The aim of the Centre is to develop and apply novel methods that can be used to determine the causes of health and disease in populations.

Work in the centre covers a large range of disease and health related outcomes, including cardiovascular disease, obesity, diabetes, cancer, mental ill-health, smoking, alcohol and physical activity. The unifying features of this work are developing and applying methods to understand causal pathways to health and disease endpoints and to improve causal inference in observational epidemiology.
Director’s message

New technologies are transforming how population-based health research can be carried out. The micro-scale ability to analyse genomes and their products, imaging techniques that allow unprecedented resolution of brain and body state and function, and new ways of collecting exposure data mean that epidemiological studies carried out today are very different from those studies on which I started my career. Indeed data production in some ways now outstrips our ability to discipline and make sense of what is collected. It is imperative that maximum value is extracted from the often publicly-funded studies that are yielding these extraordinary resources for identifying ways to improve population health. Key issues include collaboration - to ensure maximal return from investments in data generation - and the development of appropriate techniques to obtain as close to causal evidence as is possible from observational data. It is essential that such causal understanding is achieved for identifying points of leverage for improvement of population health.

At CAiTE we are committed to collaboration, both on the studies that we are fortunate enough to be current custodians of, such of the world’s leading birth cohort ALSPAC among many, and through the national and international collaborative groups that are springing up in most substantive medical fields. Our primary ambition is to develop, demonstrate and popularise the approaches to improving causal inference in population-based study data that are the focus of this report.

Professor George Davey Smith

CAUSALITY is DIFFICULT
Who caused the boat to sink?
Centre staff

At the start of the Centre in September 2007 core staff consisted of the Director (Prof G Davey Smith), deputy directors (Profs DA Lawlor and INM Day), three lecturers (Drs T Gaunt, S Rodriguez and N Timpson) and a research fellow (Dr P Guthrie). Since then we have successfully recruited staff to additional posts funded by the MRC as part of CAiTE funding and expanded considerably with posts funded from project/programme grants and fellowships awarded to CAiTE staff.

Core MRC CAiTE funding covers the salary costs of N Timpson, P Guthrie, T Palmer and B Mistry. The University of Bristol, as part of its contribution to MRC CAiTE, contributes the salaries of G Davey Smith (50% of time allocated to CAiTE), DA Lawlor (60%), INM Day (80%), D Evans (100%), T Gaunt (100%) and S Rodriguez (100%). All other staff are funded from project/programme grants or personal fellowships obtained by CAiTE staff since the centre started.

In the staff list below, where dates are not given staff have worked in the Centre since its start in September 2007.

Centre Director
Prof George Davey Smith
Professor of Clinical Epidemiology

Deputy Centre Directors
Prof Debbie Lawlor
Professor of Epidemiology
Prof Ian Day
Professor of Human Genetics

Other Centre Staff
Ms Bhavna Mistry
Centre Administrator, Public Engagement and Training Co-ordinator (started November 2008)
Dr David Evans
Senior Lecturer in Biostatistical Genetics (started November 2007)
Dr Nic Timpson
Lecturer in Genetic Epidemiology (started October 2008)
Dr Tom Gaunt
Lecturer in Bioinformatics and Molecular Genetics
Dr Santi Rodriguez
Lecturer in Population and Molecular Genetics
Dr Philip Guthrie
Research Associate in Molecular Genetics and Bioinformatics
Dr Tom Palmer
Research Associate in Biostatistics (started October 2008)
Dr Abigail Fraser
MRC Post-doctoral Fellow in Epidemiology (started September 2008)
Dr Marie-Jo Brion
Henry Wellcome Post-doctoral Fellow in Epidemiology (started September 2008)
Dr Laura Howe
Research Associate in Epidemiology (started February 2009)
Dr Li Benfield
Post Doctoral Statistician / Analyst for Carotid Ultrasound Scan Image Study (started April 2009)
Dr Tetyana Zayats
Post Doctoral Scientist in Statistical Genetics (started May 2009)
Ms Corrie MacDonald-Wallis
Research Assistant – Statistician (started October 2009)
Dr Anna-Maija Tolppanen
Post Doctoral Epidemiologist (started October 2009)

