Infectious Diseases in Resource-poor Areas of the World

Philip LaRussa Columbia University

Some of the Issues

- Burden of Disease
- Specific Pathogens/ Conditions:
 - Acute Respiratory Disease
 - Acute Diarrheal Disease
 - Tuberculosis
 - Malaria
 - Measles
 - HIV
 - Immunizations
 - Additional Resources
- Summary

WHO Projections for Selected Causes of Death



Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Medicine* [online journal], 2006, 3(11):e442 (http://medicine.plosjo urnals.org/perlserv/?re quest=getdocument&doi=10.1371/ journal.pmed.0030442)

 Shift in deaths from <u>younger to older ages</u> & from <u>communicable to</u> <u>non-communicable</u> diseases (reflective of shift to an older population)
 <u>Large declines in mortality projected</u> for all principal communicable, maternal, perinatal and nutritional causes, <u>except</u> HIV/AIDS.

• Global HIV deaths projected to rise from 2.8 million in 2002 to 6.5 million in 2030 (assumes ART coverage of 80% by 2012).

Changes in Ranking for Leading Causes of Death 2002 ® 2030

Projections of Global Mortality

Table 2. Changes in Rankings for 15 Leading Causes of Death, 2002 and 2030 (Baseline Scenario)

Category	Disease or Injury	2002 Rank	2030 Ranks	Change in Rank
Within top 15	Ischaemic heart disease	1	1	0
	Cerebrovascular disease	2	2	0
	Lower respiratory infections	3	5	-2
	HIV/AIDS	4	3	+1
	COPD	5	4	+1
	Perinatal conditions	6	9	-3
	Diarrhoeal diseases	7	16	-9
	Tuberculosis	8	23	-15
	Trachea, bronchus, lung cancers	9	6	+3
	Road traffic accidents	10	8	+2
	Diabetes mellitus	11	7	+4
	Malaria	12	22	-10
	Hypertensive heart disease	13	11	+2
	Self-inflicted injuries	14	12	+2
	Stomach cancer	15	10	+5
Outside top 15	Nephritis and nephrosis	17	13	+4
and and the second s	Colon and rectum cancers	18	15	+3
	Liver cancers	19	14	+5

doi: 10.1371/journal.pmed.0030442.t002

Mathers, Loncar, Projections of Global Mortality & Burden of Disease from 2002 to 2030. PLoS Medicine, 3(11), Nov., 2006

Ten leading Causes of Death by Income Group, 2030

Table 3. Ten Leading Causes of Death, by Income Group, 2030 (Baseline Scenario)

Income Group	Rank	Disease or Injury	Percent of Total Deaths
World	1	Ischaemic heart disease	13.4
	2	Cerebrovascular disease	10.6
	3	HIV/AIDS	8.9
	4	COPD	7.8
	5	Lower respiratory infections	3.5
	6	Trachea, bronchus, lung cancers	3.1
	7	Diabetes mellitus	3.0
	8	Road traffic accidents	2.9
	9	Perinatal conditions	2.2
	10	Stomach cancer	1.9
High-income countries	1	Ischaemic heart disease	15.8
The second state of the se	2	Cerebrovascular disease	9.0
	3	Trachea, bronchus, lung cancers	5.1
	4	Diabetes mellitus	4.8
	5	COPD	4.1
	6	Lower respiratory infections	3.6
	7	Alzheimer and other dementias	3.6
	8	Colon and rectum cancers	3.3
	9	Stomach cancer	1.9
	10	Prostate cancer	1.8
Middle-income countries	1	Cerebrovascular disease	14.4
	2	Ischaemic heart disease	12.7
	3	COPD	12.0
	4	HIV/AIDS	6.2
	5	Trachea, bronchus, lung cancers	4.3
	6	Diabetes mellitus	3.7
	7	Stomach cancer	3.4
	8	Hypertensive heart disease	2.7
	9	Road traffic accidents	2.5
	10	Liver cancer	2.2
Low-income countries	1	Ischaemic heart disease	13.4
	2	HIV/AIDS	13.2
	3	Cerebrovascular disease	8.2
	4	COPD	5.5
	5	Lower respiratory infections	5.1
	6	Perinatal conditions	3.9
	7	Road traffic accidents	3.7
	8	Diarrhoeal diseases	2.3
	9	Diabetes mellitus	2.1
	10	Malaria	1.8

Mathers, Loncar, Projections of Global Mortality & Burden of Disease from 2002 to 2030. PLoS Medicine, 3(11), Nov., 2006

Better statistics for monitoring progress:

Current reliance on predicted rather than corrected numbers



Estimates improve as more countries adopt standardized methods
Epidemic was overestimated, but it's <u>still</u> growing
Must use corrected data to compare years
There's still substantial uncertainty

World Health Statistics 2007; Ten Statistical Highlights in Global Public Health. WHO, 2007

Global Burden of Disease and Risk Factors in 2001 The World Bank, 2006

Table 1.1 Deaths and Burden of Disease by Cause—Low- and Middle-Income Countries, High-Income Countries, and World, 2001

