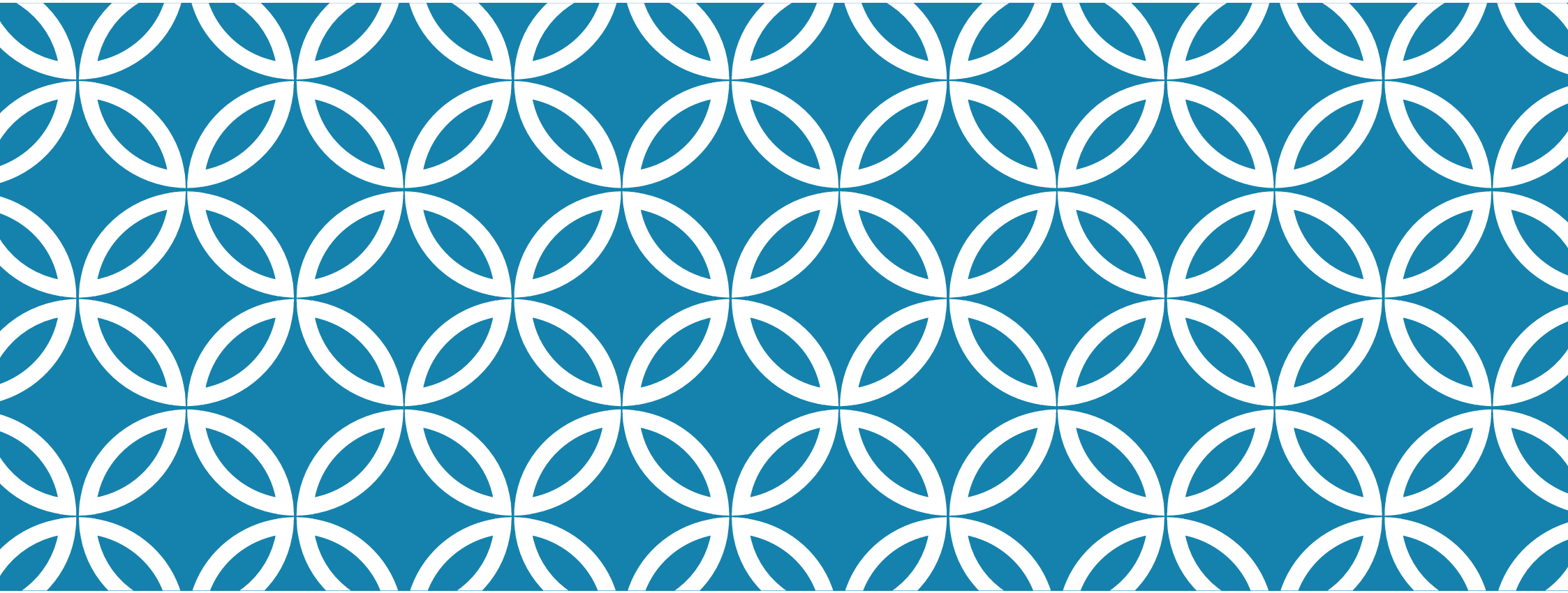
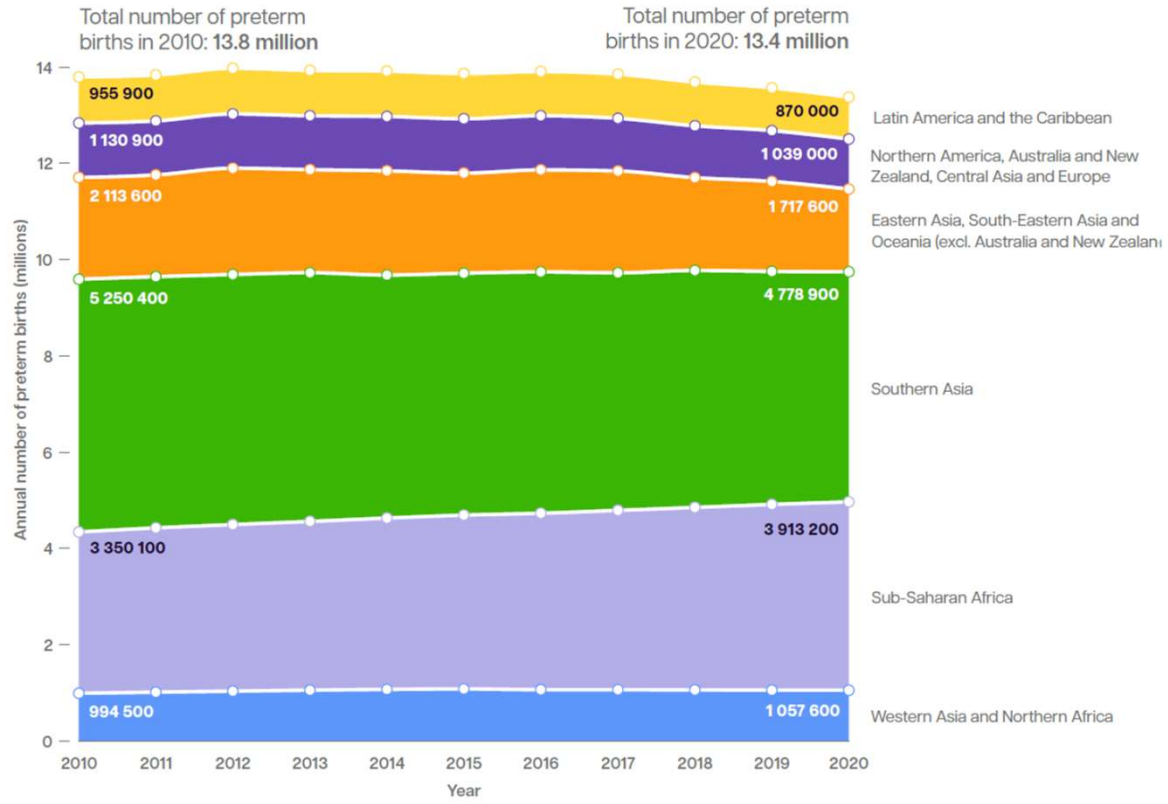
PREVENTING PRETERM BIRTH: ENHANCING OUTCOMES FOR PREEMIES