For staff profiles and a list of affiliate members and collaborators see the centre website
http://www.bristol.ac.uk/caite/
Research

Work in the centre covers a large range of diseases, risk factors and health related outcomes, including cardiovascular disease, obesity, diabetes, cancer, mental ill-health, smoking, alcohol and physical activity. The unifying features of our work are developing and applying methods to understand causal pathways to living a long and healthy life and to disease endpoints. We are particularly concerned with improving causal inference in observational epidemiology. Our research involves:

(i) identifying molecular and genetic pathways that are robustly associated with disease and health related characteristics (Molecular and genetic epidemiology);

(ii) where appropriate using genetic variants and gene expression data that are robustly related to modifiable risk factors as instrumental variables for the causal effects of these risk factors on disease (Mendelian randomization);

(iii) using family based studies (parental exposure comparisons, intergenerational studies, sibling comparisons), and family members as instrumental variables, for improving causal inference in observational epidemiology (Family based studies);

(iv) using cross-cohort comparisons, where we examine associations in cohorts from very different populations where confounding structures differ markedly, in order to explore causality (Cross cohort comparisons);

(v) developing statistical methods in the area of causal inference, particularly the use of instrumental variables analysis (Instrumental variables);

(vi) randomised controlled trials of complex population health interventions, and systematic reviews of these, particularly the long-term follow-up of intervention trials related to the developmental origins of disease (Randomised controlled trials).
Research highlights of the first 2.5 years
Molecular and Genetic Epidemiology

We have contributed to a number of genome-wide association studies of disease and health related outcomes of importance to population health, including studies of general and central adiposity, lipids, type 2 diabetes, fasting glucose, renal function, respiratory function and osteoporosis.

Dr Nic Timpson, Lecturer in Genetic Epidemiology, was joint first author of the first genome-wide study of adiposity, which was published just before the Centre opened and which identified the robust association of variation in the FTO gene with body mass index and fat mass. He has gone on to explore possible mechanisms underlying this association, and within CAiTE the use of FTO as an instrumental variable for understanding the effects of adiposity on health and disease has been extensively applied (see Mendelian Randomization).

A Common Variant in the FTO Gene Is Associated with Body Mass Index and Predisposes to Childhood and Adult Obesity

Timothy M. Frayling,1,2,3,4 Nicholas J. Timpson,1,4,5 Michael H. Weedon,1,2,6 Eleftheria Zeggini,1,6,7,8 Rachel M. Freathy,1,2,9 Cecilia M. Lindgren,1,2,5 John R. B. Perry,1,2 Katherine S. Elliott,1,2,10 Hann Lango,1,2 Nigel W. Rayner,1,2 Beverly Shields,1,2 Lynn W. Hanies,1,2 Jeffrey C. Barrett,1,2 Sian Elliott,1,2,9 Christopher J. Graves,1,2 Bridget Knight,1,2 Ann-Marie Patch,2,9 Andrew A. Ness,2 Shah Ebrahim,9 Debbie A. Lawlor,2,9 Susan M. Ring,2 Yawar Ben-Shlomo,9 Malena-Riitta Jauhiainen,1,10 Ulla Saxova,11,10 Amanda J. Bennett,5 David McLean,1,12 Luigi Ferrari,1,13 Ruth J. F. Laid,14 Ines Barroso,1,5 Nicholas J. Wareham,1,14 Fredrik Kanse,5 Katherine A. Owen,5 Lon R. Carlson,7 Mark Walker,16 Graham A. Hitman,17 Colin H. A. Palmer,14 Alex S. F. Doney,19 Andrew D. Morris,19 George Davey Smith,5 The Welcome Trust Case Control Consortium,1,2,4 Andrew T. Hattersley,1,4,5 Mark I. McCarthy1,4

