Global data for diabetes and obesity research

MEETING REPORT

INTERCONNECT: A GLOBAL INITIATIVE ON GENE-ENVIRONMENT INTERACTION IN DIABETES AND OBESITY. ***Funded by EU FP7 grant agreement 602068***

Monday 12 September 2016, European Association for the Study of Diabetes, Munich, Germany

MEETING ABSTRACT

InterConnect seeks to optimise the use of existing data to enable new research into the causes of diabetes and obesity. The variation in the risk of diabetes and obesity between different countries and continents around the world is considerably greater than the variation in risk within individual countries. This population level heterogeneity in diet, physical activity and disease outcomes is largely unexplained because physically bringing data together from cohort studies across the world is constrained by governance, ethical and legal challenges.

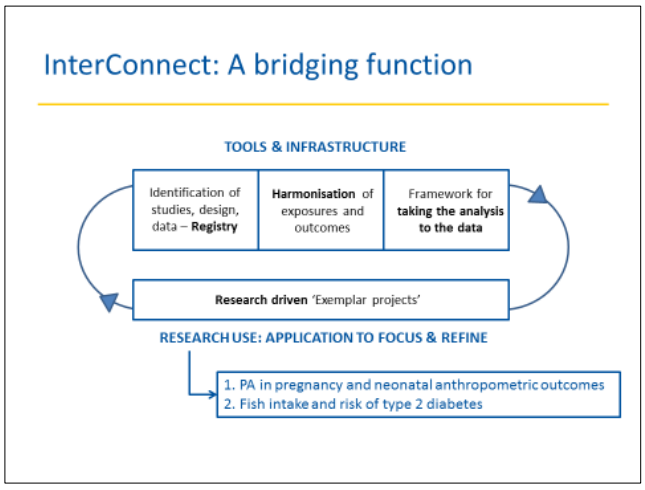
InterConnect is taking a new approach to enabling cross-cohort analyses. Rather than physically pooling data, it takes the analysis to the data - all data stays at source and only results are shared. In this way, it is possible to perform an analysis that is equivalent to a meta-analysis of harmonised individual level data and so the approach is called "federated meta-analysis". This meeting presented the findings of research projects that are underway, enabled participants to understand the contexts for research where federated meta-analysis is the method of choice and explained how to participate.

THE INTERCONNECT PROJECT (NICK WAREHAM)

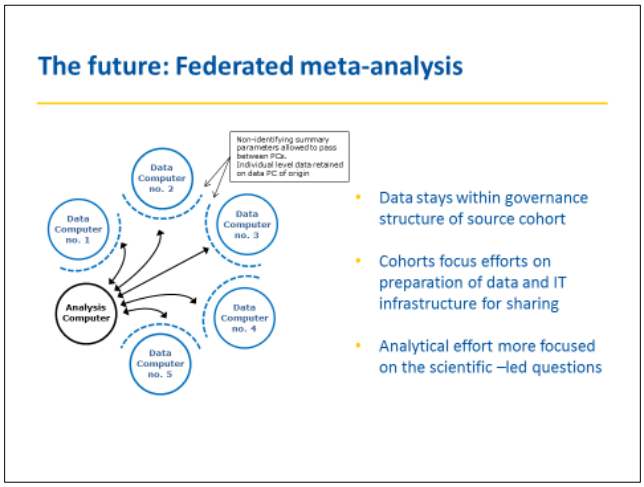
APPLYING THE INTERCONNECT APPROACH FOR FEDERATED META-ANALYSIS PROJECTS

Professor Nick Wareham, co-ordinator of InterConnect and Chair of the meeting, welcomed the participants. The aim of the Symposium was to introduce participants to the InterConnect approach and demonstrate its application. Professor Wareham explained how the InterConnect initiative had developed and that it was now beginning to deliver results that are scientifically robust and interesting.

InterConnect aims to enable others by creating the foundations for cross-cohort analyses to enable research to move from explaining the differences in risk within populations to being able to explain differences between populations. Across the many studies of diabetes and obesity there is variation in the methods used to assess exposures and outcomes. InterConnect is creating a forum for harmonising data and methods. Making the most of existing data requires harmonisation of related variables within different data sets. High quality meta-data is required to assess the degree to which this is possible. Specific algorithms can then be developed to transform the data into a common format.