BACKGROUND

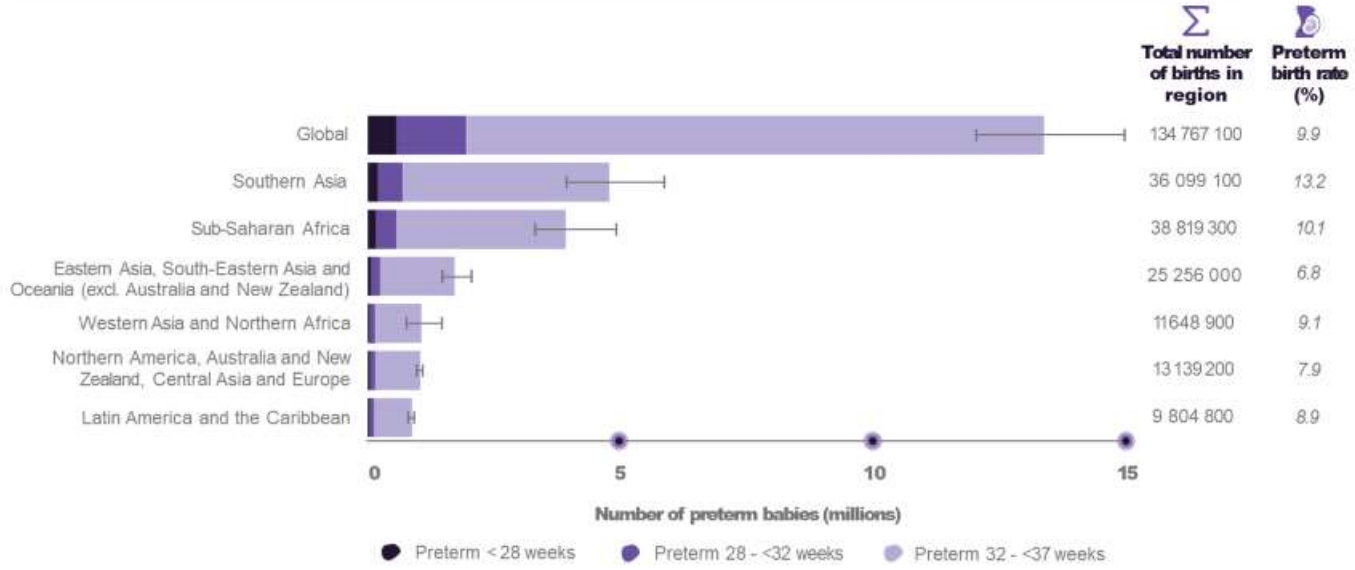
PRETERM BIRTH IS THE PRIMARY CAUSE OF INFANT MORBIDITY AND MORTALITY AND MORTALITY UNDER 5

FIGURE 2.2 Trends in annual number of preterm births by SDG region, 2010–2020



Data from WHO and UNICEF preterm birth estimates, Ohuma et al. (1).
Source: Lawn et al. (12)

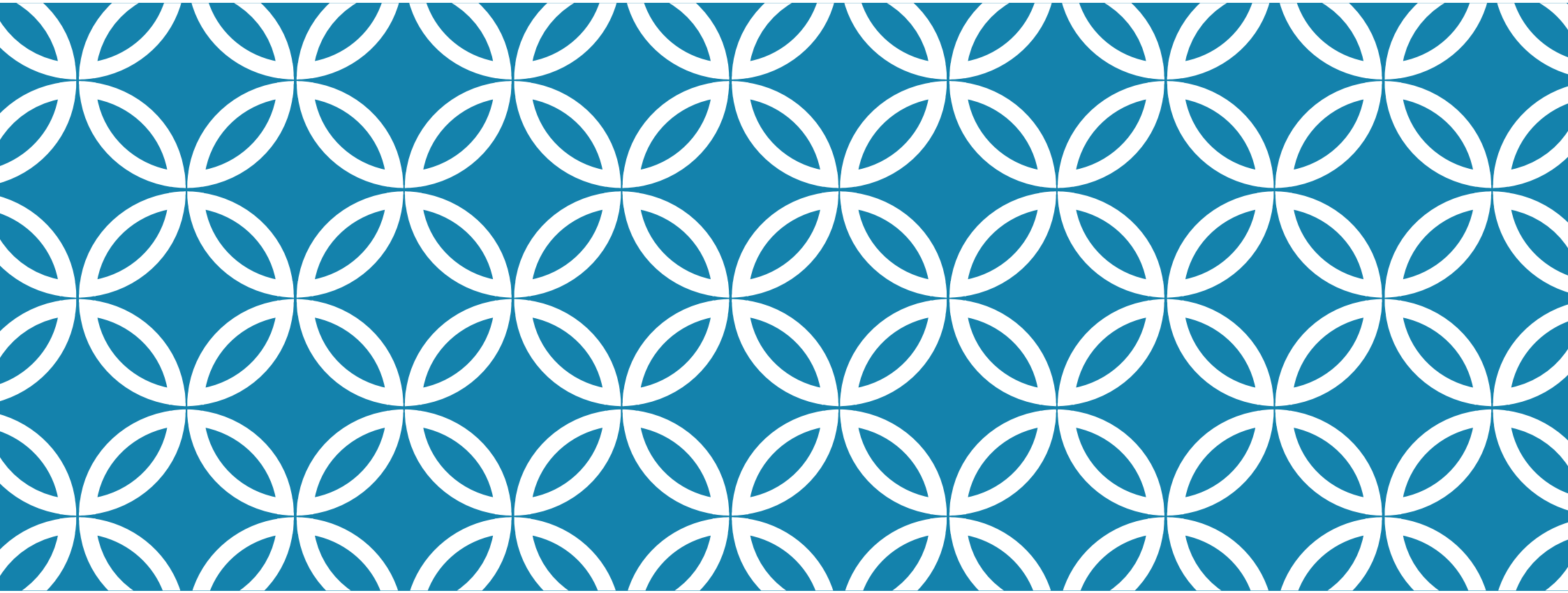
FIGURE 2.4 Preterm birth by gestational age and region in 2020