	Low- and m	iddle-income	High-	income	W	orld
	Deaths	DALYs(3,0) ^a	Deaths	DALYs(3,0)a	Deaths	DALYs(3,0) ^a
All causes						
Total number (thousands)	48,351	1,386,709	7,891	149,161	56,242	1,535 871
Rate per 1,000 population	9.3	265.7	8.5	160.6	9.1	249.8
Age-standardized rate per 1,000 ^b	11.4	281.7	5.0	128.2	10.0	256.5
Selected cause aroups:	62.come	0.00-000-000	Number in the	ousands (percent)		
I. COMMUNICABLE DISEASES, MATERNAL AND PERINATAL CONDITIONS AND NUTRITIONAL DEFICIENCIES	17,613 (36.4)	552,376 (39.8)	552 (7.0)	8,561 (5.7)	18,166 (32.3)	560,937 (36.5)
# 5 Tuberculosis	1,590 (3.3)	35,874 (2.6)	16 (0.2)	219 (0.1)	1,606 (2.9)	36,093 (2.3)
# 2 HIV/AIDS	2,552 (5.3)	70,796 (5.1)	22 (0.3)	665 (0.4)	2,574 (4.6)	71,461 (4.7)
# 4 Diarrheal diseases	1,777 (3.7)	58,697 (4.2)	6 (<.1)	444 (0.3)	1,783 (3.2)	59,141 (3.9)
Measles	762 (1.6)	23,091 (1.7)	1 (<.1)	23 (<.1)	763 (1.4)	23,113 (1.5)
#6Malaria	1,207 (2.5)	39,961 (2.9)	0 (0.0)	9 (<.1)	1,208 (2.1)	39,970 (2.6)
#1 Lower respiratory infections	3,408 (7.0)	83,606 (6.0)	345 (4.4)	2,314 (1.6)	3,753 (6.7)	85,920 (5.6)
#3Perinatal conditions	2,489 (5.1)	89,068 (6.4)	32 (0.4)	1,408 (0.9)	2,522 (4.5)	90,477 (5.9)
Protein-energy malnutrition	241 (0.5)	15,449 (1.1)	9 (0.1)	130 (<.1)	250 (0.4)	15,578 (1.0)
II. NONCOMMUNICABLE CONDITIONS	26,023 (53.8)	678,483 (48.9)	6,868 (87.0)	129,356 (86.7)	32,891 (58.5)	807,839 (52.6)
III. INJURIES	4,715 (9.8)	155,850 (11.2)	471 (6.0)	11,244 (7.5)	5,186 (9.2)	167,094 (10.9)

a. DALYs (3,0): Disability Adjusted Life Years based on a 3% annual discount rate and uniform age weights.

Death in Children, 2001

Low- and midd	le-income countri	es	High-i	income countries	
Cause	Deaths (millions)	Percentage of total deaths	Cause	Deaths (millions)	Percentage of total deaths
1 Perinatal conditions	2.49	20.7	1 Perinatal conditions	0.03	33.9
2 Lower respiratory infections	2.04	17.0	2 Congenital anomalies	0.02	20.0
3 Diarrheal diseases	1.61	13.4	3 Road traffic accidents	0.01	5.9
4 Malaria	1.10	9.2	4 Lower respiratory infections	0.00	2.5
5 Measles	0.74	6.2	5 Endocrine disorders	0.00	2.4
6 HIV/AIDS	0.44	3.7	6 Drownings	0.00	2.4
7 Congenital anomalies	0.44	3.7	7 Leukemia	0.00	1.9
8 Whooping cough	0.30	2.5	8 Violence	0.00	1.8
9 Tetanus	0.22	1.9	9 Fires	0.00	1.2
10 Road traffic accidents	0.18	1.5	10 Meningitis	0.00	1.2

Table 3.8 The 10 Leading Causes of Death in Children Ages 0-14, by Broad Income Group, 2001

Source: Authors' calculations.

70 | Global Burden of Disease and Risk Factors | Colin D. Mathers, Alan D. Lopez, and Christopher J. L. Murray

In Global Burden of Disease and Risk Factors, ed. Lopez, et. al. Chapter 2, p.29. Oxford University Press & The World Bank, 2006

Mortality, Children = 5 years by Cause, 1990 & 2001

Table 2.4 Mortality in Children Under Five by Cause, 1990 and 2001

	Low- and income (d middle- countries	East and P	Asia acific	Europ Centra	e and al Asia	Latin A and the (merica aribbean	Middle North	East and Africa	South	ı Asia	Sub-Sa Afr	aharan ica	High-i cour	income ntries	Wo	rld
Disease and indicator	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001
Acute respiratory infections Deaths (thousands) % of childhood deaths Probability of dying before age 5 per 1,000 live births	2,521 21.0 - 20	1,943 18.4 16	492 23.8 13	197 14.0 6	68 19.5 8	36 20.6 6	63 14.1 7	44 10.9 4	138 20.6 16	76 17.7 9	1,027 23.2 29	833 23.1 22	713 18.3 33	757 16.8 29	13 11.1 1	2 2.3 0	2,533 20.9 19	1,944 18.3 15
Congenital anomalies Deaths (thousands) % of childhood deaths Probability of dying before age 5 per 1,000 live births	421 3.5 3	421 4.0 3	118 5.7 3	115 8.2 4	25 7.1 3	24 135 4	30 5.1 3	41 10.1 4	22 3.3 3	41 9.5 5	196 4.2 5	142 3.9 4	41 1.0 2	58 1.3 2	19 16.3 2	18 24.6 2	440 3.6 3	439 4.1 3
Diarrheal diseases Deaths (thousands) % of childhood deaths Probability of dying before age 5 per 1,000 live births	2,362 19.7 - 19	1,599 →15.2 13	274 13.2 7	201 14.3 6	61 17.4 7	12 6.9 2	109 18.3 9	46 11.4 4	144 21.6 17	66 15.3 8	991 22.4 28	631 17.5 17	784 20.1 36	643 14.3 25	11 9.9 1	0 0.6 0	2,374 19.6 17	1,600 15.1 12
HIV/AIDS Deaths (thousands) % of childhood deaths Probability of dying before age 5 per 1,000 live births	62 0.5 - 0	→ ³⁴⁰ 3.2 3	0.0 0	5 0.4 0	0.0 0	0 0.2 0	2 0.3 0	6 1.4 1	0 0.0 0	1 0.1 0	0.0 0	14 0.4 0	60 1.5 3	313 7.0 12	0 0.0 0	0 0.1 0	62 0.5 0	340 3.2 3
Injuries Deaths (thousands) % of childhood deaths Probability of dying before age 5 per 1,000 live births	647 5.4 5	302 2.9 2	206 9.9 5	82 5.6 2	25 7.0 3	11 6.6 2	28 4.7 2	19 4.6 2	32 4.8 4	24 5.6 3	188 4.2 5	79 2.2 2	169 4.3 8	87 1.9 3	9 7.8 1	7 9.8 1	656 5.4 5	309 2.9 2
Malaria Deaths (thousands) % of childhood deaths Probability of dying before age 5 per 1,000 live births	586 4.9 - 5	1,086 10.3 9	7 0.3 0	27 1.9 1	0 0.1 0	0 0.0 0	2 0.3 0	1 0.3 0	1 0.1 0	17 3.9 2	9 0.2 0	57 1.6 2	570 14.6 26	964 21.6 36	0 0.2 0	0 0.1 0	588 4.8 4	1,086 10.2 8

