Identifying Important Life Stages for Monitoring and Assessing Risks From Exposures to Environmental Contaminants: Results of a WHO review

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Risk assessment challenge

- Susceptibility to risks from exposures to chemicals **vary with age**
  - **early life** is a particularly vulnerable period of development.

- Need to rigorously consider **changes in behavior and physiology that are related to age and life stage** for assessment of risks from exposures to chemicals.

- **Life-stage** differences in how people **interact with the environment** may be a **major determinant** of individual or populations most vulnerable to risks from particular exposures.

- Identifying the most vulnerable **age range or life stage** for a particular population and exposure scenario requires a better scientific basis.

Hazard and exposure assessment

- Available approaches are limited in scope and applicability to address full range of geographic, social, cultural and economic diversity in populations worldwide.

- In addition, there is a need to better link or coordinate hazard and exposure assessment

  – A need to identify the most vulnerable based on windows of greatest susceptibility as well as windows of highest exposure, and then to incorporate that knowledge in a population-based risk assessment

- The WHO convened a group of experts to review these issues and provide guidance on how to better identify critical life stages for use in exposure and risk assessment.

Project Objectives

For the development and application of common life stages for exposure assessment:

1. **Define age bins** by carefully identifying the particular characteristics that distinguish them

2. Decide **how finely** the overall life stages of childhood **should be divided** into age bins**.**

3. Describe how **additional factors**, such as sex, culture and geography, might modify the significance of standard age bins.

4. Recognize that there may be cases in which a **specific factor** (e.g. mouthing behavior) is a more significant indicator of exposure than age.

5. Identify the most pressing gaps in the base of scientific knowledge that would **justify standard age bins** and in the exposure factor data required to use the age bins for risk assessment.

WHO Planning Group Process

- Collected information about already implemented age-bin classification/s, and basis of these
- Reviewed literature (focus on underlying modifying factors etc)
- Prepared draft options paper for **public consultation** (web December 2011-January 2012)
- Incorporated reviewers' feedback (2012)
- Submitted article for publication (August 2013)

A life stage approach

- Life stage-specific approaches were developed for assessing risks associated with children's exposure to environmental contaminants

- Mainly to determine what the most critical "windows" of exposure are for particular health outcomes, such as cardiovascular disease, chronic diseases and cancers

Definition of Life Stage

- "A distinguishable timeframe in an individual's life characterized by unique and relatively stable behavioral and/or physiological characteristics that are associated with development and growth." (Firestone, et al., 2007)

- This approach views **childhood as a sequence of life stages**, from conception through fetal development, infancy and adolescence, rather than characterizing children as a population subgroup.

Life stages are linked to:

- Specific characteristics related to **changes in anatomy, physiology, metabolism and behavior** that can lead to differences in potential for exposure and/or risk
  - i.e. children may experience higher exposures to chemicals and greater risks from those exposures compared with adults.

Adopting a common convention for defining age groups

- **No single 'correct' set of age groups**

- However, **adopting a common convention** for defining age groups will enable scientists to better understand differences in exposure and risk across life stages

- and the factors that may account for such differences,
  - e.g. nutritional status, prevalence of certain diseases, ethnic/cultural norms regarding activity or behavior patterns, population genetic characteristics, meteorological conditions, geography, and social stress (Firestone, 2010).

- This improved understanding will facilitate health-protective decisions and policy.

Life stage-specific issues

Harmonizing exposure and risk assessment approaches and tools requires consideration of a range of life stage–specific issues:

a. identification of the relevant **changes in behavior and physiology**

b. guidance on use of available data to **identify the age range** at which important behavioral and physiological changes occur;

c. approaches for incorporating **factors influencing** age- or life stage–related differences in behavior, physiology and exposures (e.g. nutritional status and endemic disease) for populations in different geographic regions, keeping influence of social structure in mind

d. approaches for determining **age ranges** to conduct **exposure assessment** when data are limited or unavailable

e. approaches for determining **age ranges** to conduct **hazard assessment** when data are limited or unavailable

f. selection of important **age ranges** to consider in designing and conducting **exposure and health studies**

g. approaches for coordinating **windows of highest exposure** with **windows of greatest susceptibility** to hazardous effects.