PRETERM BIRTH RATES

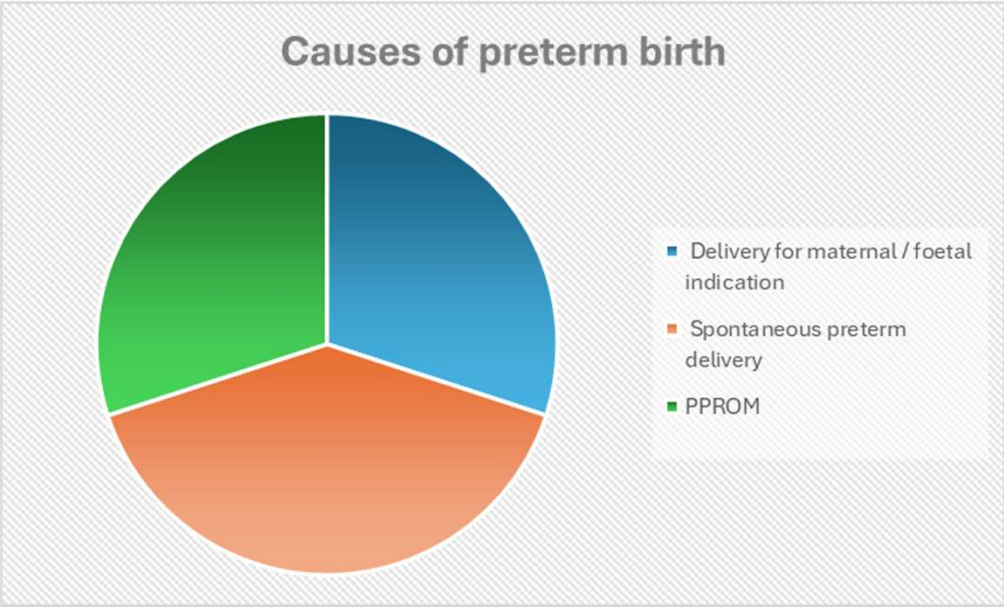
SUSTAINABLE DEVELOPMENT GOAL 3.2

By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births.



CAUSES

CAUSES OF PRETERM BIRTH



CAUSES OF SPONTANEOUS PRETERM BIRTH

Biology of control of human birth is complex and only limited information can be obtained from animal studies.

Preterm birth is one syndrome with many causes.

Basic biological mechanism – early inflammatory activation pathway

Shift in signalling between anti-inflammatory and pro-inflammatory response in preterm labour activation.

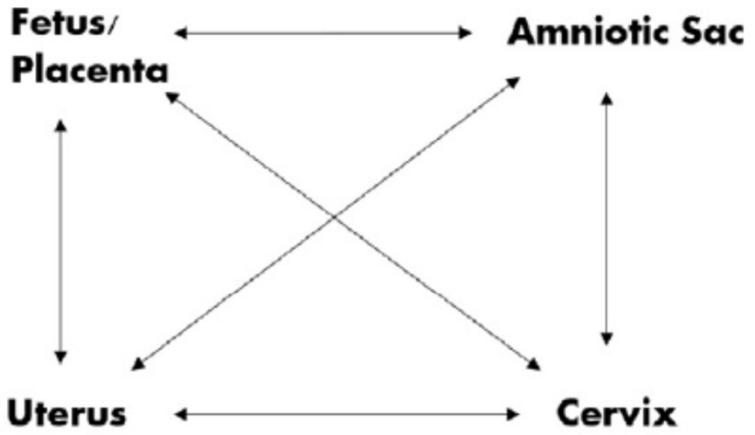
Lack of knowledge about SPB and even normal pregnancy

- Difficult to obtain tissue from pregnancies
- Limited information from animal models

Factors that can affect each "compartment"

Behaviors
Bleeding
Cervical dysfunction
Demographics
Environment
Fetal/maternal HPA axis
Genetics
Infection/inflammation
Microbiome
Race/ethnicity
Socioeconomics
Mechanical forces (stretch)
OTHER

The Complex Relationship of the "Compartments"



CAUSES OF PRETERM BIRTH

Risk factors	Examples
Age at pregnancy and pregnancy intervals	Teenage pregnancy, advanced maternal age, interpregnancy interval < 6 months
Multiple pregnancies	Twins and multiple gestation due to assisted reproduction
Infection	UTI, asymptomatic bacteriuria, Malaria, chorioamnionitis, syphilis, bacterial vaginosis
Underlying chronic medical conditions	Diabetes, hypertension, anaemia, asthma, HIV, thyroid disease
Nutritional	BMI < 19, micronutrient deficiencies – iron, zinc and folate
Lifestyle and work related	Smoking, alcohol abuse, recreational drug abuse, excessive physical labour, night shift

CAUSES OF PRETERM BIRTH

Environment	Exposure to air pollution, excessive heat stress
Maternal psychological health	Depression, stress, Gender based violence
Genetic and other	Family history, Congenital abnormalities, IUGR, periodontal disease
Vascular abnormalities	Uteroplacental ischaemia/ decidual haemorrhage
Uterus and cervix	Uterine overdistension, incompetent cervix, Pathology of Cervix
Hormonal	Progesterone deficiency
Immune	Allograft rejection, allergic phenomena

CAUSES OF PRETERM BIRTH: GENETICS

Duration of gestation determined by interaction between maternal and foetal genome.

Genome wide association studies from birth registries in different countries have identified genomic loci associated with duration of pregnancy and preterm birth.

Lack of large samples in African populations limits understanding of preterm birth genetics in this population

MICROBIOME

The vaginal microbiome varies considerably among normal individuals – influenced by factors e.g. menstruation, age, sexual activity.

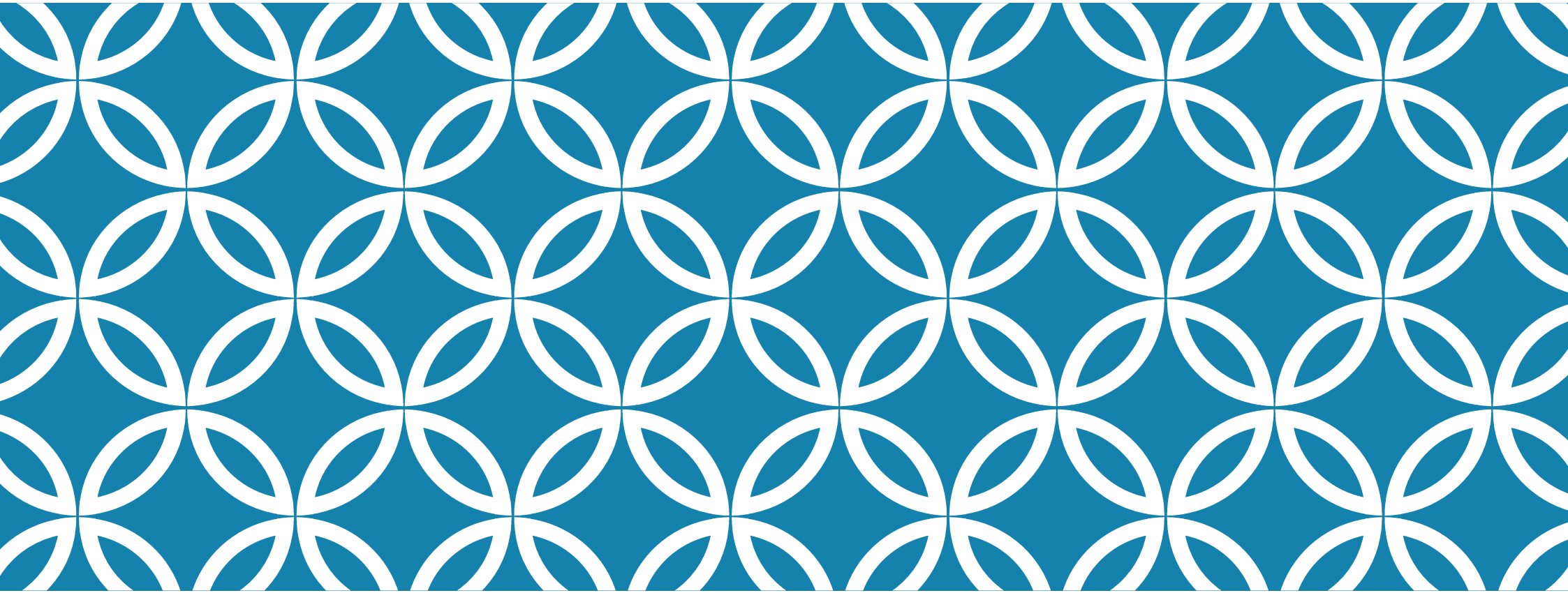
Vaginal microbiome alters in pregnancy and probably has a role in maintaining the pregnancy.

