

## The Pre-pregnancy Period

The principles of DOHaD describe how early life exposures in conception, pregnancy, infancy and childhood can have a significant impact on health and disease risk in later life. The presenters in this session sought to answer the above question by highlighting interventions that are aimed at reducing risks in the pre-pregnancy period in order to avert disease in both the mother and offspring.

According to the findings reported by Jennifer Hall et al., pregnancy intention is associated with favourable maternal and neonatal health outcomes. As a result, women with planned pregnancies were more likely to attend antenatal care (ANC) earlier and more often, take preventative actions like test for HIV and take iron/folic acid supplements etc., in comparison with women with unplanned pregnancies. To substantiate these findings, it was shown that periconceptional maternal folate status increases cerebella size growth and trajectories in the first trimester of pregnancy, which has beneficial effects on the neurodevelopmental functions (i.e. motor learning) and prevents cognitive abnormalities.

The LifeLab study identified the gaps in teenagers self-perceptions of health as a result they suggest that changing young people's health attitudes and behaviours might be a key to improve health awareness. In accordance with this, the Ntshembo research team have emphasized on the importance, not only of targeting the individuals but the community, family and adolescents in promoting health education. It is also important to note that implementing lifestyle interventions requires more than just research team work, it also requires planning, forming partnerships with stakeholders and having infrastructure to produce positive outcomes as reported by the Malaysia Jom Mama Project.

## DOHaD and Epigenetics

This session explored the relationship between genetics and epigenetics and the effects on offspring phenotype. Epigenetics is defined as changes in the genome that can affect gene expression without altering gene sequence. Matt Silver discussed nutritional epigenetics in The Gambia. He found seasonal variation in postpubertal survival, which was 10 times lower in the rainy season compared to the dry season. He also reported increased methylation in rainy vs dry season pregnancies, and methylation was associated with maternal 1-carbon nutrient biomarkers. Rebecca Richmond used Mendelian randomization to try and understand if there is a causal effect between maternal BMI and offspring BMI. Her study aimed to use large sample sizes and a genetic risk score using multiple SNP's other than just FTO, which has been used in previous studies. She reported that a greater variation of maternal BMI on fetal BMI could be explained by those extra SNP's than by using FTO alone. She reported no evidence that maternal pre-pregnancy BMI was transferred to offspring BMI once maternal genotype was considered. This was similar to previous findings. Nicole Warrington aimed to understand genetic influences on gestational weight gain. She found that the maternal genome explained maternal weight gain while the fetal genome was associated with fetal weight gain. The novel PSG5 locus was identified as having genome wide significance for gestational weight gain in the offspring genome. A substantial proportion of the variability in weight gain could be explained by common genetic variation (30-40%). Three shorter presentations were then given; Lauren Capron discussed placental gene expression and maternal distress and found no associations, however an ethnicity interaction was seen. The sample size could have limited her conclusions and so further work is needed. Vanessa Pataia investigated the effect of paternal cholestasis on sperm damage and found an association using a mouse model. Offspring had increased body weight, decreased subcutaneous fat and increased cholesterol. Kozeta Miliku showed that genetic variance associated with kidney function in adults, was also associated with kidney function in children, however microalbuminuria was not associated in children. Functional studies may establish causal genes and mechanisms underlying these associations.

Proudly brought to you by DOHaD rapporteurs:

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## Maternal ante- and post-natal depression and its impact

This year maternal mental health had its own session, a sign of the recognition of its significance in the DOHaD conversation. Maternal depression has been linked to several adverse offspring outcomes such as poor growth, behavioral problems and poor emotional adjustment. Paul Ramchandani opened the session by summarizing pertinent work done on the impact of antenatal depression (AND) on offspring outcomes. According to Paul the most exciting research questions for mental health in the next decade include establishing the extent to which the link between maternal depression and offspring outcomes is causal, and unpacking the mechanisms through which they are linked. The other presentations covered both the risk factors for and effects of maternal depression.