In Global Burden of Disease and Risk Factors, ed. Lopez, et. al. Chapter 2, p.29. Oxford University Press & The World Bank, 2006

Mortality, Children = 5 years by Cause, 1990 & 2001

Table 2.4 Continued

	Low- and middle- income countries		w- and middle- East Asia come countries and Pacific		Europe and Central Asia		Latin America and the Caribbean		Middle East and North Africa		South Asia		Sub-S Afr	Sub-Saharan Africa		High-income countries		rid
Disease and indicator	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	2001	1990	200
Measles																		
Deaths (thousands)	869	556	75	45	12	5	38		30	10	239	145	474	351	3	0	872	556
% of childhood deaths	7.2	> 5.3	3.6	3.2	3.5	2.9	6.5	0.0	4.5	23	5.4	4.0	12.2	7.8	2.5	0.1	7.2	5.2
Probability of dying before age 5 per 1,000 live births	7	5	2	1	1	1	3	0	4	1	7	4	22	13	0	0	6	4
Perinatal conditions			1															
Deaths (thousands)	2,261	2,492	480	506	83	57	162	164	141	106	906	1,066	487	573	38	32	2,298	2,524
% of childhood deaths	18.8-	>23.7	23.2	36.0	23.6	32.9	27.6	40.3	21.2	24.7	20.4	30.1	12.5	12.7	33.0	44.5	18.9	23.8
Probability of dying before age 5 per 1,000 live births	18	20	12	15	10	10	14	14	17	13	26	29	22	22	3	3	17	19
Other causes		110	100															
Deaths (thousands)	2,286	1,792	420	228	77	28	137	85	159	90	868	625	607	737	22	13	2,309	1,805
% of childhood deaths	19.0	17.0	20.3	16.2	21.9	16.3	23.2	21.0	23.8	20.9	20.0	17.3	15.5	16.4	19.1	17.9	19.0	17.0
Probability of dying before age 5 per 1,000 live births	18	15	11	7	9	5	12	7	19	11	25	17	28	28	2	1	17	14
Total																		
Deaths (thousands)	12.019	10.532	2.072	1,407	352	174	568	407	668	429	4,434	3.612	3,904	4,504	115	73	12,134	10,605
% of childhood deaths	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Probability of dying before age 5 per 1,000 live births	97	86	54	43	41	29	51	35	80	53	127	97	180	172	10	7	89	80

Sources: Estimates for 1990 are based on Murray and Lopez 1996, weighted to World Bank regions using population under five years old. Estimates for 2001 are from chapter 3 in this volume.

Note: - - not available or not applicable. Estimates of child mortality are rounded to the nearest whole number.

Relative contribution of childhood malnutrition ?

In Global Burden of Disease and Risk Factors, ed. Lopez, et. al. Chapter 2, p.30. Oxford University Press & The World Bank, 2006

Acute Respiratory Infections, Children < 5 yrs.

- About 20% of all deaths in children <5 years:
 - Pneumonia, bronchiolitis and bronchitis
 - 90% of deaths due to pneumonia
 - Delays in recognition/ treatment of pneumonia increase mortality.
- Bacterial (S. pneumoniae & H. influenzae) or viral
- Not possible to differentiate between bacterial and viral ARIs based on clinical signs or radiology
- Risk factors for higher risk of pneumonia/death:
 - Low birth weight, malnourished and non-breastfed
 - living in overcrowded conditions

http://www.who.int/fch/depts/cah/resp_infections/en/

Management of Acute Respiratory Infection(ARI) in Children <5 yrs.

- Assess children with cough or difficult breathing with case management charts
 - Also assess for signs of severe malnutrition, visible severe wasting & edema of both feet ®refer to hospital (very high risk of death from pneumonia).
 - Children with danger signs should be referred to a hospital after a dose of IM chloramphenicol.
 - If not possible, BID IM chloramphenicol for 5 days, then PO antibiotic for another 5 days.

http://www.who.int/fch/depts/cah/resp_infections/en/

Management of Acute Respiratory Infection(ARI) in Children < 5 yrs.

