 35 Years of Age or Older

Kate F. Walker, M.R.C.O.G., George J. Bugg, M.D., Marion Macpherson, M.D., Carol McCormick, M.Sc., Nicky Grace, M.A., Chris Wildsmith, B.A., Lucy Bradshaw, M.Sc., Gordon C.S. Smith, D.Sc., and James G. Thornton, M.D.et al., for the 35/39 Trial Group*

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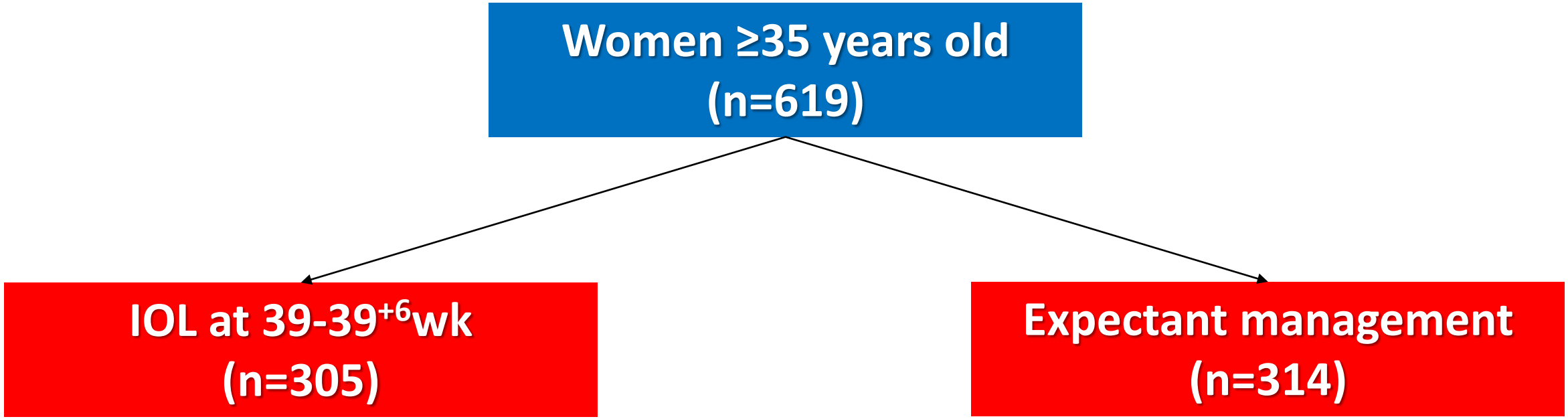
IOL in older women



- Primary outcome: CS
- The trial was not designed or powered to assess the effects of IOL on stillbirth

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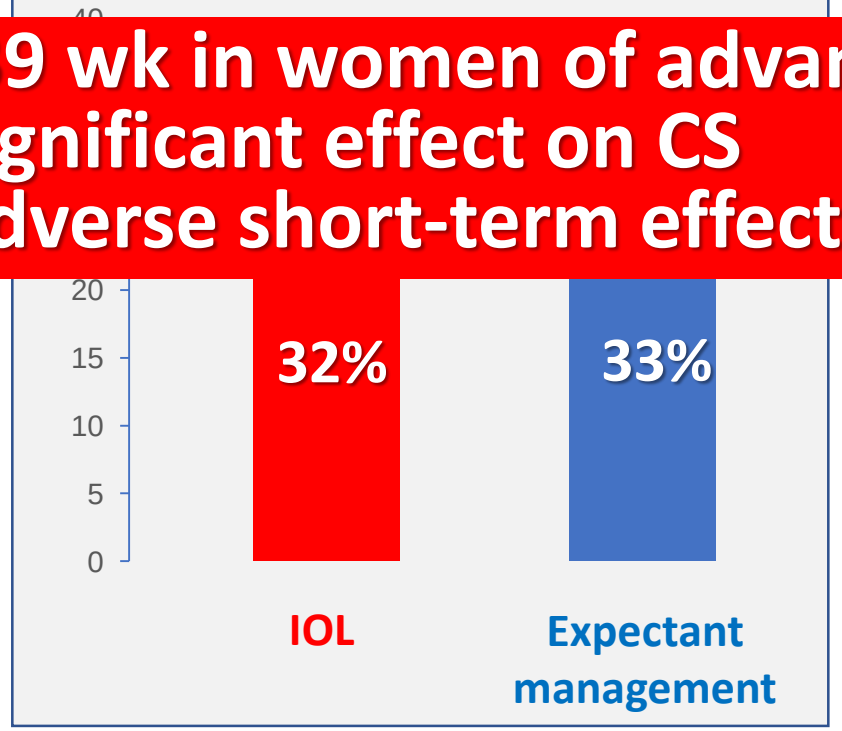
IOL in older women

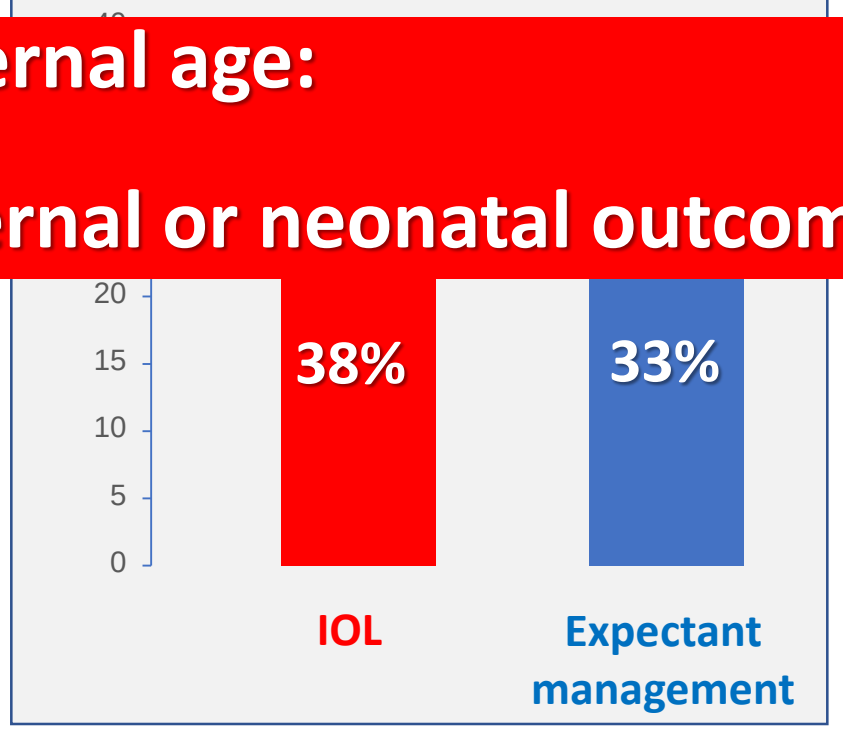
CS

RR 0·99 (0.87-1.14)



Instrumental delivery

RR 1.30 (0.96-1.77)



IOL at 39 wk in women of advanced maternal age:

- **no significant effect on CS**
- **no adverse short-term effects on maternal or neonatal outcomes**

- No maternal or infant deaths
- No Significant differences in women's experience of childbirth, adverse maternal or neonatal outcomes

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What about twin pregnancy?

