

# PRIMARY PREVENTION: Avoiding Non-Communicable Diseases by Reducing Early Life Exposure

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## BACKGROUND

Non-communicable diseases (NCDs), including cancer, cardiovascular disease and stroke, diabetes mellitus, and chronic obstructive pulmonary disease (COPD), have become the primary causes of death in both developed and developing countries. Increasingly, the global public health community is investing in clinical services and public health interventions to address the rising prevalence of these chronic diseases. In May 2012, researchers from around the world convened in Paris for the Third Prenatal Programming and Toxicology workshop, (PPTOX III), which focused on the relationships between the developmental origins of health and disease (DOHaD) and NCDs. To provide a broader forum to discuss implications of this science for the growing international efforts to combat NCDs, the National Institute of Environmental Health Sciences of the National Institutes of Health (NIH) organized a 1-day satellite symposium prior to PPTOX III entitled “Primary Prevention: Avoiding Non-Communicable Diseases by Reducing Early Life Exposure.” At this meeting, researchers highlighted emerging evidence that nutrition and environmental exposures at early stages of human development have a critical impact on subsequent risks for NCDs.

The objective of the satellite symposium was to bring together researchers who are uncovering the science behind DOHaD with public health experts who are battling the worldwide epidemic of NCDs. By sharing scientific perspectives, participants would increase awareness of the importance of early life exposures to subsequent development of NCDs and broaden the discussion of primary prevention to include reduction or elimination of harmful exposures in early life. This report summarizes the presentations given at the symposium, conclusions reached, and next steps identified.

## INTRODUCTION

**Dr. John Balbus, *National Institute of Environmental Health Sciences, NIH, Symposium Organizer***

Effectively addressing NCDs must be based on primary prevention, and not only on provision of clinical services. Global health resources are inadequate to treat the growing epidemic of NCDs, especially in poorer countries.

**Dr. Maria Neira, *World Health Organization, Symposium Co-Organizer***

This meeting is critical, as it brings together the voices of scientists and policy makers to facilitate investment in primary prevention of NCDs. Additional DOHaD research is both important and timely; NCDs are very much on the political agenda, which is advantageous in mobilizing research and affecting policy. There is a need for high-quality scientific evidence on NCDs and DOHaD to raise awareness. Sustainable development initiatives cannot be achieved without incorporation of the DOHaD paradigm.

## OVERVIEW OF NON-COMMUNICABLE DISEASES

**Ms. Ann Keeling, *International Diabetes Federation***

Non-communicable diseases create an immense burden, affecting not only individuals and their families, but also economies and health care services. NCDs, including diabetes, cardiovascular and chronic lung diseases, and metabolic syndromes, are a global epidemic and a human catastrophe. The human cost is significant: NCDs are responsible for 63 percent of global deaths and 50 percent of global disability cases, and for 9 million preventable deaths before the age of 60. Currently, there are an estimated 366 million people with diabetes, one of the most prevalent NCDs. Although the fastest increase in NCDs is in low- and middle-income countries, diabetes

is not under control in any country. NCD deaths are predicted to increase more than 50 percent by 2030, most significantly affecting young people in low- and middle-income countries, including women of childbearing age. The economic cost is considerable: it is estimated that NCD treatment will cost the global economy \$47 trillion during the next 20 years. Out-of-pocket payments for NCD treatment and care also will lead to high personal expenditure, and, in some cases, can result in or exacerbate household poverty.

The United Nations General Assembly held a high-level meeting in New York City in September 2011. The meeting marked the first time governments acknowledged NCDs as a major challenge for 21st century development and recognized the linkages between maternal and child health and NCDs. Participating governments acknowledged the severity of the NCD problem and made commitments to prevent and control NCDs, which was further discussed in a political declaration written during the meeting. The Declaration focuses on four predominantly adult risk factors related to individual behaviors and broader social determinants: poor diet, physical inactivity, tobacco use, and alcohol consumption. Although the Declaration was an important first step toward NCD prevention, a number of key challenges remain that could impede progress in combating NCDs. These include building multisectorial partnerships, addressing poverty and human rights issues, and addressing issues of blame.

## OVERVIEW OF DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE

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*Dr. Jerrold Heindel, National Institute of Environmental Health Sciences, Moderator*

*Dr. Philippe Grandjean, Harvard School of Public Health*

It is well established that NCDs in adulthood are influenced not only by genetic and adult lifestyle factors but also by environmental factors acting in early life. Early evidence of DOHaD was recognized in the 1950s and 1960s with Minamata disease and fetal alcohol syndrome. Early development is highly sensitive to toxicants and nutritional factors, to which the placenta is not an effective barrier. The extent of the toxic effects is determined by nutrient and toxicant properties, dosage amount, timing in regard to windows of vulnerability, and possible epigenetic changes that may be heritable.

