International Conference on Human Biomonitoring, Berlin

Pediatric Environmental Health:
Harmonizing Biomonitoring in Birth Cohorts

U.S. Environmental Protection Agency
Presented by Ruth Etzel, M.D., Ph.D.
Director| Office of Children's Health Protection

EPA United States Environmental Protection Agency

In 1997 the leaders of the G8 countries stated, “Protecting the health of our children is a shared fundamental value. Children throughout the world face significant threats to their health from an array of environmental hazards, and we recognize particular vulnerabilities of children to environmental threats.”

http://www.g8.utoronto.ca/environment/1997miami/children.html

ENVIRONMENTAL IMPACTS ON HEALTH

WHAT IS THE BIG PICTURE?

FACT:

23%

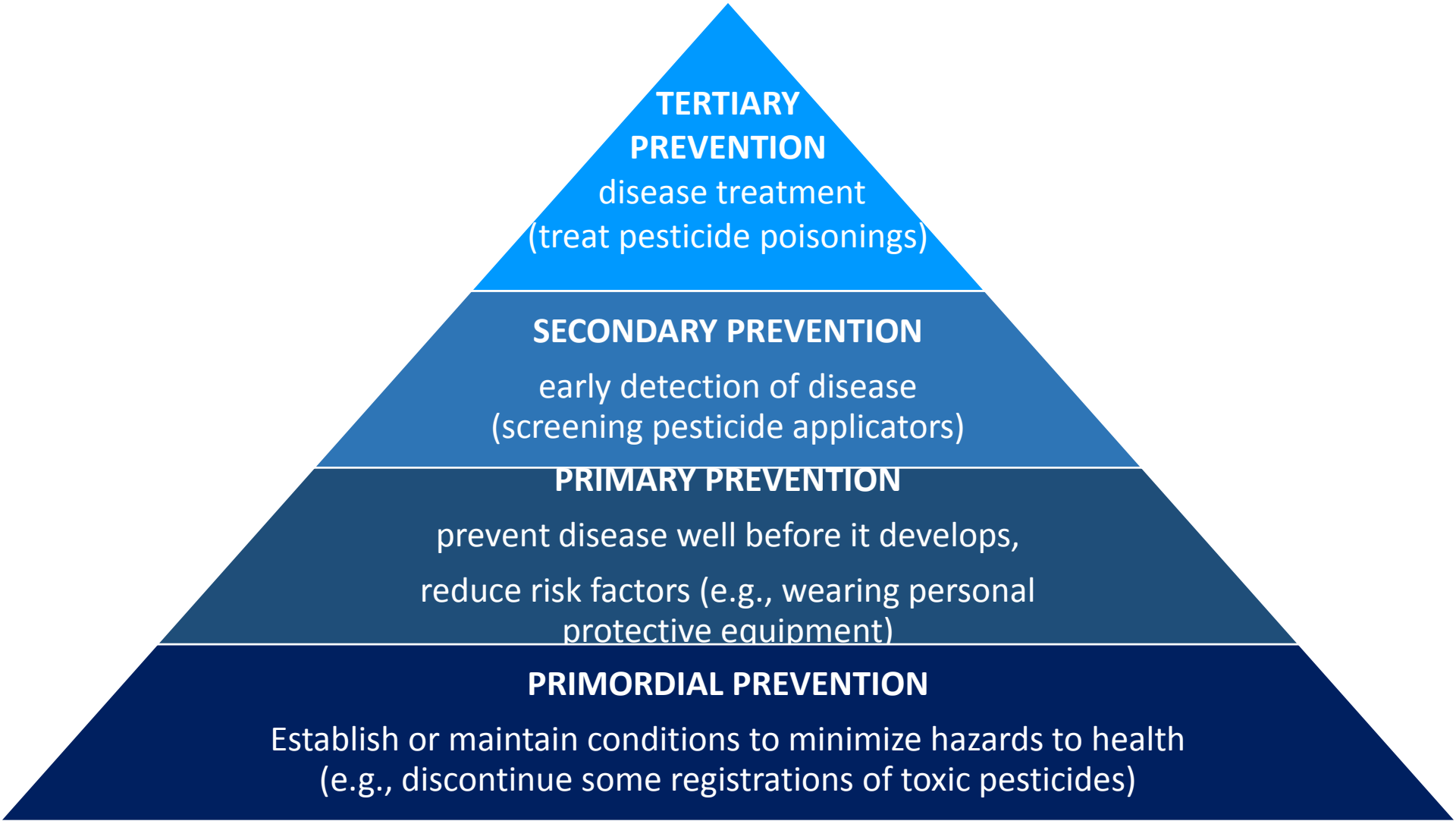
of all global deaths are linked to the environment.