Reviewed existing standardized age groups

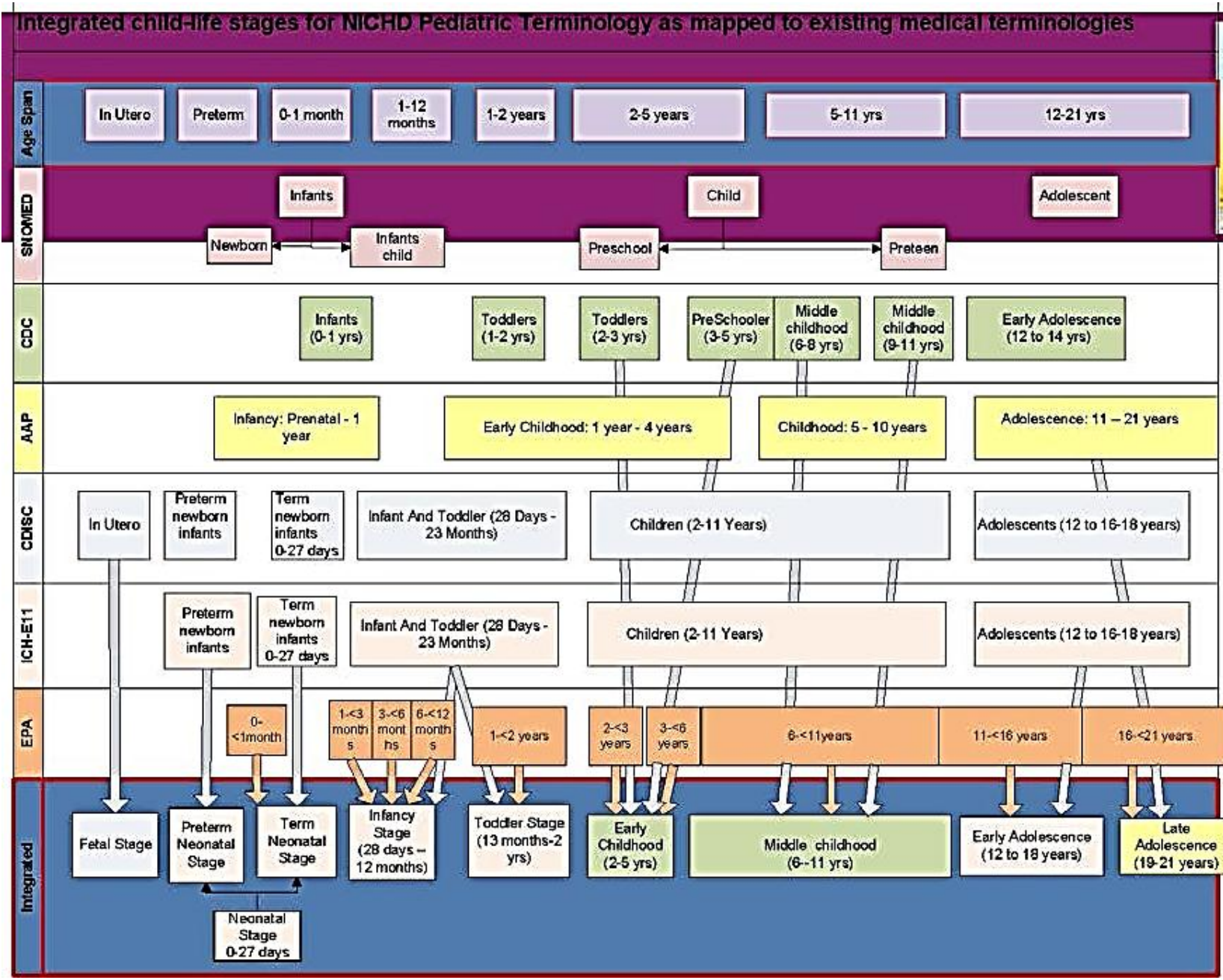
- The WHO group reviewed existing standardized age groups used by other organizations
  - e.g. U.S. Environmental Protection Agency
    - Undertaken in part to aid the US EPA in implementing regulatory initiatives requiring federal agencies to ensure that standards take into account special risks to children.

Pediatric life stage categories suggested by different agencies

Table 2. Pediatric life stage definition by different agencies

Agency	Age bracket	Descriptor	Reference
U.S. Environmental Protection Agency	Birth to <1 month	—	US EPA (2005b)
	1 to <3 months	—	
	3 to <6 months	—	
	6 to <12 months	—	
	1 to <2 years	—	
	2 to <3 years	—	
	3 to <6 years	—	
	6 to <11 years	—	
	11 to <16 years	—	
	16 to <21 years	—	
US Food and Drug Administration	—	Preterm newborn infants	US FDA (2000)
	0 to 27 days	Term newborn infants	
	28 days to 23 months	Infants and toddlers	
	2 to 11 years	Children	
	12 to 16–18 years[b]	Adolescents	
World Health Organization[a]	Birth to 28 days	Neonate	WHO (2006)
	28 days to 1 year	Infant	
	1 to 4 years	Young child	
	2 to 3 years	Toddler	
	5 to 12 years	Older child	
	12 to 18 years[c]	Adolescent	

Summary: Integrated childhood life stages (NCS 2011)



AAP: *American Academy of Pediatrics*

CDC: *Centers for Disease Control and Prevention*

CDISC: *Clinical Data Interchange Standards Consortium*

EPA: *Environmental Protection Agency*

ICH-E11: *International Conference on Harmonisation*

SNOMED: *Systematized Nomenclature of Medicine*

Searching for common physiological and behavioral changes in children

- **Physiological** and **behavioral** changes over time impacts on exposures and susceptibility
- Development occurs as a **continuum** that contributes to an exposure function over all ages
- Existing information is not adequate to construct an **exposure function** that reflects continuous behavioral and anatomical development
- **Age group "bins"** are required to provide a proxy for the continuous function.

Physiological changes relevant for risk assessment

- **Anatomical changes** from physical growth
- Changes in **toxicokinetics** and **toxicodynamics** that affect the absorption, distribution, excretion and effects of environmental contaminants.
- **These two categories are intertwined**

Physiological Changes: exposure to Environmental Contaminants

- Children's **physiology changes** over time in ways that can impact both their **exposures** to environmental contaminants and their **susceptibility** to certain health effects

- Anatomical changes relating directly to **commonly used exposure factor information** (e.g., body weight, skin surface area, skin permeability, gut absorption, and inhalation rate) are especially important for defining and applying standard age bins for risk assessment

Age bins for risk assessment: Anatomical-specific issues

- Important **developmental milestones** for anatomical changes related to physical growth in children
- For each milestone, the **range of ages** during which the anatomical characteristics are typically observed
- **Variability** among children with respect to the age of onset for the anatomical characteristics
- **Observed characteristics** associated with these milestones likely to affect children's exposure to environmental contaminants
- For those anatomical characteristics that are likely to have an important impact on exposure, **existing information** that is representative of the impact of this characteristic on exposure
- How these anatomical characteristics and milestones impact exposure by **different routes** (e.g. dermal, inhalation, and ingestion)

Table on next slide gives examples of the anatomical and physiological factors that are likely to affect children's exposures and associated developmental windows.