Link between preterm birth and microbiome of “sterile” tissues e.g. placenta.

- Microbial role possibly a trigger for preterm birth.

No single bacteria or microbial community has yet been linked with preterm birth.

Ongoing research, potential for diagnosis and intervention



PREDICTION

ROLE OF THE CERVIX IN GESTATION

Cervix primarily collagen, but internal sphincter 60% smooth muscle.

- Appears to be a specialised sphincter similar to urethra

Preterm labour associated with cervical shortening and remodelling of sphincter

- ? Collagen defect
- ?Infection
- ?early triggering of sterile inflammatory cascade

PREDICTION OF PRETERM BIRTH

Transvaginal ultrasound to measure cervical length

Biomarkers

- Serum CRP and IL6
- Cervical fibronectin
  - to confirm or refute risk of PTB in women with equivocal cervical length.

MACHINE LEARNING AND PREDICTION OF PRETERM BIRTH

Ongoing research into using machine learning to develop predictive models for risk of preterm birth using:

Cervical length

Cervical fibronectin

Cervical angle

Demographics

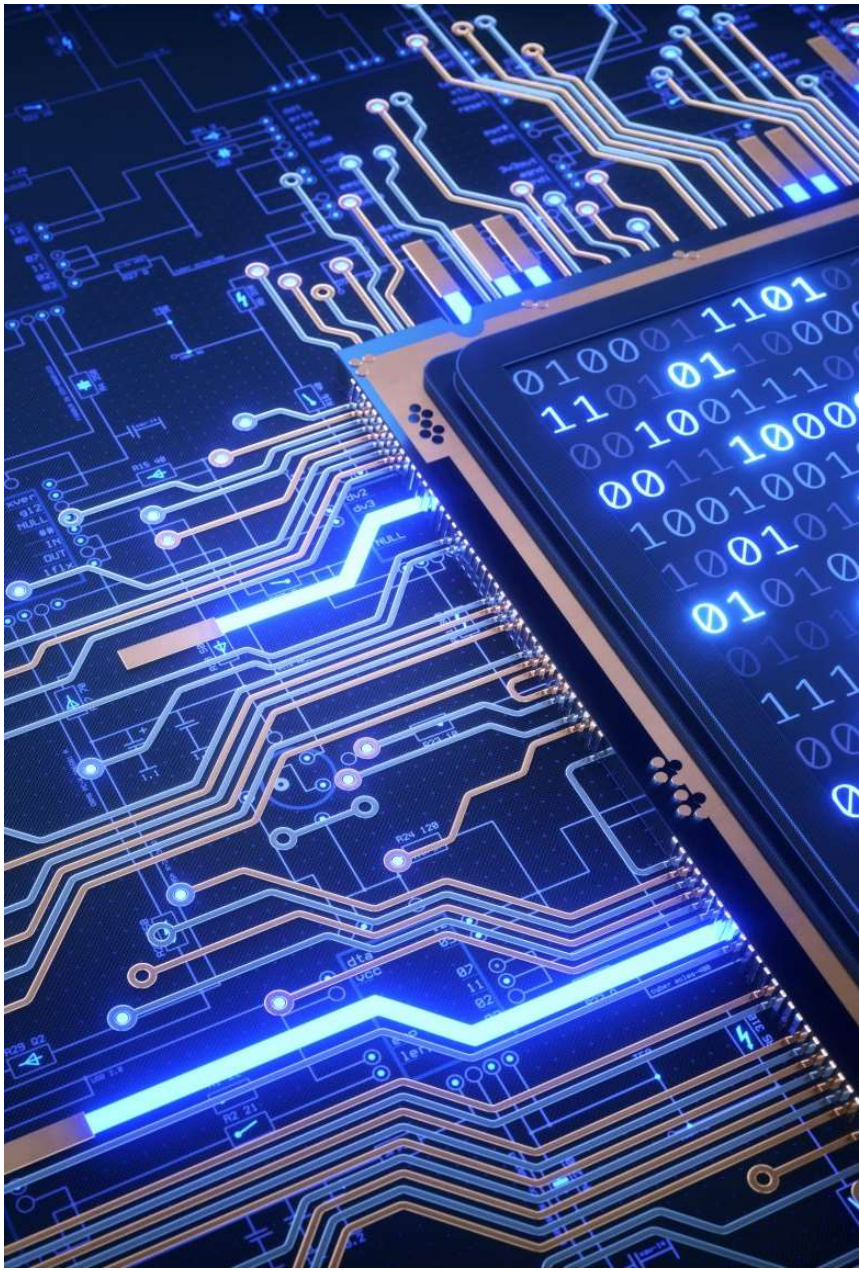
Electrohysterography

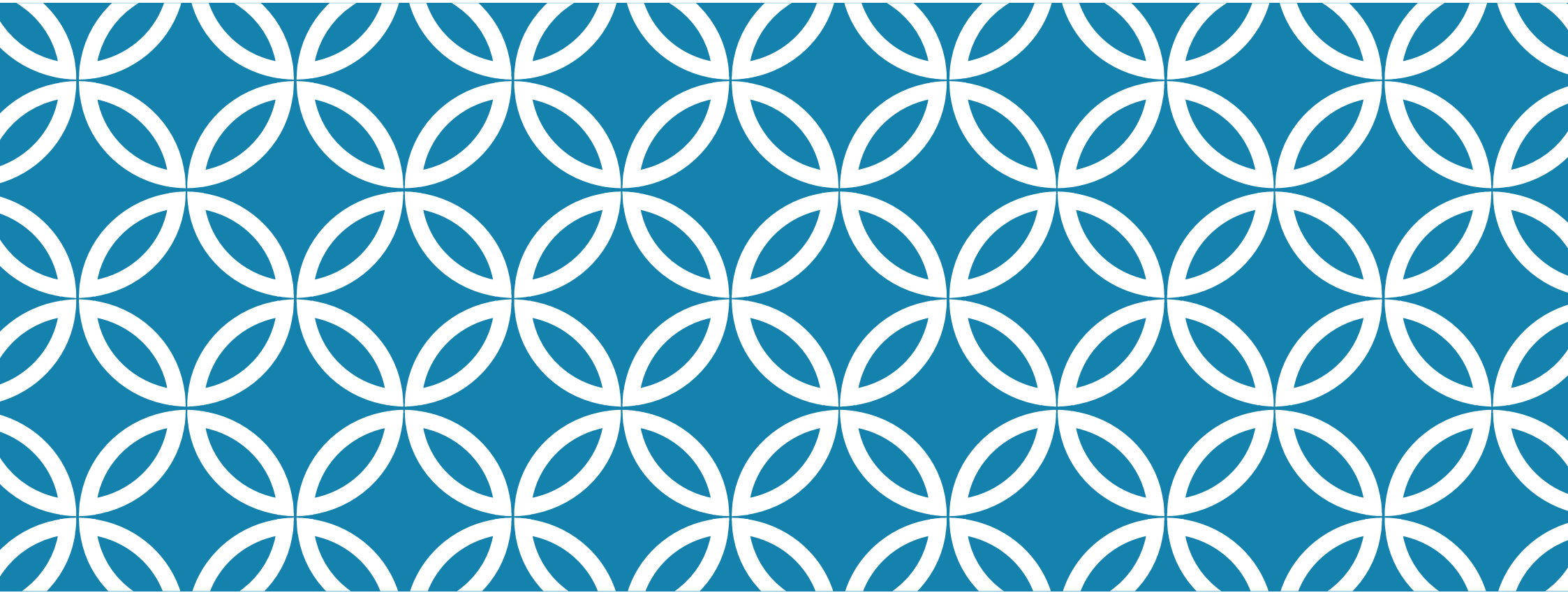
Maternal risk factors

Genetics

Micro-organisms

NB under representation of African data sets





PREVENTION

PREVENTION OF PRETERM LABOUR: CERVIX

Singleton pregnancies

- Weekly progesterone