- Severe pneumonia:
 - Give 1st dose Amoxicillin
 - Refer to hospital for IM ampicillin/penicillin
 - If not possible, PO amoxicillin for 7 days
- Non-severe pneumonia;
 - PO co-trimoxazole or amoxicillin for 5 days
- Supportive measures:
 - oral fluids to avoid dehydration, continued feeding to avoid malnutrition and antipyretics to reduce high fever

http://www.who.int/fch/depts/cah/resp_infections/en/

A.R.I. Case Management Chart

ACUTE RESPIRATORY ILLNESS CHILD AGED 2 MONTHS UP TO 5 YEARS



Acute Diarrhea

Bloody Diarrhea:

- Shigella, Salmonella, Campylobacter, enteroinvasive E. coli, Schistosoma, Entamoeba histolytica
- Pus in stool, fever, abdominal cramping, rectal pain
- No vomiting
- 1st line: Ciprofloxacin, not cotrimoxazole, check local resistance
- Watery, Non-bloody Diarrhea:
 - Cholera:
 - Associated with rice water stools, cramping, vomiting
 - No fever, rectal pain, or pus in the stool
 - Antibiotics/severe diarrhea: fluoroquinolone, check local resistance
 - Other causes:
 - Rotavirus, Norovirus, Adenovirus, Calicivirus, Norwalk, Cryptosporidium, I sosporidium, Microsporidium, Giardia......
- Is this the beginning of an outbreak?

Diarrhea Case Management Chart



* 1st line: Ciprofloxacin; do not use cotrimoxazole

Preventing Diarrhea

- Exclusive breastfeeding for up to 6 months
 - Continue breastfeeding = 2nd year
 - Nutritious/hygienically prepared complementary foods starting at
 - 6 months of age
- Use cleanest available water, protect from contamination
 - Treat water when necessary
- Hand washing with soap
- Dispose of feces in a latrine or potty
- Ensure measles immunization at appropriate age
- Specific Vaccines:
 - Vibrio cholera; Typhoid; Rotavirus

Tuberculosis: The Bad News

- Estimated 9.2 million new cases in 2006

- 83% in Africa, S.E.Asia & Western Pacific regions:
 - India> China> Indonesia> South Africa> Nigeria
- 1.7 million deaths
- 700,000 co-infected with HIV (200,000 deaths)
- Death/ disease burden in children?
 - Only smear-positive cases are reported to WHO

- XDR-TB: 500,000 cases in 2006

 Resistant to at least INH & Rifampicin (i.e. MDR-TB) <u>and</u> to any fluroquinolones, <u>and</u> to any of the 2nd line injectables (Amikacin, Kanamycin, Capreomycin).

Countries with XDR-TB confirmed cases as of February 2008





2006 Recommendations W.H.O. Global Task Force on XDR-TB

- 1 Strengthen quality of basic TB & HI V/AI DS control
- 2 Scale up programatic management of MDR-TB & XDR-TB
- 3 Strengthen laboratory services
- 4 Expand MDR-TB & XDR-TB surveillance
- 5 Develop and implement infection control measures
- 6 Strengthen advocacy, communication, social mobilization
- 7 Pursue resource mobilization at all levels
- 8 Promote research and development of new tools

Actions & Progress Since Oct. 2006

- 2nd WHO Global XDR-TB Task Force meeting in April 2008
 - XDR-TB country data included in the global TB drug resistance report (2/08)

• Missions to identify and provide support and technical assistance:

- Lesotho, Malawi, Mozambique, Namibia, Swaziland, South Africa and Zambia.
- International staff deployed in Lesotho and South Africa
- Rapid surveys completed to assess XDR-TB extent in Botswana and Swaziland.
- Generic protocols developed for countries.
- National training courses planned for Botswana, I vory Coast, Mexico and South Africa by end of 2007.
- Lesotho National Reference Laboratory restructured
 - Support from F.I.N.D.¹, Partners In Health and WHO.
- Green Light Committee strengthened to review and approve applications for 2nd line anti-TB drugs.
- TB partners/ MDR- & XDR-TB management expansion activities
 - TB C.A.P.² in infection control
 - Regional training courses in Africa, Americas, Middle East and South East Asia.
 - 1. Foundation for Innovative New Diagnostics
 - 2. Tuberculosis Control Assistance Program (USAID)

Actions & Progress Since Oct. 2006

- The Global Plan to Stop TB revised to include:
 - doubling of the numbers of MDR-TB treatments by 2015 & latest XDR-TB costings.
- Revised guidelines/ management of resistant TB in preparation:
 - includes guidance on human rights approach and community-based MDR-TB care.
- Infection control guidelines/ health care facilities in revision
 - national level infection control framework is also needed.
- Develop new approach to recording/ reporting of resistant TB
- WHO TB lab reorganized and business plan for expansion drafted.
- WHO/PEPFAR consultation:
 - recommended PEPFAR make immediately available US\$50m for TB/HIV, including funds to expand infection control, and strengthen laboratories.
- Health ministers endorsed XDR-TB emergency actions in 2007 World Health Assembly resolution
 - European Ministers back XDR-TB actions in 2007 Berlin TB Declaration.

W.H.O. Response

MDR-TB AND XDR-TB RESPONSE PLAN 2007-2008

The lives of 134,000 MDR-TB and XDR-TB patients will be saved in 2007-2008 if the US\$ 2.1billion response plan is fully funded and fully implemented.