Age Group	Anatomy/Physiology Characteristics
Birth to <1 month	Rapid growth and weight gain. Proportion of body fat increases. Increased skin permeability. Deficiencies in hepatic enzyme activity. Immature immune system functions. High oxygen requirements (leading to higher inhalation rates). Stomach more alkaline. Increases in extracellular fluid. Renal function less than predicted by surface area.
1 to <3 months	Rapid growth and weight gain. Proportion of body fat increases. Deficiencies in hepatic enzyme activity. Immature immune system functions. High oxygen requirements (leading to higher inhalation rates). Stomach more alkaline. Increases in extracellular fluid. Renal function less than predicted by surface area.
3 to <6 months	Rapid growth and weight gain. Proportion of body fat increases. Deficiencies in hepatic enzyme activity. Immature immune system functions. Increases in extracellular fluid. Renal function less than predicted by surface area.
6 to <12 months	Rapid growth and weight gain. Body fat increase begins to level off. Deficiencies in hepatic enzyme activity. Immature immune system functions. Rapid decrease in extracellular fluid. Can begin predicting renal function by surface area.
1 to <3 years	Some hepatic enzyme activities peaks, then falls back to adult range. Most immune system functions have matured. Extracellular fluid becomes more consistently related to body size.
3 to <8/9 years	Period of relatively stable weight gain and skeletal growth (as opposed to a period marked by growth spurts).
8/9 to <16/18 years	Rapid skeletal growth. Epiphyseal closure (may take until age 20). Rapid reproductive and endocrine system changes, inclusive of puberty.

Behavioral Changes: Exposure to Environmental Contaminants

- Childhood **behavior changes over time** in ways that can have an important impact on exposure to environmental contaminants.
  - Changes are linked to **physical and mental** growth
  - Can influence where children **spend their time**, what **physical activities** they engage in, and what **foods** they eat.

- To define standard age bins, aspects of behavior most important for characterizing exposure and risk must be identified as well as critical changes in these behaviors **over the course of development**, and **across populations**

Behavior-specific issues to consider

- important developmental milestones in children's behavior
- for each milestone, the range of ages during which the behaviors are typically observed
- variability among children with respect to the age of onset and the age of abandonment for these behaviors
- observed changes in behavior associated with these milestones that are likely to affect children's exposure to environmental contaminants, such as mouthing hands and objects and crawling
- for those behaviors that are likely to have an important impact on exposure, existing information that is representative of the impact of this behavior on exposure
- how these behaviors and milestones impact exposure by different routes (e.g. dermal, inhalation and ingestion).

Examples of Factors Considered in Deriving Age Groups Reflecting Behavioral Development

Age Group	Characteristics Relevant to Oral and Dermal Exposure	Characteristics Relevant to Inhalation exposure
Birth to <3 months	Breast and bottle feeding. Hand-to-mouth activities.	Time spent sleeping/sedentary.
3 to <6 months	Solid food may be introduced. Contact with surfaces increases. Object/hand-to-mouth activities increase.	Breathing zone close to the floor.
6 to <12 months	Food consumption expands. Children's floor mobility increases (surface contact). Children are increasingly likely to mouth nonfood items.	Development of personal dust clouds.
12 to <24 months	Children consume full range of foods. They participate in increased play activities, are extremely curious, and exercise poor judgment. Breast and bottle feeding cease.	Children walk upright, run, and climb. They occupy a wider variety of breathing zones and engage in more vigorous activities.
2 to <6 years	Children begin wearing adult-style clothing. Hand-to-mouth activities begin to moderate.	Occupancy of outdoor spaces increases.
6 to <11 years	There is decreased oral contact with hands and objects as well as decreased dermal contact with surfaces.	Children spend time in school environments and begin playing sports.
11 to <16 years	Smoking may begin. There is an increased rate of food consumption.	Increased independence (more time out of home). Workplace exposure can begin.
16 to <21 years	High rate of food consumption begins.	Independent driving begins. Expanded work opportunities.