  - Effective in decreasing preterm birth in a subset of women with previous PTB and cervical shortening
  - Also improves outcome of preterm neonate
  - Mechanism unclear and why it is not effective in all women.
- Daily vaginal progesterone for women without history of PTB and incidental cervical shortening
- Cervical cerclage
  - History of PTB and cervical shortening
- Cervical pessary

Multiple pregnancy

- No clear interventions to prevent preterm birth

REVIEW OF COCHRANE REVIEWS: INTERVENTIONS IN PREGNANCY TO PREVENT PRETERM BIRTH

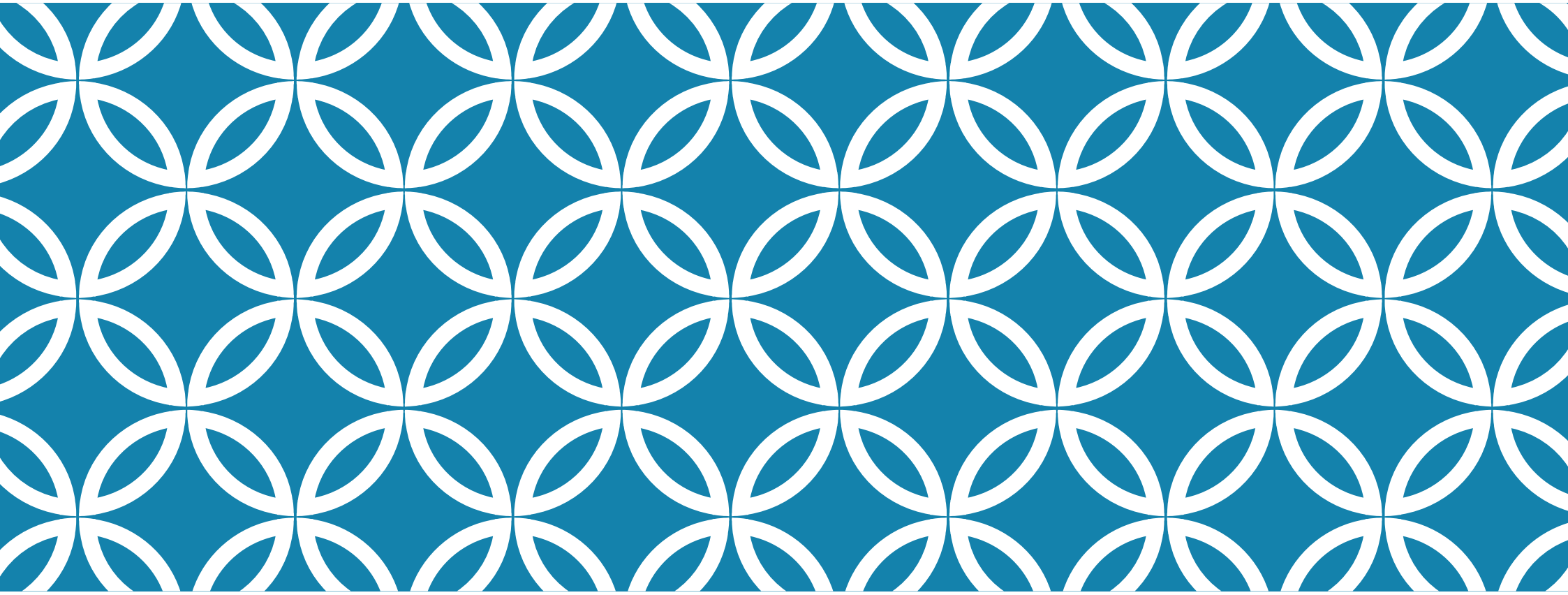
Clear Benefit:

- Midwife led continuity of care models (also decreased perinatal death)
- Screening for LGUT infection in pregnant women < 37 weeks without signs of labour, bleeding or infection.
- Zinc supplementation in women without systemic illness
- Cervical cerclage only effective in singleton pregnancy in women with high risk of PTB

REVIEW OF COCHRANE REVIEWS: INTERVENTIONS IN PREGNANCY TO PREVENT PRETERM BIRTH

Possible Benefit:

- Group antenatal care
- Vitamin D supplementation in otherwise well mothers
- Antibiotics for women with asymptomatic bacteriuria
- Pharmacologic interventions to quit smoking



IMPROVED OUTCOME

WHO GUIDELINES TO IMPROVE PRETERM BIRTH OUTCOMES (2015)

Antenatal corticosteroids recommended for pregnant women at risk of delivery between 24- and 34-weeks' gestation.