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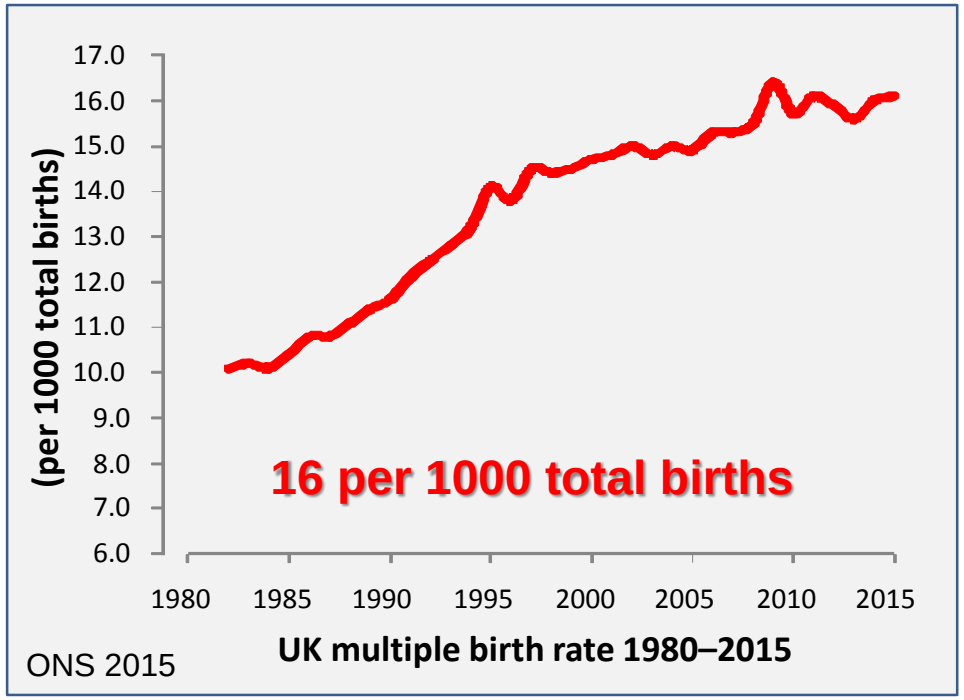

% of Births	2%
% of Stillbirth	7%
% of NND	18%
Cerebral palsy	6 times

Multiple pregnancy contributes disproportionately to stillbirths, neonatal death and cerebral palsy

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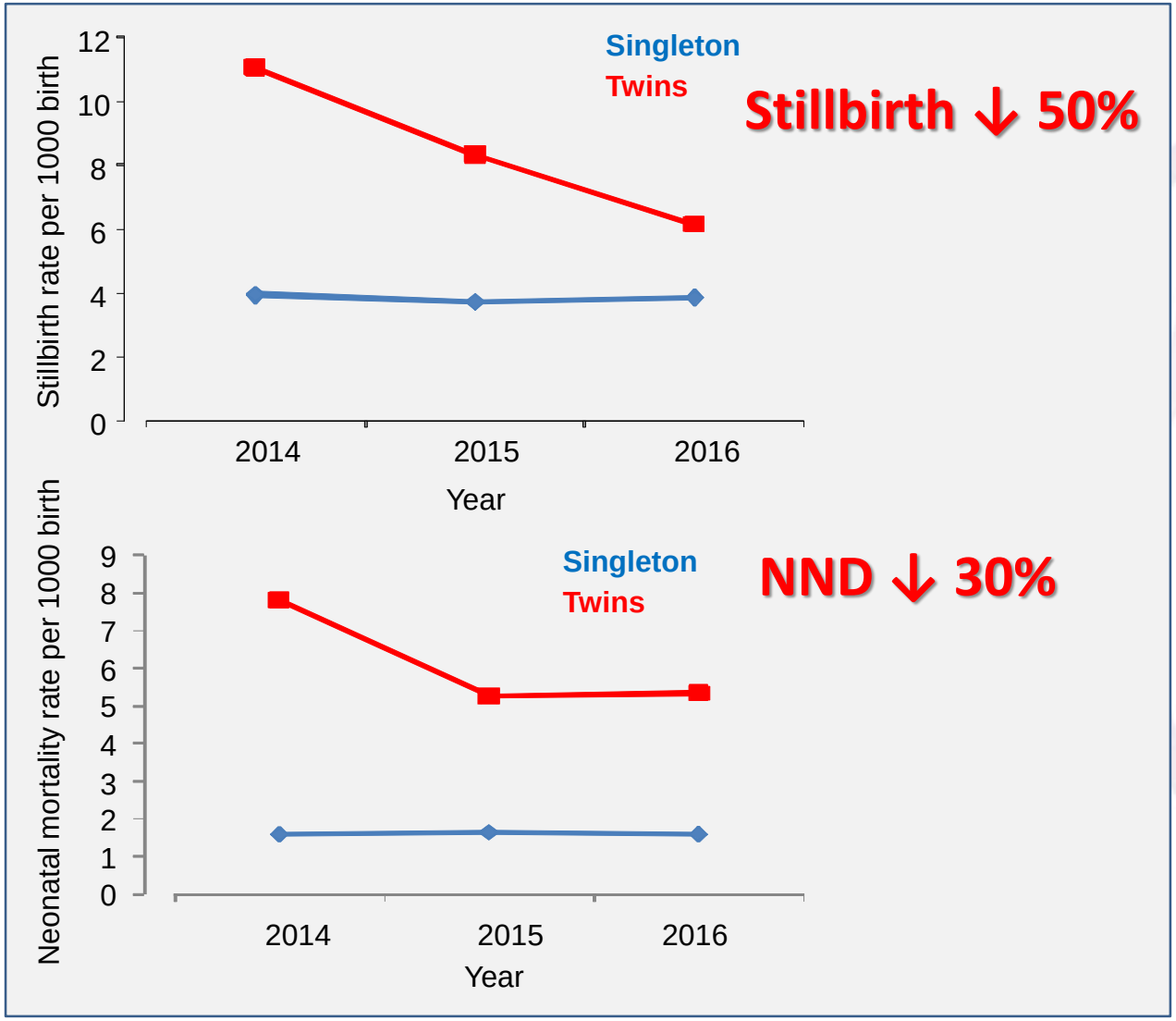
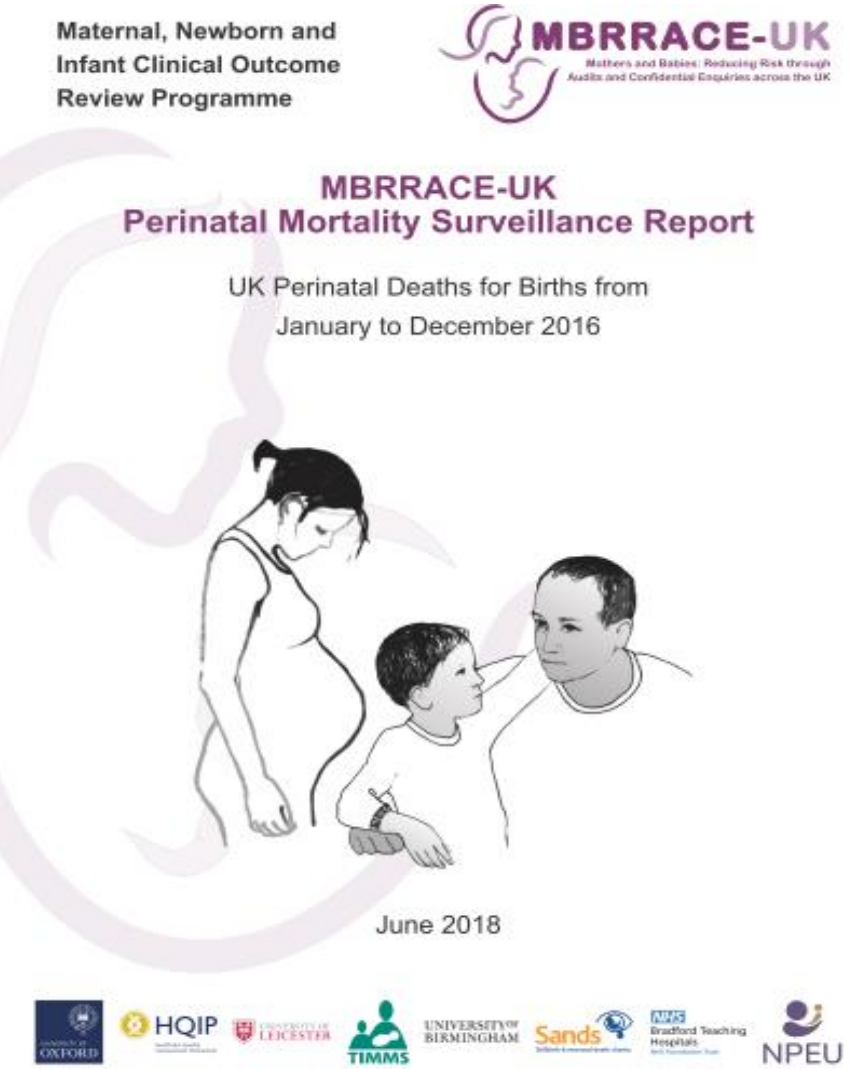
Stillbirth in twins