Modifying factors and impacts on development, exposure and vulnerability to risk

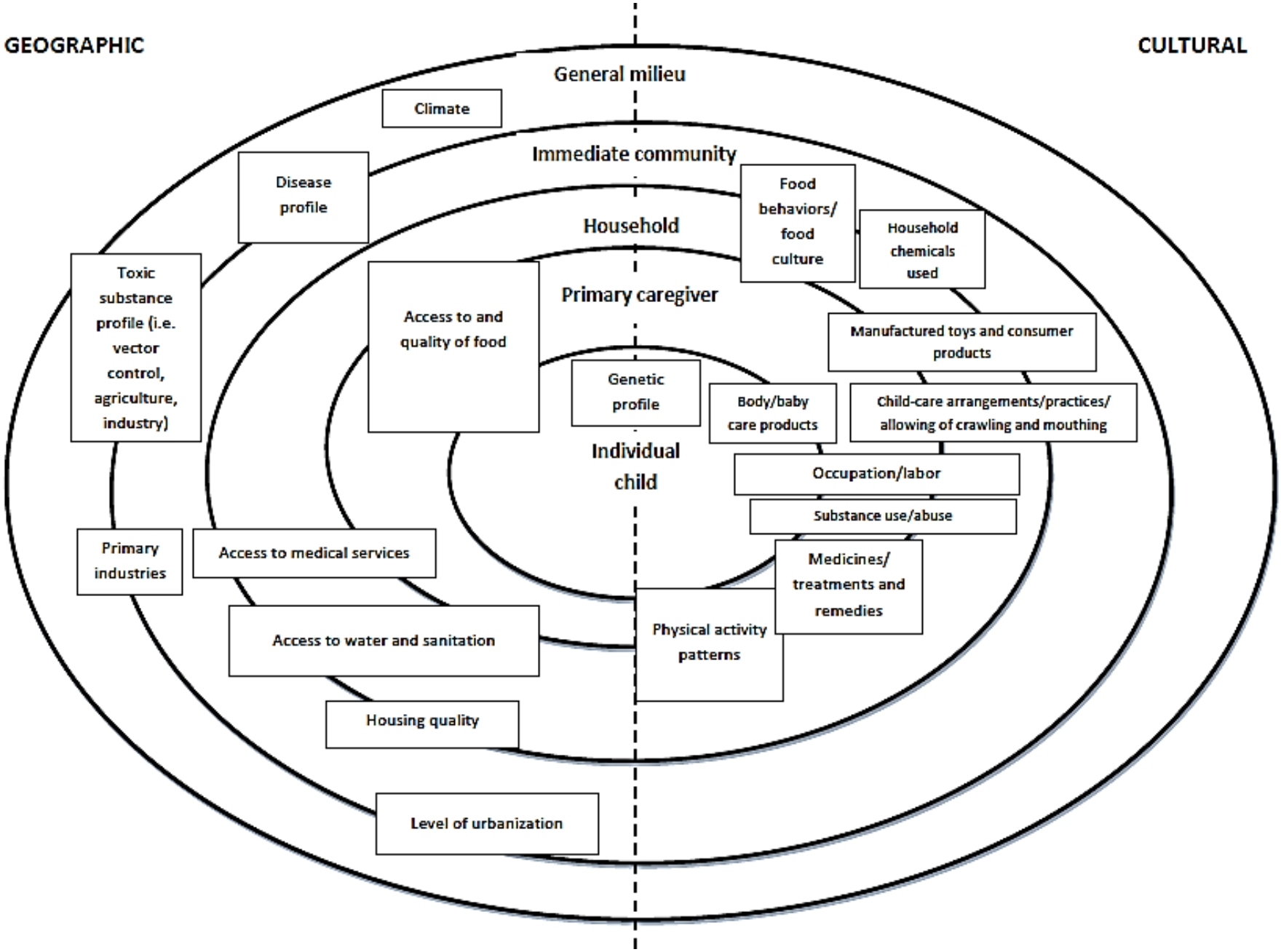
- Exposure assessment and risk assessment require **population- and community-specific** information or exposure factors that may vary significantly based on **geography and cultural practices**.

- Developed a **framework** to facilitate systematic consideration of these contextual factors for exposure and risk assessment.

Modifying factors

- A literature review was conducted to identify potential modifying factors and to explore evidence for these factors.
- For many of the potential modifying factors discussed in the literature, studies have not been conducted or published that actually associate the factors with a particular impact.
- However, the objective of the review conducted here and of the resulting framework was to consider life stage-specific aspects of these modifying factors and to understand how these are addressed by the proposed life stage–specific age bins or groups.
- In essence, as is the case for the full range of exposure-related factors, use of the age bins or groups to conduct robust assessment of exposure of and risk to specific populations will require information on national or regional modifying factors.

Framework of modifying factors for exposure associated with geography and culture



Genetic profile of child

- Exposure in utero and during early childhood is connected in a number of ways to health outcomes later in life, especially outcomes related to the development of chronic and terminal diseases.

- For example, chemical exposures in utero result in gene expression changes in the fetus (i.e. epigenetic changes) that may confer susceptibility to disease

- The influence of the mother and/or immediate caregivers in terms of their own exposure to chemicals via substance use or abuse, nutrition and use of body care products and household chemicals is therefore of particular importance in determining the exposure of the fetus in utero and of the child in early childhood

Modifying Factors and Impacts on Development, Exposure, and Vulnerability to Risk

- Exposure and risk assessment requires **population and community specific** information on exposure factors

- This may vary significantly based on **geographical location , type of living environment** or **cultural contexts and practices**

Geographic factors

- In many instances, exposure relates to both the climate and the toxic substance profile of an area or region.