That's roughly **12.6 million deaths** a year.

Source: WHO. http://www.who.int/quantifying_ehimpacts/publications/PHE-prevention-diseases-infographic-EN.pdf?ua=1

Levels of Prevention

(example: pesticide poisonings)



Hierarchy of Studies (According to Scientists)

- Randomized Controlled Trial
- Prospective Cohort Study
- Case-Control Study
- Cross-sectional Study
- Case Series
- Case Study

Hierarchy of Studies (According to Scientists)

- ~~Randomized Controlled Trial~~
- Prospective Cohort Study
- Case-Control Study
- Cross Sectional Study
- Case Series
- Case Study

Hierarchy of Studies (Politicians)
All Politics is Local

- Case Study (personal story)
- Case Series
- Cross-Sectional Study
- Case-Control Study
- Prospective Cohort Study
- Randomized Controlled Trial

Many countries planned birth cohort studies to better understand environmental risk factors for childhood outcomes.

Emerging evidence that the environment contributes to causation of disease in children

Early in the new millennium, large-scale longitudinal birth cohort studies were being planned or launched in several countries

- Identify causal relationships between environmental exposures and child health outcomes
- Determine factors relating to many different outcomes (therefore cost-efficient)
- Minimize recall bias

During the last century…

- Nutrition experts conducted longitudinal cohorts – evaluate multiple aspects of child nutrition (but neglected to include chemicals and environmental factors)
- Social scientists conducted longitudinal cohorts – evaluate multiple aspects of stress (but neglected to include chemicals and environmental factors)
- Environmental scientists conducted longitudinal cohorts– evaluate multiple aspects of exposure to lead (but neglected to include exposure to mercury)

We cannot solve our problems with the same thinking we used when we created them.

Albert Einstein

Moving from “boutique” to “harmonised”

Environment and Child Health International Birth Cohort Group

Effort to bring together the next generation of large-scale birth cohorts from different parts of the world:

Japan

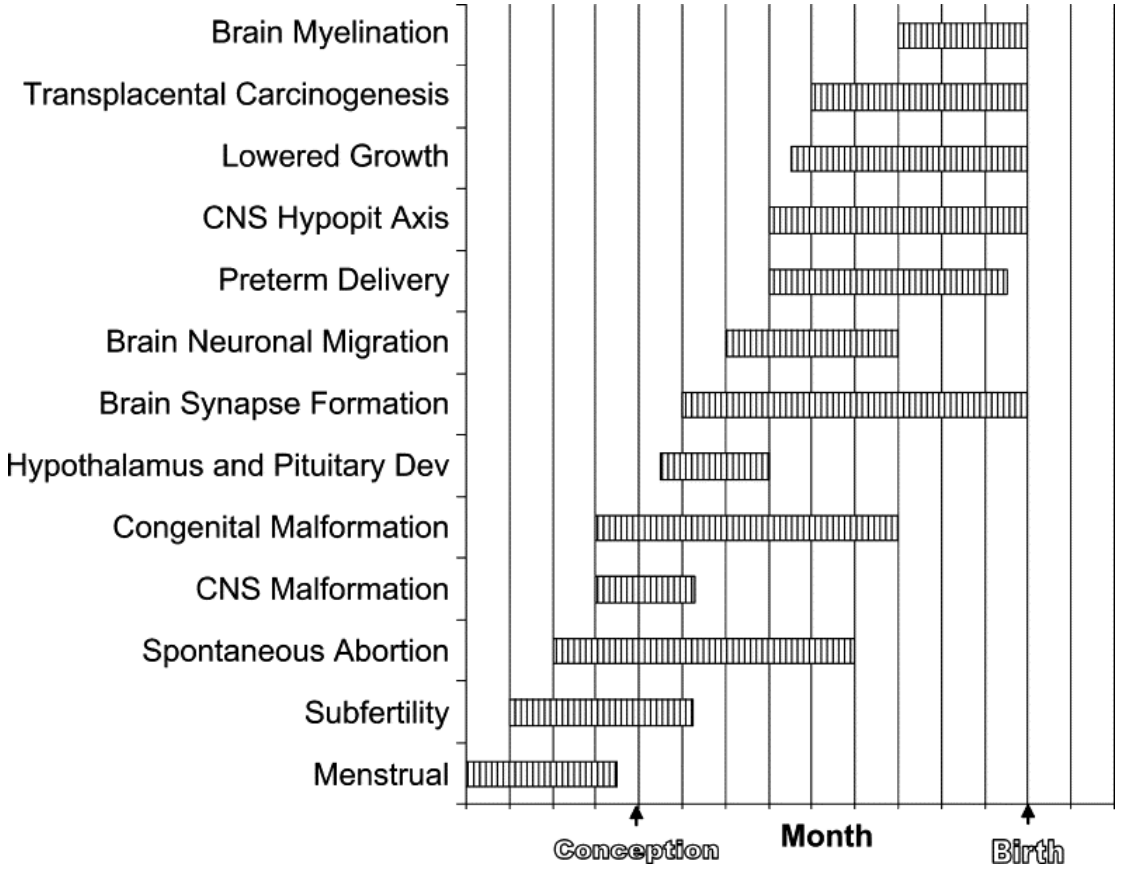
Shanghai, China

France

USA

Germany*

Schematic of the development of the relationship between the timing of an environmental insult (from preconception through birth) and "windows" of susceptibility by system.



From Silbergeld and Patrick, 2005

"Window of susceptibility" for the next generation of large-scale birth cohort studies

- Protocols were being shaped
- Biomarkers were being selected
- Measurements were being validated

- When this window closed the chance to influence protocol development disappears

What are the advantages of coordinating birth cohort studies?

- Common protocol elements will enable data to be combined (if desired) to look at rare childhood outcomes
- Even large cohorts (100,000 children) cannot study very rare diseases
- Common protocol elements allow comparison of results

Comparison of Results

- Need for set of “core” measurements
  - Specific questions and biomarkers of exposure

  - Measured at same time period in infant's life
  - Using similar case definition
  - Using similar age of inclusion
  - Using similar analytical methods

What are the advantages of coordinating birth cohort studies?

Huge burden with regard to choice of protocols, biological and environmental measurements, experience in piloting and validation, reviewing the literature

Studies in Environment and Child Health International Birth Cohort Group

	Shanghai Birth Cohort Study	The Etude Longitudinale Française depuis l'Enfance	Japan Environment and Children's Study	The Unites States of America National Children's Study
Expected number of participants	4,000 couples	400 families; 18,312 infants; 18,024 mothers	100,000 participants	100,000 children
Followed up	2 years of age	3 years of age	13 years of age	21 years of age
Time periods of evaluation	Preconception Pregnancy: ≤ 16 weeks 22-28 weeks 32-36 weeks Birth 42 days 6 months 12 months 24 months	 Birth 2 months 3-10 months 12 months 24 months 3 year	Pregnancy: ≤ 12 weeks 12-24 weeks Birth 1 month 6 months 12 months 18 months Childhood every 6 months 2-12 years	Pregnancy: before 20 weeks after 20 weeks Birth 3 months 6 months 9 months 12 months 18 months Childhood every 6 months 2-5 years Youth (years): 7, 9, 11, 13, 15, 17, 19, 21
Funding	Shanghai Municipality Bureau of Health	French Ministries of Health, Environment and Research and "Investing for the future program"	Japanese Parliament	United States Congress
Website	www.shyou-sheng.net	www.elfe-france.fr	www.env.go.jp/en/chemi/hs/jecs	www.nationalchildrensstudy.gov

Process of Coordination

- September 2011, Barcelona, International Society of Environmental Epidemiology
- October 2011, Baltimore, USA, International Society of Exposure Science
- December 2011 Bonn, Germany
- February 2012, Kitakyushu, Japan
- June 2012, Shanghai, China
- September 2012, Seattle, WA, USA, International Society of Exposure Science
- May 2013, Bethesda, MD, USA
- August 2013, Basel, Switzerland
- November, 2013, Nagoya, Japan
- October 2014, Cincinnati, Ohio, USA, International Society of Exposure Science
- August 2015, Lyon, France, IARC

Discussing the possibility to coordinate on diverse issues:

- Case definitions
- Collecting, storing and processing biological samples
- Timing of collection of environmental samples
- Data organisation
- Statistical analyses
- Information technology
- Building capacity
- Ethical issues

Discussing the possibility to coordinate on biomarkers:

- Mercury
- PCBs
- PBDEs
- Phthalates
- Organophosphates

Benefits of coordination efforts:

- Investigators shared experience, knowledge, and technologies (e.g. detailed information about specimen containers that are free of contaminants)
- Round-robin analyses
- Enhanced attention of policymakers to understanding children's exposures