Obesity is a serious international health problem that increases the risk of several common diseases. The genetic factors predisposing to obesity are poorly understood. A genome-wide search for type 2 diabetes-susceptibility genes identified a common variant in the FTO (fat mass and obesity associated) gene that predisposes to diabetes through an effect on body mass index (BMI). An additive association of the variant with BMI was replicated in 13 cohorts with 38,759 participants. The 1.86% of adults who are homozygous for the risk allele weighed about 3 kilograms more and had 1.67-fold increased odds of obesity when compared with those not inheriting a risk allele. This association was observed from age 7 years upward and reflects a specific increase in fat mass.
Senior academics in CAiTE were successful in obtaining two of the Wellcome Trust Genome Wide association grants – one, awarded to Professor George Davey Smith, to examine extreme obesity in young adults and the second to Professor Debbie Lawlor to examine maternal pregnancy and later life phenotypes. Genome-wide association studies require collaboration across custodians of a large number of study datasets and academics from a range of disciplinary backgrounds. CAiTE prides itself in having contributed to these endeavours both as partners and leaders.

In addition to genome wide association studies our research involves more disease focused approaches and Dr Tom Gaunt, Lecturer in Bioinformatics and Molecular Genetics, was successful in obtaining funds from the British Heart Foundation (BHF) to use the Human-cardiovascular disease 44.5K array of ~2,000 established loci across a range of cardiovascular, metabolic and inflammatory phenotypes in the British Women’s Heart and Health Study. As with the genome-wide work, we recognise the importance of large-scale collaborative efforts in this area and are working closely with PIs, from other UK institutions, who were successful in the same BHF call. To date work with the cardiochip has identified genetic variants robustly associated with variation in lipid levels and apolipoprotein levels and a large number of papers exploring different aspects of the genetics of cardiovascular disease are currently at different stages of preparation.

Dr David Evans, Senior Lecturer, has obtained an MRC New Investigator Research Grant to examine the effect of common disease genetic variants on transcriptomic and early life phenotypes which will elucidate the mechanisms through which these genetic variants affect disease risk. To date work has focused on variants that affect bone mineral density and menopause.

Mendelian Randomization

Mendelian randomization studies aim to use genetic variants to make causal inferences about modifiable (non-genetic) risk factors for disease and health related outcomes. This methodology has been pioneered by Professor George Davey Smith, Director of MRC CAiTE. Since George Davey Smith and Shah Ebrahim's initial paper (International Journal of Epidemiology 2003;32:1-22) proposing this approach as a means of improving causal inference in observational epidemiology the use of Mendelian randomization has grown rapidly in popularity.

We have used the approach to examine the causal effect of: C-reactive protein on cardiovascular and metabolic outcomes; adiposity on vascular and metabolic outcomes, bone mass and cancer; maternal adiposity in pregnancy on offspring obesity risk; folate or homocysteine on mental health, cardiovascular outcomes and bone health and of alcohol intake on blood pressure and cancer. Using Mendelian randomization is central to the large MRC grant awarded to Professor Debbie Lawlor to examine the causal effect of variation in vitamin D levels on metabolic and cardiovascular and also to the Wellcome Trust award to Dr Sarah Lewis (CAiTE affiliate member) examining the causal influence of mother’s dietary intake during pregnancy on brain development and cognitive ability and to several other grants on which CAiTE members are co-applicants. This approach is also central to three postdoctoral fellowship awards obtained since the opening of the Centre: Dr Abigail Fraser; (MRC) Dr Marie-Jo Brion (Wellcome Trust); and Dr Rachel Freathy (Wellcome Trust).

Our Mendelian randomization studies use results from research in genetic and molecular epidemiology (see above). In particular we have used variants identified in genome-wide association studies as genetic instrumental variables for Mendelian randomization studies. Mendelian randomization studies are also informed by our research into statistical methods for causal inference (see below under Development of statistical methods for causal inference).
Family Based Studies

Professors Debbie Lawlor & George Davey Smith have used family based study designs to explore causal inference in a number of areas for several years. This work continues to form a central part of the work of CAiTE and is being enhanced by new developments and understanding of instrumental variables analysis. Debbie Lawlor is editor of a recently published OUP book on the use of family based studies to improve causal inference and this approach is being used by several of the postdoctoral fellows in CAiTE. For example, Dr Marie-Jo Brion, has examined four different approaches to causal inference in examining the effect of maternal smoking in pregnancy and child psychological problems. One approach was to compare associations of maternal smoking in pregnancy with offspring outcomes to the equivalent associations of paternal smoking at the time of their partner’s pregnancy. The assumption here is that if there is a causal intrauterine effect one would anticipate stronger associations of mothers smoking than fathers smoking. This was the case, and together with other approaches to causal inference, we concluded that maternal smoking in pregnancy was causally (via intrauterine mechanisms) related to offspring conduct problems in childhood.