- 24 mg Dexamethasone or betamethasone in divided doses.
- PPROM, gestational diabetes and maternal hypertension are not a contraindication.
- Don't use if there is evidence of chorioamnionitis.
- Repeat dose if delivery has not occurred within 7 days.
- Not recommended for elective CS 34 to 37 weeks

ANTENATAL CORTICOSTEROIDS

First published 1972

SA 2017 –ACS coverage of preterm births 44%

ANTENATAL CORTICOSTEROIDS (WHO 2022)

ACT trial (2015) found that upscaling use of steroids in LMICS could harm mothers and babies, particularly an increase in infection

WHO then conducted ACTION-1 trial to determine use of ACS in LMICS.

WHO found that a course of ACS reduced neonatal death and did not cause harm to mother or baby

ANTENATAL CORTICOSTEROIDS (WHO 2022 CONT)

WHO recommend ACS therapy be used in mother at risk of preterm birth between 24 and 34 weeks gestation provided the following criteria are met:

- Gestational age assessment can be accurately determined.
- There is a high likelihood of preterm birth within 7 days
- There is no clinical evidence of maternal infection.
- Adequate childbirth support is available, including the ability to safely manage preterm labour and birth.
- The preterm neonate can receive adequate care including resuscitation, KMC, thermal care, feeding support, infection treatment and respiratory support, including CPAP as needed

ANTENATAL CORTICOSTEROIDS COCHRANE 2020

A single course of antenatal corticosteroids to accelerate foetal lung maturation in pregnant women decreases:

- Perinatal death
- Neonatal death
- Respiratory distress syndrome

Corticosteroids probably decrease:

- Intraventricular haemorrhage
- Developmental delay in children

Benefit of steroids is the same in high, middle and low income settings

Any steroid (even incomplete course) has benefit

TOCOLYTICS

Tocolytics are not recommended in imminent preterm delivery to improve neonatal outcome

Tocolysis with calcium channel blockers (nifedipine), betamimetics, magnesium sulphate, oxytocin receptor antagonists all effective relative to placebo

Prolonging preterm gestation for a few days does not impact outcome, but tocolysis allows time for administration of steroids and transfer to higher level of care

WHO RECOMMENDATIONS TO IMPROVE PRETERM BIRTH OUTCOMES (CONT)

MgSO4 is recommended in imminent preterm delivery below 32 weeks gestation to prevent CP

- Probably also decreases severe IVH

Routine antibiotic use is not recommended in pregnant women with imminent preterm delivery with intact membranes and no signs of infection

Antibiotics (erythromycin) are recommended in women with PPROM

Routine delivery of preterm infants by CS is not recommended, irrespective of presentation (cephalic / breech)

WHO RECOMMENDATIONS TO IMPROVE PRETERM BIRTH OUTCOMES (CONT)

Thermal care

- Kangaroo care for all neonates < 2000 grams who are clinically stable.
- Unstable infants should be nursed in a neutral thermal environment.
- Plastic wrapping for transfer of preterm babies to prevent heat loss.

CPAP as soon as respiratory distress syndrome is diagnosed.

Surfactant for preterm infants who are intubated and ventilated within two hours of birth

Start at 30% supplemental oxygen, only increase if preterm neonate bradycardic or hypoxic

PREGNANCY INTERVENTIONS TO IMPROVE OUTCOMES IN PRETERM NEONATES

No clear evidence:

- Maternal probiotic supplementation

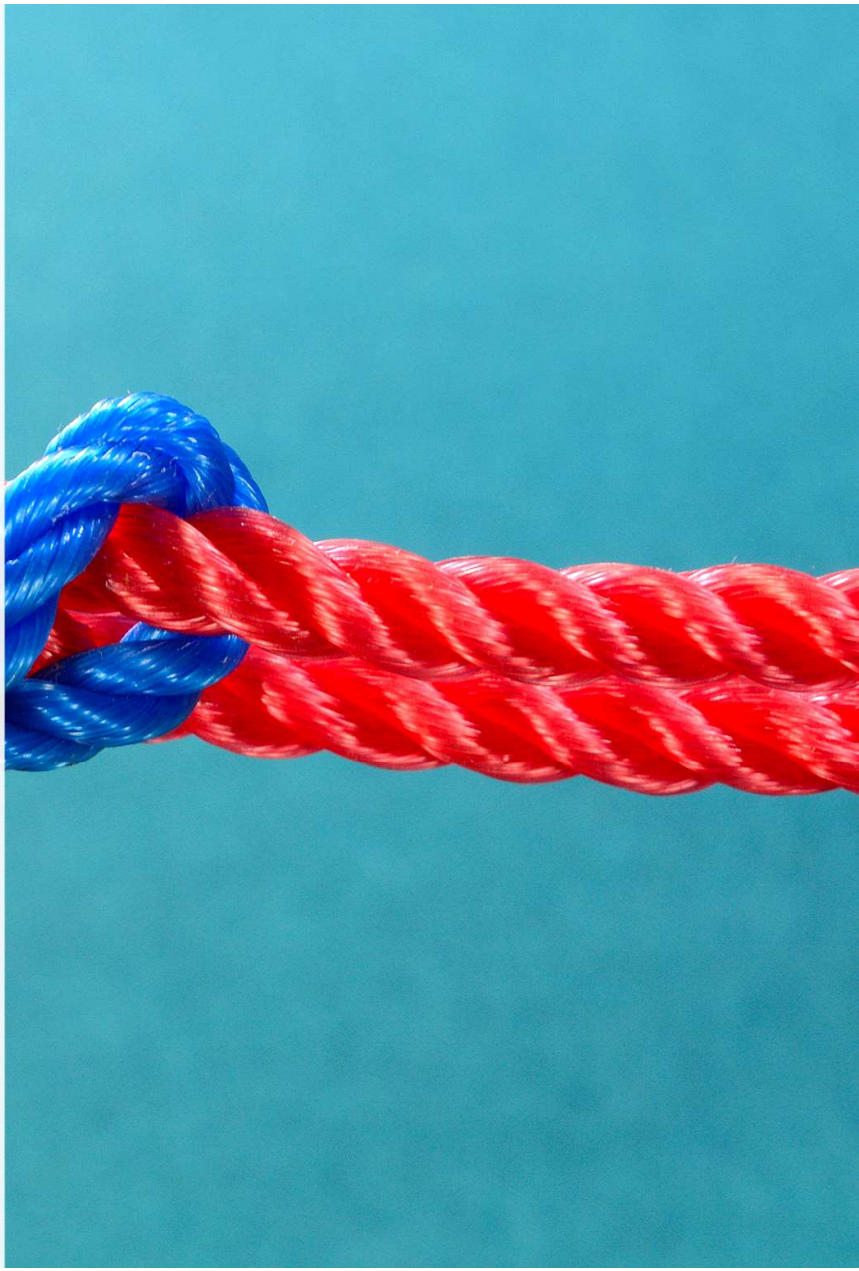
Some evidence, but research ongoing:

- Maternal immunisation for HiB and influenza
- NB Wits research into maternal GBS immunisation

COCHRANE DELAYED CORD CLAMPING

Delayed, rather than early, cord clamping may reduce the risk of death before discharge for babies born preterm.