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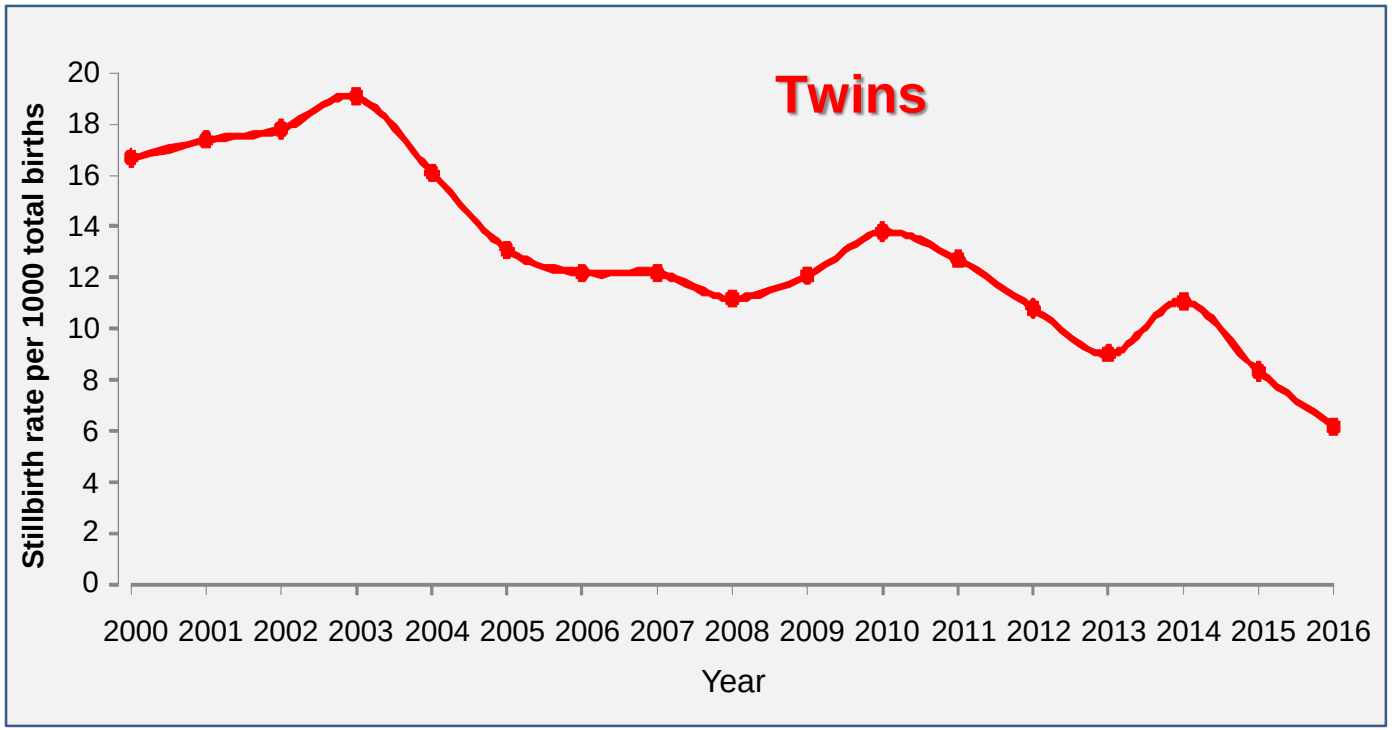
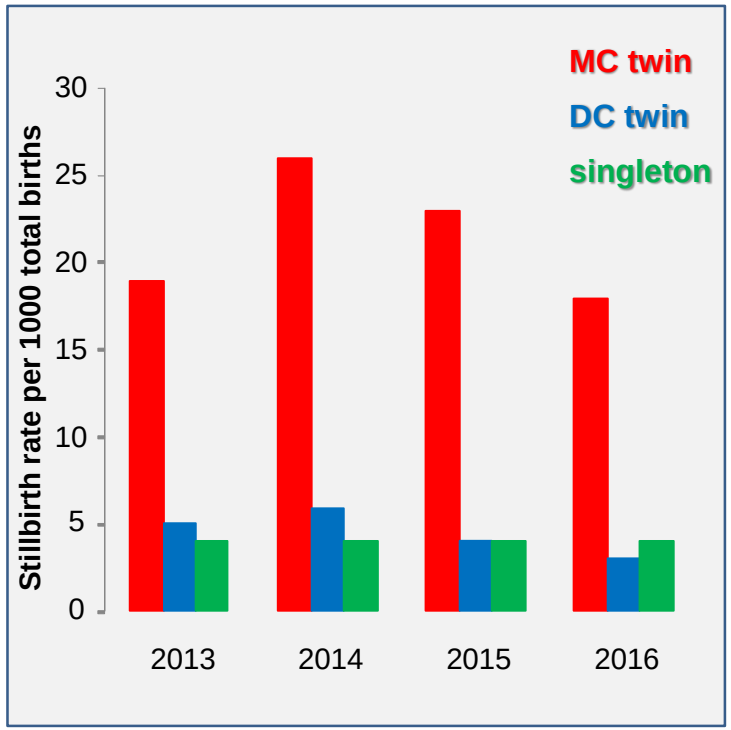
Stillbirth in twins