Cross cohort comparisons

Over the last 12 months we have developed collaborations with leads of cohort studies in very different populations in order to undertake cross-cohort comparisons and use these to make causal inference. The underlying idea is that if confounding explains an association in one population then one would expect no association in another population with a very different confounding structure to the initial population. For example, Dr Marie-Jo Brion, Wellcome Trust post doctoral fellow, spent 6 months working in Pelotas, Brazil, developing collaborations between the Pelotas birth cohorts and the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort based at the University of Bristol. In one study she demonstrated that whilst breast feeding was strongly socially patterned in ALSPAC (mothers from higher socioeconomic background and with greater education being more likely to breastfeed), this was not the case in Pelotas. Since there are concerns that many of the associations of breastfeeding with long-term outcomes such as obesity and cardiovascular disease in later life might be explained by residual confounding due to socioeconomic position, we reasoned that if this were the case we would expect no association in the Pelotas cohorts where breastfeeding was not related to socioeconomic position. We found that in ALSPAC breast feeding was associated with future adiposity, blood pressure and IQ, whereas in Pelotas the only association was with IQ. These findings are consistent with long-term follow-up of a breast feeding promotion trial (see section below on randomised controlled trials) that also suggested breast feeding is causally related to future IQ, but not to adiposity or blood pressure.
Maternal smoking in pregnancy and child psychological problems:

Disentangling causal and non-causal effects

Marie-Jo Brion PhD, Cesar Victora PhD, MD, Alicia Matijasevich PhD, MD, Bernardo Horta MD, Luciana Anselmi PhD, Colin Steer MSc, Ana Maria B Mcaczes MD, Debbie A Lawlor PhD, MB, ChB, George Davey Smith MD, DSc, F Med Sci

ABSTRACT

Objective: To explore associations of maternal prenatal smoking and child psychological problems and to determine the role of causal intrauterine mechanisms.

Patients and Methods: Maternal smoking and child psychological problems were explored in two birth cohorts in Pelotas, Brazil (n=509; random sub-sample) and ALSPAC, Britain (n=6,735). Four approaches for exploring causal mechanisms were applied: 1) cross-population comparisons between a high income and a middle-income country, 2) multiple adjustment for socioeconomic and parental psychological factors, 3) maternal-paternal comparisons as a test of putative intrauterine effects; and 4) search for specific effects on different behavioural subscales.

Results: Socioeconomic patterning of maternal prenatal smoking was stronger in ALSPAC compared with Pelotas. Despite this difference in a key confounder, consistency in observed associations was found between these cohorts. In both cohorts, unadjusted, maternal smoking was associated with greater odds of offspring hyperactivity, conduct/externalizing problems, and peer problems, but not with emotional/externalizing problems. After adjusting for confounders and paternal prenatal smoking, only the association with child conduct/externalizing problems persisted in both cohorts (conduct problems in ALSPAC OR=1.24, 95% CI: 1.07 to 1.46, p=0.005; externalizing in Pelotas OR=1.82, 95% CI: 1.19 to 2.78, p=0.005; ordinal odds ratios for maternal smokers having offspring with higher scores). Maternal smoking associations were stronger than paternal smoking associations in both cohorts, although statistical evidence that these associations differed was weak in one cohort.

Conclusions: Evidence from four approaches for exploring causal inference suggest a possible intrauterine effect of maternal smoking on offspring conduct/externalizing problems.
Development of statistical methods for causal inference

Traditionally epidemiologists have used multivariable generalised linear regression models to make causal inference from observational epidemiology with the explicit assumption that all potential confounding factors have been measured (accurately) and correctly included in the regression models. Prospective studies, particularly with the removal of early years of follow-up, are used to minimise the risk of reverse causation. This approach has undoubtedly had major successes, for example in identifying the adverse health impacts of cigarette smoking, high blood pressure and high cholesterol. However, this approach has also had its notable failures, for example the causal claims for hormone replacement and cardiovascular disease protection in women and for antioxidant vitamin supplementation and the protection from cancer and cardiovascular disease.

