

# Background to the Cape Town Manifesto: harnessing the power of the normal

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Cape Town was a highly appropriate place to launch the Developmental Origins of Health and Disease (DOHaD) Society's manifesto (see below) at the 9th International Congress in November 2015. Much of the work of members of the Society concerns the developmental origins of non-communicable diseases (NCDs) including cardiovascular disease, diabetes, bone and joint disorders, obstructive lung disease and some cancers, along with their major risk factors of which obesity is foremost in importance. Following the Political Declaration of the United Nations General Assembly on the prevention and control of NCDs in September 2011, which put NCDs centre stage on the global health agenda for the first time, and which acknowledged the importance of development in setting the risk for these diseases, the importance of addressing the problem has been emphasized in the Sustainable Development Goals, announced in September 2015: Target 3.4 is 'By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and wellbeing'. As long ago as 2008, the World Health Organization reported that 80% of deaths from NCDs occur in low-middle income countries,<sup>1</sup> and that globally these diseases account for more than 60% of all deaths. By 2014, more than 1.9 billion adults were overweight or obese, with 600 million obese;<sup>2</sup> this compares with 37 million people with HIV/AIDS.<sup>3</sup> Childhood overweight and obesity has increased at a rate 30% greater, and there are now more overweight and obese children in low and middle income countries than high income countries. These conditions are becoming so common as to be normal in parts of sub-Saharan Africa, where the number of overweight children almost doubled from 5.4 to 10.3 m from 1990 to 2014. Whilst this might prevent the overweight or obese child from feeling, or being treated as, unusual, it opens up the prospect of complacency, if public health services see no need to address the 'new normal'. This was one of the reasons for producing the Cape Town Manifesto of the Society as a statement of commitment to action.

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Coupled to this concern about inaction is the problem that addressing the challenge of obesity takes DOHaD into the realm of post-normal science (P.D. Gluckman, personal communication). Such science is defined<sup>4</sup> as 'the application of science to public issues where facts are uncertain, values in dispute, (but the) stakes high and decisions urgent'. This is not the science with which many of us, and the agencies which fund our research, are familiar: most of us are steeped in conceptual frameworks which are still dominant – Popper's doctrine of scientific progression by falsification of hypotheses<sup>5</sup> and Kuhn's of scientific revolution by paradigm shifts.<sup>6</sup> They don't help us to argue for greater attention to the importance of normal development, about which there is still so much that we do not know.

This is not helped, either, by the fact that to the non-specialist, or even to the general public, while it is obvious that development is important it happens as a normal part of life. Why worry about it? Practically everyone appreciates that the complex human body arises from the fertilized egg by a process of cell division and specialization. It is also well known that the process must stop, except for those cell types which are continually renewed such as in the skin or the gut. This limit, which Hayflick<sup>7</sup> demonstrated to be at about 47 cell divisions in contrast to the Nobel laureate Carrel's concept that all cells would be immortal *in vitro*, would not surprise most people. Even without specialized knowledge, many people would be happy with the idea that our development is 'programmed', a process largely determined by the genes we inherited from our parents and present in the fertilized eggs. The rediscovery of developmental epigenetics at the end of the 20th Century has challenged this view, but its implications are still not widely appreciated.

Uncertainties about which individuals, or which groups, in a population are at particular risk of later NCDs makes the task of the DOHaD advocate harder still. After all, variation in phenotypic traits is normal: it is the reaction norm described over a century ago by Woltreck for the water flea.<sup>8</sup> It is fundamental to evolution, as a part of the triad with inheritance and selection which Darwin recognized. And much work in developmental biology at the turn of the 20th Century, specifically in embryology, concerned the elucidation of fundamental processes which did not vary between individuals, or even between species.

When faced with the relentless rise in the prevalence of NCDs in low to middle income countries, and also in lower socioeconomic status and educational attainment groups in high income countries, it is easy to be pessimistic about the consequences of human nature. After all, it is normal to wish for some positive economic progress, however small. It is normal to want to reduce the labour and cost of shopping and cooking by eating at fast food outlets. It is normal to adopt labour-saving technology which reduces physical activity. Freeing time from domestic chores can help women in particular to undertake paid work, increasing household income even if it challenges breast feeding practices or children's diets. It is normal to enjoy screen-based recreational activities, for example watching sport on TV rather than playing it. Factors which exacerbate or contribute to risk of NCDs are a normal part of contemporary human life.

Unfortunately, it is also normal to discount risk, or even to ignore it altogether. Few of us have any education in how to assess financial or health risks, let alone in statistics. We buy lottery tickets when the chance of winning is vanishingly small. We struggle to deal with a news item about a medical discovery, for example that exposure to a food additive is claimed to increase the risk of a rare cancer by 20%. And we plan to take adopting a healthier lifestyle much more seriously later in our lives. Against this background, how are the normal processes underlying DOHaD, and the normative behaviours which may increase risk from early development onwards, to be understood more widely and their relative importance to be appreciated? Perhaps by giving some thought to how we can harness the power of the normal. There may be several ways of doing this.

First, we should recognize that, by definition, it is normal to conform to social norms. The adherence to dietary patterns during pregnancy, for example, does not necessarily indicate a lack of willingness to provide what is thought to be the best nutritional environment for both the mother and baby. There is a very wide range of traditional diets across cultures which are consumed in preparation for or during pregnancy: lots of fruit, or eggs, or butter for example. These are often rigidly adhered to, as women, their partners and their families believe that they are doing the right thing. While some such diets might seem potentially harmful to nutritionists, rather than viewing their consumption as a sign of ignorance, we should harness this willingness to conform to what is thought to be best. We need to provide better information and ensure its uptake and dissemination, from opinion formers to the wider population. This may mean communicating through channels which we would not usually think relevant as biomedical scientists or doctors.

