

EUCCONET Science Meeting - EUCCONET workshop

Name of principal organiser: V.W.V. Jaddoe		
Address: P.O. Box 3000 CA Rotterdam, the Netherlands		
Telephone: + 31 10 704 34 05	Fax: + 31 10 704 46 45	Email: v.jaddoe@erasmusmc.nl
Title of meeting/workshop: DOHaD 2012 satellite meeting: New developments in developmental epidemiology		
Location of meeting: Rotterdam, the Netherlands		
Dates: From: December 6 th , 2012 To: December 7 th , 2012		
Organisation sponsoring meeting (if any): Eucconet Companies		

1) SCIENTIFIC SUMMARY

Summary

The Developmental Origins of Health and Disease (DOHaD) hypothesis proposes that adverse environmental exposures in early life lead to early developmental adaptations. These adaptations may be beneficial for short term survival, but may lead to diseases in later life, such as cardiovascular disease, type 2 diabetes, respiratory diseases and psychopathology. This hypothesis was primarily based on historical cohort studies, but led to the start of numerous prospective pregnancy and birth cohort studies in different countries all over the world. Many of these cohorts started in European countries during the last 10 years, and have led to hundreds of publications in peer reviewed journals and to important insights in determinants and consequences of various developmental trajectories in fetal life and early childhood. ***The main objective of the DOHaD 2012 satellite meeting was to bring junior and senior researchers together who are involved in Developmental Epidemiology research in Europe.*** There were state of the art and recent research lectures. Plenary and parallel session were focused on adverse fetal exposures; air pollution; asthma; behavior; bone health; brain imaging; cardiovascular development; cognition; epigenetics; genetics; growth; metabolomics; methodological approaches; nutrition; obesity; placenta function. More than 200 researchers from more than different 20 countries participated in the meeting. These researchers came from various European cohorts which participate in the EUCCONET Consortium. During the meeting, various opportunities to develop European and other international collaborations were discussed.

Description of the scientific content of and discussions at the event

General

Many European research groups started birth cohort studies during the past 10 to 15 years. The focus of these birth cohorts is to explore the growth, development and health from early childhood into adulthood. This interest is largely based on the Developmental Origins of Health and Disease (DOHaD) hypothesis, which proposes that adverse environmental exposures in early life lead to early developmental adaptations. These adaptations may be beneficial for short term survival, but may lead to diseases in later life, such as cardiovascular disease, type 2 diabetes, respiratory diseases and psychopathology. This hypothesis was primarily based on historical cohort studies, but led to the start of numerous prospective pregnancy and birth cohort studies in different countries all over the world. ***The main objective of the DOHaD 2012 satellite meeting was to bring junior and senior researchers together who are involved in Developmental***

Epidemiology research in Europe. There were state of the art and recent research lectures. Plenary and parallel sessions were focused on adverse fetal exposures; air pollution; asthma; behavior; bone health; brain imaging; cardiovascular development; cognition; epigenetics; genetics; growth; metabolomics; methodological approaches; nutrition; obesity; placenta function. More than 200 researchers from more than different 25 countries participated in the meeting (Table 1). These researchers came from various European cohorts which participate in the EUCCONET Consortium. During the meeting, various opportunities to develop European and other international collaborations were discussed. The program of the meeting is given in detail in the annexes. Briefly, during two days, there were 4 plenary sessions, 14 parallel sessions and 2 poster sessions. During these sessions, in total 131 presentations were given.

**Table 1.
Countries from participants**

Europe

Austria
Belgium
Denmark
France
Germany
Greece
Ireland
Italy
Norway
Poland
Spain
Sweden
Switzerland
The Netherlands
United Kingdom

Other countries

Brazil
Canada
India
Indonesia
Jamaica
Japan
New Zealand
Singapore
USA
Venezuela

Program summary

Day 1 Morning session (Thursday 6/12/12; 9.00 - 12.30)