Global Response Plan	2007	2008	<u>Total</u>
MDR-TB Cases on Treatment	60,000	100,000	160,000
XDR-TB Cases on Treatment	6,000	10,000	16,000
Lives Saved	49,000	85,000	134,000
US\$ Total	\$882m	\$1,273m	\$2,155m

Tuberculosis: The Good News

- =26 million treated with WHO DOTS strategy¹
- 2005 targets for case detection (=70%) & cure (=85%) met in Western Pacific Region & 26 countries¹
- TB/HIV or MDR-TB cases far fewer than anticipated¹
- Global TB epidemic on the threshold of decline²
 - Incidence rate stable/falling in all WHO regions
 - Millennium Development Goal 6 to halt & begun to reverse incidence of TB, will be achieved before target date of 2015
 - 4 regions on track to halve prevalence & death rates by 2015 vs.1990 levels
 - Africa and Europe not on track to reach these targets:
 - » large increases in the incidence of TB during the 1990s.

1. World Health Statistics 2007; Ten Statistical Highlights in Global Public Health. WHO,2007

2. Global Tuberculosis Control 2008: SURVEILLANCE, PLANNING, FINANCING. WHO 2008





Regional Variation in Incidence of Malaria

Incidence of Clinical Malaria Episodes

Map 3. Estimated incidence of clinical malaria episodes-caused by any speciesresulting from local transmission, country level averages, 2004 (2)

0.00 0

Incidence of P. falciparum Episodes



World Malaria Report, 2005. W.H.O. (http://rbm.who.int/wmr2005/index.html)

Malaria transmission areas and reported P. falciparum resistance, 2004



P. Vivax resistance:

- Sulfadoxine-pyrimethamine in many areas
- Chloroquine in Indonesia, East Timor, Papua New Guinea and other parts of Oceania and Peru.

P. Malariae:

 Chloroquine resistance in Indonesia

Malaria

- 40% of the world's population still at risk
- 3 million acute illnesses
- 1 million deaths/year
 - 90% of deaths are in Sub-Saharan Africa:
 - Most efficient parasite (P.falciparum)
 - Most efficient vector (A.gambiae ss)
 - Africa's leading cause of under-five mortality (20%)
 - Responsible for 10% of Africa's overall disease burden

Malaria

- In areas with high malaria transmission:
 - 40% of public health expenditures
 - 30-50% of inpatient admissions
 - Up to 50% of outpatient visits
 - Major cause of anaemia/ children & pregnant women, low birth weight, premature birth and infant mortality
- P. vivax & falciparum most common
 - Most deaths are due to falciparum
- Sub-Saharan Africa:
 - 60% of cases of worldwide
 - 75% of falciparum cases
 - =80% of malaria deaths
 - Falciparum → 18% of all deaths in children = 5yrs.

Roll Back Malaria Program

- Goal:
 - Halve the burden/ endemic countries by 2010
- Insecticide-treated Nets for =60% of children = 5 yrs. & to Pregnant Women:
 - Pyrethroid insecticides
 - Africa/ 2001: only 3% of kids = 5yrs. (0.1-63%)
- Indoor Residual Spraying
- Larviciding for vector control:
 - Oiling of waste water collections
 - Temephos or Insect Development Inhibitors (IDI) for clean waters
 - Larvivorous fish for ornamental waters.

Roll Back Malaria Program

- Prompt & Effective treatment:
 - Artemisinin-based combination therapy
 - 10-20 times more expensive than chloroquine
 - Home management for children = 5 yrs
 - Train mothers & provide pre-packaged high-quality meds
- Intermittent Preventative Therapy for pregnant women in Sub-Saharan Africa:
 - Sulphadoxine-pyrimethamine x2 after the 1st trimester
 - Consider endemnicity, drug resistance, HIV, P. vivax

Measles

- Burden of Disease:
 - Estimated 30-40 million cases annually?
 - Case fatality ratios: 1–5% to 10–30%
 - Highly contagious
 - In 2002:
 - Estimated 610,000 deaths (540,000 in children < 5 yrs)
- Complications:
 - Severe measles / malnourished, vitamin-A deficient, HIV-infected
 - Otitis media, Blindness, Encephalopathy, Diarrhea, Pneumonia & Death

Measles

- Measles Initiative, 2001
 - Collaborative effort:
 - WHO, American Red Cross, CDC, UN Foundation, UNICEF
 - Goal: cut deaths due to measles by 90% by 2010 (vs. 2000)
 - Global vaccination campaigns in Africa:
 - 1st dose at 9 months of age or shortly thereafter
 - "2nd opportunity for measles vaccination"
 - Vaccinate those not yet vaccinated or vaccinated at 6 months
 - Vaccinate those in the target population (5-19 yrs) regardless of history of disease or prior vaccination
 - Repeat every 3-4 years?

Measles

Measles Initiative, 2001

- Progress:

- =217 million African children vaccinated (2001-5)
- 75% decrease in deaths in Africa:
 - 506,000 in 1999 ® 126,000 in 2005
- Expansion to Asia & all 6 WHO regions
- Vitamin A, deworming meds, insecticide-treated bed nets



Estimated number of people living with HIV and adult HIV prevalence



Number of people living with HIV
% HIV prevalence, adult (15-49)

This bar indicates the range around the estimate

*Even though the HIV prevalence rates have stabilized in sub-Saharan Africa, the actual number of people infected continues to grow because of population growth. Applying the same prevalence rate to a growing population will result in increasing numbers of people living with HIV.



