

Preventing Preterm Birth: What Can Be Done with What We Know Now?



James A. Litch MD, DTMH

Every Premie-SCALE

Global Alliance to Prevent Prematurity and Stillbirth (GAPPS), Seattle Children's

18 February 2015



Overview

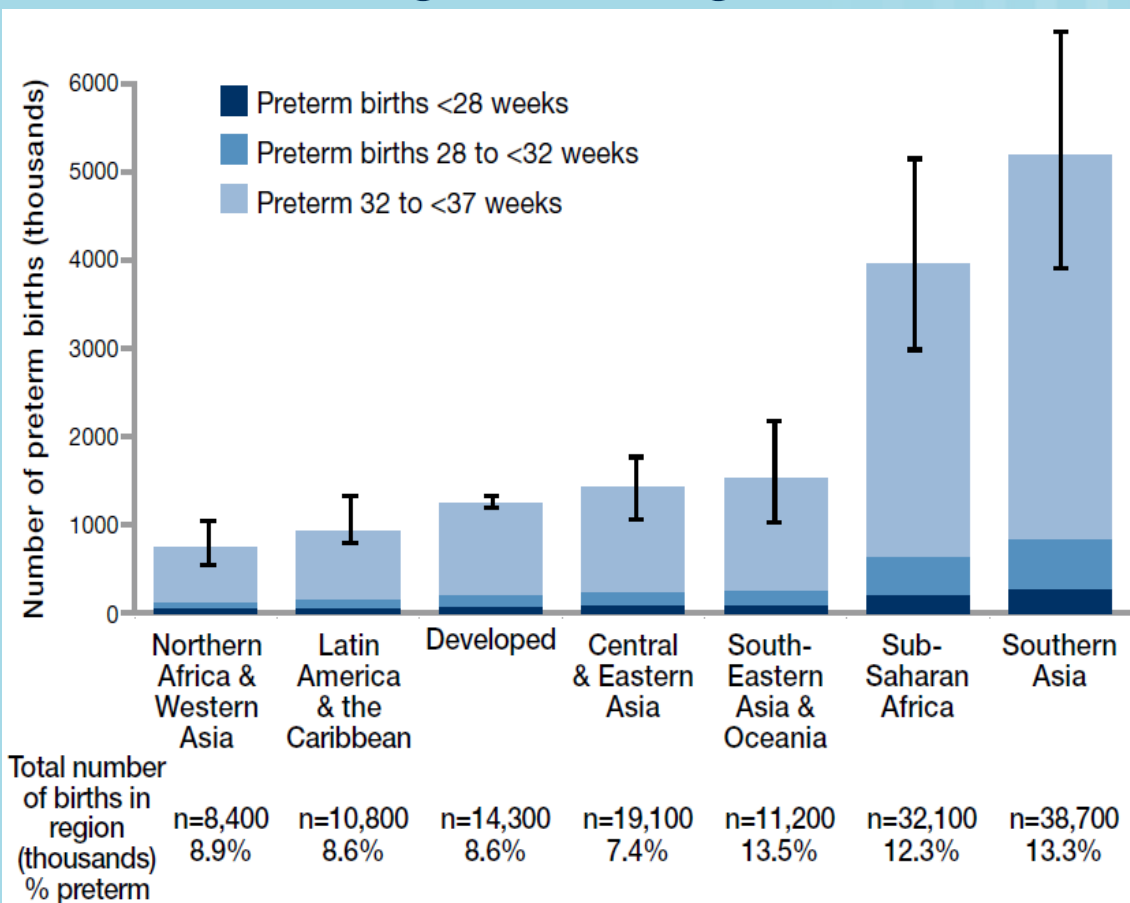
High level review of the state of the evidence for interventions to prevent preterm birth.

How do interventions that prevent preterm birth compare with PTL management and PTB care?

Explore a rationale for how to move forward given what we know.