In econometrics instrumental variables analysis has been increasingly used in recent decades to make causal inference with observational data. An instrumental variable is one that is robustly associated with the main risk factor of interest but is not associated with potential confounding factors and is only associated with the outcome of interest through its association with the risk factor of interest. In our Mendelian randomization work (see above) we use genetic variants as instrumental variables to examine the causal effect of modifiable (non-genetic) risk factors on outcomes. Central to this work is the assumption that genetic variants are unlikely to be related to the large number of socioeconomic and behavioural characteristics that confound conventional multivariable regression models.
approaches (something that we have demonstrated empirically) and that genetic associations cannot be explained by reverse causation.

The use of genetic instrumental variables is relatively new and there are several aspects of instrumental variables analysis that require further development to enhance their value to epidemiology and population health sciences. We have an MRC methodology grant, joint with the University of Leicester, that funds several aspects of this work and have contributed a number of research papers in this area. Dr Tom Palmer leads much of this work and has recently developed methods for estimating causal odds ratios and risk ratios using genetic instrumental variables and for the use of multiple genetic variants (each with different underlying biological mechanisms) to increase statistical efficiency and provide further evidence of causal effects. This work is done in collaboration with colleagues in the Department of Econometrics and Mathematics at the University of Bristol, as well as with other external colleagues.

Improving measurements in observational studies

A further aspect of improving causal inference is by improving the accuracy and number of repeat (over time and by different family members) measurements within the cohort studies that we use. Dr Laura Howe, post doctoral researcher, has compared the accuracy of health visitor records of infant weight and height that were collected in the whole ALSPAC cohort on a sub-group who had research clinic measurements and found the health visitor records to be largely accurate. In ALSPAC information is collected on both parents and their offspring allowing for some characteristics reports by parents to be compared to those of the offspring. Where possible we emphasise accurate objective measurements, such as movement sensors to assess physical activity in our cohort studies and trials. Drs Laura Howe, Abigail Fraser and Corrie MacDonald-Wallis are working closely with Dr Kate Tilling (Reader in Biostatistics, Department of Social Medicine, University of Bristol and affiliate member of CAiTE) to develop methods for appropriate analysis of repeat measurements, such as repeat anthropometry and blood pressure, in order to accurately assess the impact of these across the life course on later health related outcomes.

Randomised controlled trials

Much of the work in MRC CAiTE is focused on improving causal inference in observational epidemiology. This is important because for many potential interventions it is unfeasible or unethical to randomise study participants and where this is not the case the expense and ethical implications of randomised experiments necessitates best prior (observational) evidence on which to select interventions. However, we also contribute to randomised controlled trials. We have a particular interest in trials of early life population interventions that can potentially be used in the future to explore developmental origins.
of health and disease and may be useful for exploring gene-environmental intervention interactions. Professor George Davey Smith and Professor Richard Martin (an affiliate member of MRC CAiTE) are co-applicants on the long-term follow-up of the Promotion of Breastfeeding Intervention Trial, a randomised controlled trial in Belarus that originally allocated the mothers of 17,046 healthy term infants to a breast feeding promotion intervention or not. This has been used to demonstrate that breast feeding has long term beneficial effects on child IQ, but does not seem to have long term effects on child obesity or associated cardiovascular risk factor risks.

Professor Debbie Lawlor is PI of a recently completed pilot and feasibility study examining a school based intervention to improve physical activity and diet in early childhood and is currently applying for funds to complete the full-scale randomised controlled trial of this intervention. Professor George Davey Smith, working with groups in Birmingham, Cardiff, Aberdeen and Hyderabad, instigated follow-up of experimental studies of manipulation of the antenatal and early postnatal diet, and work on these studies is ongoing.