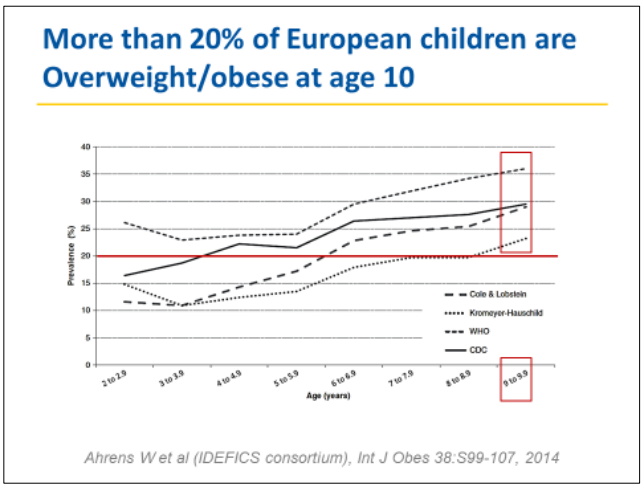
InterConnect is applying the approach to a number of exemplar projects that address research questions of aetiological and public health interest. These exemplars help to understand and address the real-life issues that affect implementation and also ensure that the tools and infrastructure are aligned to their research use. The exemplars enable InterConnect to engage researchers, develop specific resources for data harmonisation derived from practical needs and begin to establish a collaborative network for federated meta-analysis.



Data sharing - physically bringing data together - presents governance, ethical and legal challenges. To address this, InterConnect is developing a global collaborative 'data access and results sharing' network, providing a new approach that is secure, scalable and sustainable. A federated process means that participant data from contributing studies is held securely on geographically dispersed, study-based computers. Analyses are requested remotely and performed locally, so all data stays at source and only results are shared. In this way, InterConnect aims to enable others to conduct cross-cohort research.

1. PHYSICAL ACTIVITY IN PREGNANCY AND NEONATAL ANTHROPOMETRIC OUTCOMES

WHY THIS QUESTION IS IMPORTANT (GERNOT DESOYE)



Professor Desoye explained that this topic is of enormous health relevance. While it is common knowledge that the world is facing an obesity epidemic, it is less well-known that at least 20% of European children are overweight or obese by the age of 10, and that neonates born overweight have higher risks of developing metabolic syndrome and type 2 diabetes. Gestational diabetes also increases the risk of childhood obesity, setting up a vicious cycle. Lifestyle modifications such as physical activity in overweight women can potentially improve outcomes. The effect of physical activity on birth weight may depend upon the intensity of exercise undertaken and the period of pregnancy during which it occurs but studies to date are small and there is a need for evidence on a on a larger scale.

SYSTEMATIC REVIEWS OF MATERNAL PHYSICAL ACTIVITY IN PREGNANCY AND OFFSPRING BIRTH SIZE (SILVIA PASTORINO)

Dr Pastorino presented evidence from a systematic review of studies that have investigated physical activity in pregnancy and offspring birth size, with conflicting and inconclusive results. These show high levels of heterogeneity. She went on to explain the benefits that federated meta-analysis can bring to reach a better understanding of current research, as the process allows individual participant meta-analysis without physical pooling of data and reduces heterogeneity by harmonising physical activity measures and includes the same number and types of confounders.

TECHNICAL SET UP & HARMONISATION FOR FEDERATED META-ANALYSIS (TOM BISHOP)

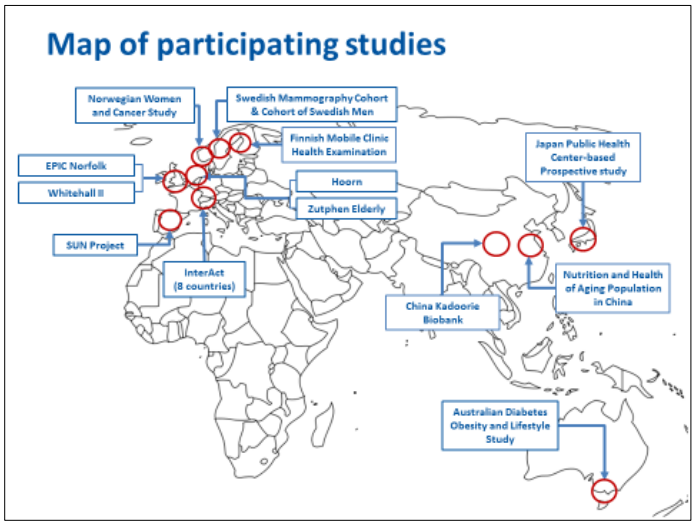
Tom Bishop explained how the team worked with collaborating cohorts to set up and harmonise the data. Seven participating studies had set up a local server as a node in the network and the data had been harmonised ready for analysis. Tom outlined the steps in the harmonisation process, using duration of moderate-vigorous leisure time physical activity as an example. The InterConnect team guided the server set up and data upload for each study, coded the harmonisation rules and then implemented an analysis on each study's server through remote access. Tom went on to explain the technical process of joining InterConnect in some detail, noting that while some work and cost is involved, it is readily achievable with the support of the InterConnect team and the server can be re-used for further research questions.

