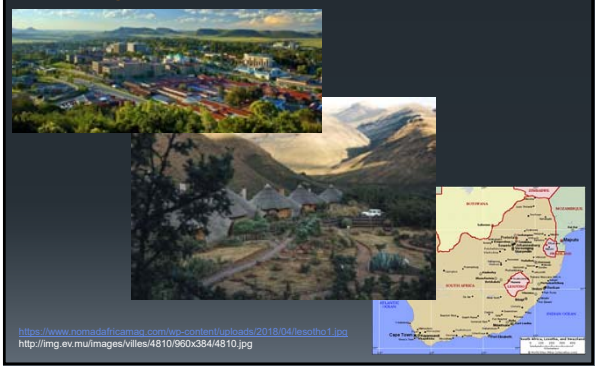
Under-5 Mortality

March 10th, 2020

Rajesh K. Daftary, MD, MPH
University of California San Francisco
School of Medicine
Department of Emergency Medicine

Background



https://www.nomadafricamag.com/wp-content/uploads/2018/04/lesotho1.jpg
http://img.ev.mu/images/villes/4810/960x384/4810.jpg

The Big Picture

https://i1.wp.com/jonathanpearson.net/wp-content/uploads/2016/03/forest.png

Learning Objectives

- Review historical trends in child mortality
- Define Millennium Development Goal 4 (MDG-4) and Sustainable Development Goal 3.2
- Identify current progress in mortality reduction
- Identify major causes of domestic and international mortality
- Identify and describe effective interventions

Historical Trends in Child Mortality

- Under-5 mortality = *probability* of dying by 5th birthday/1000 live births
- Why under 5?
  - Shift in major causes of mortality
  - Early life causes have less of an impact afterwards
- U5MR has plummeted since the 19th century
  - Role of modern transition / standard of living increase
  - Advances in science and technology
  - Public health campaigns

Historical Trends in Child Mortality

- Rate of U5MR (CMR) was halved 1960-1990
  - Developing world
  - 88-93/1000
  - 12.4 million deaths in 1990
  - Large inequities
- 1990 World Summit for Children
  - Goal: reduction to 70/1000 or 1/3 by region
  - 10-year goal
  - Unsuccessful
    - Slowing in reduction: 2.5% annual decrease-> 1.1%

Black, R. E., Morris, S. S., & Bryce, J. (2003). Where and why are 10 million children dying each year? *Lancet , 361*, 2226-34.

MDG-4

Millennium Declaration by the United Nations (2000)

Every individual has the right to dignity, freedom, equality, and a basic standard of living that includes freedom from hunger and violence, and encourages tolerance and solidarity

MDG-4

- 2002 – Office of Economic Cooperation and Development
  - Release of the Millennium Development Goals (MDG)
    - Health
    - Economic
    - Education
    - Environmental
- MDG-4: Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate
  - Target: 31/1000
  - Required an average 4.4% annual reduction globally

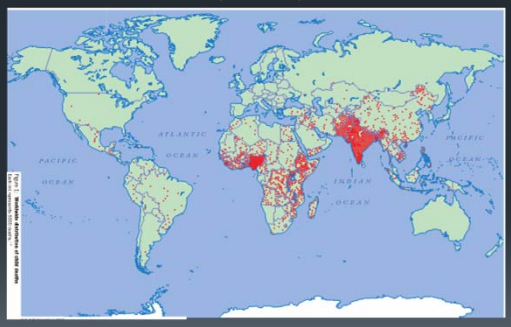
Black, R. E., Morris, S. S., & Bryce, J. (2003). Where and why are 10 million children dying each year? *Lancet , 361*, 2226-34.

Target Countries

- Low/Middle Income (LMIC) vs High Income Countries (HIC)
  - 18x more likely to die before 5
  - 42 countries account for 90% of deaths
  - 68 countries account for 97% of deaths
- Highest rates in Sub-Saharan Africa and Southern Asia

Countdown Coverage Writing Group. (2008). Countdown to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. *Lancet , 371*, 1247-58.

