7th INTERNATIONAL SYMPOSIUM ON
CHILDREN'S ENVIRONMENTAL HEALTH

MINISTRY OF ENVIRONMENT OF JAPAN

14 to 16 December 2008

Tokyo, Japan

BIRTH COHORT STUDIES IN DEVELOPING COUNTRIES

GLOBAL AND LOCAL CHALLENGES

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Public Health and Environment
World Health Organization

WHO

The children of today live in environments that are vastly different than those of a few generations ago

This is telescoped in low and middle-income countries.

The children of today are exposed to:

- Transition from agrarian to urbanized industrial societies
- Increasing production and use of chemicals
- Movement of hazardous wastes across national borders
- Global climate change
- Emerging and re-emerging risks: EDCs, nanoparticles, atmospheric brown clouds, ….

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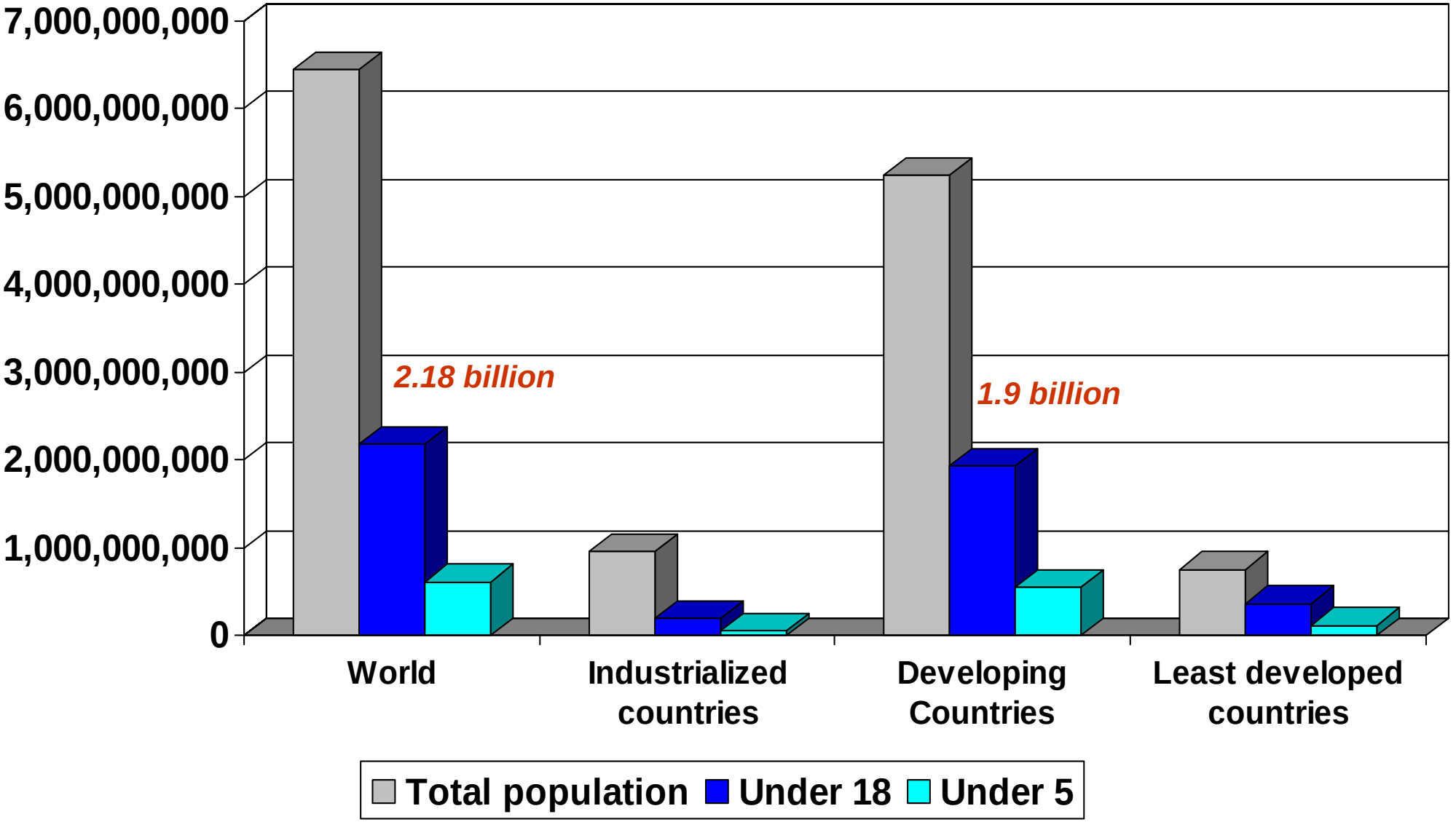
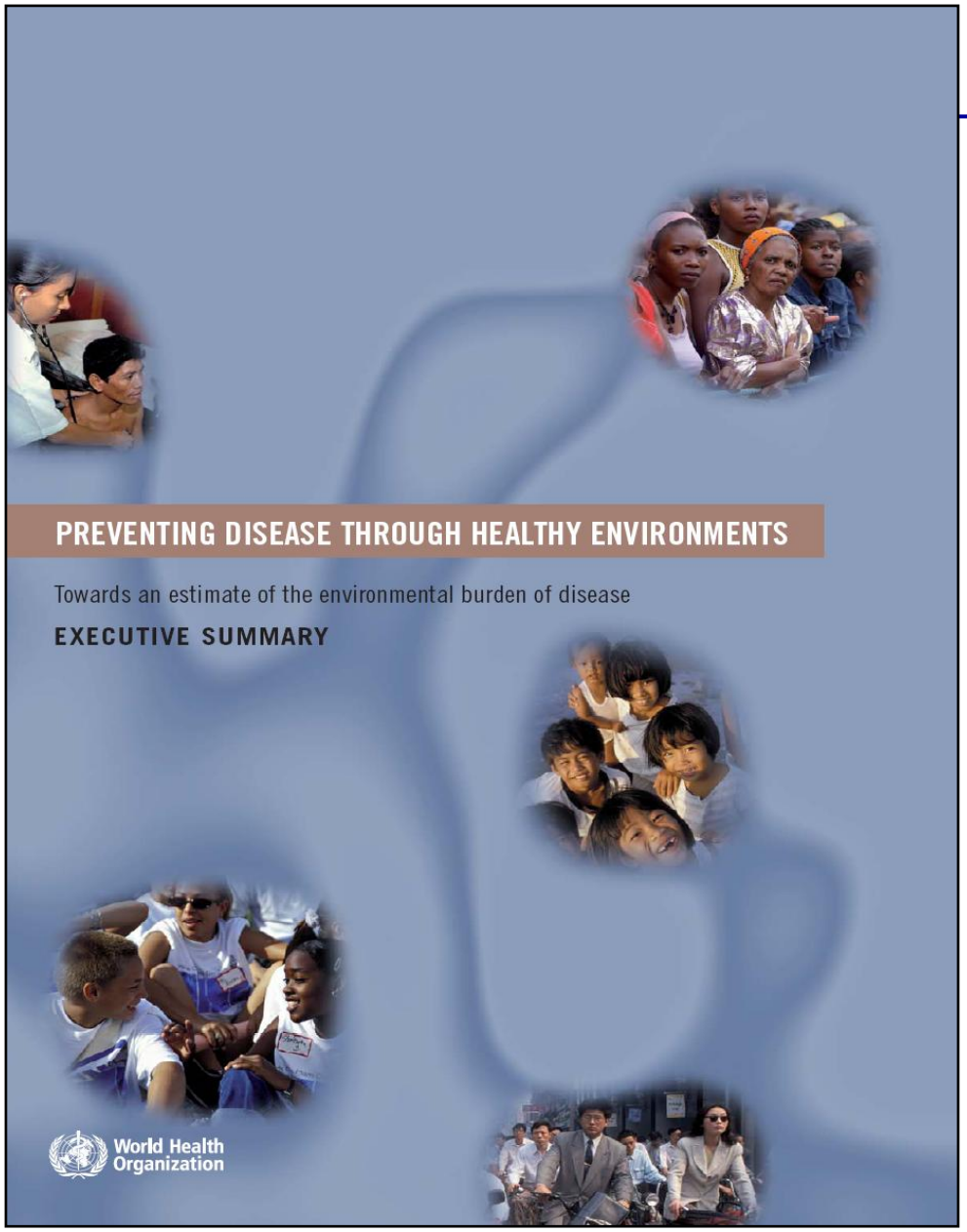
Risks are enhanced in countries undergoing industrial transition – *is there locally relevant data?.*