Known examples of DOHaD are not exceptions. Rather, they are the new paradigm; epigenetic changes add plausibility and mechanisms to that paradigm. However, researchers have been confronted with an obstacle to their complete understanding of DOHaD. Its effects are often underestimated for a variety of reasons, including: non-specific effects are sensitive to confounding; complex causation may hide the effects of single factors; the level of effect may depend on the exact time of exposure; the total effect may become apparent only years or decades later; and the end result may be affected by compensation mechanisms.

*Professor Mark Hanson, University of Southampton*

Birth weight, even within the normal range, is inversely linked to metabolic syndrome in adulthood. In the Southampton Women's Survey, dietary patterns of low prudence before pregnancy are associated with increased blood supply to the fetal liver and larger babies. Nutritional status during pregnancy also has been associated with epigenetic changes: low carbohydrate intake in early pregnancy is associated with methylation changes in cord blood and with adiposity later in childhood. This finding is significant because it provides a biomarker of impact later in life. Researchers also have observed paternally induced transgenerational environmental reprogramming of metabolic gene expression in mammals, which also may affect offspring health.

There is a strong case for early life intervention in order to address the impact of nutritional abnormality in the prenatal environment. This intervention is especially important for groups with a low education quotient, as research has suggested that lower levels of education are associated with unhealthy diet. A broad spectrum of public education regarding early life nutritional intervention is necessary to reduce NCDs. Education programs should target adolescent boys and girls, as the Life Lab program at the University of Southampton does. These programs also should ensure that community leaders and teachers are well versed in NCD prevention techniques, which also would contribute to the overall success of a society-wide effort.

**Dr. Linda Birnbaum, *National Institute of Environmental Health Sciences, NIH***

A number of environmental exposures have been linked with health and disease. For example, prenatal and early life exposures to arsenic have been linked to COPD and lung cancer, and exposures to tobacco smoke and diethylstilbestrol (DES) have been linked to obesity. Epigenetics is an important mechanistic pathway for these influences. Epigenetic changes, such as changes in methylation and histone modification, are critical for development, but are also a target of environmental agents. For example, exposures to DES and bisphenol A (BPA) have been linked to dose-related changes in mRNA expression and to later life increased cancer risk.

Thinking of the environment more broadly and mining the toxicological literature for clues on etiologically relevant exposures are important next steps in addressing NCDs and DOHaD. As global DOHaD research develops, focusing that research on prevention rather than on treatment will become significantly more important.

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**IMPLICATIONS OF EARLY LIFE EXPOSURES FOR NON-COMMUNICABLE DISEASES**

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**Sir Peter Gluckman, *University of Auckland***

There is a need for policies that will encourage early life interventions to reduce NCDs. Although there is clear evidence for DOHaD, evidence does not automatically make policy. In fact, DOHaD has been largely ignored in reducing NCD burden. The 2011 UN political declaration and 2010 World Health Organization report, for example, focus primarily on modifying adult behaviors to combat NCDs. In order to move DOHaD into the policy arena, the idea that NCDs are a matter of voluntary adult choices must be challenged. Policy changes are more likely to be successful where measurable indicators of NCD risk reduction are currently available, such as epigenetic indicators of adult health and disease.

Although it is necessary to include DOHaD in the global effort to reduce NCDs, introducing its tenets will likely be a controversial move. Policy is always a matter of political compromise; while policy is largely value-driven, science is often left out of the valuation process, and it will be difficult to convince people to alter their life routines significantly based on scientific findings.

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**CLOSING PANEL AND DISCUSSION**

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**Ms. Christine Hancock, *C3 Collaborating for Health***

**Ms. Génon Jensen, *Health and Environment Alliance***

**Dr. Cristina Rabadán-Diehl, *National Heart, Lung, and Blood Institute, NIH***

**Ms. Johanna Ralston, *World Heart Federation***

**Dr. Kwok-Cho Tang, *World Health Organization***

The panelists discussed the ways in which their organizations are currently addressing the issue of DOHaD and NCDs. The organizations universally support efforts to increase societal education, beginning with communities and spreading to a larger number of scientists and public policy makers, as an important first step in NCD prevention. Additionally, the represented organizations work to support scientists by building their research capacity and disseminating the results of their work to the public, health care professionals, and policy makers.

In subsequent discussions, the symposium participants identified several recommendations aimed at reducing the global burden of NCDs:

1. The science of DOHaD must be communicated to the public, educators, and policy makers.
2. Prevention of disease must be integrated into broader social and economic development efforts.
3. Partnerships between key stakeholders—including global food and beverage industries, nongovernmental organizations, philanthropic bodies, academia and governments, and especially between wealthier and poorer countries—should be developed to encourage a more wholistic life-course approach to reverse the NCD epidemic.

## NEXT STEPS

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The satellite symposium provided reflection of the current state of DOHaD with regard to NCDs and the conflicted interests of the public, scientists, and policy makers. Although clear progress has been made in understanding the science of DOHaD and the potential impact on NCD prevention, progress hinges on advancing the dialogue and expanding the discussion to a variety of stakeholders.

A meeting is planned for 2013 in Singapore for this purpose, and a commentary for *The Lancet* is in preparation to continue raising awareness of the role of DOHaD in the prevention of NCDs.

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