A Syndrome of PTB - Preterm Births by Gestational Age and Region for 2010



- 75% of preterm deaths are in Sub-Saharan Africa and Southern Asia.

- 85% of PTB are born from 32-37 weeks.

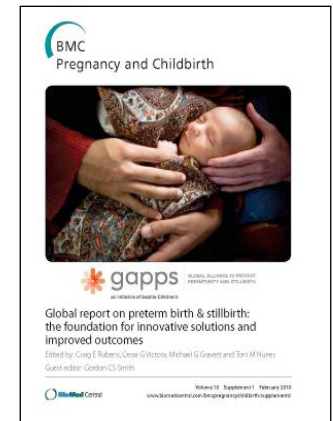
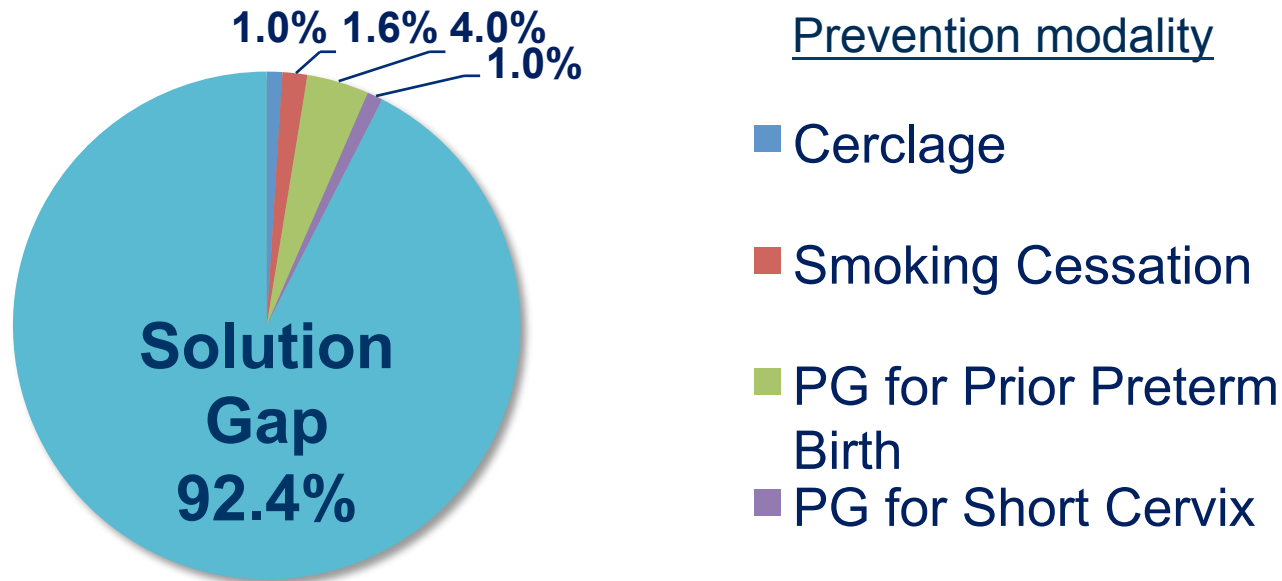
- Level of care is determined by gestational age.

Preterm Prevention: Social, Biological, and Clinical Risk Factors for Preterm Birth

- Chorioamnionitis
- Bacterial vaginosis
- Periodontal disease
- Maternal morbidity
- Incompetent cervix
- Low pre-pregnancy weight
- Poor weight gain
- Twins, triplets
- Congenital malformations
- Genetics
- Prior preterm birth
- Poor nutrition
- Poor pregnancy weight gain
- Maternal age
- Inter-pregnancy interval
- Marital status
- Poverty
- Black race
- Tobacco use
- Substance use
- Stress
- Physical exertion

Preterm Prevention: The Need for New Solutions

Percentage of preterm births preventable by current modalities in HICs



Not included: reduction of non-medically indicated induced preterm birth, or the impact on readily available contraception for birth timing and spacing.