Translation of research findings

As the centre’s name implies our aim is to improve causal inference in observational epidemiology and also to ensure that findings from such research are appropriately translated, ultimately into improving population health. To this end we work closely with the UKCRC Centre for Development and Evaluation of Complex Interventions for Public Health Improvement (DECIPHer), which is co-directed by Professor Rona Campbell from the Department of Social Medicine (University of Bristol) and run jointly with the Universities of Cardiff and Swansea. Professor Debbie Lawlor is a collaborator with DECIPHer. There are several ways in which findings from our work will be translated into population health benefit.

i. Translation from observational science to new intervention trials

Results from our observational studies (using the causal approaches described earlier) will highlight key areas where there is a strong prior for causality and hence where there would be high value in funding appropriate randomised trials. In some instances our observational causal work will highlight areas where intervention trials are not warranted. For example, our work using genetic variation in the CRP gene suggests that investment in trials of drugs that reduce CRP levels as a means of preventing cardiovascular disease are not warranted.

ii. Translation from observational science to pharmacoepidemiology

An example of this work is provided in the recent publication that used CETP gene polymorphisms to separate the mechanism-based and off-target actions of CETP-inhibitors. Cholesteryl ester transfer protein (CETP) inhibitors raise high density lipoprotein cholesterol (HDLc) and therefore it was assumed that CETP-inhibitor drugs would provide a valuable means for preventing cardiovascular disease in those at high risk (in particular those with low HDLc). However, a large randomised trial of torcetrapid, the first-in-class CEPT-inhibitor, found that it caused an unexpected elevation in blood pressure and an overall increase in cardiovascular disease events. Since other classes of CETP-inhibitors were being trialled as these results were published it was important to quickly understand whether the blood pressure elevation was due to CETP-inhibition per se (and therefore likely to occur with all drug classes) or was an off-target effect of torcetrapid (and possibly something that would not occur with other CETP inhibitors). Using CETP gene polymorphisms our work suggested that CETP inhibition did not result in elevate blood pressure and hence it would be ethical to continue to trial other classes of CETP inhibitors (all be it with continued monitoring of blood pressure, other cardiovascular risk factors and events) with the possibility that their reduction in HDLc would result in reduced cardiovascular events.
**iii. Translation from intervention studies to public and clinical health policy**

Through our links with DECIPHer, and their links to relevant public health policy makers, and our own experience of working with key organisations responsible for national and international clinical and public health policy we will ensure that findings from our primary research are translated into policy where this is appropriate. Professor Debbie Lawlor is a board member of the MRC's Populational Health Sciences Network and provided comments on an earlier draft of that Network's recent publication on a translational framework for public health research (http://www.biomedcentral.com/content/pdf/1471-2458-9-116.pdf).

**Future plans**

Many of the grants, postdoctoral fellowships and PhD studentships obtained during the first 2.5 years of MRC CAiTE (see below) will direct much of the next 2.5 years work of the Centre. These will add substantially to research in the key overlapping areas highlighted above. Additional areas that we plan to expand in the next 2.5 years include:

**i. Epigenetics.**

We are currently beginning MRC funded pilot work that aims to assess the magnitude of both intra- and inter-individual variation in DNA methylation in the Avon Longitudinal Study of Parents and Children (ALPSAC) cohort, to establish the fidelity of DNA methylation patterns over time and accrue pilot data on the relationship between specific exposures (including maternal diet, smoking and alcohol consumption in pregnancy) and DNA methylation status and, in turn, DNA methylation patterns and specific phenotypic traits. These traits include offspring and maternal adiposity, intelligence, respiratory, vascular and metabolic traits and age at menarch (in daughters) and menopause (mothers). This work is in close collaboration with Dr Caroline Relton from the University of Newcastle (CAiTE collaborator) and is being extended to India-based studies funded by a Wellcome Trust award to George Davey Smith. The initial results of this pilot work are very exciting and with Dr Relton and others we are applying for major grant funding to integrate epigenetic measures as intermediate phenotypes within expanded Mendelian randomization designs, a method we refer to as genetical epigenomics.