Child Deaths (2000)



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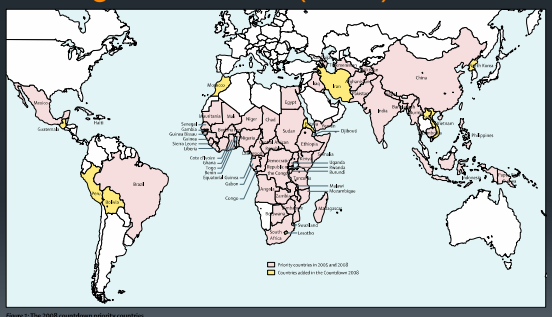
Target Countries (2008)



Countdown Coverage Writing Group. (2008). Countdown to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. *Lancet* , *371*, 1247-58.

Target Countries

Total Deaths (2000)		Probability of Death (2000)	
Country	Under-5 deaths	Country	U5MR
India	2,402,000	Sierra Leone	316
Nigeria	834,000	Niger	270
China	784,000	Angola	260
Pakistan	565,000	Afghanistan	257
DR Congo	484,000	Liberia	235

Black, R. E., Morris, S. S., & Bryce, J. (2003). Where and why are 10 million children dying each year? *Lancet* , *361*, 2226-34.

Was MDG-4 Successful?

- Overall reduction rate of 53%
  - 43/1000
  - Fell short of total goal of 31/1000
- 4 million fewer deaths/year in 2015 (compared to 2000)
- Regional variations in success
  - Sub-Saharan African countries experienced a two-fold increase in reduction rates
    - 2.947 million fewer deaths annually by 2015
  - Asia experienced a 50% increase in reduction rates (compared to pre-MDG implementation in 2000)

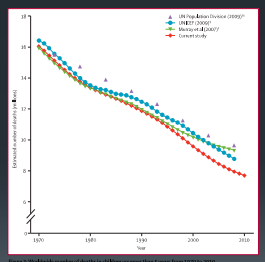
Target Countries

Total Deaths		
Country	2000	2017
India	2,402,000	1,040,000
Nigeria	834,000	790,000
Pakistan	565,000	340,000
DR Congo	484,000	250,000

Black, R. E., Morris, S. S., & Bryce, J. (2003). Where and why are 10 million children dying each year? *Lancet* , *361*, 2226-34.

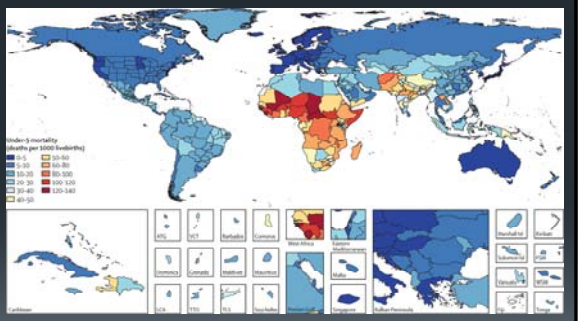
Progress

- Downtrend in under 5 mortality
  - 1990: 12.4 million deaths
  - 2000: 10.8 million
  - 2010: 7.6 million
  - 2015: 5.9 million
- Neonatal mortality
  - slow to change



Rajaratnam et al. (2010). Neonatal, postneonatal, childhood, and under-5 mortality for 187 countries, 1970-2010: a systematic analysis of progress towards Millennium Development Goal 4. *Lancet* , *375*, 1988-2008.
Liu et al. (2012). Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet*, 379:2151-2161.

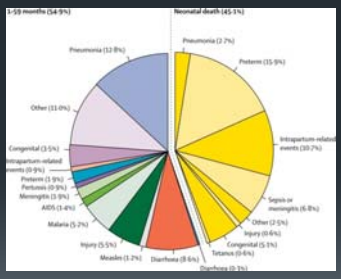
Under-5 Mortality (2015)