Is the "epidemiological transition" detected?

Children in the world



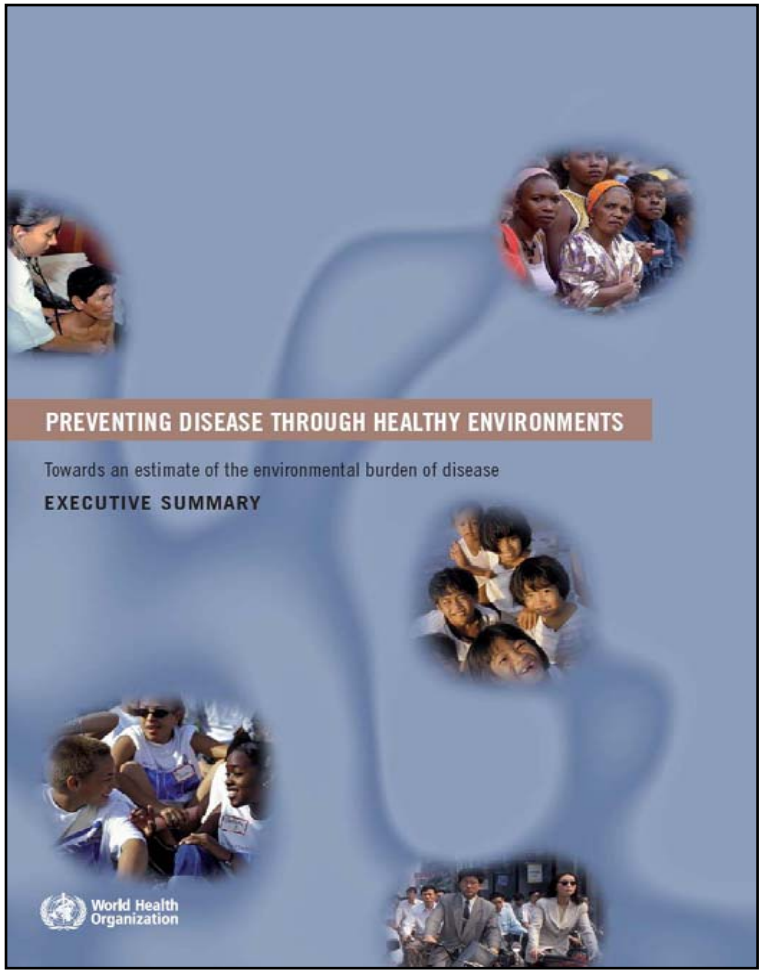


HOW DO SPECIFIC DISEASES AND INJURIES RELATE TO ENVIRONMENTAL RISK FACTORS ?

WHICH REGIONS AND POPULATIONS ARE THE MOST VULNERABLE

Environmental factors contribute to 85 of the 102 major diseases of the World Health Report (2004)

Burden of disease attributable to environmental factors



- **24% of global disease burden**
  (healthy life years lost)
- **23% of <u>all</u> deaths**
  (premature mortality)
  - ***25% in developing countries***
  - ***17% in developed regions***
- ***36% of deaths in children 0-14 years***

Environmentally-related diseases in children

- **On average, children in developing countries lose 8-times more *healthy life years* per capita than children in developed countries**
- **In very poor regions of the world, the disparity is greater: n° of healthy life years lost due to lower respiratory infection is 800 times greater per capita**
- **Mental retardation caused by lead in gasoline is 30 times higher in areas where it is used, if compared with areas where it was banned**