Risk factors and associated interventions before and between pregnancy

EVERY
PREEMIE
SCALE

How Great Is The Risk?		
Pregnancy in adolescence	+	Increased prevalence of anemia, pregnancy-induced hypertension, low birthweight, prematurity, intra-uterine growth retardation and neonatal mortality
Birth spacing	+	
Short intervals		PTb: OR 1.45, LBW: OR 1.65
Long intervals		PTb: OR 1.21, LBW: OR 1.37
Pre-pregnancy weight status	+	
Underweight		PTb: OR 1.32, LBW: OR 1.64
Overweight & obesity		PTb: OR 1.07 Maternal overweight is a risk factor for many pregnancy complications including hypertensive disorders, gestational diabetes, postpartum hemorrhage, stillbirth, congenital disorders Both underweight and overweight women have a higher chance for requiring obstetric intervention at delivery
Micronutrient deficiencies	+/-	
Folic acid		Folic acid deficiency is definitively linked to neural tube defects (NTDs) in newborns
Iron		Anemia increases the risk for maternal mortality, low birthweight, preterm birth and child mortality
Chronic diseases	+	
Diabetes mellitus		Babies born to women with diabetes before conception have a much higher risk of stillbirths, perinatal mortality, congenital disorders, as well as spontaneous pregnancy loss, preterm labor, hypertensive disorders, and delivery by cesarean birth
Hypertension		
Anemia		A study shows that anemia before conception increases the risk of low birthweight (OR 6.5)
Poor mental health (especially depression) and Intimate partner violence	++	Increased risk for preterm birth, low birthweight and depression during pregnancy and the postpartum period IPV-PTb OR: 1.37, LBW OR: 1.17 Also increased risk for spontaneous pregnancy loss, stillbirth, gynecological problems including sexually-transmitted infections, depression
Infectious diseases	++	
STIs - syphilis HIV/AIDS Rubella		Infectious diseases increase the risk for spontaneous pregnancy loss, stillbirths and congenital infection
Tobacco use	++	A single study shows risk for PTb OR: 2.2 Smoking increases the risk for spontaneous pregnancy loss, placental disorders, congenital malformations, sudden infant death syndrome, stillbirths and low birth weight

For magnitude of risk:

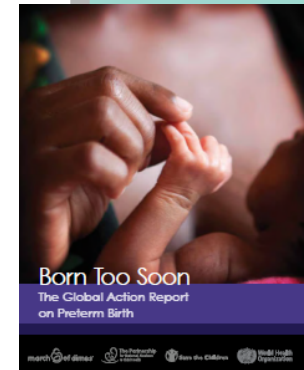
++ means strong evidence of risk and implicated in biological pathways leading to preterm birth and low birthweight

+ means moderate evidence of risk on preterm birth and low birthweight

+/- means weak evidence of risk on preterm birth and low birthweight

Acronyms used: PTb = preterm birth; OR = odds ratio; IPV = intimate partner violence

Source: Barros et al., 2010; Bhutta et al., 2011a; Goldenberg et al., 2008; Iams et al., 2008