Second, we should recall that it is normal for adolescents to want to rebel against the normative behaviours of their culture, at least to some extent. There are several recent examples of social, cultural and political movements which have been fuelled by the desire of young people to see change and to demand action. We need only think of climate change, financial probity or concerns about surveillance and data security to

realize how powerfully the socially networked 'voice' of the young can be. When asked, most teenagers say that one of their aspirations is to have a happy relationship and a healthy family. So why don't they care about the information which DOHaD research has revealed on the processes underlying the health of the next generation? Maybe because we just have not told them about it.

Third, there are some aspects of our lives which we believe to be so fundamental, so widely accepted, that we consider them to be normal and do not always stop to ask if they are in operation: human rights are a good example. The right to healthy development is framed in the United Nations Convention on the Rights of the Child. This is part of the International Covenant on Economic, Social and Cultural rights adopted by the United Nations in 1966. The 'enjoyment of the highest attainable standard of physical health' is part of Article 12 of this covenant (see *The Lancet* 386:2366, 12 December 2015) and of course young people should be central to achieving this goal, for their future as well as that of the next generation. Maybe in DOHaD we have not occupied the high moral ground sufficiently and made a clear demand that this human right be met under all normal circumstances.

It was with some of these considerations in mind that I drafted a Manifesto for the Society, which was skilfully edited by members of the Society's Council into the document which follows. We hope that members and others can use it to advocate that meeting its goals is a perfectly normal expectation, and should be a normal ambition, everywhere.

## The Cape Town Manifesto: November 2015

### *A healthy start builds a bright future*

Research in the field of DOHaD shows that the environment in which the embryo, fetus and young child grow and develop influences not only life course health and wellbeing but also the risk of later NCDs. Important aspects of the environment include maternal, fetal and infant malnutrition (including excess or insufficient macro- and micronutrients), toxins (e.g. maternal smoking or environmental chemical exposure), pregnancy in teenagers or older women and psychological or physiological stress. The NCDs include obesity, type 2 diabetes, hypertension, coronary heart disease, chronic lung and kidney disease, musculoskeletal disorders, some cancers and some mental illness.

Mothers are central to these inter-generational effects on health, because the embryo, fetus and young child depend on them for nutrition and nurturing. However, unhealthy behaviour and exposure to harmful environments in fathers may also increase the risk of NCDs in the next generation, through biological effects on the sperm as well as social factors.

Whether acting through the mother, father or directly on the infant and child, adverse environmental exposures during early development shape the body's responses to later challenges

such as unhealthy diets, sedentary lifestyle, inadequate sleep, excess screen time, high levels of stress and exposure to environmental toxicants. These biological responses are exacerbated by the rapid changes in lifestyle occurring between generations with urbanization and socio-economic progress in low- and middle-income countries, in migrants and displaced populations. Reducing the burden of NCDs across the life course thus requires interventions to promote healthy early development, beginning even before conception, as well as interventions aimed at sustaining health in children, adolescents and adults.

Harmful environments during early development may cause failure to achieve full physical and mental potential, and a loss of human capital. Combined with increased susceptibility to NCDs, this widens inequalities in health and has adverse economic consequences for individuals, families and communities. Moreover, an unhealthy lifestyle in prospective parents, along with NCDs such as diabetes, cardiovascular disease or obesity before conception and in pregnancy, passes greater risk of NCDs to the next generation. This perpetuates cycles of poor health, reduced productivity and shorter life expectancy, trapping populations in a trough of low human capital from which they cannot easily escape.

Against this challenging picture, pioneering DOHaD research provides grounds for optimism. Appropriate interventions during adolescence and the reproductive years will not only promote the health of the current generation but may also ensure a healthy life course for future children and grandchildren. The importance of the adolescent and preconception phases of the life course is now recognized in the United Nations Sustainable Development Goals and the Global Strategy for Women's, Children's and Adolescents' Health (2016–2030). The insights from DOHaD can help to leverage human capital across generations, of vital importance for meeting these goals.

DOHaD researchers are actively engaged in devising and evaluating primary interventions to promote a healthy start to life. They are also focusing on counteracting the effects of a poor start to life in order to reduce later NCD risk, by identifying biomarkers that could help susceptible individuals and populations to reduce such future risk. Building upon these foundations, the members of the International Society for Developmental Origins of Health & Disease have set targets for research, education and advocacy, applicable to both high and low income countries. They aim to:

- Promote and disseminate DOHaD concepts to the public and to government and non-government organizations, so as to increase awareness of the transgenerational benefits of a healthy start to life.

- Support optimal timing of pregnancy, healthy weight, good macro- and micronutrient status, physical activity, sleep and other behaviours in women and their partners before, during and after pregnancy.
- Reduce the prevalence of smoking and substance abuse in pregnancy.
- Reduce the incidence of gestational diabetes and its consequences.
- Promote positive maternal mental health and reduce rates of untreated depression and anxiety in pregnancy.
- Support breastfeeding, healthy complementary feeding, regular physical activity, a healthy lifestyle and parenting skills, to exploit critical windows of opportunity for the optimal physical and mental development of children.
- Promote healthy childhood growth, reduce stunting and obesity.
- Promote school attendance and health literacy in adolescents and young adults to improve behaviours including diet, physical activity, sleep and avoidance of toxicant exposure.

These goals reflect the Society's commitment to engaging in research at the highest level; to inspiring and training future researchers and educators; to advocating for interventions based on DOHaD concepts with civil society, government and non-government and other organizations; and to engaging all stakeholders in building new initiatives to promote a healthy start to life for all members of the next generation.

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