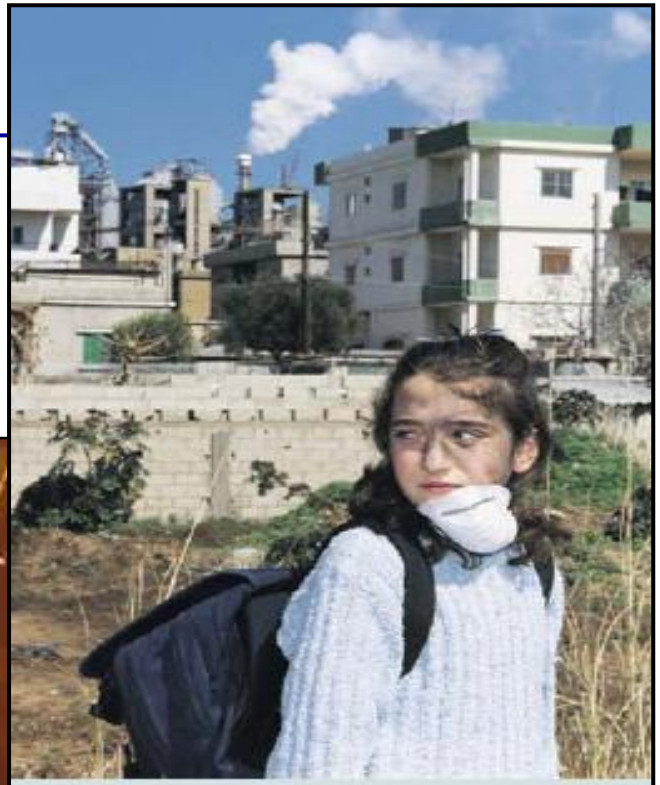
PREVENTING DISEASE THROUGH HEALTHY ENVIRONMENTS: Towards an estimate of the global burden of disease

Cooking and heating with solid fuels over an open fire in Latin America. Many women and children in developing countries are thus exposed to very high concentrations of indoor air pollution, a major risk factor for respiratory infections.

Credit: Nigel Bruce/University of Liverpool

A child directly exposed to tailpipe emissions from an automobile, which may heighten environmental exposue to lead in countries where leaded gasoline has not yet been phased out.

Credit: Harmut Schwarzbach/Still Pictures



A schoolgirl with a face mask for protection from smokestack pollution emissions of factories in her neighbourhood in the eastern Mediterranean region.

Credit: Munir NASA/UNEP/Still Pictures

Japan

Population	128.1 mio
GNI/capita	31 410 US$
% urbanization	66%
% people living in cities greater than 100 000 inhabitants	64%
Population below the poverty line (national)	NA
Population below the poverty line (international, <$1/day)	NA
Under age 5 mortality rate	4/1000 live births
Life expectancy	82 years

Environmental burden of disease for selected risk factors, per year

Risk factor	Exposure		Deaths /year	DALYs/ 1000 cap /year
Water, sanitation and hygiene (diarrhoea only)	Improved water: Improved sanitation:	100% 100%	-	0.2
Indoor air	SFU% households:	<5%	-	-
Outdoor air	Mean urban PM10:	33 ug/m3	23 800	0.9
Main malaria vectors	No transmission			
Main other vectors	None			

COUNTRY PROFILE – ENVIRONMENTAL BURDEN OF DISEASE - JAPAN

Environmental burden by disease category [DALYs/1000 capita], per year

Disease group	World's lowest country rate	Country rate	World's highest country rate
Diarrhoea	0.2	**0.3**	114
Respiratory infections	0.1	**0.5**	56
Malaria	0.0	**0.0**	32
Other vector-borne diseases	0.0	**-**	4.2
Lung cancer	0.0	**0.8**	2.5
Other cancers	0.5	**2.6**	4.1
Neuropsychiatric disorders	1.4	**1.6**	4.4
Cardiovascular disease	1.3	**2.8**	13
COPD	0.0	**0.3**	4.7
Asthma	0.3	**1.0**	2.4
Musculoskeletal diseases	0.5	**1.0**	1.5
Road traffic injuries	0.3	**0.3**	10
Other unintentional injuries	0.9	**1.3**	19
Intentional injuries	0.1	**0.8**	7

Other indicators	
Use of leaded gasoline (2004)	No
Overcrowding	NA
Malnutrition (% stunting)	NA

Every year more than 3.000.000 children under 5 die due to diseases linked to the environment

- **Diarrhoeal disease** **1.800.000**
- **Respiratory diseases** **1.000.000**
- **Malaria/vector-borne disease** **1.000.000**
- **Poisonings/Injuries** **300.000**