Regional HIV and AIDS statistics and features, 2003 and 2005

REGION	Adults (' children livi	15+) and ng with HIV	Adults (15+) newly infect	and children ed with HIV	Adult (prevale	(15-49) nce (%)	Adult (15+) and child deaths due to AIDS			
	2005	2003	2005	2003	2005	2003	2005	2003		
Sub-Saharan Africa	24.5 million [21.6? 27.4	23.5 million [20.8? 26.3	2.7 million [2.3? 3.1 million]	2.6 million [2.3? 3.0 million]	6.1 [5.4? 6.8]	6.2 [5.5? 7.0]	2.0 million [1.7? 2.3 million]	1.9 million [1.7? 2.3 million]		
North Africa and Middle East	440 000 [250 000? 720	380 000 [220 000? 620	64 000 [38 000? 210 000	54 000 [31 000? 150 000	0.2 [0.1? 0.4]	0.2 [0.1? 0.3]	37 000 [20 000? 62 000]	34 000 [18 000? 57 000]		
Asia	8.3 million [5.7? 12.5 million]	7.6 million [5.2? 11.3 million]	930 000 [620 000? 2.4	860 000 [560 000? 2.3	0.4 [0.3? 0.6]	0.4 [0.2? 0.6]	600 000 [400 000? 850	500 000 [340 000? 710		
Oceania	78 000 [48 000? 170	66 000 [41 000? 140	7200 [3500? 55 000]	[4300-69 000]	0.3 [0.2? 0.8]	0.3 [0.2? 0.7]	3400 [1900? 5500]	2300 [1300? 3600]		
Latin America	000] 1.6 million [1.2? 2.4 million]	000] 1.4 million [1.1? 2.0 million]	140 000 [100 000? 420	130 000 [95 000? 310	0.5 [0.4? 1.2]	0.5 [0.4? 0.7]	59 000 [47 000? 76 000]	51 000 [40 000? 67 000]		
Caribbean	330 000 [240 000? 420	310 000 [230 000? 400	37 000 [26 000? 54 000]	34 000 [24 000? 47 000]	1.6 [1.1? 2.2]	1.5 [1.1? 2.0]	27 000 [19 000? 36 000]	28 000 [19 000? 38 000]		
Eastern Europe and Central Asia	000] 1.5 million [1.0? 2.3 million]	000] 1.1 million [790 000? 1.7	220 000 [150 000? 650	160 000 [110 000? 440	0.8 [0.6? 1.4]	0.6 [0.4? 1.0]	53 000 [36 000? 75 000]	28 000 [19 000? 39 000]		
North America, Western and Central Europe	2.0 million [1.4? 2.9 million]	1.8 million [1.3? 2.7 million]	65 000 65 000 [52 000? 98 000]	65 000 65 000 [52 000? 98 000]	0.5 [0.4? 0.7]	0.5 [0.3? 0.6]	30 000 [24 000? 45 000]	30 000 [24 000? 45 000]		
TOTAL	38.6 million [33.4? 46.0	36.2 million [31.4? 42.9	4.1 million [3.4? 6.2 million]	3.9 million [3.3? 5.8 million]	1.0 [0.9? 1.2]	1.0 [0.8? 1.2]	2.8 million [2.4? 3.3 million]	2.6 million [2.2? 3.1 million]		



Impact of AIDS on life expectancy in five African countries, 1970– 2010



Source: United Nations Population Division (2004). World Population Prospects: The 2004 Revision, database.



HIV prevalence (%) among pregnant women attending antenatal clinics in sub-Saharan Africa, 1997/98? 2004



Median HIV prevalence (%) 10 Côte d'Ivoire **Burkina Faso** 5 Ghana Senegal 0 1999? 2001 1997? 2002 2003 2004 1998 2000

Note: Analysis restricted to consistent surveillance sites for all countries except South Africa (by province) and Swaziland (by region)

Sources: Ministry of Health (Mozambique); Department of Health (South Africa); Ministry of Health and Social Welfare (Swaziland); Ministry of Health and Child Welfare (Zimbabwe); Adapted from Asamoah-Odei, et al. HIV prevalence and trends in sub-Saharan Africa: no decline and large subregional differences. Lancet, 2004 (Ethiopia); Ministry of Health—National AIDS/STD Control Programme (Kenya); Ministry of Health (United Republic of Tanzania); Conseil national de lutte contre le sida et les IST (Burkina Faso); Centers for Disease Control and Prevention (CDC)—GAP—Côte d'Ivoire (Côte d'Ivoire); Ghana Health Service (Ghana); Conseil National de Lutte Contre le SIDA (Senegal).



HIV prevalence (%) by gender and urban/rural residence, selected sub-Saharan African countries, 2001? 2005



Sources: Demographic and Health Survey reports (Lesotho, Zambia, Kenya, Burkina Faso, Ghana, Guinea and Senegal) (2001–2005). Nelson Mandela Foundation (South Africa) (2005). Ministry of Health (Uganda). Tanzania Commission for AIDS (UR Tanzania) (2005).



Comparison of 2003 and 2005 data on the coverage of antiretroviral therapy, access to mother-to-child prevention services and coverage of HIV-infected mothers who received antiretroviral prophylaxis to prevent mother-to-child transmission in low and middle income countries





Comparison of 2003 and 2005 data on the expansion of antiretroviral therapy and coverage of HIV-infected mothers who received antiretroviral prophylaxis in three sub-Saharan African countries



Sources: Individual country reports (2005).