PHYSICAL ACTIVITY DURING PREGNANCY EXEMPLAR PROJECT – RESULTS (KEN ONG)

Dr Ong presented the first results of InterConnect, analysing the association between physical activity during pregnancy on birth weight using six geographically dispersed studies. The first analytical results were robust and consistent, demonstrating that the InterConnect approach provides informative results, much more so than a literature based analysis. The analysis showed a consistently null association between birth size and physical exercise taken in the first trimester and demonstrated that heterogeneity significantly decreased by consistent adjustment. Further analyses were planned, to look at the effect of physical activity in the third trimester and also to incorporate further studies. Professor Wareham welcomed questions and responses from the floor at this point, with discussions arising in relation to the choice of exemplar research question and the implications of the results for public health.

2. FISH INTAKE AND RISK OF TYPE 2 DIABETES

WHY THIS QUESTION IS IMPORTANT (NITA FOROUHI)



It is expected that fish intake is likely to be beneficial for the prevention of type 2 diabetes, based on the benefits for cardiovascular health. Yet previous published meta-analyses found heterogeneity with associations between fish intake and type 2 diabetes incidence varying between positive, inverse or null, based on geographic location. Past limitations were that only total fish intake was assessed but not types of fish (e.g. fatty fish, lean fish and shellfish) or cooking methods; contaminants/pollutants might also contribute. Systematic reviews did not include unpublished results. High heterogeneity in meta-analyses was observed and might be caused by different confounding structures of included studies as well as by different fish exposures (for instance, as portions sizes varied across studies).

Dr Forouhi outlined the advantages that the InterConnect approach brought to this research, in an attempt to reduce heterogeneity and harmonise to common formats. The exemplar team now have meta-data from all studies that have agreed to participate and collaboratively this working group has agreed on variables and an analysis plan. Server and IT set up for the cohorts in the fish intake exemplar are progressing well and the final phase of running the analysis should take place at the beginning of 2017. The team reached out to all cohorts who might have data and had already published, or not yet done so, with the aim of encouraging greater representation.

IDEAS FOR FUTURE RESEARCH PROJECTS (MATTHIAS SCHULZE AND NITA FOROUHI)

Professor Schulze opened this session by outlining the potential of InterConnect for further studies on diet and diabetes risk, outlining the project ideas from the InterConnect consortium members:

1. Exploratory dietary patterns
2. Gene-diet Interaction: TCF7L2
3. Legume consumption

All 3 projects will form new exemplars for InterConnect. Professor Schulze focused on the first two exemplar ideas. The first project aims to cross-validate previously described dietary patterns across different populations to strengthen the evidence-base for overall dietary patterns in diabetes prevention. The second project aims to investigate gene-diet interaction on the risk of type 2 diabetes of TCF7L2 gene variants and the intake of dietary fibre, coffee and macronutrients. Dr Forouhi focused on the third of these new exemplars, legume intake and type 2 diabetes. This topic is of increasing relevance as many dietary guidelines recommend reduction of red and processed meat intake. Legumes provide a suitable alternative protein source, yet there is limited and conflicting past evidence on legumes intake and diabetes, and in some populations legumes are a significant part of the staple diet but health effects are unknown. There is much research to be done in these important areas, and Symposium participants were invited to get in touch if they would like to be involved in any of the 3 new diet-related exemplar projects.

VISION AND PLACE FOR FEDERATED META-ANALYSIS (NICK WAREHAM)

Professor Wareham noted that the InterConnect initiative is now starting to deliver results with public health implications without any access to or visibility of individual-level data. Internationally, it is increasingly harder to share data and so this represents a very useful approach to enabling cross-cohort analyses. Although time and some investment is required to set up the infrastructure locally, Professor Wareham reiterated that it can be re-used through upload of additional sub-sets of data to address new questions, with studies remaining in complete control of data – unlike central deposition. Unlike traditional meta-analysis, studies do not need to perform any analyses – work follows role and the analysis is done in real time with no wait for outputs from study analysts.