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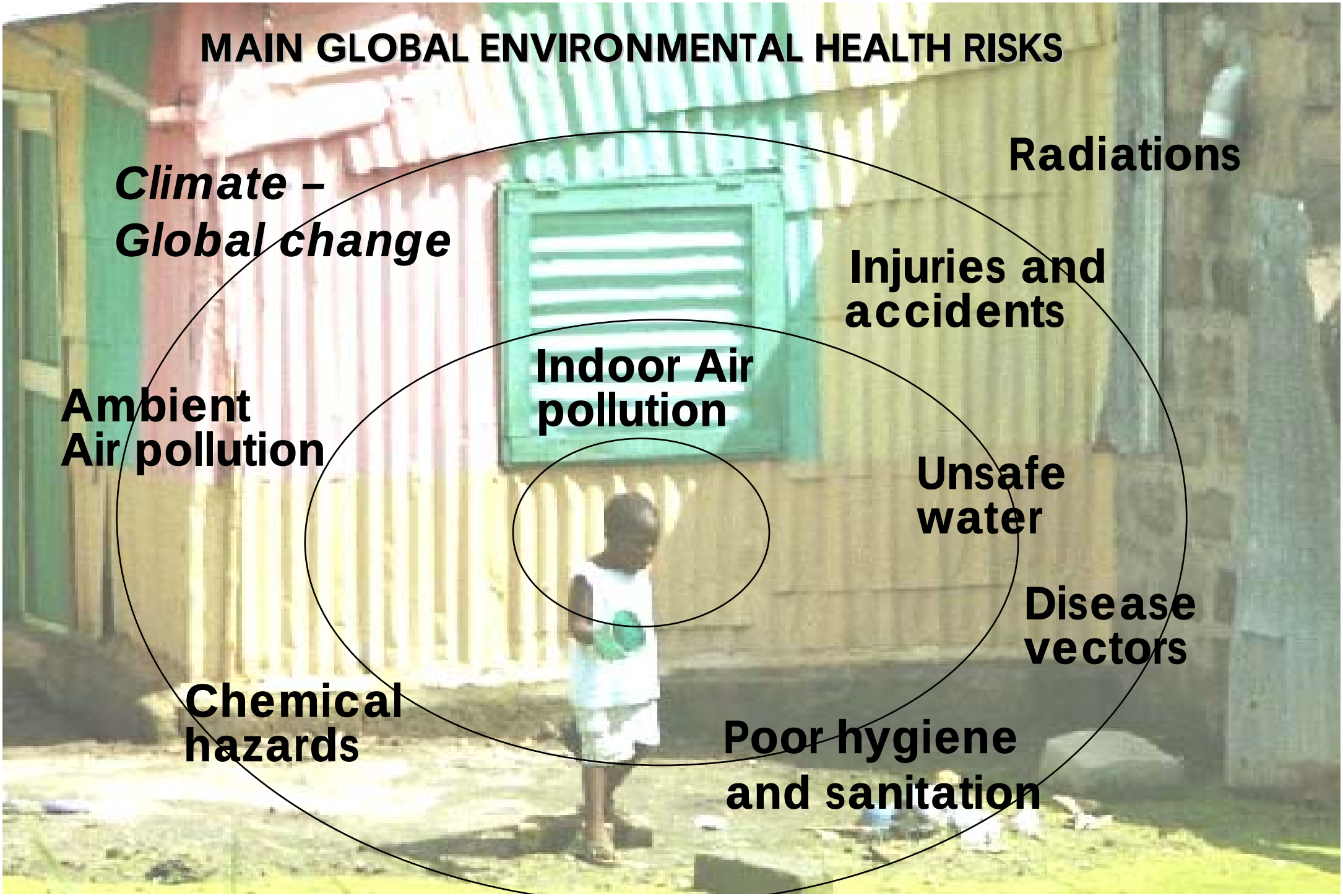
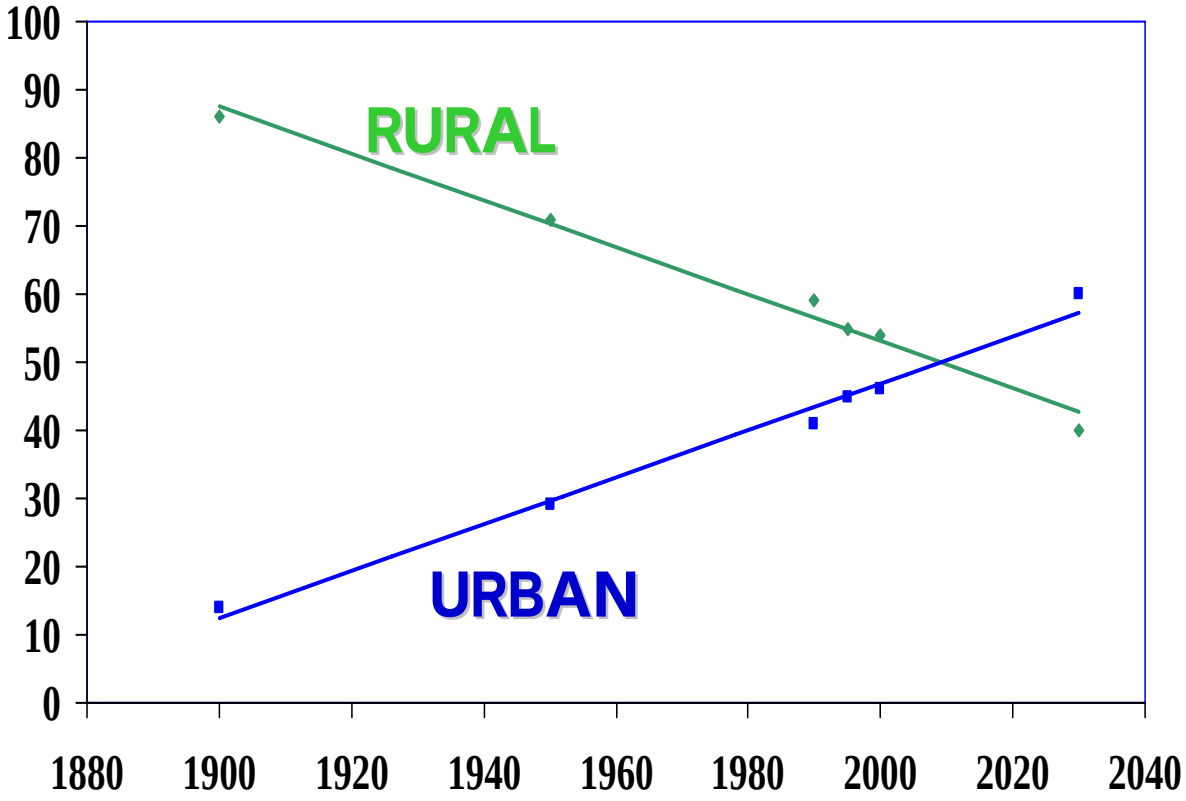
What happens with those who survive ?


MAIN GLOBAL ENVIRONMENTAL HEALTH RISKS
Climate –
Global change
Radiations
Injuries and
accidents
Indoor Air
pollution
Ambient
Air pollution
Unsafe
water
Disease
vectors
Chemical
hazards
Poor hygiene
and sanitation

URBANIZATION TRENDS



World's annual urban growth rate at 1.8% vs. rural growth rate of 0.1 %

World's urban population will go from 2.86 billion (in 2000) to 4.98 billion by 2030

High-income countries will account for only 28 million out of the 2.12 billion increase