- The toxic substance profile refers mainly to the history of chemical use in that area, often related to the area's primary industry

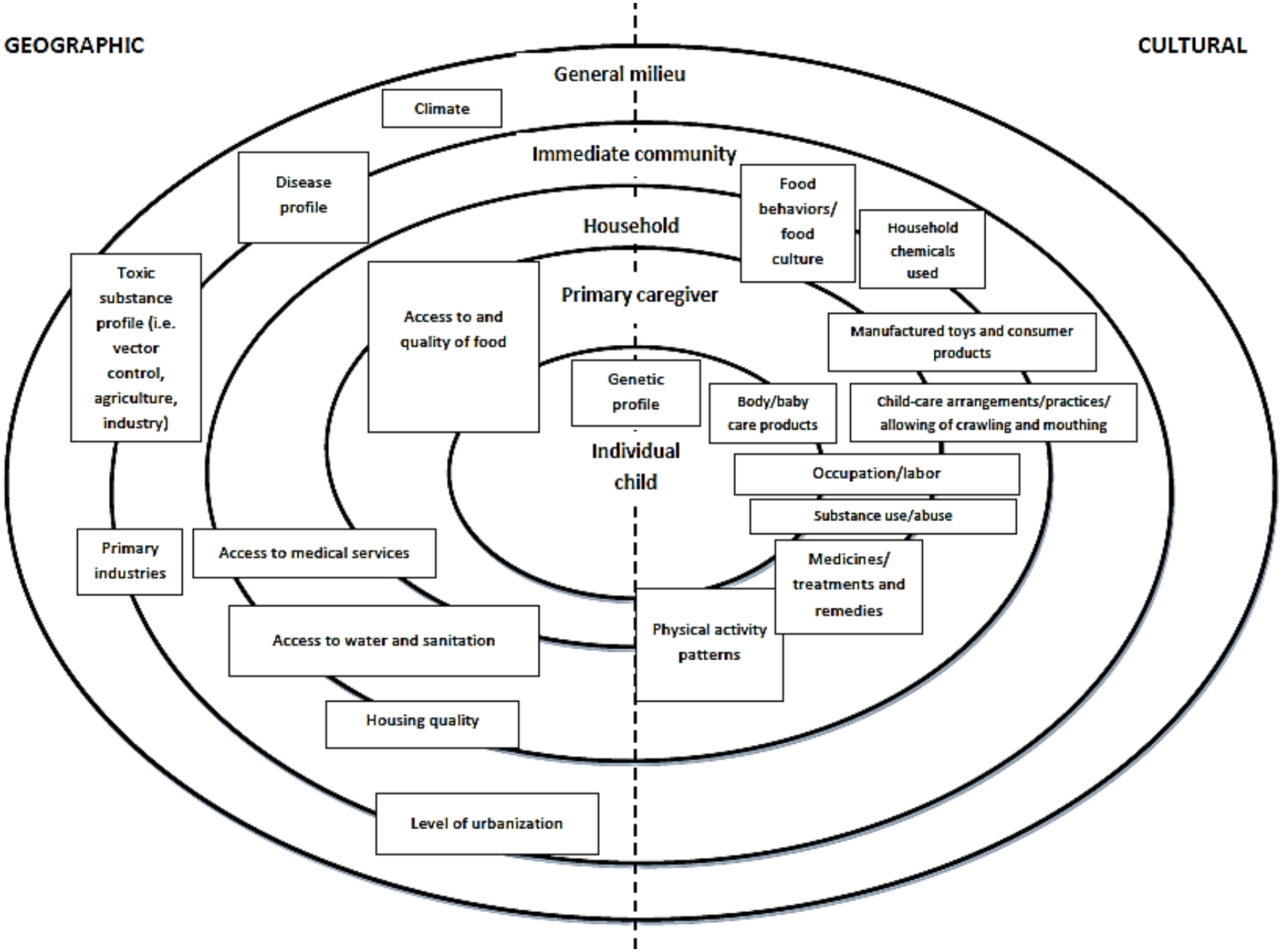
- Another key geographic factor relates to the quality of housing and the materials used for building, as well as for heating and cooking indoors

Geographical , social and cultural modifying factors

- Developed a framework with **five levels or layers** of impact
  - Individual (child or fetus)
  - Primary caregiver/mother/immediate caregivers
  - Household
  - Immediate community
  - Extended community or general milieu

- Different **geographical , social and cultural** modifying factors that operate on these levels or layers are suggested
  - Interactions often intersect
  - Levels or layers of impact may combine in different ways in different contexts.

Framework of modifying factors for exposure associated with geography and culture



Geographic factors

1. **Climate (impacts on level of general milieu)**
   - Includes reference to **disease profile** and specific environmental adaptations, e.g. malaria
   - Often associated with **crawl/play areas** for children (inside and outside)
   - To a large extent determines the **infectious disease profile** of people (e.g. malaria, respiratory conditions)
   - Living at different **altitudes** may result in adaptations during pregnancy and early childhood

2. **Disease profile (impacts on levels of general milieu and immediate community)**
   - **Reclaimed land** for residences (e.g. landfills, rubbish dumps), low lying areas, groundwater
   - **Disease/vector control** measures (for example, DDT is still used to control malaria in some areas)
   - **Socio-economic drivers of disease** occurrence (social epidemiology, for example combination of factors that results in high levels of HIV infection in particular places)

Geographic factors

3. **Toxic substance profile (impacts on levels of general milieu and immediate community)**
    - **Disease/vector control measures** (for example, DDT is still used to control malaria in some areas)
    - **Level of urbanization** (often associated with exposure to traffic-related pollutants like lead, and carbon monoxide and carcinogenic compounds such as benzene and PAHs) (also associated with play areas for children) (also associated with access to medical care) (also associated with specific toxic substance that have a history in that area)
    - **Primary industry** (for example, agricultural areas and pesticide exposure)

4. **Primary industries (impacts on levels of General Milieu and Immediate Community)**
    - Air, ground and water pollution from industry

Geographic factors

5. **Levels of urbanization (impacts on levels of general milieu and immediate community)**
    - Proximity to industry
    - Proximity to major roads
    - Associated with play areas for children (inside or outside)
    - Associated with access to medical care