There is insufficient evidence to show what duration of delay is best,

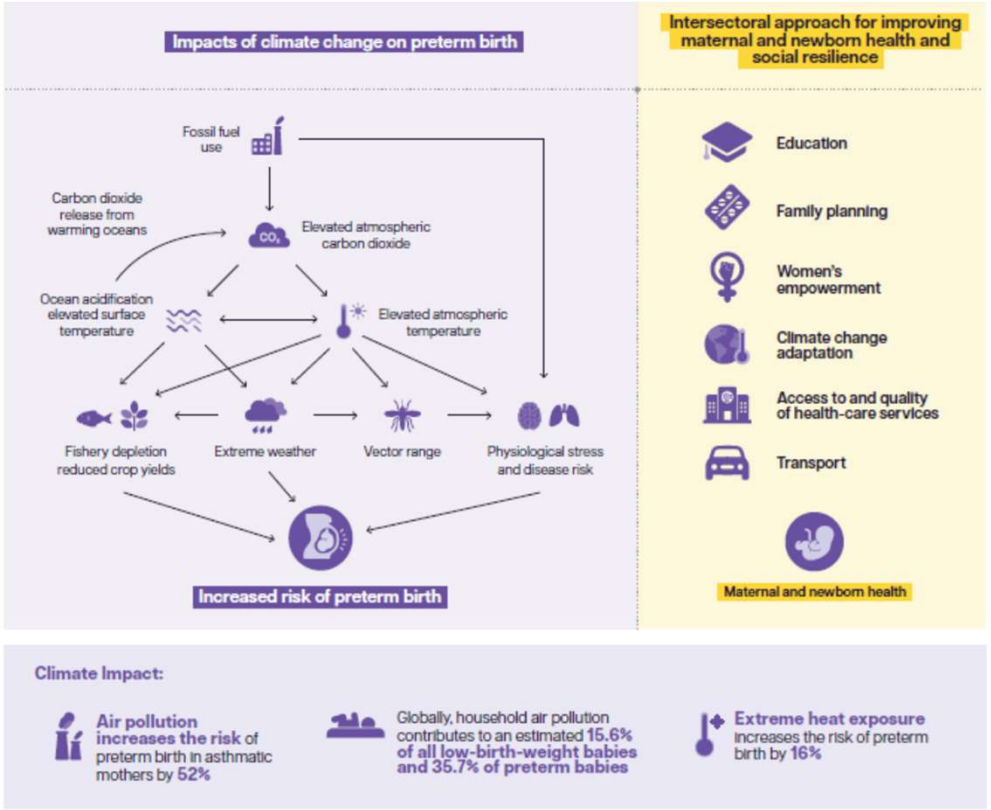


ANTENATAL INTERVENTIONS TO PREVENT SB, FOETAL LOSS AND PERINATAL DEATH (REVIEW OF COCHRANE REVIEWS)

Clear benefit

- Balanced protein/ energy supplementation
- Prevention of malaria (insecticide treated mosquito nets)
- Midwife led antenatal care
- Training traditional birth attendants
- Computerised antenatal CTG

CLIMATE CHANGE AND PRETERM BIRTH

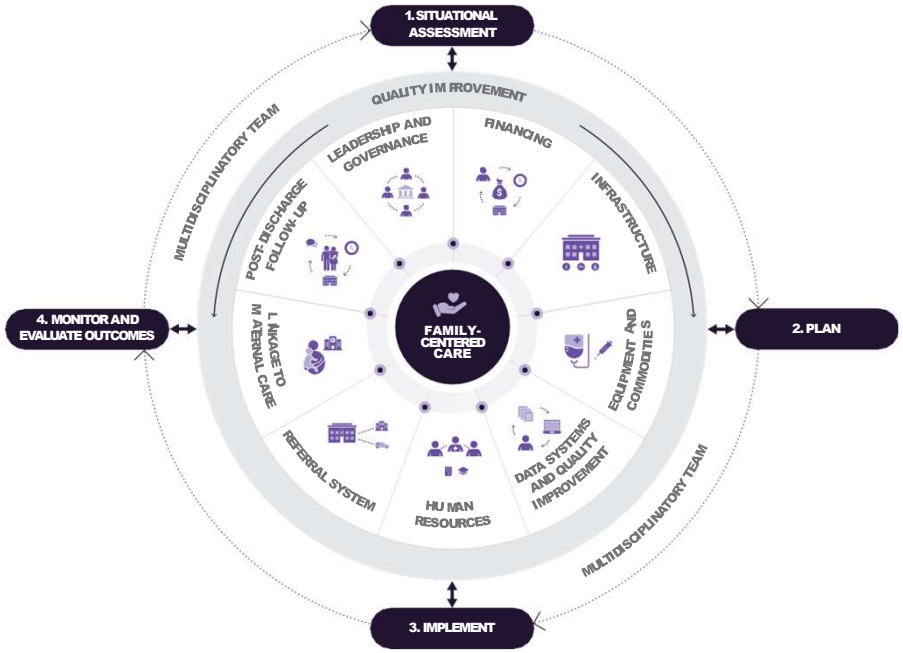


FIGO PREMPREP-5 INITIATIVE

- Five simple initiatives that can be implemented globally to improve outcomes of preterm infants:
  - Antenatal corticosteroids
  - Intrapartum magnesium sulphate
  - Delayed cord clamping by one minute
  - Early feeding with breast milk
  - Immediate Kangaroo Mother Care


Decade of action
on preterm birth
PMNCH for Women's Children's and Adolescents' Health
World Health Organization
unicef
UNFPA