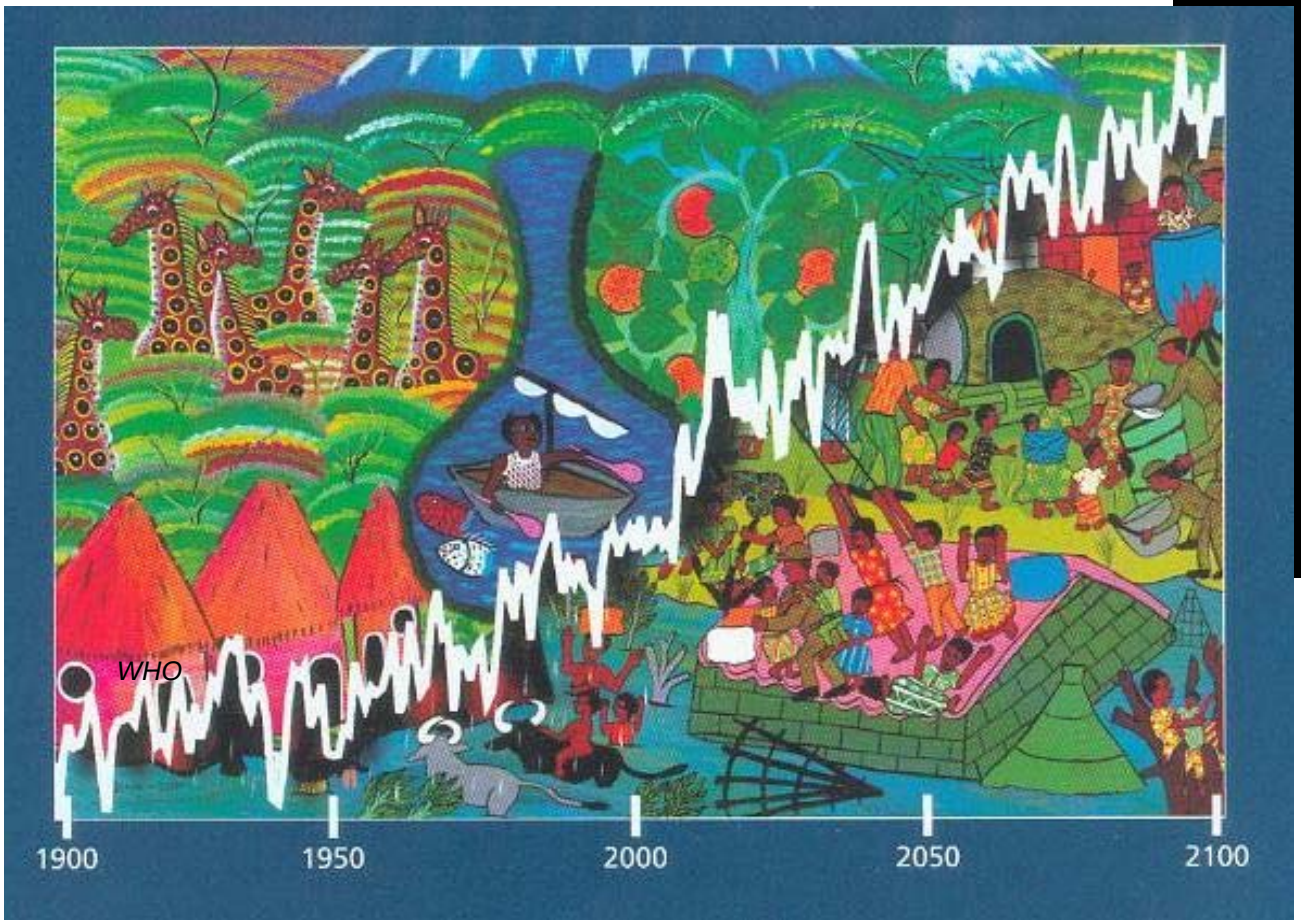
2004-5 UN-HABITAT
State of the world's cities'

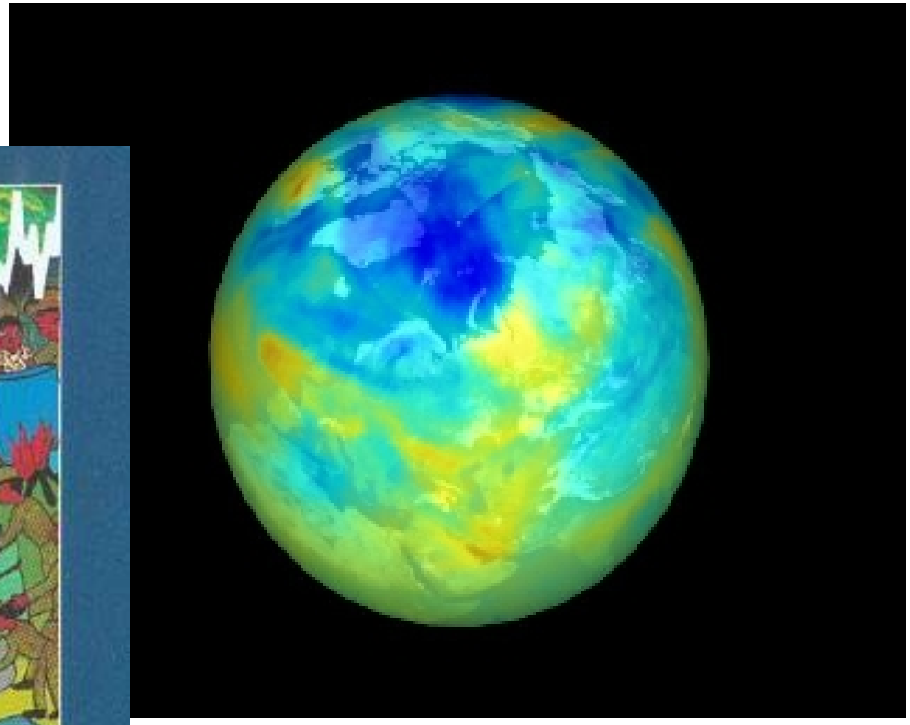
Urbanization trends - as cities grow anarchically,

- Slums emerge near industrial sites, power stations, garbage dumps, busy roads without services, degrading the natural environment.
- Housing is unsafe, no ventilation, no natural light, prone to fire
- In areas with dust, smoke, noise pollution, disease vectors
- Chemicals unsafely stored and dumped
- Pollutants released by factories and vehicle exhaust fumes
- Slum children are especially vulnerable
- Child labor develops…

Urbanization and its consequences on children
P. Mehta, ICCW News Bull. 1992

GLOBAL ENVIRONMENTAL CHANGE





Ozone Hole
svs.gsfc.nasa.gov

Global warming

Ozone depletion

Why and how are children vulnerable to climate change?