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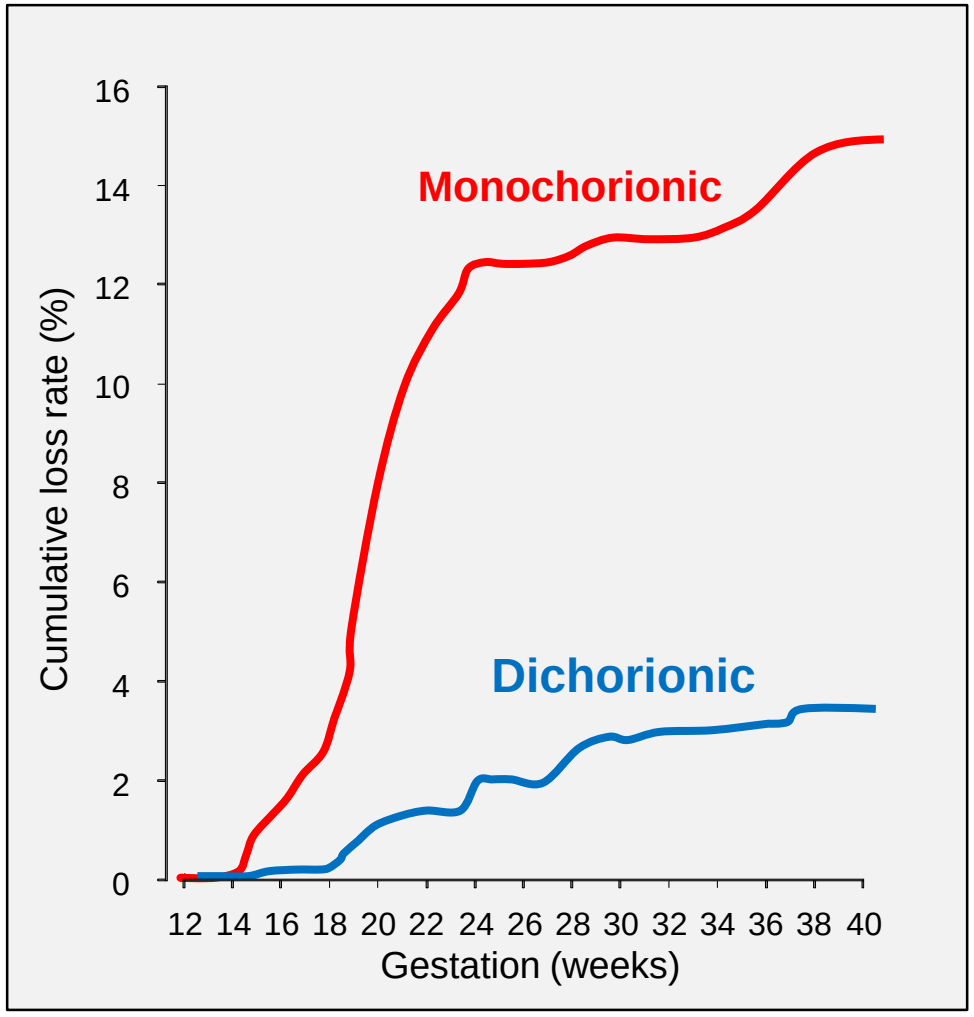
Stillbirth in Twins

The hidden mortality of monochorionic twins



	MC	DC
Fetal loss:		
Pregnancies (%)	*12.7*	*2.5**
Fetuses (%)	*12.2*	*1.8**
Perinatal loss:		
Pregnancies (%)	*4.9*	*2.8*
Fetuses (%)	*2.8*	*1.6*

* P<0.05

Sebire NJ et al., BJOG 1997

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What are the causes of stillbirth?

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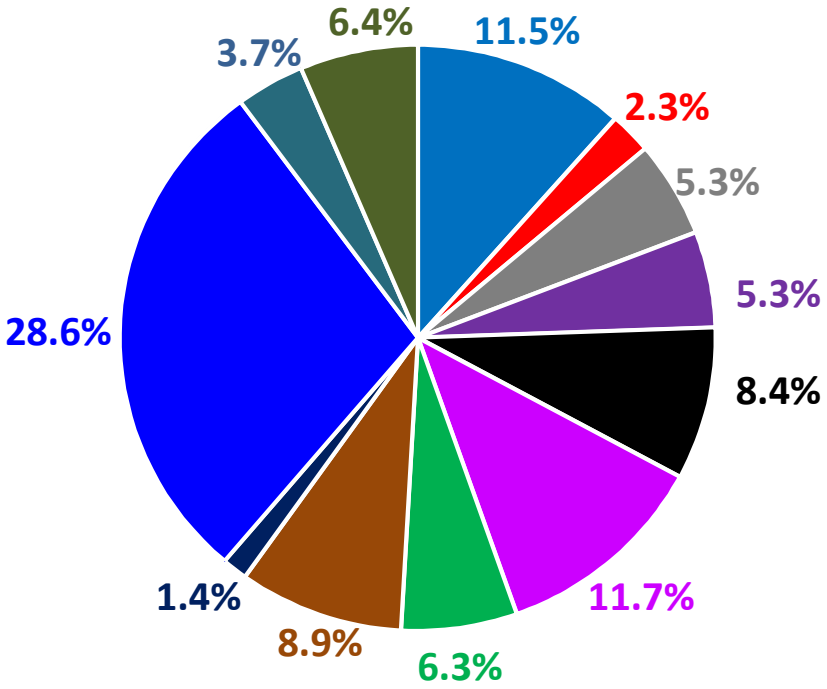
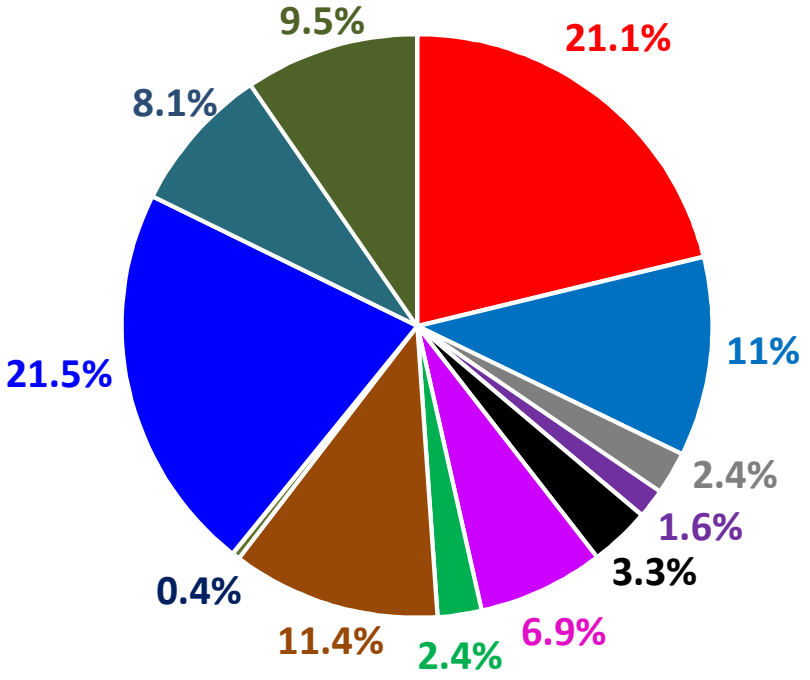
Stillbirth in Twins