The meeting was opened by Prof H. A. Büller, Chair of the Board of Director from the Erasmus University Medical Center. The first session was focused on early nutrition. Plenary

speakers were Dr. V.W.V. Jaddoe, Prof. D.A. Lawlor and Prof. K.M Godfrey. During these sessions recent results and potentials for future studies were discussed related to maternal nutrition and life style during pregnancy, maternal obesity during pregnancy and maternal and infant vitamin D levels. Dr. Jaddoe discussed results of prospective studies on the life style related and socio-economic risk factors and cardiovascular consequences of specific fetal growth patterns. Prof. Lawlor presented evidence from both intervention and observational studies using designs that might help to better understand causal effects of maternal adiposity on childhood outcomes. Prof. Godfrey presented a review of current evidence for the adverse effects of low maternal and childhood vitamin D levels on childhood outcomes. After this plenary session, the parallel sessions were started focused on obesity, pre-pregnancy health, environmental exposures and epigenetics.

Day 1 Lunch poster session (Thursday 6/12/12, 12.30 -13.30)

During the lunch break, we organized a poster session. These posters were presented by the authors and focused on adverse fetal exposures, air pollution, asthma, behaviour, bone health, brain imaging, cardiovascular development, cognition. Most participants participated in this poster session.

Day 1 Afternoon session (Thursday 6/12/12; 13.30 – 17.15 hrs)

This afternoon session started with parallel sessions focused on air pollution, asthma, behavior and infant growth and nutrition. We closed the first day with a plenary session focused on the recent advances in genetic approaches. Results from recent genome wide association studies, genome sequence data and application of these methods in multi-ethnic populations were discussed by leaders in this field (Dr. F. Rivadeneira, Prof. T.M. Frayling, Dr. N. Timpson, Dr. S. Grant). Dr. Rivadeneira presented analysis approaches of genetic data from a multi-ethnic cohort of children. He provided an overview of the methodology applied to guarantee unbiased analyses, the major challenges we are confronted with and the array of opportunities that working with multi-ethnic data can provide. Prof. Frayling presented results of various European studies focused on genetic studies that might help to explain the observed associations of low birth weight with type 2 diabetes in later life. He showed that genetic studies offer the opportunity to study multiple variants that combined explain appreciable proportions of phenotypic variation and can be used to test the causal relationship between associated metabolic traits, including those relevant to the development origins of disease. Dr Timpson presented the design of the UK10K study, which contains 4000 population based samples with low read depth whole genome sequence data, and a series of new analytical opportunities. He also discussed new lessons to learn when trying to incorporate these data into efforts to further understand the aetiology and impact of early life

health, and the potential for European level collaboration. Dr. Grant presented his work on the genetics of childhood obesity, not only based on his own database but also in the meta-analysis setting, primarily within the Early Growth Genetics (EGG) consortium.

Day 2 Morning session (Friday 7/12/12; 9.00 - 12.30)

The first session on the second day was focused on specific methodological issues that are important and relevant for most cohort studies. Plenary speakers were Prof. A.J. Wilcox, Prof. G. Davey-Smith, Dr. E. Aagaard-Nøhr and Prof. H.W. Tiemeier. Methodological issues that were discussed included bias and confounding, Mendelian randomization, and non-response and loss to follow-up in large cohort studies. Prof. Wilcox discussed limitations of current studies focused on the fetal origins of disease, These studies should not neglect the possibilities of toxic exposures during pregnancy (including infections and medications) that produce cancer, infertility, and other impairments in adulthood - risks with well-established causal mechanisms and unquestioned public health urgency. Prof Davey Smith discussed the potential to incorporate 'omic' data, including metabolomic and epigenomic data in analytical approaches to explore causality. Dr. Aagaard-Nøhr presented her studies that examined the consequences of non-participation at recruitment and loss to follow-up on descriptive measures and exposure-outcome associations. Her results indicate that obtaining a random sample of all births is an impossible task and that internal validity should be given higher priority than external validity. Prof. Tiemeier presented analytical approaches to explore the association of early exposures on child mental health. After this plenary session, the parallel sessions were started focused on fetal exposures, maternal and child nutrition and childhood health.

Day 2 Lunch poster session (Friday 7/12/12, 12.30 -13.30)

During the lunch break, we organized a poster session. These posters were presented by the authors and focused on epigenetics, genetics, growth, metabolomics, methods, nutrition, obesity, and placenta function.