The prevalence of and postnatal depression (PND) is quite high in India as reported by Meera Gandhi. Several social factors increase the risk of maternal depression in Indian slums with more educated women being less at risk. In rural South Africa depression is highly prevalent among HIV positive pregnant women, with HIV diagnosis during pregnancy increasing the risk. Rates of parenting stress are also high in HIV positive women, however these associations may be quite complex as risk factors for one disorder may be protective against another. Dietary quality is also associated with PND as seen in the Norwegian study MoBa, as is pre-pregnancy obesity according to a study from University of Helsinki. The latter is attenuated by depressive symptoms during pregnancy.

Results from the ALSPAC Study in the UK show that both maternal ante- and post-natal depression are associated with depression in the offspring at 18 years of age. After adjusting for the sex of the offspring, ante-natal depression increased the risk of depression in girls more than in boys and vice versa for the boys. Maternal postnatal depression is also linked to offspring anxiety disorder at 18 years. A Californian study shows that AND is more strongly associated with persistent than transient offspring obesity. The general consensus among the researchers present was the need for further work to elucidate causality pathways.

B I N G O				
Speaker bashes previous work	Repeated use of "um..."	Speaker sucks up to host professor	Host Professor falls asleep	Speaker wastes 5 minutes explaining outline
Laptop malfunction	Work ties in to Cancer/HIV or War on Terror	"...et al."	You're the only one in your lab that bothered to show up	Blatant typo
Entire slide filled with equations	"The data clearly shows..."	FREE Speaker runs out of time	Use of Powerpoint template with blue background	References Advisor (past or present)
There's a Grad Student wearing same clothes as yesterday	Bitter Post-doc asks question	"That's an interesting question"	"Beyond the scope of this work"	Master's student bobs head fighting sleep
Speaker forgets to thank collaborators	Cell phone goes off	You've no idea what's going on	"Future work will..."	Results conveniently show improvement

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# Developmental Origins of HEALTH AND DISEASE



9th WORLD CONGRESS CAPE TOWN, SOUTH AFRICA

10 NOVEMBER 2015

## DOHAD and fetal, neonatal and infant growth standards

This session presented new/refined standards for assessing fetal and neonatal growth, while identifying factors which may influence early growth and current gaps in this area.

INTERGROWTH-21st project:

Stephen Kennedy, Oxford University, UK and Fernando Barros, Federal University of Pelotas, Brazil WHO growth standards are a globally utilised tool for assessing growth from birth to 5 years. However, they do not cover growth in utero which may have a significant impact on growth trajectories in the post-natal period. The INTERGROWTH-21st study has recently filled this gap by providing prescriptive international standards for fetal growth and new born size for gestational age across 8 sites (USA, UK, Brazil, Kenya, Oman, Italy, China and India). Fetal and newborn size were found to be comparable across populations when growth constraints were minimal and can therefore compliment the WHO standards to provide internationally relevant standards of growth through pregnancy to 5 years of age.

Additionally, a secondary aim of this study showed that deeper neonatal phenotyping and therefore functional characterisation of the new born (beyond low birth weight/preterm birth classification) provides useful clinically relevant information for targeting interventions. The influence of maternal HIV-infection perinatal outcomes Speaker: Joris Hemelaar, Oxford University, UK ART naïve maternal HIV infection is associated with an increased risk of preterm birth, low birth weight, small-for-gestational age infants and still birth, with one preterm birth every 7 minutes in Sub-Saharan Africa in 2013 being due to HIV infection (200/day). Neonatal and infant body composition. Speaker: Joris Hemelaar, Oxford University, UK Fat mass varies greatly between neonates born with similar birth weights and these differences in adiposity may be predictive of metabolic risk in later life. However, no clinically applicable marker for predicting neonatal fat mass exists and there is a lack of reliable, population based, longitudinal data on body composition through infancy.

## NOTICES

- Meet the Mentor participants will be allowed to take their lunch into the auditorium with them for the session during lunchtime.

- DOHaD Society Annual General Meeting will take place in the auditorium 1 from 17:00

- Congress Dinner: Ticket holders can utilise the shuttle service departing from outside the CTICC between 18:45 and 19:30.

- Anneke Kempe will no longer be presenting abstract 5071. She will instead be presenting abstract 4708 "Exploring women's fear of childbirth in a high maternal mortality setting on the Arabian Peninsula". This will take place on Wednesday, 11 November, POD 4 at 10h35.