Preconception and ANC Interventions

EVERY
PREEMIE

	Stillbirth	Preterm birth	Perinatal mortality	Small for gestational age	Neonatal mortality
Preconception and antenatal interventions					
Iron supplementation	..	0.88 (0.77-1.01)	0.90 (0.68-1.19)
Iron and folic acid supplementation	..	1.55 (0.40-6.00)	0.81 (0.51-1.30)
Multiple micronutrient supplementation	0.95 (0.85-1.06)	0.99 (0.97-1.02)	0.96 (0.84-1.10)	➔ 0.87 (0.83-0.92)	1.01 (0.89-1.16)
Calcium supplementation	..	➔ 0.76 (0.60-0.97)	0.90 (0.74-1.09)	1.01 (0.84-1.21)	1.07 (0.39-2.95)
Balanced energy protein supplementation	➔ 0.62 (0.40-0.98)	0.96 (0.80-1.15)	..	➔ 0.68 (0.49-0.89)	0.63 (0.37-1.06)
Tetanus toxoid immunisation	➔ 0.06 (0.02-0.2)
Haemophilus influenzae type b vaccine	1.69 (0.41-6.94)	1.37 (0.20-9.16)
Influenza virus vaccine	..	0.77 (0.36-1.64)
Syphilis screening and treatment	➔ 0.18 (0.10-0.33)	➔ 0.36 (0.27-0.47)	➔ 0.20 (0.13-0.32)
Intermittent preventive treatment for malaria in pregnancy	0.96 (0.72-1.27)	0.86 (0.62-1.21)	0.83 (0.66-1.05)	➔ 0.65 (0.55 - 0.77)	➔ 0.69 (0.49-0.98)
Insecticide-treated bednets	➔ 0.65 (0.55 - 0.77)	..
Maternal anthelmintic treatment	..	0.88 (0.43-1.78)	0.97 (0.68,1.40)
Lower genital infection screening and management					
Lower genital infection screening and management	..	➔ 0.55 (0.41-0.75)
Prophylactic antibiotics	..	0.96 (0.70-1.33)	0.80 (0.31-2.06)	1.29 (0.42-3.96)	..
Antibiotic prophylaxis for group b streptococcus colonisation	0.19 (0.01-3.82)
Antibiotics for bacterial vaginosis	..	0.88 (0.71-1.09)	0.71 (0.36-1.39)
Asymptomatic bacteriuria treatment	..	0.37 (0.10-1.36)
Periodontal disease management	➔ 0.49 (0.26-0.94)
Antihypertensive for mild-to-moderate hypertension	1.14 (0.60-2.17)	1.02 (0.89-1.16)	0.96 (0.60-1.54)	1.04 (0.84-1.27)	0.79 (0.14-4.34)
Magnesium sulphate for prevention of pre-eclampsia	0.99 (0.87-1.12)	..	0.98 (0.88-1.10)	..	1.16 (0.94-1.42)
Calcium supplementation for hypertension	0.90 (0.74-1.09)	➔ 0.76 (0.60-0.97)	0.86 (0.70-1.07)	1.05 (0.86-1.29)	..
Antiplatelets for pre-eclampsia	1.15 (0.88-1.49)	➔ 0.92 (0.88-0.97)	0.89 (0.74-1.08)	➔ 0.90 (0.83-0.98)	0.89 (0.64-1.22)
Preconception diabetes education	..	0.83 (0.62-1.12)	➔ 0.31 (0.19-0.53)
Optimum vs suboptimum glucose control	0.51 (0.14-1.88)	..	➔ 0.40 (0.25-0.63)
Education/psychotherapy to quit smoking	..	0.79 (0.52-1.21)
Nicotine replacement therapy	..	➔ 0.77 (0.61-0.97)
Incentives to quit smoking	..	0.49 (0.22-1.08)
Prenatal antidepressants	..	➔ 1.55 (1.38-1.74)

Source: Bhutta ZA et al, Lancet Every Newborn Series 2014

Using investments wisely – across the continuum of care

Prevention of preterm birth

- Preconception care package especially family planning
- Smoking cessation
- High risk pregnant women (PG to prevent recurrent preterm birth)
- Antenatal care package including nutrition
- Effective maternal childbirth care for obstetric complications

Management of preterm labor

- Prophylactic corticosteroids
- Antibiotics for pPROM
- Tocolytics to slow down labor

Premature newborn care

- Essential Newborn Care and Special Care for PT/LBW
- Neonatal resuscitation
- Continuous Skin-to-Skin Care
- Management of premature complications especially respiratory distress syndrome, infections and jaundice
- Comprehensive neonatal intensive care

Reduction of preterm birth

Mortality reduction among babies born preterm

The High Cost of Preterm Birth

- Estimated annual societal economic burden in the United States
>\$26.2 billion (\$51,600 for every infant born preterm)
- Average hospital length of stay

Term infant	1.5 days
Preterm infant	13 days

- Average first-year medical costs, including both inpatient and outpatient care

Term infant	\$3325
Preterm infant	\$32,325

1.