Singleton pregnancies



Twin pregnancies



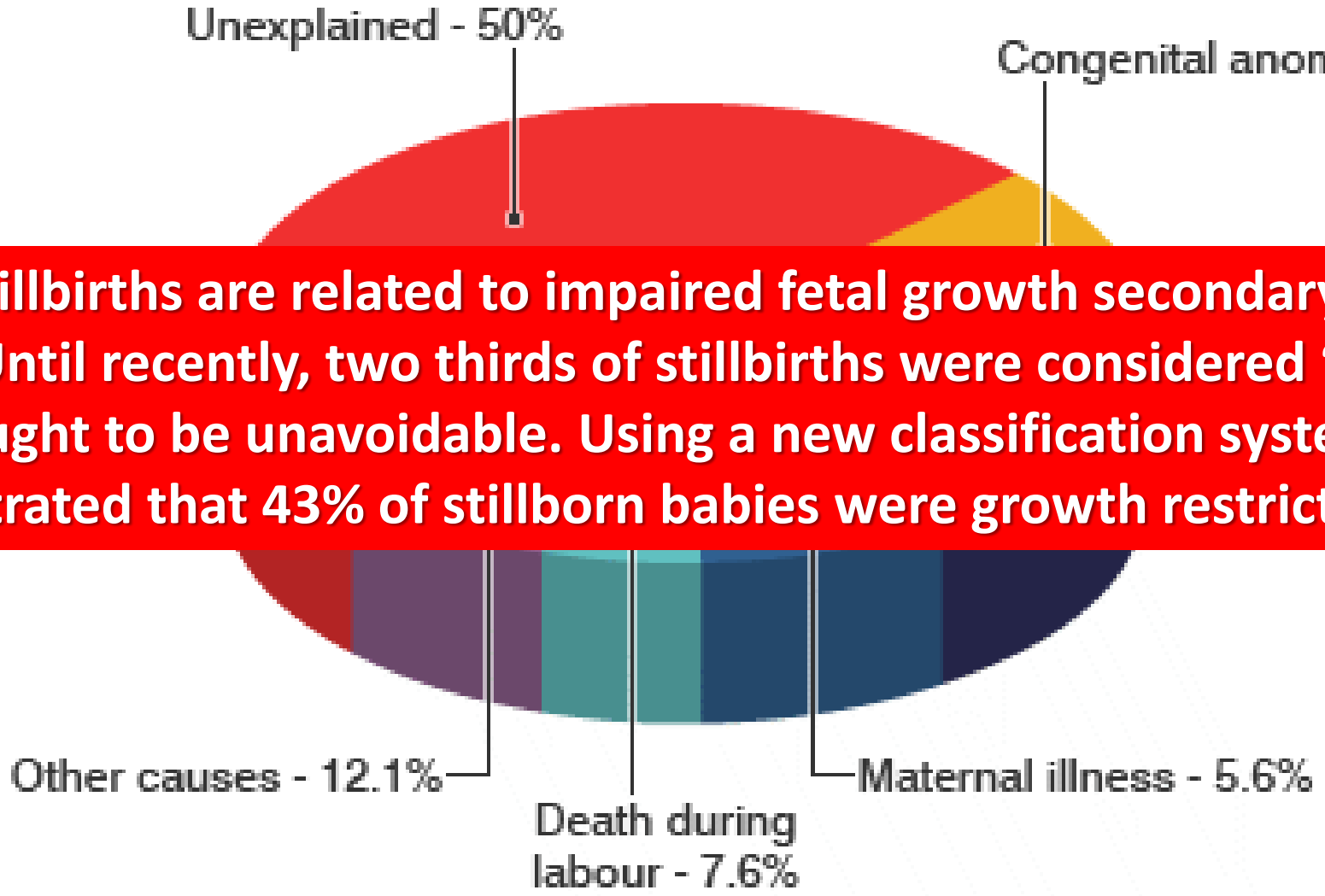
Specific placental conditions
Infections
Mechanical
Hypertensive disorders of pregnancy
Unclassified
Associated obstetric factors

Specific fetal conditions
Maternal disorders
Antepartum or intrapartum haemorrhage
Major congenital anomaly
Unexplained
IUGR

n=246 twins
n=3017 singletons

CMACE Report 2009

CAUSES OF STILLBIRTHS IN ENGLAND, WALES AND N IRELAND IN 2006

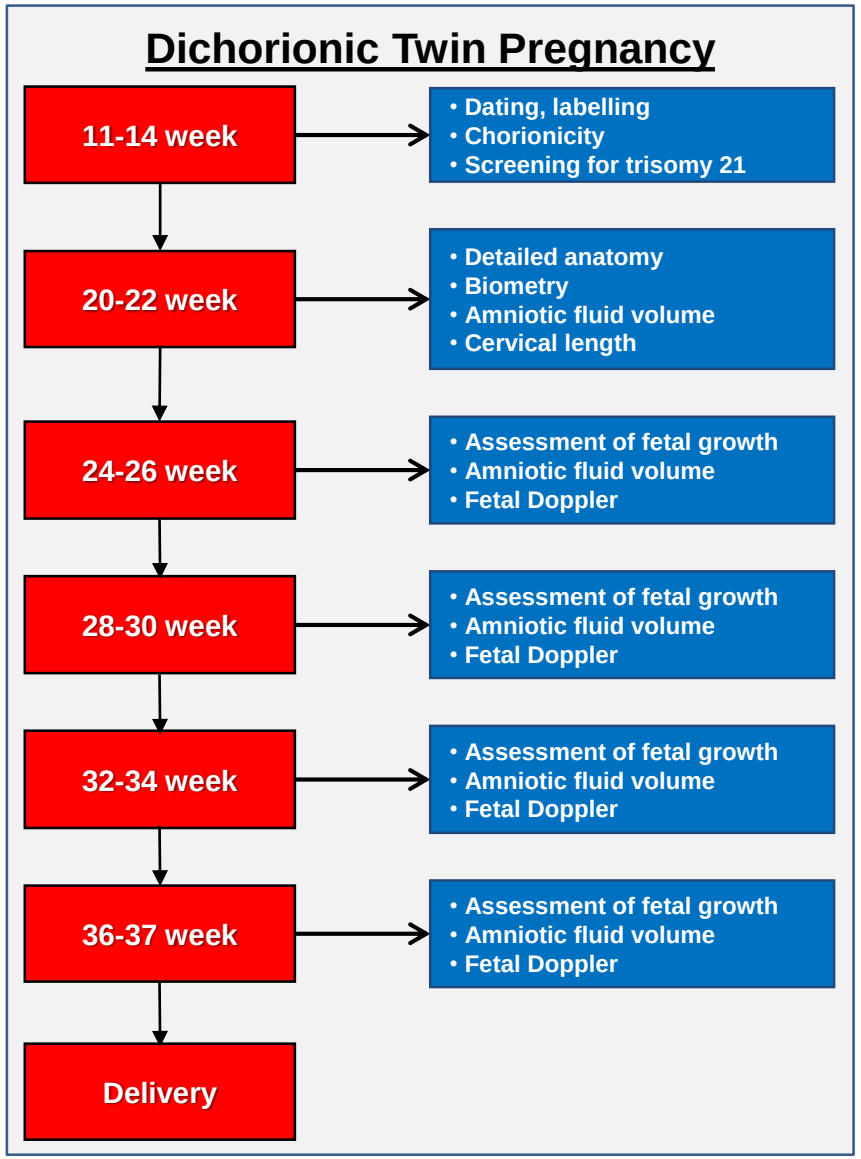


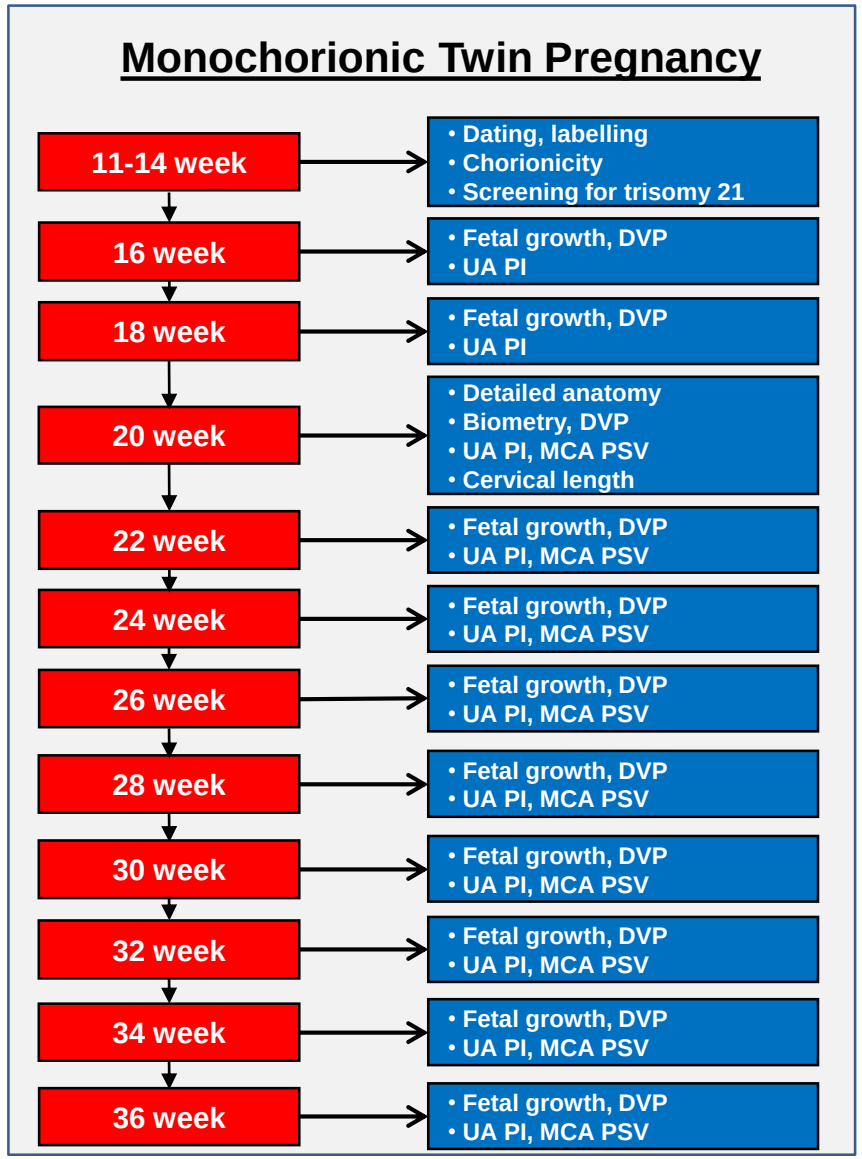
Over half of stillbirths are related to impaired fetal growth secondary to placental dysfunction. Until recently, two thirds of stillbirths were considered 'unexplained' and therefore thought to be unavoidable. Using a new classification system, however, it has been demonstrated that 43% of stillborn babies were growth restricted.