Modality	Mechanism	Increased Exposure
Metabolic	• > Respiratory rate • > Metabolic rate • > Water demand per unit body mass	• Air pollution, allergens • Malnutrition, thermal extremes • Gastrointestinal Diseases, dehydration
Behavioral	• > Outdoor time • > Vigorous activity • < Ability to avoid unhealthy situations • < Swimming capacity	• Infectious diseases, air pollution, UV radiation, thermal extremes, allergens • Weather extremes, UV radiation, thermal extremes • Drowning
Physiology	• > Surface area: volume • < Detoxifying capacity • < Skin development • < Immunity	• Infectious diseases, UV radiation • Air pollution, infectious diseases, thermal extremes • UV radiation • Infectious diseases, allergens/mycotoxins
Time	• > Latency for genetic/long-term effect • > Lifetime exposure time	• UV radiation, malnutrition, allergens
Development	• Undergoing development	• Malnutrition, stunting, psychosocial trauma • Morbidity and quality of life

(> indicates greater, < indicates less)

Figure 3. *Modalities and mechanisms by which children may be more susceptible to climate change than adults.*

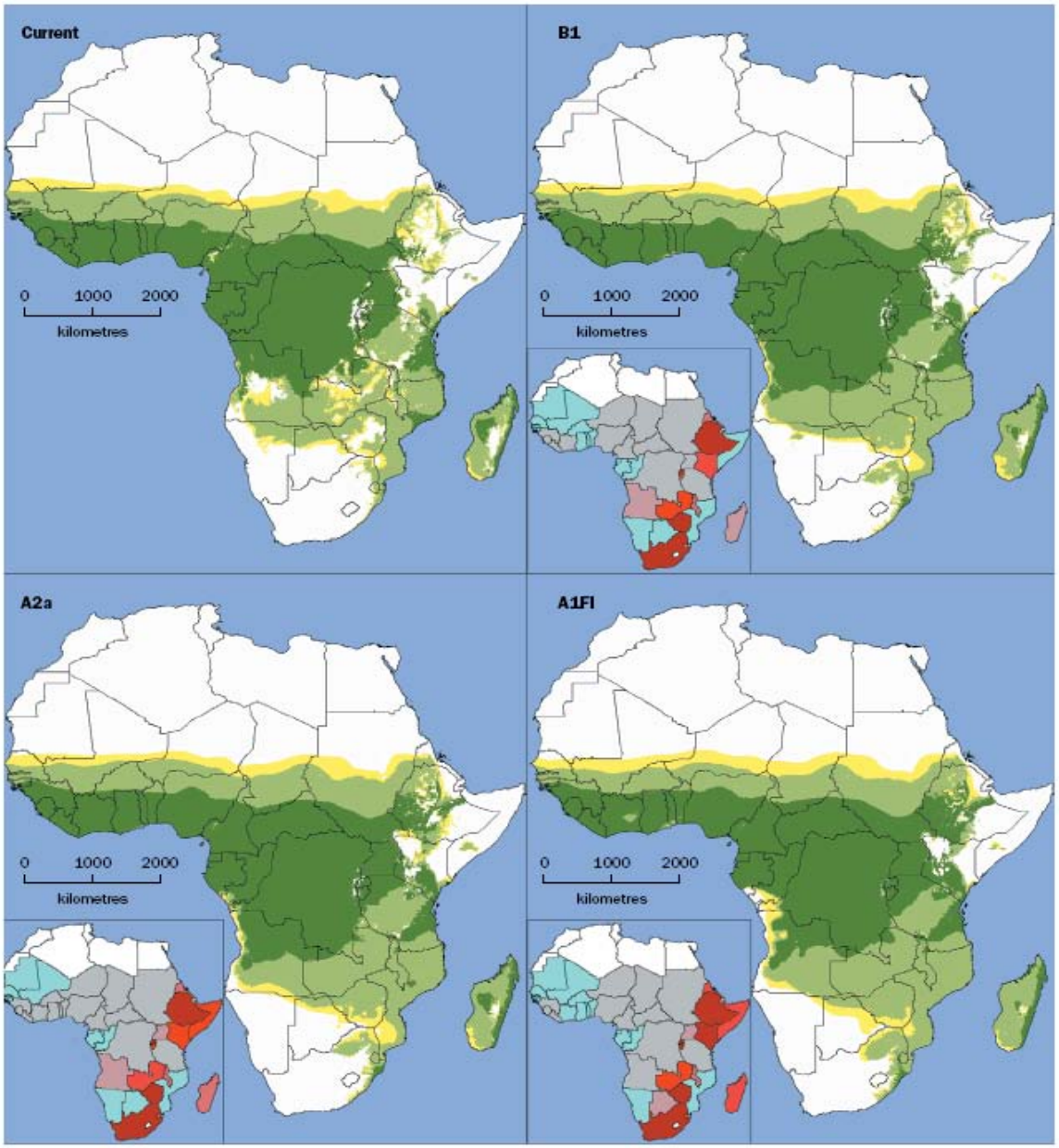
Global warming – potential health impacts

Direct Effects:

- Respiratory problems
- Weather disasters: death, injuries, trauma, disease
- Dehydration and diarrhoeal disease
- Thermal extremes: heat stroke

Indirect Effects:

- Food scarcity: malnutrition, growth retardation, developmental delay
- Malaria, dengue fever, and other vector-borne diseases
- Increased aeroallergens: asthma, allergies