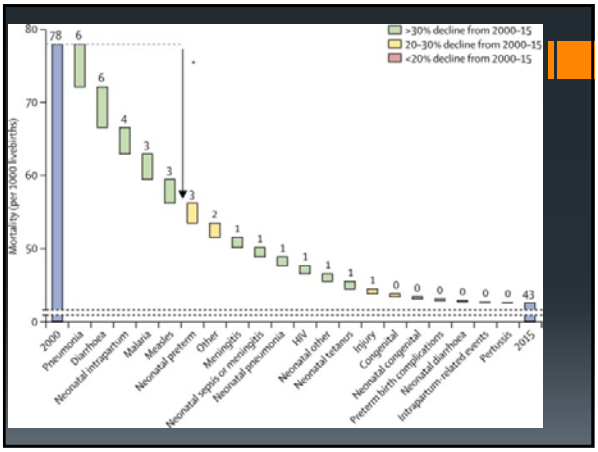
The Lancet 2016 388, 1725-1774DOI: (10.1016/S0140-6736(16)31575-6)

Causes of Mortality (2015)

- 5.942 million deaths
  - Preterm
  - Pneumonia
  - Intrapartum
- 45% in neonatal period
  - Preterm
  - Intrapartum
  - Sepsis
- 54% in 1 m/o-59 m/o
  - Pneumonia
  - Diarrhea
  - Injuries
  - Malaria



The Lancet 2016 388, 3027-3035DOI: (10.1016/S0140-6736(16)31593-8)

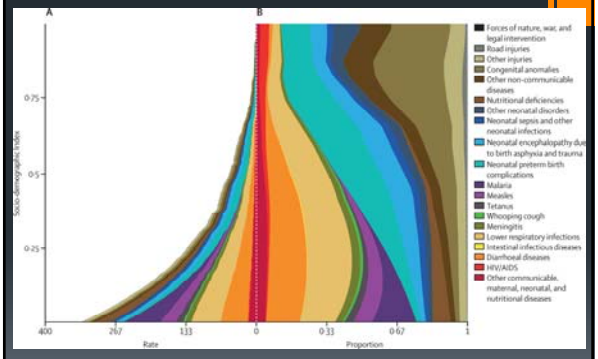


	Estimated number (UR; millions)	Cause specific mortality rate (per 1000 livebirths)
Children aged 0–59 months		
Preterm birth complications	1·055 (0·935–1·179)	7·555 (6·696–8·442)
Pneumonia	0·920 (0·812–1·117)	6·589 (5·815–7·996)
Intrapartum-related events	0·651 (0·598–0·778)	4·950 (4·283–5·569)
Diarrhoea	0·526 (0·418–0·691)	3·767 (2·993–4·955)
Sepsis/meningitis	0·517 (0·488–0·547)	3·701 (2·922–4·436)
Congenital abnormalities	0·512 (0·455–0·606)	3·664 (3·256–4·338)
Other conditions	1·720 (1·662–2·051)	12·314 (11·467–14·682)
Neonates aged 0–27 days		
Preterm birth complications	0·944 (0·812–1·066)	6·761 (5·959–7·632)
Intrapartum-related events	0·632 (0·550–0·723)	4·562 (3·937–5·177)
Sepsis/meningitis	0·401 (0·280–0·522)	2·874 (2·005–3·739)
Congenital abnormalities	0·301 (0·260–0·382)	2·169 (1·861–2·735)
Pneumonia	0·158 (0·113–0·219)	1·134 (0·793–1·753)
Tetanus	0·034 (0·018–0·084)	0·243 (0·129–0·601)
Diarrhoea	0·017 (0·010–0·070)	0·121 (0·072–0·504)
Other conditions	0·185 (0·142–0·240)	1·327 (1·017–1·719)
Children aged 1–59 months		
Pneumonia	0·762 (0·651–0·943)	5·455 (4·661–6·752)
Diarrhoea	0·509 (0·401–0·661)	3·645 (2·872–4·730)
Injuries	0·327 (0·272–0·410)	2·341 (1·944–2·938)
Malaria	0·306 (0·225–0·452)	2·193 (1·613–3·237)
Congenital abnormalities	0·209 (0·165–0·259)	1·496 (1·178–1·853)
Meningitis	0·115 (0·093–0·152)	0·825 (0·662–1·087)
Preterm birth complications	0·111 (0·061–0·168)	0·791 (0·438–1·202)
AIDS	0·086 (0·076–0·101)	0·614 (0·541–0·722)
Measles	0·074 (0·038–0·268)	0·529 (0·274–1·920)
Intrapartum-related events	0·054 (0·028–0·092)	0·388 (0·201–0·657)
Pertussis	0·054 (0·052–0·056)	0·387 (0·377–0·427)
Other conditions	0·654 (0·536–0·803)	4·681 (3·815–5·752)

Uncertainty range (UR) is defined as the 2·5–97·5 centile. Other conditions among children aged 1–59 months included causes originated during the perinatal period, cancer, severe malnutrition, and other specified causes. Intrapartum-related events were formerly referred to as "birth asphyxia".