Other causes: Pre-eclampsia (2.8%); Infection (2.7%); Unclassifiable (0.6%); Accident (0.1%); Other specific causes (5.9%)

SOURCE: CEMACH 2006/2007

Twin Pregnancy: ultrasound monitoring





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When should we deliver uncomplicated twins?

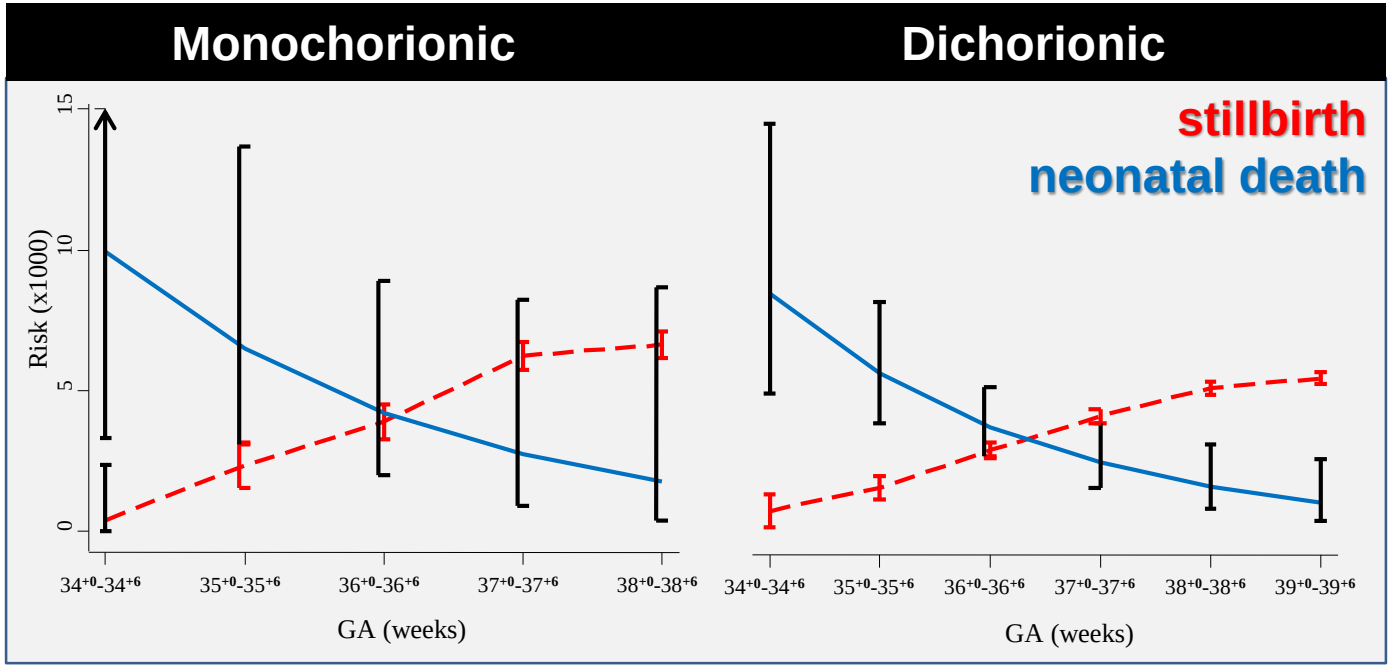
Optimal Timing of Delivery

Prospective risk of stillbirth/neonatal complications

BMJ

Prospective risk of stillbirth and neonatal complications in twin pregnancies: systematic review and meta-analysis

- 25,946 twin gestations
- Delivery at:
  - 36^{+0} - 36^{+6} weeks in MCDA
  - 37^{+0} - 37^{+6} weeks in DCDA



Cheong-See *et al* BMJ 2016

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NICE 2019

Timing of Delivery in Multiple Pregnancy

- DCDA twins: from 37^{+0} wk
- MCDA twins : from 36^{+0} wk after a course of steroids
- MCMA twins : 32^{+0} to 33^{+6} wk after a course of steroids
- TCTA or DCTA triplet: from 35^{+0} wk after a course of steroids

- If declines elective birth → weekly appointments with specialist obstetrician
  - ultrasound scan (including assessment of AFV and umbilical artery doppler)
  - fortnightly growth scans

National Institute for Health and Care Excellence (2019) Twin and triplet pregnancy. Available from https://www.nice.org.uk/guidance/ng137

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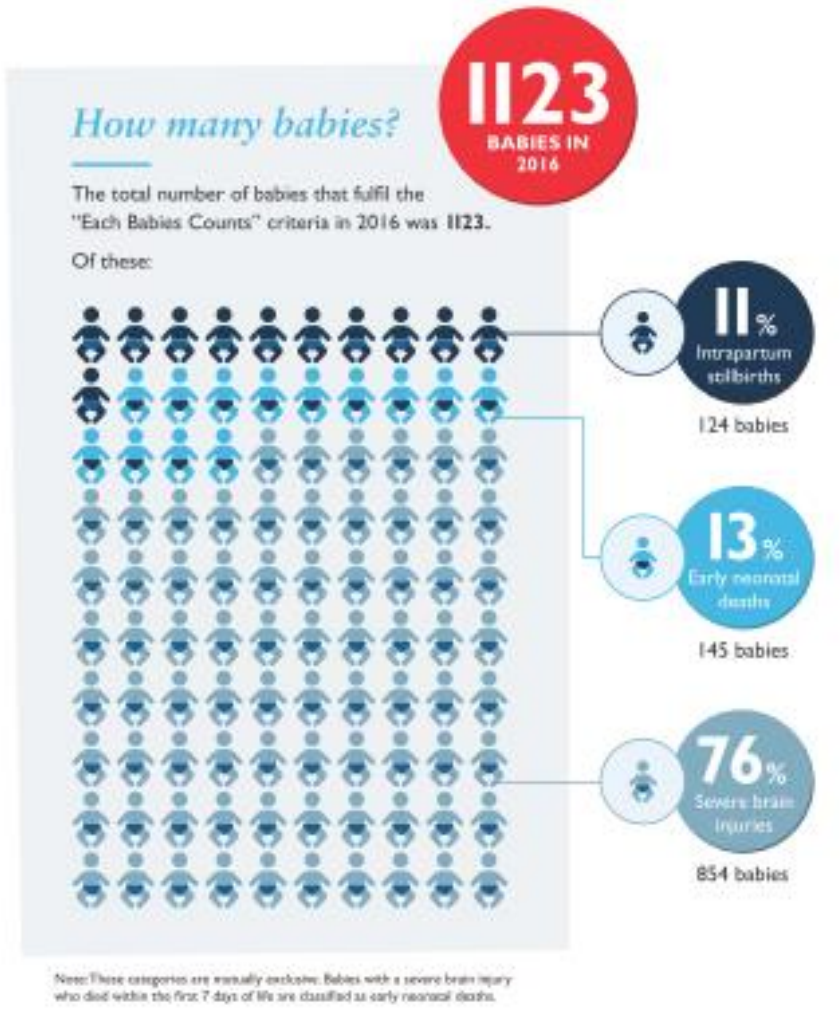
Update on national projects