Impact of three scenarios on New HIV infections in sub-Saharan Africa, 2003–2020





Impact of AIDS-related deaths in sub-Saharan Africa, 2003–2020





Diarrhea, malnutrition, & pediatric mortality Francistown, Botswana, Nov 2005-April 2006



Findings: Stool testing

- Stool samples from inpatient children with diamhea tested by CDC-Atlanta
 - Cryptosporidium-60%
 - Enteropathogenic E. coli (EPEC)-50%
 - Salmonella 38%
 - Shigella 17%
 - Norovirus 21%
- Multiple pathogens suggest general contamination of water and environment

Findings: Case-control study Risk factors for diarrhea

AOR* (95% CI)
50.0 (4.5 - 100)
3.7 (1.5 - 9.1)
3.0 (1.1 - 8.6)
2.6 (1.1 – 6.3)
2.5 (1.1 - 5.0)

Findings: Diarrhea inpatients

Feeding of infants <12 months

Milk provided	Mother HIV positive (n=55)	Mother HIV negative (n=26)
Breastfeeding	0	35%
Formula	73%	15%
Cow milk (UHT)	25%	35%
Cow milk (raw)	11%	15%
Nomilk	2%	8%

Findings: Diarrhea inpatients Mortality (n=153)

- High mortality: 22% (33/153) died
- Risk factors for death
 - Kwashioukov RR 2.0, 95% CI 1.1-3.8
 - Only 1/16 (6%) breastfeeding children died (ns)
 - infant age 1 month; also receiving cow milk and formula
- Not associated with death
 - Maternal HIV status
 - Infant HIV status
 - Socioeconomicstatus
 - Water source
 - Urban vs. rural residence
 - Specific pathogen

•Mortality in formula-fed = 32/137 (23%)?



14th Conference on Retroviruses and Opportunistic Infections

Prevention of HIV Transmission from Breastfeeding

HOW EFFICACIOUS ARE SHORT-COURSE ARVs IN MOTHER-TO-CHILD-TRANSMISSION AT ABOUT 6 WEEKS IN BREASTFEEDING AFRICAN WOMEN. 1995-2005?

ATTRITION OF EFFICACY DUE TO BREASTFEEDING





LeRoy V, WHO 2006



What is the risk of post-natal transmission due to breastfeeding?

Breastfeeding and HIV International Transmission Study – BHITS

- Estimated rate of breastfeeding transmission was 0.74%/mth
- This risk was roughly constant over the 24 month period
- Carries a risk of about 8 96/100 child years of breastfeeding

BHITS Study Group, JID 2004



AT 18 MONTHS: MORE BREASTFED INFANTS INFECTED BUT: MORE FORMULA-FED INFANTS DIED

18m:	HIV+	Dead
Breast:	9.5%	8.5%
Formula:	6.0%	10.7%



EARLY MORTALITY IS HIGHER IN FORMULA-FED THAN BREASTFED [+ AZT] INFANTS: BOTSWANA

IS THERE OVERALL BENEFIT TO EARLY BREASTFEEDING CESSATION [GROUP A] vs CONTINUED BREASTFEEDING [GROUP B]?



Kuhn L, CROI 2007, ZEBS

 6 month Transmission in exclusively Breast fed infants

> Maternal CD4 <200 vs. >200: 34% vs.17%

- Why not use formula if there's no difference in survival?
 - Formula is expensive
 Hard to supply

RISK FACTORS FOR POSTNATAL TRANSMISSION

Maternal Factors
 Low CD4
 Infant Factors

Breastmilk Factors

 Non-Exclusive Breastfeeding

Duration
 Viral Factors



3. WHEN TO RECOMMEND EXCLUSIVE BREASTFEEDING OR FORMULA FEEDING

Infant Mortality Rate>25/1000 live births Exclusive breastfeeding for 6 months [early cessation].

Infant Mortality Rate<25/1000 live births: Replacement feeding from birth

Piwoz EG et al, J Nutrition 2005

WHO Recommendations



HIV and Infant Feeding Technical Consultation Geneva, October 25-27, 2006 CONSENSUS STATEMENT

- The most appropriate infant feeding option for an HIV-infected mother should continue to depend on her individual circumstances, including her health status and the local situation, but should take greater consideration of the health services available and the counselling and support she is likely to receive.
- Exclusive breastfeeding is recommended for HIV-infected women for the first 6 months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time.
- When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIVinfected women is recommended.

Vaccines in the Pipeline

- HIV ????
- TB ?
- Malaria ??
- Cholera
- Other Diarrheal agents

Unknowns

- Avian Influenza
 - Sporadic -> Endemic -> Epidemic -> Pandemic?
 - W.H.O. 5-year Strategic Plan:
 - Strengthen the early warning system.
 - Intensify rapid containment operations.
 - Build capacity to cope with a pandemic
 - stockpiles of oseltamivir
 - Coordinate global scientific research & development
 - Rapid development/distribution of a pandemic strain vaccine
- SARS

Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO

18 March 2008

Country	200	03	2004		200	2005		2006		007	2008		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	8	5
Cambodia	0	0	0	0	4	4	2	2	1	1	0	0	7	7
China	1	1	0	0	8	5	13	8	5	3	3	3	30	20
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	4	1	47	20
Indonesia	0	0	0	0	20	13	55	45	42	37	12	10	129	105
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	3	2
Lao People's Democratic Republic	0	0	0	0	0	0	0	0	2	2	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	1	1	0	0	1	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	5	5	106	52
Total	4	4	46	32	98	43	115	79	86	59	24	19	373	236
Fotal number of cases includes	number of deaths	100%	70)%	4	4%	69	%	69	%	79	%	6	3%

WHO reports only laboratory-confirmed cases. All dates refer to onset of illness.