Table 2: Estimated numbers of deaths by cause and cause-specific mortality rate in 2015

The Lancet 2016 388, 3027-3035DOI: (10.1016/S0140-6736(16)31593-8)



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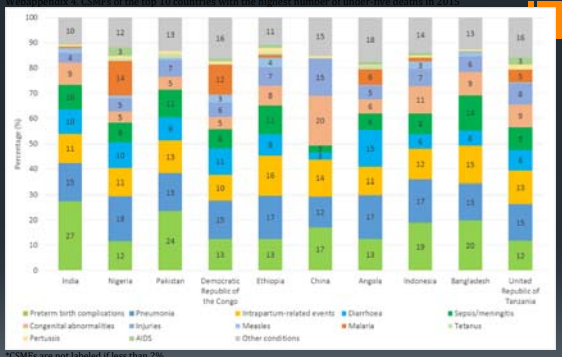
Variations by mortality strata

U5MR Mortality Strata (x/1000)	# of countries	% of total deaths	Causes
Very high (≥ 100)	7	20%	• Pneumonia • Malaria • Diarrhea
High (75-<100)	17	23.7%	• Pre-term birth • Pneumonia • Intrapartum
Medium-High (50-<75)	20	11%	
Medium (25-<50)	36	34.9%	
Low (10-<25)	54	9%	• Congenital abnormalities • Preterm birth complications • Pneumonia • Intrapartum
Very Low (<10)	60	2%	• Congenital abnormalities • Preterm birth complications • Injuries

Webappendix 5. CSMFs of the 10 countries with the highest U5MR in 2015

*CSMFs are not labeled if less than 2%
Countries are ordered from the highest U5MR to the lowest from left to right.
The Lancet 2016 388, 3027-3035DOI: (10.1016/S0140-6736(16)31593-8)

Webappendix 4. CSMFs of the top 10 countries with the highest number of under-five deaths in 2015



*CSMFs are not labeled if less than 2%
Countries are ordered from the highest number of under-five deaths to the lowest from left to right.

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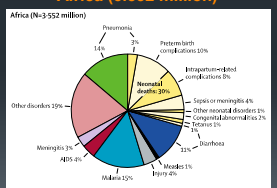
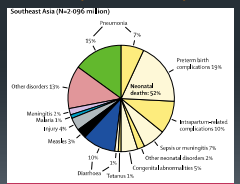
Regional Variation (2010)

Africa (3.552 million)



SE Asia (2.096 million)



Liu et al. (2012). Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet*, 379:2151-2161.

Impact of Malnutrition

- Malnutrition
  - Not reported as direct cause
  - Major precipitant
    - 53% of all deaths
    - Mild malnutrition: 2x risk of death
    - Moderate to severe malnutrition: 5-8x risk of death
  - Correlation to death (> -1 SD):
    - Diarrhea: 61%
    - Malaria: 57%
    - Pneumonia: 53%
    - Measles: 53%

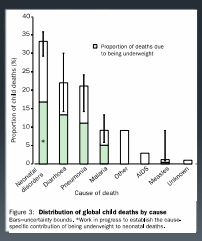


Figure 3: **Distribution of global child deaths by cause**
Bars=uncertainty bounds. *Work in progress to establish the cause-specific contribution of being underweight to neonatal deaths.

Black, R. E., Morris, S. S., & Bryce, J. (2003). Where and why are 10 million children dying each year? *Lancet* , *361*, 2226-34.