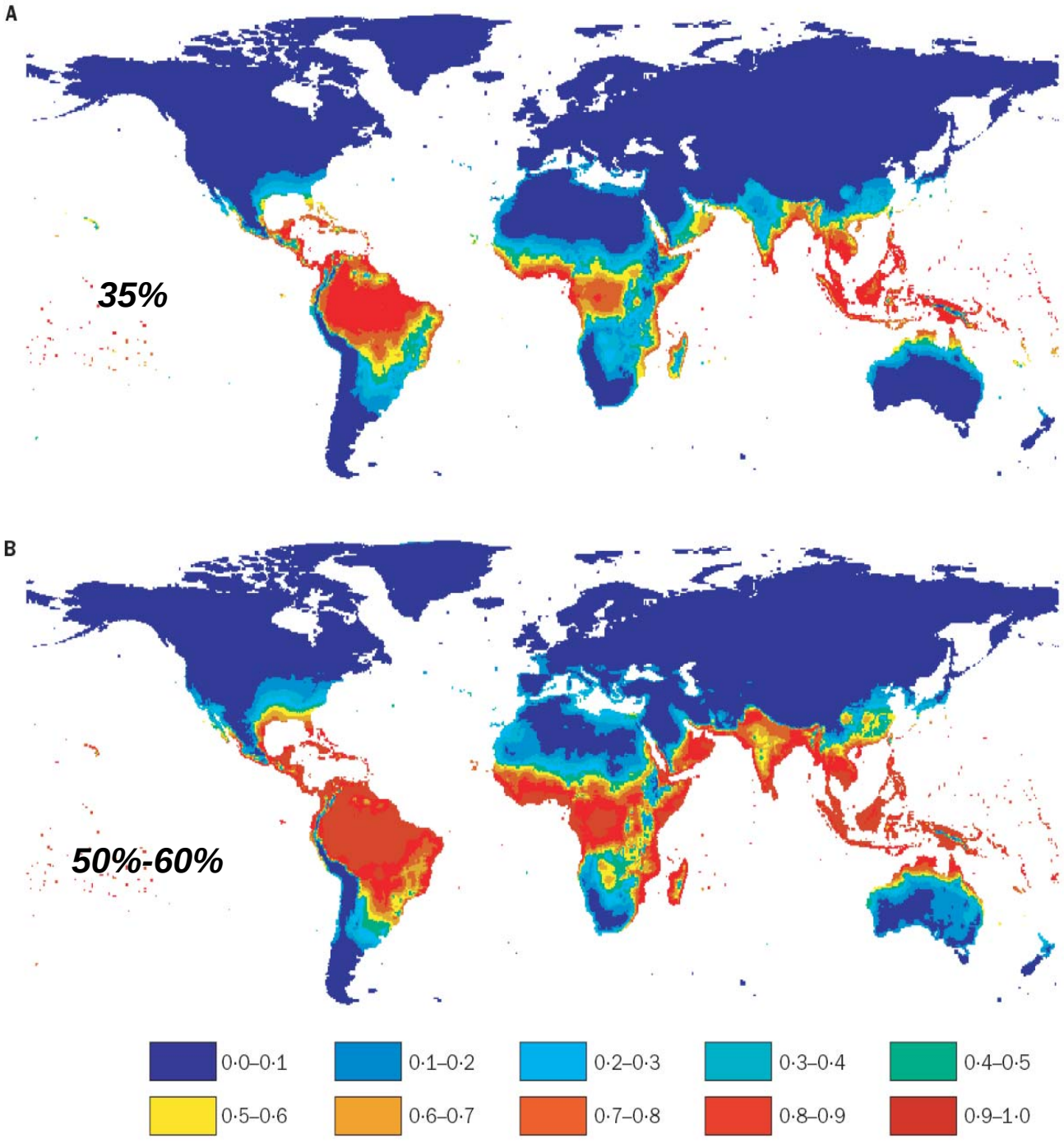


(Tanser et al, Lancet, 2003)

Future climate change and malaria

1.1 million death/year – most of them children!

Climate change is likely to change transmission – *but to what extent?*



Future climate change and dengue

Increase in the the proportion of global population exposed to dengue from 35% to 50- 60% by 2085.

Hales et al, Lancet 2002

GLOBAL ENVIRONMENTAL CHANGE AND CHILD HEALTH

- **Ozone Depletion**
  - Melanoma, Non-Melanoma Skin Cancer,
  - Immune Damage, Cataracts
- **Global Warming**
  - Increased heat related deaths
  - Increased air pollution related illness
  - Injury, death from extreme weather events
  - Increased waterborne diseases
  - Changes in vector/rodent-borne illness
- **Globalization of travel and food**
  - Infectious disease increase
- **Chemicals**
  - Effects of long-term, low dose exposure

Promotion of international collaborative research

NIEHS-WHO Grant for the promotion of collaborative international research enables to promote cooperation and networking -

- **Asthma and respiratory diseases** **(Australia & India)**
- ***Carbon particles in macrophages*** ***(UK and 10 countries)***
- **Arsenic in pregnant women** **(Thailand & USA)**
- **Biomarkers of PAH exposure** **(Thailand, Czech Republic)**
- **POPs in breast milk** **(Mexico & Canada)**
- **Long-term cohort studies** **(15 countries)**

Longitudinal cohort studies on CEH

WHO Informal Consultations *(co-sponsors: NIH, USEPA, CDC)*

Are LTS feasible in developing countries?

Oct 2003 (Glion, Switzerland)

What are the key issues for harmonized international work ?

July 2004 (PAHO, USA 2004)

Need for "core" hypotheses

Nov 2004 (Cuernavaca, Mexico)

Set of measurements required and a "matrix"

Aug 2005 (Bangkok, Thailand)

Longitudinal cohort studies on CEH

Core hypothesis on:

1. **RESPIRATORY EFFECTS**
2. **PREGNANCY OUTCOME**
3. **NEURODEVELOPMENT**
4. **GROWTH AND DEVELOPMENT**
5. ***INJURIES***
6. **BIRTH DEFECTS**
7. **CHILDHOOD CANCER**

Longitudinal cohort studies on CEH

SPECIMENS FOR COLLECTION

Blood (maternal, paternal, child, cord)
Amniotic fluid
Placenta
Meconium
Urine (maternal, child)
Semen
Hair
Nails
Bucal swabs
Vaginal/cervical swabs
Saliva
Tooth
Stools

Other
ENVIRONMENTAL

TIMING OF SAMPLE COLLECTION
Enrolment, 2nd and 3rd trimester
Birth, 3-6-12 months, yearly
Other

TECHNIQUES (standard and "omics")