Source: Y. Oyelese, MFM, UTHSC



Estimated Lives Saved of Premature Babies if Universal Coverage of Care Interventions Achieved – LiST Analysis

Intervention reaching 95% coverage	Also saves mothers or other babies	By 2015		By 2025	
		% deaths averted	Lives saved	% deaths averted	Lives saved
Family planning*	M, SB, N	24	228,000	→ 32	345,000
Antenatal corticosteroids	N	40	373,000	→ 41	444,000
Antibiotics for pPRoM	N	9	85,000	9	101,000
Immediate assessment and simple care of all babies	N	5	44,000	5	53,000
Neonatal resuscitation	N (SB)	7	65,000	7	77,000
Thermal care	N	15	142,000	16	171,000
Kangaroo mother care	N	48	452,000	→ 48	531,000
Interventions implemented together	M, SB, N	81	757,000	84	921,000

Note: interventions marked with M will also save maternal lives, SB would avert stillbirth, and N will save newborns dying from causes other than preterm birth.

* Family planning scaled to 60% coverage or to a level whereby the total fertility rate is 2.5.

Note that obstetric care would also have an impact, but is not estimated separately

520,000 lives (55%) saved of premature babies if adequate management of preterm labor and birth.

921,000 lives (84%) saved if family planning included in model.

Where 15 million preterm babies receive care



Photo: GAPP/Seattle's Children

High-income countries
Access to full intensive care
(1.2 million preterm babies)



Photo: Bill & Melinda Gates Foundation/Frederic Courbel

Middle-income countries
Neonatal care units
(3.8 million preterm babies)



Photo: Save the Children

Low-income countries
Home birth and care at home
(5.6 million preterm babies)