Day 2 Afternoon session (Friday 7/12/12; 13.30 – 17.15 hrs)

This afternoon session started with parallel sessions focused on maternal and pregnancy health, allergy and cardiovascular outcomes. We closed the second day with a plenary session focused on the recent advances in epigenetic approaches. Results from recent studies focused on epigenetic changes as a consequence of fetal famine exposure or air pollution were presented. Also, recent developments of genome wide methylation study approaches were discussed by leaders in this field (Dr. B.T. Heijmans, Dr. A. Baccarelli

Prof. C. Relton). Dr Heijmans presented his work on identification of epigenomic marks that are susceptible to the (prenatal) environment and to establish their contribution to human disease. His work was mainly but only based on the Dutch Hunger Winter, a well-documented human proxy of animal experiments of malnutrition during gestation. Dr. Baccarelli demonstrated that altered DNA methylation in blood and other tissues is associated with environmentally-induced disease, such as cardiovascular disease and asthma. He proposed possible models for the interplay between fetal and early-life exposure to environmental toxicants and the human epigenome in the developmental origins of human disease. Finally, Prof. Relton presented her work on genome-wide DNA methylation data (such as the Illumina HM450 BeadChip data), together with possible strategies for reducing the dimensionality of such data. She presented on possible strategies for future collaboration for GWAS of DNA methylation data that will in due course facilitate meaningful cross cohort comparison. The meeting was closed by the dean of the Erasmus University Medical Center Rotterdam (Prof. H.A.P. Pols)

During both the plenary and parallel session, there was a remarkable interaction between the presenters and the other participants. Many discussions were focused on ways to collaborate between cohorts, and on standardization and harmonization of methods. The main outcomes of these discussions are given below.

Results and impact of the event on the future directions of the field

General

The ambition of this meeting was to bring together leaders and junior researchers from major European child cohorts focused on the growth, development and health from childhood to adulthood. The meeting was linked to the DOHaD Society (www.mrc.soton.ac.uk/dohad). We aimed to provide an overview of new developments in developmental epidemiology, compare practices, exchange experience and other tools, and encourage future collaboration projects analyses.

Existing collaborations

During the meeting results from various European level collaborations were presented. These include:

- CHICOS: Developing a Child Cohort Research Strategy for Europe Consortium
- EAGLE : Early Growth and Longitudinal Epidemiology Consortium
- EGG: Early Growth Genetics Consortium
- ENRIECO: Environmental Health Risks in European Birth Cohorts Consortium

Various results of these collaborations have already been published in peer reviewed journals. These examples led to the initiation of various new analyses within these collaborations.

New collaborations

During the meeting, various initiatives for further collaboration were launched. These collaborations include:

- European collaboration on combined epigenetic studies. Several studies in Europe, such as ALSPAC (UK), Generation R (Netherlands), INMA (Spain) have started genome wide methylation data. We discussed plans for starting collaborations to standardize and harmonize data analyses and perform combined discovery and replication analyses.
- Mendelian Randomization Studies. Mendelian randomization can be used to explore the causality for observed associations. Various Mendelian randomization studies have already been performed to assess the causality for many associations in adults (eg. Inflammation and cardiovascular disease; obesity and cancer). Planned combined analyses include exploration of the analyses of maternal smoking during pregnancy with childhood obesity, blood pressure and asthma. European cohorts that will probably participate in these analyses include ALSPAC (UK), DNBC (Denmark), Generation R (Netherlands), GINI (Germany), INMA (SPAIN), LISA (Germany), MOBA (Norway).
- Metabolomics: Recent technological advances enable high throughput metabolomic analyses in large samples. During the meeting several possibilities for performing these analyses in the European Birth cohort were discussed. We expect the participating cohorts will apply for funding on European level to perform the analyses in their subjects.

Final remarks

In summary, the EUCCONET – DOHAD 2012; New Development in Developmental Epidemiology Meeting was a great success. We welcomed junior and senior researchers from various European countries who shared their ideas for current and future research projects. The meeting has led on specific ideas and plans for future collaborative studies.