6. **Housing quality (impacts on levels of immediate community and household)**
    - Building materials, ventilation, paints used, asbestos
    - Sources of **fuel** for heating and cooking (see paraffin, coal and wood)
    - Reclaimed land for residences (e.g. landfills, rubbish dumps), low lying areas, groundwater

Geographic factors

7. **Access to services (impacts on levels of immediate community and household and primary caregiver)**
    - Access to clean water
    - Access to sanitation
    - Access to medical care

8. **Access to and quality of food (impacts on household, primary caregiver and individual child)**
    - Access and quality restricted by drought, flooding or other weather-related events
    - Quality of food (e.g. pesticide residues, steroid hormonal residues, additives for food preservation and enhancement, antimicrobials in animal feed)

Modifying factors to exposure associated with social and cultural practices and contexts

Cultural factors may modify a range of exposure-related practices:

- **Physical activity patterns and contact** with different surfaces
- The uses of **particular medicines and treatments** (especially in traditional contexts)
- **Exposures related to work and labor practices**, especially in terms of farm workers and their exposure to pesticides and chemicals, as well as practices such as recycling/reclaiming of electronics, scavenging on dumpsites and artisanal mining.
- **Practices around food and feeding** (especially related to women's practice of breastfeeding and how it impacts their other activities) is an important factor in determining the exposure of children to environmental contaminants

Modifying factors to exposure associated with social and cultural practices and contexts

The behavioral modifying factors that potentially operate or combine with the levels of impact to produce particular impacts (via exposure) are:

1. **Substance use/abuse (impacts on the levels of household and primary caregiver and individual)**
    - Smoking, alcohol and medicine/substance use/abuse during pregnancy
    - Smoking, alcohol and medicine/substance use/abuse by people in immediate surroundings during early childhood
    - Smoking, alcohol, solvents, other substance use by young children and early teenage years

Modifying factors to exposure associated with social and cultural practices and contexts

2. **Household chemicals used (impacts on the levels of immediate community and household)**
   - Affects inhalation and dermal exposure
   - Associated with play areas for children, indoor/outdoor crawling and mouthing

3. **Manufactured toys and consumer products (impacts on the levels of immediate community and household and primary caregiver)**
   - Chemicals used to manufacture toys
   - For example, lead used in paint/coating materials
   - Plastics
   - Synthetic fibers and textiles

4. **Body/baby care products (impacts on the levels of primary caregiver and individual)**
   - Chemicals used to manufacture care products
   - Baby powders and lotions
   - Detergents

Modifying factors to exposure associated with social and cultural practices and contexts

5. **Child-care arrangements/practices/allowing of crawling and mouthing (impacts on the levels of immediate community and household and primary caregiver)**
    - Activity patterns associated with the physical state of childhood (being an infant, toddler, child, pubescent etc.), such as crawling, mouthing etc. are considered.
    - Playing and/or crawling inside or outside (associated with climate conditions)
    - Childcare arrangements (how much is an infant picked up or played with)
    - Mouthing (again, inside or outside play areas)
    - Household chemicals on surfaces (inhalation and dermal exposure)

Modifying factors to exposure associated with social and cultural practices and contexts

6. **Physical activity patters (impacts on the levels of household and primary caregiver and individual)**
    - Possibility to play outdoors
    - Type of toys determines activity patterns
    - Ways of measuring activity patterns also important
    - Standard definitions of developmental milestones measures in different contexts often adjusted (individual indicators related to the domains of languages and socialization, almost never related to physical growth and the attainment of motor skills)

Modifying factors to exposure associated with social and cultural practices and contexts

7. **Food behaviors/food culture (impacts on levels of immediate community and household and primary caregiver)**
    - Urban and rural food availability
    - Poverty – income as well as own food production
    - Differential understanding of nutritional value and what makes “good” food
    - Secular trends: over past century, better nutrition (plus social factors around childcare) has resulted in higher stature and earlier onset of puberty in certain populations
    - History of pesticide/chemical use in an area
    - Practices and beliefs around breastfeeding and breastfeeding interval
    - Livelihood strategies and the role of women (associated with breastfeeding interval and the introduction of other foods)
    - The beliefs of parents around “normal” growth/development.
    - Levels of heavy metals and toxic substances in human milk
    - Food additives (preservatives and colorants)

Modifying factors to exposure associated with social and cultural practices and contexts

8. **Occupation/Labor (impacts on the levels of household and primary caregiver and individual)**
    - Marginalized groups with few choices in work/income are often exposed with lack of legislation or control over working conditions and occupational safety
        - Those working in agriculture are particularly highlighted, for exposure to pesticides in their work and home environments
    - History of pesticide and/or chemical use in a particular environment (long term presence of certain chemicals)
    - Outsourced tasks that are done in households (beedie rolling, reclaiming and recycling materials (heavy metals from car batteries and electronics lead & mercury
    - Artisanal mining around the world
    - Hazardous child labor
    - Livelihood activities (associated with the economic circumstances and activities of the household (e.g. farming)

Modifying factors to exposure associated with social and cultural practices and contexts

9. **Medicines/Treatments and remedies (impacts on the levels of household and primary caregiver and individual)**

- Various traditional ways of understanding disease and consequent treatment
- Effects (often unintended) on common illnesses among infants and young children
- Example of “impila” (*Callilepis laureola*) for protection in utero and in early childhood
- Antenatal “modes” of care: e.g. “Isihlambezo” or traditional herbal antenatal care (also Ayurvedic medicine, Chinese herbal remedies)
- “Muti” medicine/generic names for certain “concoctions”
- Geophagic practice among different populations
- Remedies for pregnant women
- Remedies for infants and small children
- Effect of medicines on activity patterns; interaction of medicines with environmental contaminants in the body

Methodological considerations

- Particular study designs → data needed to evaluate exposure to environmental chemicals and risks at different developmental stages of a child's life.