Neonatal Mortality (2008)

- Accounts for 41% of total U5M
  - 28 days vs 1800 days
  - 30x Risk
  - 99% of neonatal deaths in LMIC
- Greatest risk of death: first 24 hours
- Slowest group of decline
- Linked to maternal mortality
  - 500,000 deaths per year
  - Lifetime risk: 1/10 in some regions

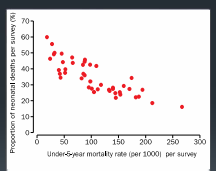


Figure 2: **Relation between under-5-year mortality rate and percentage of these deaths in neonates**
Each dot=one survey.

Lawn, J. E., Cousens, S., & Zupan, J. (2005). 4 millions neonatal deaths: When? Where? Why? *Lancet* , *365*, 891-900.
Black et al. (2010). Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet* , *375*, 1969-87.

Neonatal Mortality

- Causes
  - Preterm
  - Infection – Pneumonia, Sepsis
  - Asphyxia – Intrapartum ischemic injury
  - Tetanus
- Low birth weight infants have worse outcomes
  - IUGR
  - Prematurity
  - Linked to maternal health

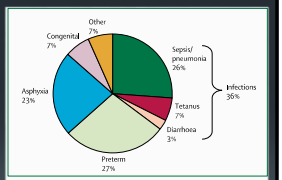


Figure 4: **Estimated distribution of direct causes of 4 million neonatal deaths for the year 2000**
Based on vital registration data for 45 countries and modelled estimates for 147 countries.

Lawn, J. E., Cousens, S., & Zupan, J. (2005). 4 millions neonatal deaths: When? Where? Why? *Lancet* , *365*, 891-900.

Risk of Death By Day of Life

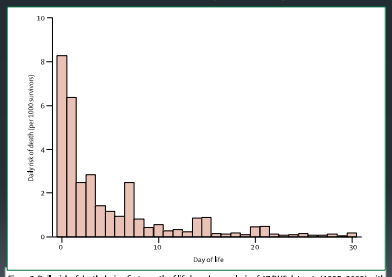


Figure 3: Daily risk of death during first month of life based on analysis of 47 DHS datasets (1995–2003) with 10 048 neonatal deaths
Deaths in first 24 h recorded as occurring on day 0, or possibly day 1, depending on interpretation of question and coding of response. Preference for reporting certain days (7, 14, 21, and 30) is apparent.

Lawn, J. E., Cousens, S., & Zupan, J. (2005). 4 millions neonatal deaths: When? Where? Why? *Lancet* , *365*, 891-900.

Mortality in the US (2018)

- Child mortality in children aged 1-4: 0.932/1000/yr
- U5MR: 6.53/1000 live births (UNICEF)

Comparison: Deaths/1000 live births (2011)

	0-6 days (Early Neo)	7-28 days (Late neo)	29-364 days (Post-neo)	1-4 years	Under 5y
Worldwide	16.1	5.2	16.0	16.5	52.8
Developing	17.7	5.8	17.8	18.4	58.5
Developed	2.6	0.8	1.9	1.2	6.6
USA	3.1	0.8	2.0	1.2	7.1

Lozano, et al. (2011) Progress towards Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis. *Lancet*, 378:1139-1165.

Sustainable Development Goals (2015)

- 3.2: End preventable deaths of newborns and children under-5 by 2030
- Equates to mortality rate of 25 child deaths/1000 live births
- 12 neonatal deaths/1000 live births

The way forward…

Interventions

Task:

- X-axis: Major causes of mortality
- Y-axis: Proposed interventions
- Challenge: Mark the boxes where an intervention has a measureable and evidence based impact on mortality
- Hint: Interventions can be effective against more than one cause

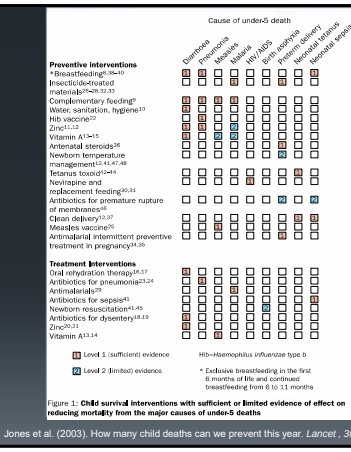


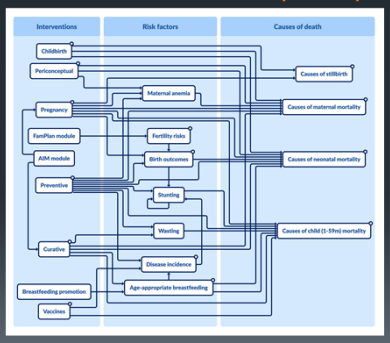
Figure 1: **Child survival interventions with sufficient or limited evidence of effect on reducing mortality from the major causes of under-5 deaths**

Jones et al. (2003). How many child deaths can we prevent this year. *Lancet* , *362*, 65-71.