Summary

- Better data to make predictions & direct allocation of resources
- Integrated approach to health care:
 - Emphasis on preventative interventions?
 - Clean water
 - Good nutrition
 - Immunizations:
 - Enteric & Resp. pathogens, Malaria TB, HIV ???
 - Education re risky behavior: sexual, dietary, smoking.....
 - Education/Economic Development:
 - Jobs ® better living standards, health care, pay taxes
 - Better housing & sanitation
 - Access to adequate treatment for acute illnesses:
 - DOTS for TB; for HIV?



		Globa	L.				
Population data in thousand	ş 1					10	
1	2005	2004	2003	2002	2001	2000	1990
Total population	6'445'633	6'370'429	6'295'235	6'219'879	6'144'133	6'067'816	5'264'584
Live births	133'294	132'800	132'390	132'076	131'875	131'806	135'847
Surviving infants	125'993	125'403	124'893	124'476	124'167	123'983	126619
Pop. less than 5 years	615'567	613'757	612'543	611'917	611'841	612 267	624'369
Pop. less than 15 years	1'816'346	1'817'504	1'819'715	1'822'126	1'823'611	1'823'303	1'708'411
Female 15-49 years	1'664'988	1'644'088	1'622'582	1'600'518	1'577'934	1'554'874	1'311'452
Number of reported cases							
Diphtheria	\$229	9'864	6781	9235	10'356	9'594	23'864
Measles	580'287	504'689	677'297	585'957	832'954	836'338	1'374'083
Mumps	019/002	004/210	3341003	4//0/9	412341	344'093	-
Pertussis	121'608	236'844	106'584	136'372	168'533	186'151	476'377
Polio	2'296	1'258	784	1'922	498	2'971	23'366
Rubella	207300	308'219	321180	031'571	836'349	071'280	
Rubella (CRS)	37	88	99	75	50	181	-
Tetanus (neonatal)	9780	9'294	8'999	11762	14'510	15'335	25'293
Tetanus (total)	15'516	13'347	14'369	18781	22'894	18'939	64'378
Yellow fever	588	1'344	672	705	620	684	4'336
Percentage of target populat based on WHO-UNICEF estim TT3plus and YFV are based on	ion vaccinated, ates 2 reported coverage	by antiger	ı			e	
BCG	83	83	82	81	80	80	81
DTP1	88	87	87	86	85	85	88
DTP3	78	77	75	74	74	73	75
HepB3	55	51	46	40	35	33	1
Hib3	21	20	19	17	14	13	1
MCV	77	76	75	74	74	73	73
Pol3	78	77	76	75	74	74	75
TT2phus	57	51	52	54	52	53	43
VEU	43	36	32	30	21	26	4

WHO vaccine-preventable disease monitoring system, 2006 global summary

28 million infants not immunized (DTP3), 2005



() WHO

192 WHO Member States.

"Developing"* countries with % of districts achieving at least 80% DTP3 coverage, 2005



Source: WHO/UNICEF estimates and WHO/IVB database, 2006

192 WHO Member States.

The containing and makes tabled in the oblightation relead of mit shap to be imply the experimenof any optimic whatsoever on the part of the World Health (Organization concerning the legal status of any country, tarritory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted limes on maps represent approximate border limes for which there may not yet be full agreement. @ WHO 2006. All rights reserved



Slide Date: October 06

Polio Eradication Progress, 1988 - 2005



Resources

- <u>http://www.who.int/child-adolescent-</u> <u>health/publications/pubemergencies.htm</u>:
 - Acute Respiratory Infections in children
 - ARI Case management charts
 - Diarrhoea Treatment Guidelines
 - Diarrhoea Case management charts
 - Guidelines for the control of shigellosis
 - Integrated Management of Childhood Illness (IMCI)



No Benefit of Early Cessation of Breastfeeding at 4 Months on HIV-free Survival of Infants Born to HIV-infected Mothers

Zambia Exclusive Breastfeeding Study

Mases Sinkala, Louise Kuhn, Chipepo Kankasa, Prisca Kasonde, Cheswa Vwalika, Mwiya Mwiya, Nancy Scott, Katherine Semrau, Grace Aldrovandi, Donald M. Thea

> Ministry of Health, Zambia Columbia University, New York Boston University Children's Hospital of Los Angeles UTH, University of Zambia



Benefits of exclusive breastfeeding on early postnatal transmission through 4 months



Increased transmission due to non-exclusive BF: (as time-dependent) Relative Hazard 3.4 (95% CI: 1.7-7.2)

Was Weaning in Group A Successfully Achieved?

2

Duration of breastfeeding by random group assignment



How abrupt?					
Stopped within:	Percent				
0-2 Days	70				
2-7 Days	25				
7-14 days	4				
15+ days	1				

3

Was There Overall Benefit to Early Cessation vs. Continued Breastfeeding?

Over all HIV-free Survival among Children without HIV & still Breastfeeding at 4 Months of Age by Group Assignment



In Group A, Was There Benefit to Compliance with Early Cessation of Breastfeeding? Effects differed by stage of maternal disease

HIV-free Survival among Children without HIV & still Breastfeeding at 4 Months of Age - <u>As Practiced</u>



Was Early cessation of BF Harmful to HIV-infected Children?

Survival of HIV-infected Children with Positive Results before 4 Months of Age by Group Assignment



Conclusions

- There is no net benefit to early cessation of breastfeeding among HIV-exposed children living in resource-poor areas.
- Continued breastfeeding may be more beneficial for children of mothers with high CD4 counts.
- Exclusive breastfeeding in the first 4 months significantly reduces HIV transmission through breastmilk.
- Early cessation of breastfeeding is particularly dangerous for children who are HIV-infected prior to 4 months of age.