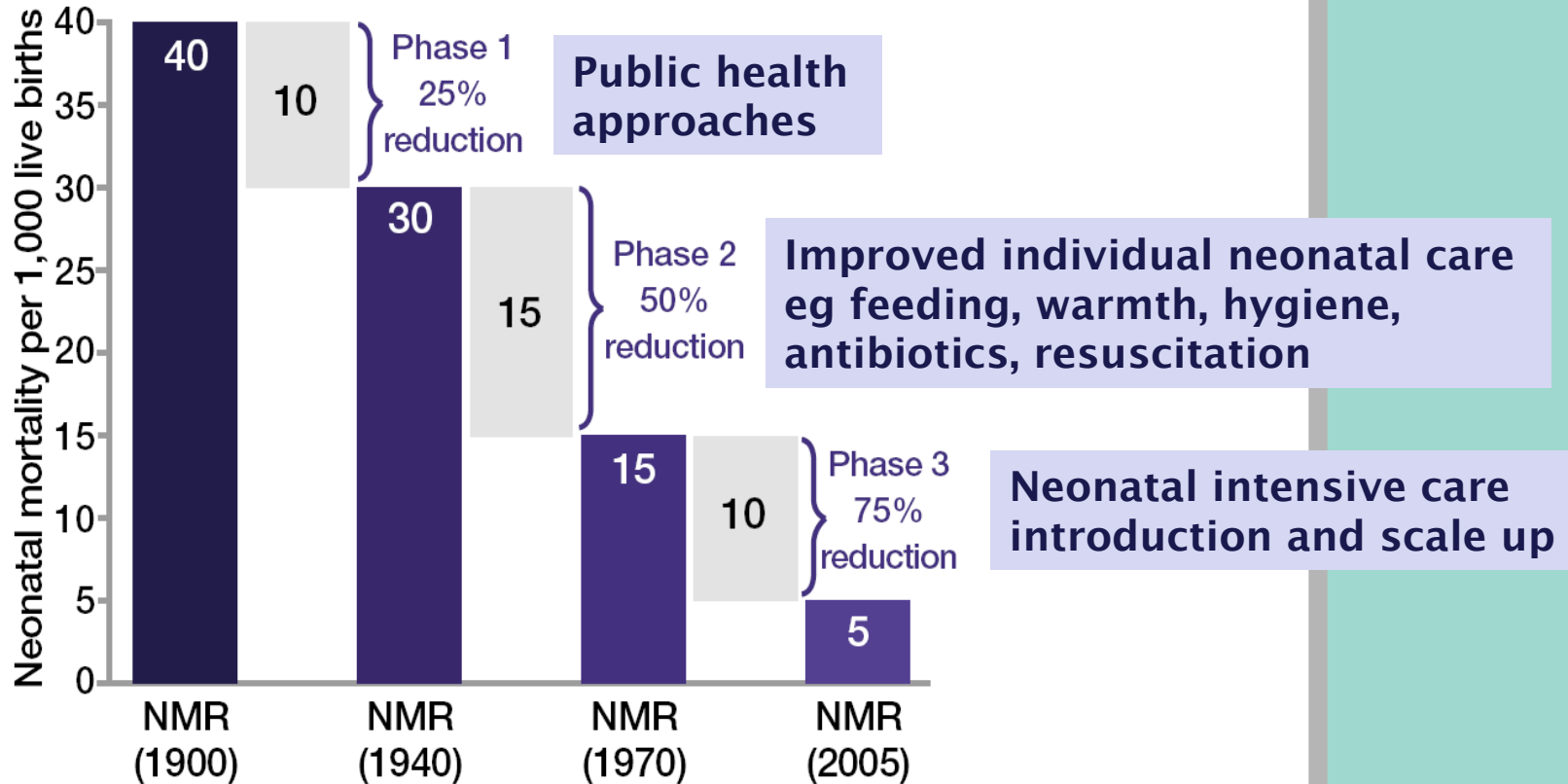
Photo: Pep Bonet/NOOR/Save the Children

Low-income countries
Facility births but limited space, staff and equipment
(4.4 million preterm babies)

Can we reach scale with care interventions that require high functioning care facilities?



Many premature babies can be saved before neonatal intensive care becomes available



Over 60% reduction can be achieved before neonatal intensive care and history shows the impact would be huge

Data sources for UK and US historical data: (CDC, 2012, Office for National Statistics, 2012, NIH, 1985, Smith et al., 1983, Jamison et al., 2006, Lissauer and Fanaroff, 2006, Baker, 2000, Philip, 2005, Wegman, 2001). With thanks to Boston Consulting Group

Accelerate prevention of preterm birth

What have we learned from the evidence?

Preterm birth is a syndrome with shared pathways and risk factors, resulting in many potential intervention points.

Prevention interventions to reduce preterm birth can impact a number of related outcomes including mortality.

Context matters – has a remarkable impact on the measure of effect.

Existing global health investments can reduce PTB, while working to develop effective care systems to further reduce PTB mortality.

Evaluate as we go forward. Effectiveness studies can inform difficult decisions.

Learn by doing. Programs with strong evaluation components can inform further investment.



EVERY
PREEMIE
SCALE

Accelerate prevention of preterm birth

The LINC approach?

This is not “business as usual”:

- Coordinate and leverage existing programs and investments that are currently advancing and implementing LINC interventions.
- Integrate across RMNCH for a major cause of child mortality. These activities would also contribute to a reduction in maternal and newborn mortality.
- Gather evidence and inform next steps as we go forward.



Questions/Discussion