Professor Wareham also explained that InterConnect is not an analytical consortium, but rather seeks to enable ad hoc consortia to form within a framework with each able to decide its own way of working. InterConnect has facilitated this process through exemplar studies, and hopes in time to broaden the range of studies that are included as they are currently primarily from Europe. Professor Wareham invited members of the audience to become involved with this initiative in a number of ways: by indicating that they would like their study to be included in the InterConnect registry (email InterConnectRegistry@mrc-epid.cam.ac.uk), by participating in one of the new diet exemplar questions and/or by devising and leading new exemplar research questions with support from the InterConnect team.

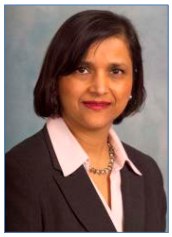
DISCUSSION

A wide-ranging discussion followed, touching upon exemplar studies, technical issues in the harmonisation process and data protection. Professor Wareham emphasised that researchers have a moral responsibility to better use existing global data, and the need to encourage funders and other stakeholders to support this process. Professor Wareham drew the meeting to a close and thanked participants for attending and for their welcome contributions to the meeting.

SPEAKER BIOGRAPHIES

Mr Tom Bishop, Senior Data Scientist, InterConnect, MRC Epidemiology Unit, University of Cambridge, UK. Tom is a Senior Data Scientist in the Aetiology of Diabetes and Related Metabolic Disorders programme, and is responsible for the technical delivery of the InterConnect project. Tom has a Master's degree in mechanical engineering from Cambridge University.

Professor Gernot Desoye, Director of Research, Department of Obstetrics and Gynaecology, Medical University Graz, Austria. Prof Desoye's research focuses on effects of maternal lifestyle (nutrition, physical activity), obesity and diabetes on placental development and function and how this affects fetal development and the neonatal phenotype. He coordinated the recent FP7-project (DALI) that studied lifestyle interventions in pregnancy for gestational diabetes prevention. Currently, he leads the placenta work package of the FP7-project EarlyNutrition. Prof Desoye is a board member of the International Association of Diabetes in Pregnancy Study Groups (IADPSG) and of the EASD Diabetic Pregnancy Study Group (DPSG).



Dr Nita Forouhi, Group Leader, Nutritional Epidemiology Programme, MRC Epidemiology Unit, University of Cambridge, UK. Her research focuses on the link between diet, nutrition and risk of diabetes, obesity and related disorders. She is also an Honorary Consultant Public Health Physician and member of the Diabetes Atlas committee of the International Diabetes Federation (IDF). She trained in Medicine in Newcastle and Edinburgh, and in Epidemiology and Public Health in London and Cambridge..

Dr Ken Ong, Group Leader, Growth and Development Programme, MRC Epidemiology Unit, University of Cambridge, UK. Dr Ong leads the Unit's Growth and Development programme. His research identified rapid postnatal growth, weight gain and reproductive timing as determinants of, and also potential targets for the prevention of, childhood obesity, type 2 diabetes and related disorders. Dr Ong obtained his PhD in Paediatrics following research at the Universities of Oxford and Cambridge, using large population-based studies to explore gene-environment interactions in fetal and early childhood growth.

Dr Silvia Pastorino, Career Development Fellow, MRC Epidemiology Unit, University of Cambridge, UK. Dr Pastorino is involved in the coordination and research development of international consortia as part of the InterConnect project. Dr Pastorino obtained her PhD in Epidemiology and Public Health at University College London investigating dietary and anthropometric determinants of type 2 diabetes.

Professor Matthias Schulze, Head, Department of Molecular Epidemiology, German Institute of Human Nutrition Potsdam-Rehbruecke, Germany. Prof Schulze was appointed as full Professor at the University of Potsdam and Head of the Department of Molecular Epidemiology at DIfE in 2010. His research interests are methodological approaches for dietary pattern analyses, metabolic and genetic predictors of type 2 diabetes, interaction between genetic factors and diet in the development of type 2 diabetes, and risk prediction modelling.

Professor Nick Wareham, Director MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine, UK. Prof Wareham is an Honorary Consultant at Addenbrooke's Hospital, Cambridge and Co-Director of the Institute of Metabolic Science. He was formerly a Wellcome Trust Senior Fellow in Clinical Science in Cambridge. Professor Wareham was the coordinator of the InterAct EU FP6-funded project, which investigated how genes and lifestyle factors interact to lead to type 2 diabetes. His work on gene-environment interaction is based on quantitative trait studies and large-scale population-based cohort studies. Prof Wareham is co-lead of the ADDITION study, a trial of screening for diabetes and intensive cardiovascular risk reduction undertaken in three European Countries.