Interventions

- Lancet 2003 meta-analysis:
  - At least one intervention for every cause
  - Exception: neonatal asphyxia
- New data (2008):
  - CPAP
  - Maternal interventions

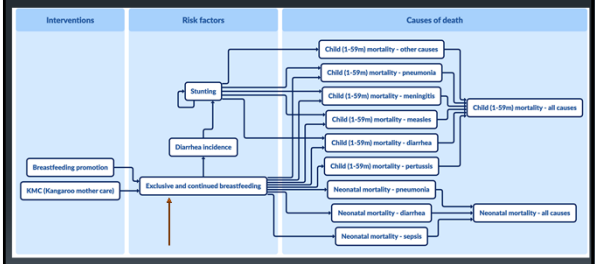
The Lives Saved Tool (LiST)



Interventions

- Exclusive breastfeeding (EBF)
  - 0-6 months
  - Early initiation (1 hour post delivery)
  - Target coverage 90%
  - Wide amount of variation
- Complementary breastfeeding
  - 6-24 months

Impact of Breastfeeding

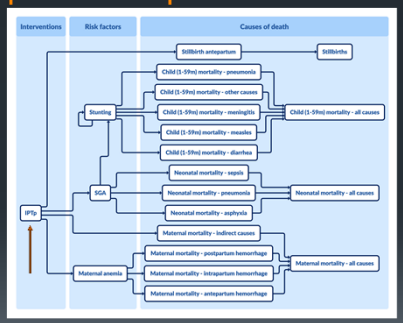


Lives Saved Tool listvisualizer.org; Retrieved March 6th, 2020

Interventions

- Intermittent Preventive Treatment in pregnancy (IPTp) for malaria
  - Scheduled administration of three doses of antimalarials during pregnancy, regardless of malaria infection
  - Reduces maternal mortality
  - Reduces maternal and fetal anemia
  - Reduces low birth weight

Impact of IPTp

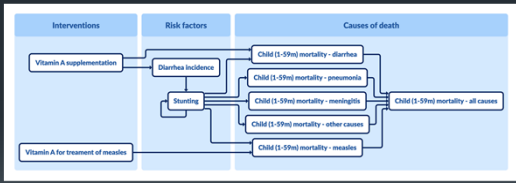


Lives Saved Tool listvisualizer.org; Retrieved March 6th, 2020

Interventions

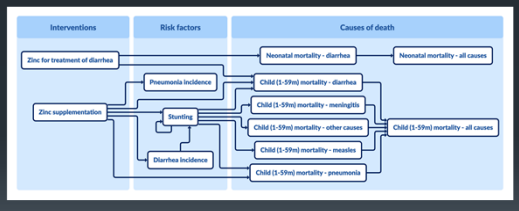
- Vitamin A – Two doses per year from 6 - 59 m/o
  - Reduces incidence: diarrhea
  - Treatment for measles
  - Treatment for malnutrition
    - Improving nutrition status reduces overall mortality
- Zinc
  - Reduced severity of diarrheal illness in micronutrient deficiency

Vitamin A Supplementation



Lives Saved Tool listvisualizer.org; Retrieved March 6th, 2020

Impact of Zinc: Supplementation and Treatment



Lives Saved Tool listvisualizer.org; Retrieved March 6th, 2020

Interventions

- 99% coverage rate of interventions would:
  - Reduce 6.3 million deaths
  - Achieve MDG-4 goal
  - Assumes 90% coverage of EBF

Jones et al. (2003). How many child deaths can we prevent this year. *Lancet* , *362*, 65-71.