- Hazel Inskip will be presenting on "Engaging Teenagers to Improve Lifelong Nutrition: The LifeLab Experience". This will take place during Breakout Session iv number 3 at 13:30.



## Breastfeeding: Putting Science into Practice

Four breastfeeding research luminaries presented a fascinating global overview of breastfeeding patterns and trends (Cesar Victora), determinants (Linda Richter) and intervention evidence (Nigel Rollins). The session chair, South Africa's own Jerry Coovadia, began the session by highlighting that the study of breastfeeding is largely a question of science trying to catch up with what we already know, that breastfeeding is beneficial to both infant and mother. This argument was substantiated by Victora's overview of the findings of 28 systematic reviews on breastfeeding just published in *Acta Paediatrica* (Supplement, Dec, 2015). Coovadia also intimated that the practice of breastfeeding is under threat. Using South Africa as an example, he highlighted how fear of HIV transmission alongside aggressive marketing by the formula industry has resulted in suboptimal breastfeeding. The threat of industry also was evident in data Rollins presented on the economic value of the formula market, particularly in emerging markets. The formal presentation began with Victora, who gave participants a sneak-peak of data on global patterns and trends of breastfeeding, which will be published in *The Lancet* early next year.

Linda Richter's presentation followed, providing rich insight into why we find such large variations in breastfeeding practices over time and between populations. Using data from the 1970s until mid-2014 and an ecological approach, she presented a range of determinants from individual beliefs, e.g. milk insufficiency, and family support to the ways our very societies are structured in terms of social norms, labour (more women working), policies (maternity leave), health systems (training of workers), and market economies where formula continues to be marketed aggressively. Rollins then provided evidence from a review of breastfeeding interventions that have targeted health systems, home/family environments, work environments and combinations thereof. While impact has varied, the evidence shows that combined interventions have the best results, but that the mix needs to vary by context. The results also give hope that practices can be changed, albeit against a backdrop of industry marketing and poor enforcement of the Code against the Marketing of Breastmilk Substitutes. Though the challenges of shifting breastfeeding practices were highlighted by all of the presenters, the overall tenor of the session was one of passion, determination and hope, guided centrally by a desire to improve the health outcomes of both children and their mothers.

## Gestational diabetes and it's impact

John Newman et al. opened the session by outlining the principles of DoHad and the cycle of life (see diagram below) in determining the long term effects of gestational diabetes mellitus (GDM) in the offspring. In the Born Cycle study, they found that regular exercise didn't prevent the recurrence of GDM but instead increased maternal fitness and psychological wellbeing. Several DOHaD speakers presented on their work and made the following conclusions:

- Vulnerable Windows Cohort Study, showed that greater maternal weight gain in pregnancy and lower birth BMI are associated with lower beta cell function. However, faster postnatal growth is associated with lower insulin sensitivity.
- Monash University Study reported an unexpected and lower estimated fetal weight at 32-34 weeks and lower birth weight. Preliminary data indicated that fetal kidney volume is normal in GDM

## DOHaD Hot Topics

The DOHAD hot topics break out session featured a range of talks tackling environmental factors that may impact fetal development and postnatal outcomes. Some of the topics addressed the negative impact of intrauterine exposure to infection, alcohol and cigarette smoking as well as the positive effects of nutritional supplementation on birth outcomes. The impact of maternal obesity and in vitro fertilisation from donor eggs on intrauterine organ development was also discussed.

Various studies looked at the effect of maternal obesity on fetal kidney development and on metabolic programming in human populations in an indigenous Australian cohort (Kirsty Pringle et al) and from the perspective of experimental mice studies (Alcazar, M. A al).

Emily Dorey's presented a paper that also examined the effect of alcohol exposure during the periconceptional period on renal dysfunction. In this paper, she outlined an experimental genetic study that was conducted in rats that demonstrated altered renal gene expression and metabolism following exposure to alcohol.

Addressing the problem of preterm births is a major public health priority and understanding factors which may predispose to preterm birth is key. Thais Pereira outlined a case-control study that was conducted in the Brisa Birth Cohort in Brazil and colleagues looked at the potential role of counter-regulatory cytokine (CRC) in predicting preterm birth. This was achieved by investigating the relationship between Interleukin 10 (IL-10) and Transforming Growth Factor  $\beta$  (TGF- $\beta$ ) with the risk of preterm birth. Low levels of IL-10 and TGF- $\beta$  individually or in combination were associated with increased odds of preterm birth.