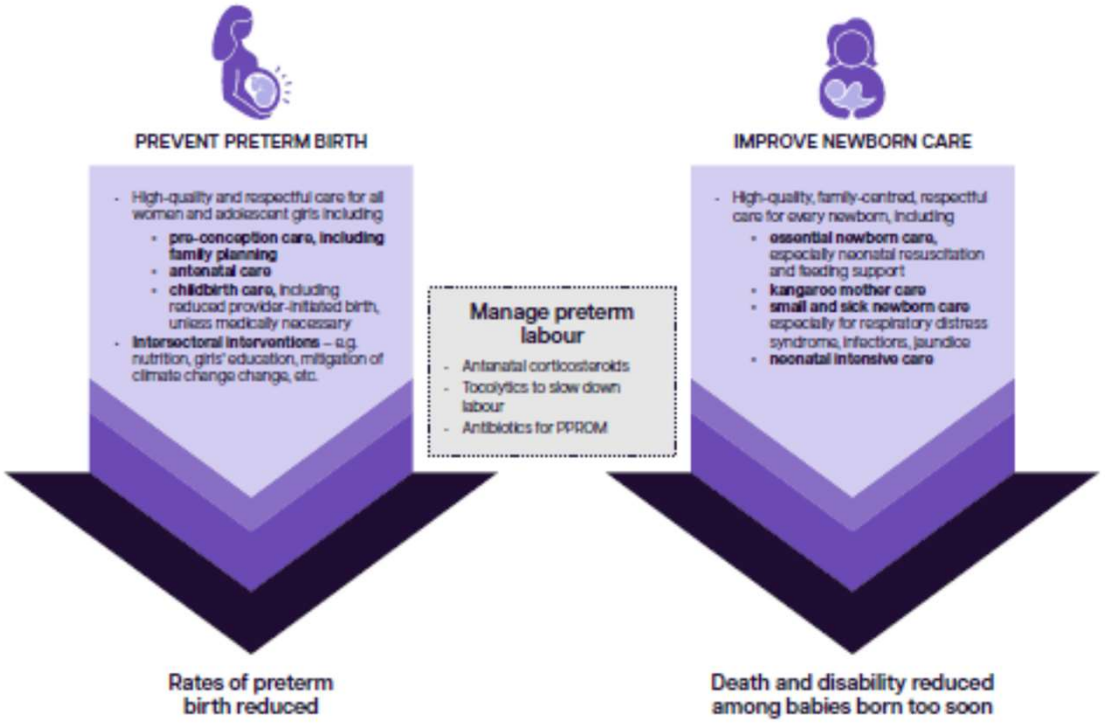
FIGURE 5.4 Implementation of small and sick newborn care (with the baby and their family at the centre)



Four steps adapted from Knippenberg et al. (23). Wheel adapted from (24) and the WHO-UNICEF 10 core component model for small and sick newborn care scale-up (22).

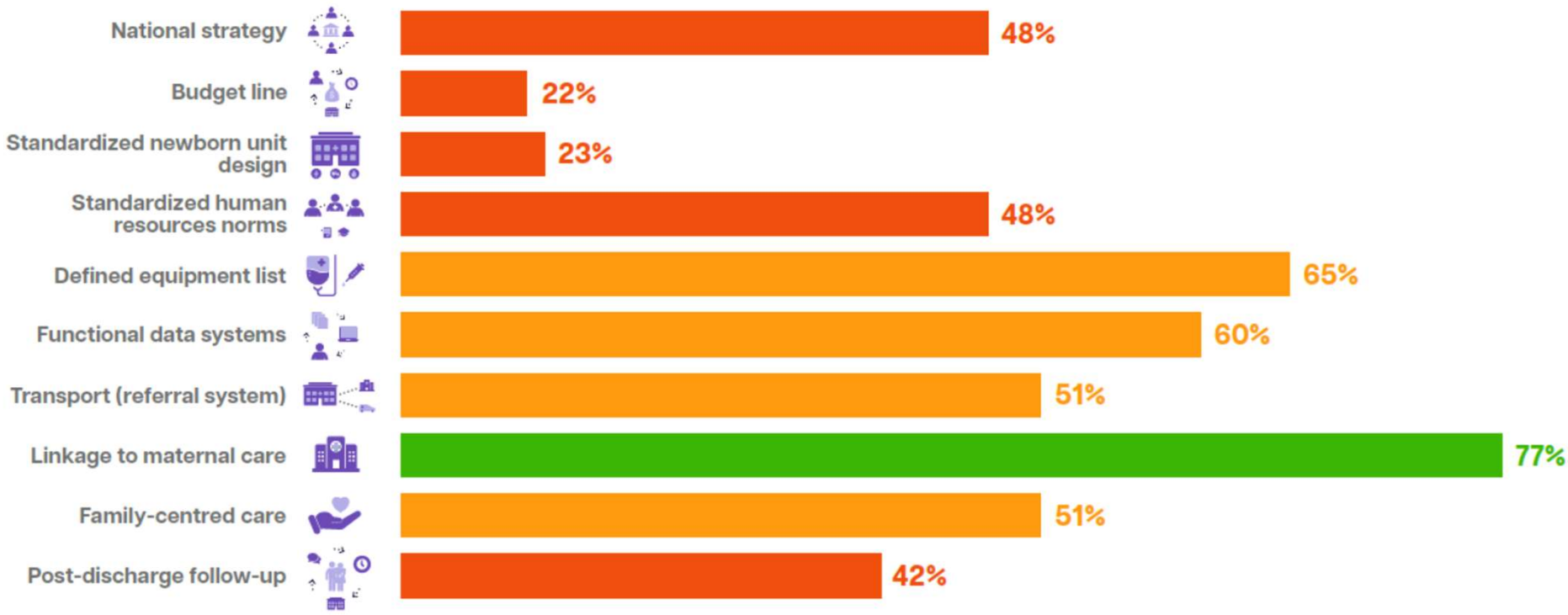
Two priority tracks

FIGURE 7.1 Twin tracks to reduce the burden of preterm birth and unlock human capital



PPROM preterm prelabor rupture of membranes

FIGURE 5.5 Status of the WHO/UNICEF 10 core component model for scaling up small and sick newborn care in 106 countries, based on reporting for ENAP/EPMM




The more things change, the more they are the same.
Alphonse Karr
BrainyQuote

CONCLUSION

Preterm birth is a health priority in South Africa

Even in the new world of AI, simple interventions have significant impact

- Corticosteroids
- Magnesium sulphate
- Delayed cord clamping
- KMC
- Breastfeeding

THANK YOU

REFERENCES

1. WHO recommendations on interventions to improve preterm birth outcomes 2015
2. Best practice and research clinical obstetrics and gynaecology 2018.
3. Effective and simple interventions to improve outcomes of preterm infants worldwide: The FIGO Premprep -5 initiative Hall et al 2023
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5. Cochrane review library