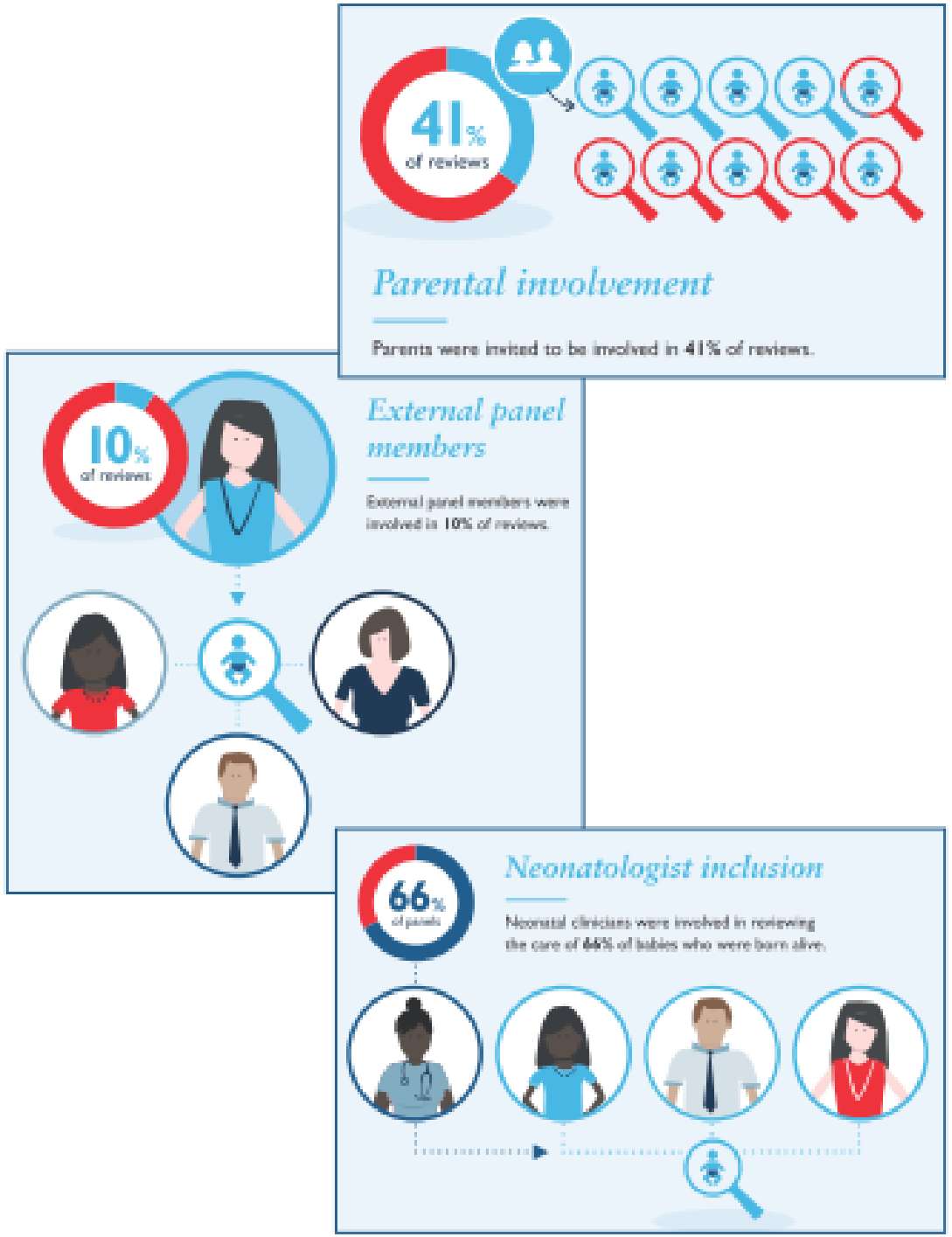
each baby COUNTS.

RCOG's national quality improvement programme to reduce the number of babies who die or are left severely disabled as a result of incidents occurring during term labour.

each baby COUNTS.

71% babies might have had a different outcome with different care

On average 7 critical contributory factors for each baby where different care might have had made a difference to the outcome.


41%
of reviews
Parental involvement
Parents were invited to be involved in 41% of reviews.
10%
of reviews
External panel members
External panel members were involved in 10% of reviews.
66%
of panels
Neonatologist inclusion
Neonatal clinicians were involved in reviewing the care of 66% of babies who were born alive.

Guidelines

Workload

The labour ward coordinator must remain supernumerary at all times and should not be caring for women during the antenatal, intrapartum or postnatal period.

Escalating high activity

There must be a clear escalation policy in place and a culture that empowers staff to escalate when the workload is becoming difficult to manage. All members of staff, irrespective of their role or grade, should feel empowered to inform senior midwives, managers and consultants when concerns arise both within their own specialty but also on behalf of another specialty. The consultant obstetrician should always be informed when labour ward activity is high.

Cross-site communication

Women receiving care from multiple units must have an individualised management plan for antenatal, labour and postnatal care that outlines the roles and responsibilities of each site to avoid any confusion. All sites should be able to readily access a woman's notes whether they be hand-held or electronic.

Local guidelines

There must be a clear policy to ensure that local guidelines are updated in line with national guidance. Appropriate resources and staff time must be allocated to facilitate this. Where units decide to deviate from national guidance, this should be clearly documented and units should undertake regular review of local deviations from national guidance. All guidelines should be reviewed in light of incidents to ensure that they improve care as intended.

Migration of boundaries

Teams should protect against migration of boundaries by ensuring that real practice reflects practice as described in guidelines. Audit identifies where migrations from safe practice are occurring, but it is only through a process of quality improvement or changing unworkable guidelines that these migrations can be corrected.

Anaesthetic care

A decision about the purpose of transfer to theatre and urgency of any birth should be made together with the anaesthetist before transfer to theatre. The degree of urgency should be reviewed on entering theatre before the WHO check, and the obstetrician should confirm the degree of urgency directly to the anaesthetist.