	Estimated under-5 deaths prevented	
	Number of deaths (×10³)	Proportion of all deaths
Preventive interventions		
Breastfeeding	1301	13%
Insecticide-treated materials	691	7%
Complementary feeding	587	6%
Zinc	459 (351)*	5% (4%)*
Clean delivery	411	4%
Hib vaccine	403	4%
Water, sanitation, hygiene	326	3%
Antenatal steroids	264	3%
Newborn temperature management	227 (0)*	2% (0%)*
Vitamin A	225 (176)*	2% (2%)*
Tetanus toxoid	161	2%
Nevirapine and replacement feeding	150	2%
Antibiotics for premature rupture of membranes	133 (0)*	1% (0%)*
Measles vaccine	103	1%
Antimalarial intermittent preventive treatment in pregnancy	22	<1%
Treatment interventions		
Oral rehydration therapy	1477	15%
Antibiotics for sepsis	583	6%
Antibiotics for pneumonia	577	6%
Antimalarials	467	5%
Zinc	394	4%
Newborn resuscitation	359 (0)*	4% (0%)*
Antibiotics for dysentery	310	3%
Vitamin A	8	<1%

*Numbers represent effect if both levels 1 (sufficient) and 2 (limited) evidence are included, value number in brackets shows effect if only level-1 evidence is accepted. Interventions for which only one value is cited are all classified as level 1.

Table 2: **Under-5 deaths that could be prevented in the 42 countries with 90% of worldwide child deaths in 2000 through achievement of universal coverage with individual interventions**

Coverage (2000)

Highest	Lowest
Breastfeeding (6-11 months, 90%)	NVP + replacement feeding (5%)
Measles vaccine (68%)	Newborn Resuscitation (3%)
Vitamin A (55%)	Insecticide treated malarials (2%)
Clean delivery (54%)	Hib vaccine (1%)
Tetanus Toxoid (49%)	IPTp (1%)
EBF (39%)	Zinc (0%)

Jones et al. (2003). How many child deaths can we prevent this year. *Lancet* , *362*, 65-71.

Coverage (2008)

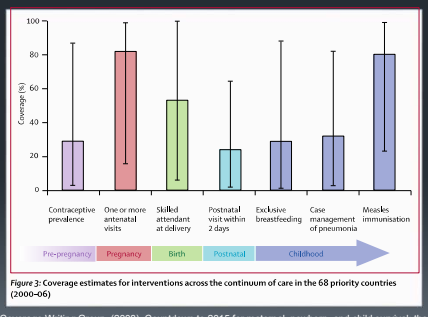


Figure 3: Coverage estimates for interventions across the continuum of care in the 68 priority countries (2000–06)

Countdown Coverage Writing Group. (2008). Countdown to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. *Lancet* , *371*, 1247-58.

Coverage (2010)

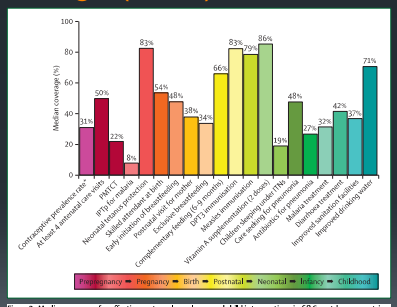


Figure 2: **Median coverage for effective maternal, newborn, and child interventions in 68 Countdown countries**
Data are most recent available estimates since 2000. PMTCT=prevention of maternal to child transmission of HIV.

Bhutta et al. (2010). [illegible] and child survival. *Lancet*, 375, 2032–44.

Coverage

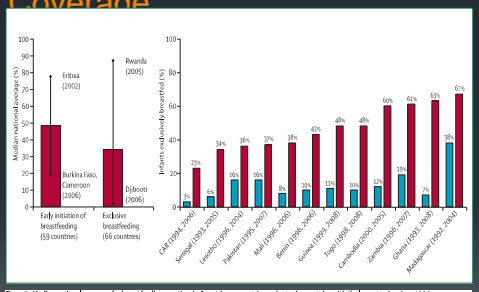


Figure 5: **Median national coverage for breastfeeding practices in Countdown countries and rates in countries with the largest gains since 1990**
(A) Median national coverage in Countdown countries. Data are most recent estimates since 2000; error bars show the highest and lowest coverage estimates in Countdown countries since 2000. (B) Percentage of infants younger than 6 months who were exclusively breastfed, in selected Countdown countries with highest rates of increase since 1990. Source: UNICEF Global Database (November, 2009). Compiled from Multiple Indicator Cluster Surveys, Demographic and Health Surveys,

Bhutta et al. (2010). [illegible] and child survival. *Lancet*, 375, 2032–44.