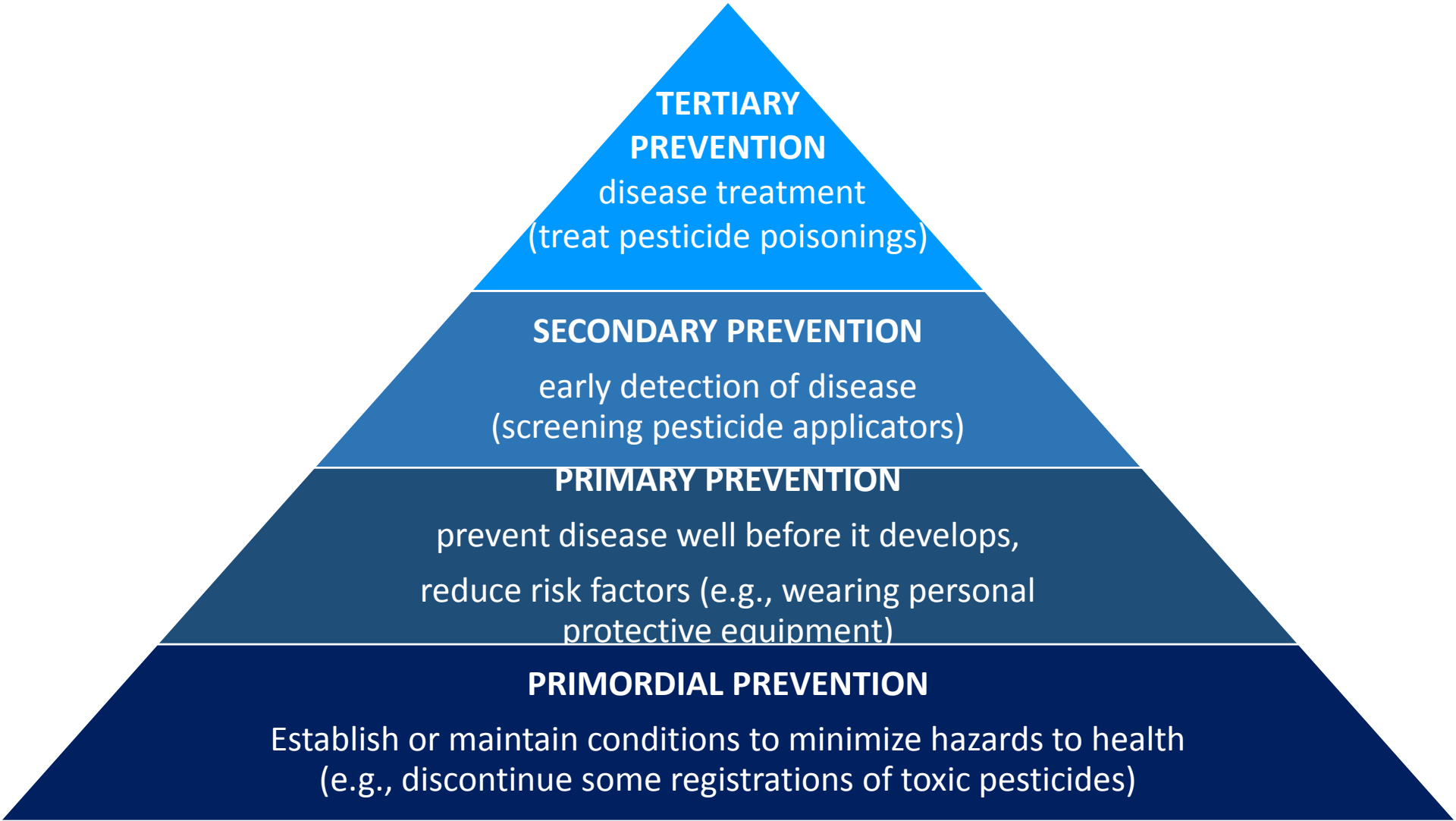
Challenges in harmonization:

- Harmonization must conform to objectives and logistics of the individual studies
- Desynchromized start of the cohorts in different countries
- Differences in choice of sample and specimen, collection intervals, and analytes

Hierarchy of Studies (Politicians)

- Case Study - HBM makes pollution personal
- Case Series
- Cross Sectional Study
- Case-Control Study
- Prospective Cohort Study
- Randomized Controlled Trial

Ultimate Goal of Cohort Studies: Primordial Prevention



Contact

Ruth Etzel, M.D., Ph.D., Director

Office of Children's Health Protection

Environmental Protection Agency

HTTP://WWW2.EPA.GOV/CHILDREN

(202) 564-2188