- **The most suitable approach for the determination of exposure and risk at different life stages is the longitudinal birth cohort study.**

- Several such studies are being planned or are under way in various parts of the world.

- Expensive undertaking -- most of these studies have been undertaken in high-income countries.

  - WHO held several consultations to promote longitudinal cohort studies (2003–2007), which resulted in the publication of **"A Guide to Undertaking a Birth Cohort Study: Purposes, Pitfalls and Practicalities"** as a supplement to the journal *Paediatric and Perinatal Epidemiology* (Golding et al., 2009)

Cross-population applications

- **For measurements of developmental stages and growth** in babies and young children, across different **genetic, social and economic contexts** cross-cultural (or, rather, cross-population) application of **standard measures** must be considered

Cohort studies

- In the past 20 years, birth cohort studies to assess the risks to developing children from exposure to chemicals have been undertaken in many countries.

- **To increase the sample size, investigators working on these older cohort studies are now making an effort to pool their data.**

- Their efforts are hampered by the fact that the **older studies did not use agreed-upon** disease outcome definitions, time periods of measurement or methods for measuring biomarkers and chemical contaminants in air, water and food.

- **This makes pooling data extremely difficult, if not impossible.**

New birth cohort studies

- To avoid problems in the new birth cohort studies, WHO is currently working with investigators from various countries undertaking large-scale birth cohort studies

- **to invest time up front to agree** on when during pregnancy, infancy and childhood to assess disease outcomes, measure biomarkers and measure environmental exposures.

- **A harmonized set of age bins for assessing exposures will greatly enhance the ability to conduct cohort studies that can then be combined in the future, yielding studies with more power to identify positive results.**

Key issues for applying age bins to assess exposure and risk

When to use age bins?

- **Depends on the purpose of assessments**

- For outcomes with known windows of susceptibility -- the **age associated** with this window should be assessed

- Where a **unique window of susceptibility cannot be identified** and an assessment is required **to evaluate potential for highest exposures** compared against potential for impacts at multiple developmental time points, use of these age bins is encouraged to develop estimates of life stage-specific exposures.

Applying age bins to support life stage-based exposure assessment

- When assessing long-term exposures to environmental toxicants, it is desirable to integrate age-specific values for both exposure and toxicity/potency, where such data are available and appropriate (US EPA, 2005a).

- Historically, chronic risks, including cancer risks, have been assessed assuming that risk is proportional to the lifetime average daily dose for a "typical" adult.

- A life stage integrative approach is a departure from this approach, because it assesses risk by summing time-weighted exposures or risks across all relevant age groups, including those of childhood, adulthood and old age, as well as maternal-fetal exposures during pregnancy, and then averages across the total exposure period.

When assessing risks from exposure to carcinogens with a mutagenic mode of action, the US EPA applies different toxic potency adjustments for exposure of children less than 2 years of age and between 2 and 16 years of age

Table 5. Integrating the US EPA's *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (US EPA, 2005a) with the *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (US EPA, 2005b)[a]

Exposure age groupings	Exposure duration (years)	Age-dependent adjustment factor (ADAF)
Birth to <1 month	0.083	10×
1 to <3 months	0.167	10×
3 to <6 months	0.25	10×
6 to <12 months	0.5	10×
1 to <2 years	1	10×
2 to <3 years	1	3×
3 to <6 years	3	3×
6 to <11 years	5	3×
11 to <16 years	5	3×
16 to <21 years	5	1×
>21 years (21 to <70 years)	49	1×

[a] Cancer potency adjustments, or age-dependent adjustment factors, apply only to carcinogens that act via a mutagenic mode of action.

Source: US EPA (2005b)

Variability is a key challenge

- Children of the same age can exhibit tremendous variability in development and behavior.
- A challenge for identifying fixed age ranges to use for assessing children's exposure and risk.
- Remains useful to address this variability in development of the exposure factor data while maintaining a standard set of age bins.
- With sufficient data, the standardized bins facilitate understanding of the contextual and confounding factors that are driving differences in exposure and risk, even within each bin.

Representativeness

- Another challenge when assessing children's exposure is the extent to which the available exposure data represent the population of interest (Thompson, 1999).
- Exposure data are collected for a specific group of people, in a specific place and at a specific time.
- They can be used in a risk assessment only to the extent that they are sufficiently relevant to the population being assessed in the current time and place.
- The rapid pace of social and behavioral change may diminish the relevance of study data.
- In addition, social and behavioral differences may be significant from one community to another and from one population to another.
- Here again, the need for a common exposure metric facilitated by a standard set of life stages will improve understanding of similarities and differences among and across study populations.

Coordinating exposure and hazard assessment

- A need to better link or coordinate hazard and exposure assessment (the need to identify the most vulnerable based on windows of greatest susceptibility as well as windows of highest exposure and then to incorporate that knowledge in a population-based risk assessment).

- Approaches for coordinating and linking exposure and hazard assessment will necessarily be fit to purpose.

- If risk for a specific health outcome with known life stage–specific etiology is being assessed, then the window of exposure associated with the known window of biological susceptibility should be assessed, and the full set of recommended age bins need not be considered.