The DOHAD hot topics break out session featured a range of talks tackling environmental factors that may impact fetal development and postnatal outcomes. The session started off with a presentation by Dr Rihlat Said Mohammed who presented on the relationship between exposure to infectious environment in early life and metabolic outcomes in early adulthood. Exposure to infectious environment and body weight during infancy are associated with an increase of the concentration of CRP in young adulthood. Growth in infancy and adiposity in adulthood are associated with waist circumference, fasting glucose and SBP in young adulthood. Dr William Johnson presented on the impact of prenatal nutritional supplementation on fetal growth and birth outcomes. In a study set in the Gambia, women were randomised into four intervention arms. The study was carried out during the rainy and dry seasons to control for the potential season effect. The impact of supplementation showed a positive impact among those who had greater weight gain during pregnancy. Supplementation had a differential positive impact on fetal biometry.

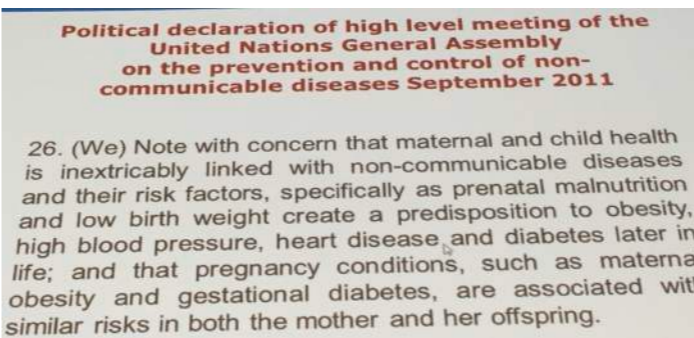


## DOHaD Opening Plenary

Monday the 9th of November saw the 9th Annual DOHaD Congress kick-off in earnest with the official opening of proceedings being initiated by a truthsayer followed by numerous distinguished guests facilitated by Lisa Mickelsfield.

Among the guests to grace the stage was Mark Hanson, President of the DOHaD Society. Special thanks was extended to Shane Norris and the conference management team for making this congress a resounding success. Mark noted the steady increase of membership over the years buttressed by the current representation of no less than 58 countries globally. Of particular importance is the plight of maternal and child health and nutrition. Emphasis was placed on the Cape Town Manifesto which is available for comment on the DOHaD Society website. Following Mark was Tim Armstrong from the WHO, who explained the role and mandate of the World Health Organisation. Noting that the global shift in the burden of disease has placed non-communicable diseases on the global agenda.

The Honorable Lokman Hakim Sulaiman, Deputy Director-General for Public Health for the Department of Health in Malaysia, treated delegates to an insightful look at preconception care and the JOM Mama project. Matthew Gillman, from Harvard concluded the proceeding with his discussion through, theory, evidence, and policy.



## Neuro-developmental programming

The session on programming of infant neurological development and neuro-behaviour was chaired by Prof Linda Richter. All the speakers kept to their time allocation and presented cutting edge research that examined and outlined various methodological issues and theoretical models to address the complex issues of reliable estimation of early infant and childhood cognitive function and behaviour. Barak Morgan kicked off the session with a uniquely theoretically rich presentation of neurobehavioural programming by early social adversity. In this paper he discussed various learned behaviours in the child in relation to maternal care (sensitivity) and he examined from an evolutionary perspective whether or not commonly perceived maladaptive behaviours were pathological or an adaptive advantage. The range of papers presented extended from the effect that maternal mental illness during pregnancy and the postnatal period had on infant cognition and emotion and on preschoolers' capacity to complete executive functioning tasks to the effects of maternal supplementation and diet on post partum depression and cognition and behaviour in South African school children. Salient point that emerged were that even subtle maternal anxiety and depression during the antenatal period may cognitive function of offspring to the extent that they might underlie a propensity to infant hypervigilance and anxiety. Conversely, the role of breast milk and maternal mindfulness might have a significant impact on preventing mental illness in their offspring at various developmental stages in their lifecourse.