STORAGE

Biomarkers of exposure, outcome and susceptibility

A matrix for sampling and data collection

Time point	*Antenatal*	*Birth*	*Week 6*	*Month 6-9*	*Year 1*	*Year 2*	*Year 3*	*Year 4*	*Year 5*
Visit	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
	Clinical Assessments and Questionnaires : X = Essential X = Optional								
Inclusion/exclusion criteria, PIC, repeat consent for biological samples	X	X	X	X	X	X	X	X	X
Contact Details	X								
Demographic Data	X								
Family and Lifestyle Questionnaire	X		X	X	X	X	X	X	X
Maternal Medical History	X								
Paternal Medical History			X						
Maternal Physical Examination	X	X			X	X	X	X	X
Maternal Physical and Mental Health	X		X	X	X	X	X	X	X
Pregnancy, Delivery and Neonatal Record		X							
Maternal Food Frequency & Diet Questionnaire (while breastfeeding)	X		X	X	X	X			
Child Food frequency & Diet			X	X	X	X	X	X	X
Developmental Assessment			X	X	X	X	X	X	X
Child medical history			X	X	X	X	X	X	X
Child Physical Examinations		X	X	X	X	X	X	X	X
Record Of Vaccination			X	X	X	X	X	X	X

A matrix for sampling and data collection

Time Point	*Antenatal*	*Birth*	*Week 6*	*Month 6-9*	*Year 1*	*Year 2*	*Year 3*	*Year 4*	*Year 5*
Visit	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
Biological Samples X = Essential X = Optional									
Cord blood (or cord slice)		X							
Placenta		X							
Meconium		X							
Breast Milk			X						
Maternal Blood Sample	X								
Child Blood Sample			X	X	X	X	X	X	X
Child Faecal Sample			X	X	X	X	X	X	X
Maternal Urine	X								
Child Urine			X	X	X	X	X	X	X
Hair			X	X	X	X	X	X	X
Teeth									X
Environmental Questionnaires & Measures									
Environmental Questionnaire	X		X	X	X	X	X	X	X
Outdoor Air Quality	X				X	X	X	X	X
Water Quality	X				X	X	X	X	X
Indoor Air Quality	X				X	X	X	X	X

Longitudinal cohort studies on CEH

Other need/issues identified

- **Terminology/definitions**
- **Environmental "history"**
- **Informatics' support**
- **Capacity building**
- **Biostatistics**
- **Funding: seed, bilateral and main**
- **Ethical aspects**
- **Community involvement/incentives**

Outcomes:

-White paper (publication)

- Guidance paper

- Hypotheses

- Measurements

- *Specialized WG*

- *Harmonized protocols*

Country	Objectives/Outcomes
Thailand	Biological, psychosocial, and moral development in Thai children, from the perinatal period to adulthood
Cuba	Injuries and respiratory morbidity in children
Guatemala	Growth and development in children and cardiovascular risk factors and economic productivity in adults in relation to prenatal and childhood nutrition
Dominican Republic	Cooking with charcoal indoors and respiratory illnesses infants and young children
Chile	Ambient air pollution and respiratory disorders in children
Brazil	Social inequities and health outcomes in children
China	Folic acid supplements before an early in pregnancy and risk of neural tube defects
South Africa	Health and development of children born in a 7 week period in 1990 in the Greater City of Johannesburg
Peru, India, Êthiopia, Viet Nam	Causes and consequences of childhood poverty
Multinational	Growth and nutrition

New studies

- Seoul, Korea (10.000)
- CHILD Canada (5.000)
- Paarl, South Africa (1000)
- Peel, Australia (1500)
- Barwon, Australia (1000)
- Athens, Greece (500)
- Other…

Guide to Undertaking a Birth Cohort Study

- Based on the outcome of the four consultations
- Plus input of academia, governmental and non-governmental organizations in different countries, with different backgrounds – and a shared concern about the environmental health of children and future adults.
- Prepared by ALSPAC
- Publication: March 2009

  Pediatric and Perinatal Epidemiology, 23 (Suppl 1),…2008

Guide to Undertaking a Birth Cohort Study

I. WHY CARRY OUT A LONGITUDINAL SURVEY?

II. WHO SHOULD BE STUDIED AND WHEN IN A LONGITUDINAL BIRTH COHORT?

III. THE OVERALL PLACING AND MANAGEMENT STRUCTURE OF A LONGITUDINAL BIRTH COHORT

IV. IMPORTANCE OF BIOLOGICAL SAMPLES IN LONGITUDINAL BIRTH COHORT STUDIES

V. CHOICE OF TYPES OF SAMPLE TO COLLECT IN LONGITUDINAL BIRTH COHORT STUDIES

VI. IMPORTANCE OF A GENETIC COMPONENT

VII. NESTING SUB-STUDIES AND RANDOMISED CONTROLLED TRIALS WITHIN BIRTH COHORT STUDIES

VIII. ETHICS AND GOVERNANCE FOR A LONGITUDINAL BIRTH COHORT

IX. SOURCES OF DATA FOR A LONGITUDINAL BIRTH COHORT

X. HOW MANY SUBJECTS ARE NEEDED IN A LONGITUDINAL BIRTH COHORT?

XI. THE FUNDING OF COHORT STUDIES

Guide to Undertaking a Birth Cohort Study

X. INFORMATION TECHNOLOGY (IT)

XI. TAKING AND STORING BIOLOGICAL SAMPLES FOR LONGITUDINAL BIRTH COHORTS

XII. EXTRACTING, STORING AND DISTRIBUTING DNA FOR A BIRTH COHORT STUDY

XIII. CHOICE OF ENVIRONMENTAL COMPONENTS

XIV. ASSESSING DIET IN BIRTH COHORT STUDIES

XV. OUTCOME MEASURES

XVI. ENROLMENT AND RESPONSE RATES

XVII. PREPARATION, PILOTING AND VALIDATION PRIOR TO STARTING A BIRTH COHORT STUDY

XVIII. DATA ORGANISATION

XIX. THE IMPORTANCE OF A COLLABORATING CENTRE TO GUIDE COMPARATIVE DATA COLLECTION

International collaboration on LTCS is crucial – it enables:

- **Identify critical <u>environmental</u> health issues**
- **Improve detection of environmental factors and emerging health threats (sentinel cases or events).**
- **Baseline information & characterization of patterns of children's EH**
- **Comparability of data across countries**
- **Transfer of knowledge and study technologies**
- **Efficient use and sharing of resources**
- **A sufficiently large cohort on "rare" diseases**

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PROMOTE SAFER ENVIRONMENTS FOR CHILDREN ...AND ALL