- If some uncertainty about the key drivers of a particular outcome or these are multifactorial and complex, information on critical windows of susceptibility should be mapped to exposure-related age bins for further assessment and/or data collection.

WHO recommendation on harmonized early life age groups

- To harmonize exposure assessment for comparison across time, place and culture, we need to define a standard framework within which to analyze population-specific information.

- Defining standard age ranges for children will also facilitate collection of data and analyses of aggregate exposure and cumulative risk.

- Given the range of scientific and policy-related needs for a harmonized set of age groups, the following tiered set of early life age groups (Table 6) is recommended for international use to facilitate some level of consistency with recently developed age grouping guidance currently in use in some regions:

  – **Tier 1:** Adopt guidance similar to the US EPA's (2005) recommended childhood
  – **Tier 2**: Consolidate some of the age groups defined above in order to reduce the burden of developing age-specific exposure factor data for different countries or regions.

Table 6. WHO-recommended tiered set of early life age groups

Life stage descriptor	Tier 1 age groups	Tier 2 age groups
Preconception	Preconception	—
Fetal	Prenatal	Conception to birth
Newborn (neonatal)	Birth to <1 month	Birth to <1 month
Infant	1 to <3 months	1 to <12 months
	3 to <6 months	
	6 to <12 months	
Toddler	1 to <2 years	1 to <2 years
Early childhood	2 to <3 years	2 to <6 years
	3 to <6 years	
Middle childhood	6 to <11 years	6 to <11 years
Early adolescence	11 to <16 years	11 to <16 years
Late adolescence	16 to <21 years	16+ years

Example when to use Tier 1

- Preferred in those cases where significant differences in exposure early in life can greatly impact health risks from acute or sub-chronic exposure to toxins.

- For example, fluid consumption on a body 600 weight basis is on average almost 3 times greater shortly after birth (birth to < 1 month) than for infants 601 6 to <12 months of age and almost twice the time-weighted average for the entire first year of life (Table 7 on next slide).

Table 7. Recommended mean drinking water ingestion rates, consumers only,[a] by age group

Age group	Intake (mL/kg body weight per day)	Ratio to adults ≥21 years
Birth to <1 month	137	9
1 to <3 months	119	7
3 to <6 months	80	5
6 to <12 months	53	3
1 to <2 years	27	2
Time-weighted average for birth to <12 months	78	5
≥21 years (adults)	16	1

[a] Consumer-only intake represents the quantity of water consumed only by individuals that reported consuming water during the survey period.

Source: Data from Recommended Values for Drinking Water Ingestion Rates, Table 3-1 (http://www.epa.gov/ncea/efh/pdfs/efh-chapter03.pdf) in US EPA (2011).

Discussion

- The above recommendation builds on several recent activities and fills gaps identified in recent publications that focus on assessing risks from exposures of children to environmental contaminants.

- The US EPA document titled *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (US EPA, 2005b) presents recommended age bins for children based on physiology and behavior.

- The scope of this document narrowly focuses on birth through 18 years of age and is designed specifically to promote a more uniform approach for exposure assessments conducted across US EPA program offices and regions.

Discussion

- Prenatal and preconception periods were identified as important periods for consideration in assessing health risks from early life exposures, and these life stages were added to the US EPA-recommended age bins in the US EPA (2006) document titled *A Framework for Assessing Health Risks of Environmental Exposures to Children*.

- The WHO document titled *Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals* (WHO, 2006) cites the US EPA guidance document (US EPA, 2006) in the exposure section.

- However, the lack of harmonization in determining age ranges for life stages became apparent during development of the WHO (2006) document.

Discussion

- In a few instances, life stages defined at the beginning of the document consistent with WHO terminology were slightly different from the US EPA-recommended exposure bins that were used in the exposure chapter of the WHO (2006) document.

- Even with the focus on children in these three documents, there is not a uniform approach for identifying the important life stage (age range), exposure factors specific to the exposure/risk assessment question of interest or the characteristics of a particular population that might modify these.

- In addition, very few institutions outside the United States have addressed this issue, and there are likely some different factors that might be important for non-U.S. populations that should be considered for a harmonized approach.

Discussion

- While there is no single “correct” means of choosing a common set of age groups to use internationally in assessing early life exposure and risk, use of a set of defined age groups is recommended to facilitate comparisons of potential exposures and risks around the globe.

- Application of these age groups for robust assessment of exposure and risk for specific populations will then require country- or region-specific exposure factor information as well as local environmental monitoring data (and/or characterization of local sources).

Conclusions

- We propose a harmonized set of age bins for assessing risks from exposures to chemicals for global use.
- The two-tiered set of early life age groups will facilitate consistency with recent guidance in use in some regions.
- A harmonized set of age bins will greatly enhance the ability to combine results from longitudinal birth cohort studies.
- Application of these age groups for exposure assessment for specific populations requires region-specific exposure factors and environmental monitoring data.

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Identifying important life stages for monitoring and assessing risks from exposures to environmental contaminants: Results of a World Health Organization review ☆,☆☆

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ABSTRACT

In this paper, we summarize exposure-related issues to consider in determining the most appropriate age ranges and life stages for risk assessment. We then propose a harmonized set of age bins for monitoring and assessing risks from exposures to chemicals for global use. The focus is on preconception through adolescence, though the approach should be applicable to additional life stages. A two-tiered set of early life age groups is recommended. The first tier involves the adoption of guidance similar to the childhood age groups recommended by the U.S. Environmental Protection Agency, whereas the second tier consol-

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