Baby deaths in the UK
The national picture for 2017

MBRRACE-UK
Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

760,169 births
of babies delivered from 24 weeks of pregnancy, excluding terminations of pregnancy

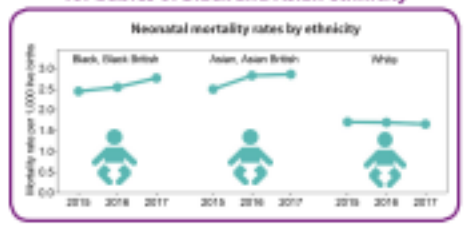
2,840 stillbirths — **1,267** neonatal deaths

Overall reduced mortality rates between 2013 and 2017

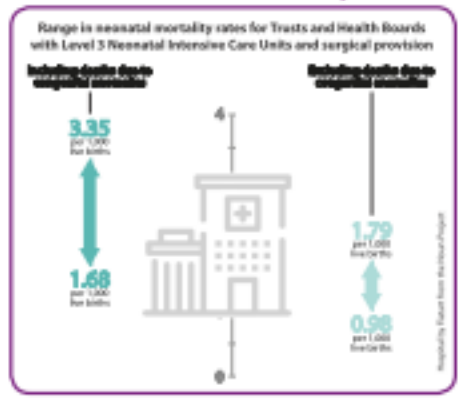
Largest fall in mortality rates in babies delivered at term

* in 2017 compared with 2013
† a baby born at any time during pregnancy who lives, even briefly, but dies within 4 weeks of birth
‡ between 37+0 and 41+6 weeks of pregnancy
§ between 24+0 and 36+6 weeks of pregnancy

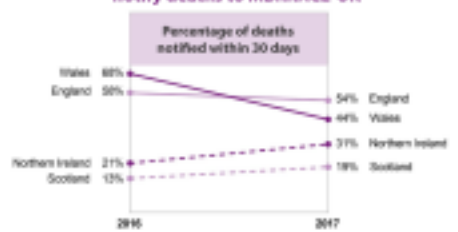
Neonatal mortality rates remain high for babies of Black and Asian ethnicity



Congenital anomalies account for wide variation in neonatal mortality rates



Reduced variation in the time taken to notify deaths to MBRRACE-UK



Only **half of deaths** were notified within the MBRRACE-UK benchmark period of 30 days

Baby deaths in the UK

The national picture for 2017

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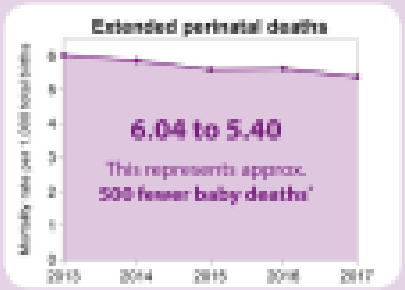
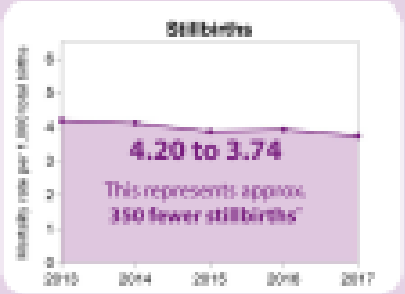
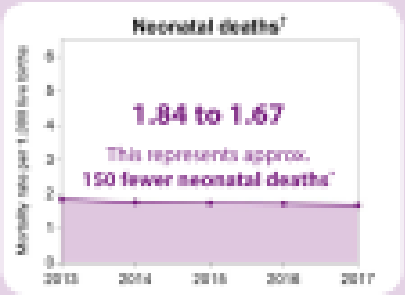
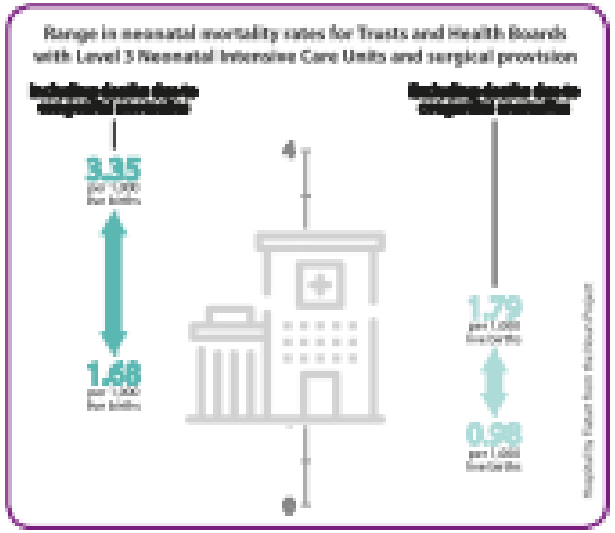


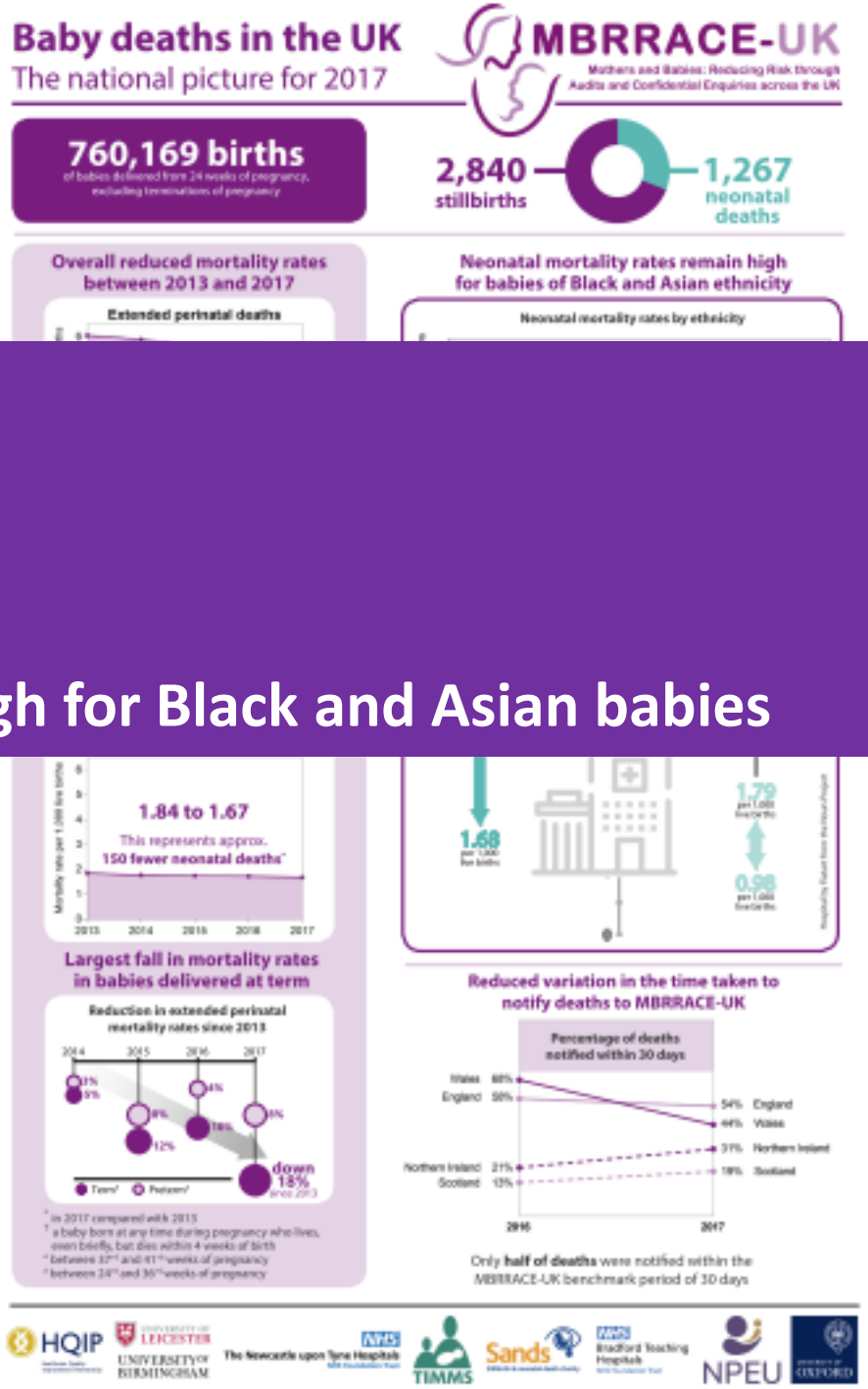




Neonatal mortality rates remain high for babies of Black and Asian ethnicity

Congenital anomalies account for wide variation in neonatal mortality rates





- ↓ perinatal death
- ↓ stillbirth
- ↓ intrapartum stillbirth
- ↓ unexplained stillbirth
- Mortality rates remain high for Black and Asian babies

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Thank you