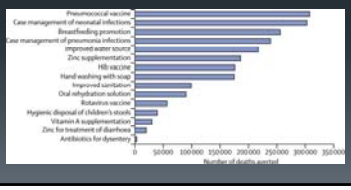
Coverage

- Cost: Bryce et al (2005)
  - Implementation of 23 known effective interventions
    - 42 target countries with 90% mortality
    - 18 scheduled contacts for mother and child
    - Packaging of services at community level
    - Assume: 99% coverage
    - Does not include structural/training cost
    - Conclusion
      - $5.1 billion USD annually
      - $887 per life saved

Bryce, J., Black, R. E., Walker, N., Bhutta, Z. A., Lawn, E. J., & Steketee, R. W. (2005). Can the world afford to save the lives of 6 million children each year. *Lancet*, *365*, 2193-2200.

Coverage: Pneumonia and Diarrhea Interventions

- Account for 35% of all deaths (2 million in total)
- If known interventions were scaled to 80% coverage
  - 1.4 million deaths could be averted
  - Total cost of $6.715 billion



Postnatal (newborn	Hospital	Community	Household
Immediate thermal care	✓	✓	✓
Initiation of exclusive breastfeeding (within first hour	✓	✓	✓
Hygienic cord and skin care	✓	✓	✓
Neonatal resuscitation with bag and mask (professional health worker	✓	✓	-
Case management of neonatal sepsis, meningitis and pneumonia	✓	✓	-
Kangaroo mother care for preterm and for less than 2000g babies	✓	✓	-
Management of newborns with jaundice	✓	✓	-
Surfactant to prevent respiratory distress syndrome in preterm babies	✓	-	-
Continuous positive airway pressure (CPAP) to manage babies with respiratory distress syndrome	✓	-	-
Extra support for feeding small and preterm babies	✓	✓	-
Presumptive antibiotic therapy for newborns at risk of bacterial infections	✓	-	-
Infancy and Childhood			
Exclusive breastfeeding for 6 months	✓	✓	✓
Continued breastfeeding and complementary feeding from 6 months	✓	✓	✓
Prevention and case management of childhood malaria	✓	✓	✓
Vitamin A supplementation from 6 months of age	✓	✓	✓
Comprehensive care of children infected with or exposed to HIV	✓	✓	-
Routine immunization and *H. influenzae*, meningococcal, pneumococcal and rotavirus vaccines	✓	✓	✓
Management of severe acute malnutrition	✓	✓	-
Case management of childhood pneumonia	✓	✓	✓
Case management of diarrhoea	✓	✓	✓

The Partnership for Maternal, Newborn & Child Health. 2011. A Global Review of the Key Interventions Related to Reproductive, Maternal, Newborn and Child Health (RMNCH). Geneva, Switzerland: PMNCH.

The Three Delays: Current work by UCSF EM Faculty

- Delay in recognition of illness severity
  - Nursing eduction
- Delay in transport to a health facility
  - Prehospital systems/emergency medical services
- Delay in adequate care upon arrival at a health facility
  - Basic Emergency Care course
  - Curriculum for Pediatric Emergency Medicine
  - Residency training program in Uganda, Tanzania

Conclusions

- Major progress has been made in under 5 mortality
- 5 million children are likely to die this year
- Known interventions exist for every major cause of mortality
  - Coverage rates are a challenge

Future

- Maternal care
  - Maternal mortality exceedingly high
  - Female education impacts:
    - Child mortality
    - Maternal mortality
  - Family planning
- Community based interventions
- Packaged services
- Scale up of primary health care delivery
- Novel interventions
  - Community based neonatal care, treatment of sepsis
  - Vaccine development
- Impact of climate change
  - Food and water insecurity
  - Civil unrest
  - Migration
  - Vector transmission

Questions?