**ii. Genotype based recall studies.**

A further MRC funded pilot (to DA Lawlor) is currently examining MRI determined fatty liver in adolescents recalled on the basis of extreme homozygotes for genetic variants associated with adiposity. The aim of this study is to contribute to a larger body of work concerned with the causes and consequences of non-alcoholic fatty liver disease. More broadly it will contribute to evaluating the potential of genotype based recall as an efficient research approach for use with expensive and time-consuming but very accurate phenotypic measurements. Our plan is to use this approach in the future for a number of phenotypic measurements such as dietary challenge experiments.

**iii. Expression studies.**

Dr Nic Timpson is currently leading an MRC funded pilot study examining the effects of variants in predicted microRNA binding sites on mRNA expression levels. Genetic variation is associated with mRNA expression levels in a heritable fashion and has been mapped in humans and model organisms as expression quantitative trait loci (eQTL). We aim to recognise this type of variation and assess, in a translational manner, the implications of this for both gene expression and complex phenotypes. In the future we hope to be able to use expression data and determinants of this in causal inference using similar approaches to those used in our Mendelian randomization studies.

**iv. Exploring the use of genetic variants to refine the utility of biomarkers.**

Genetic variants have the potential to define subgroups of the population in whom established biomarkers work well and those in whom they do not work. We have a small CRUK grant that is funding pilot work to explore this possibility with the example of prostate specific antigen (PSA) and prostate cancer. This study will explore the genetic contribution to very low PSA levels in order to determine whether in the populations there are PSA ‘non-responders’ or ‘hypo-responders’ in whom PSA
cannot act as a prostate cancer biomarker. If this work establishes value then we plan to expand it to other areas.

v. Gene copy number variation
Gene copy number variation (CNVs) are a wide-spread phenomenon, currently known to affect nearly 8,500 loci. The change in copy number of a gene will, in many cases, impact on protein quality, and as such is likely to have a functional role in human health. Despite the potential importance of CNVs in human health, the difficulty in assaying sequences that differ in number rather than content has meant that progression of research in this area has been limited. Dr Philip Guthrie and Prof Ian Day have developed a novel high-throughput liquid-phase CNV assay (Amplification Ratiometry Control System - ‘ARCS’) which is inexpensive and generic, and will therefore be widely applicable to the determination of CNV class distribution in large cohorts. We are currently preparing manuscripts for an ‘ARCS’ methods paper and a copy number/phenome scan paper for the copy number variable haptoglobin duplicon. In the future we plan to use ARCS in a wide range of CNV genetic association studies.

vi. Whole genome sequence data
Prof George Davey Smith is co-applicant on a recently awarded large Wellcome Trust Strategic grant that will resequence the whole genome of 2000 ALSPAC participants, as well as participants in the TwinsUK cohort (PI of TwinsUK: Prof Tim Spector, CAiTE collaborator). This level of detailed genomic information has incredible potential for expanding our work in molecular genetic epidemiology, Mendelian randomization and use of genetic variants to refine biomarker accuracy. However, it also raises a number of challenges related to data handling, analysis and interpretation and ethical issues. Thus, in the immediate future CAITE staff (primarily Dr Nic Timpson and Prof George Davey Smith) will work with the Wellcome Trust and national and international collaborators to develop guidance for the use of such data.

vii. Expanding family based studies
Profs George Davey Smith and Debbie Lawlor, together with Dr Tom Palmer, are developing instrumental variables analyses for use with family data. We are also developing new family methods, such as spousal comparisons, and enhancing collaborations with colleagues in Denmark, Norway and Sweden where large scale record linkage facilitates the development and use of these family based methods. A key component of the next ALSPAC core renewal will be methods for obtaining prospective information on the offspring (led by Debbie Lawlor and George Davey Smith) of the ALSPAC children who are currently aged 18. This will provide the most detailed intergenerational study with detailed biological and phenotypic data across three generations. This will be used to further extend our family based studies and also our molecular genetic epidemiology (including exploring epigenetics and family of origin effects) and hence Mendelian randomization studies.
Grants

1. Research grants with CAiTE Staff as principal investigators

2009


6. Lawlor DA (PI), Davey Smith G, Callaway M, Ash-Miles J, Day CP. A genome based recall pilot study to compare use of liver enzymes, ultrasound scan and magnetic resonance imaging for identifying non-alcoholic fatty liver disease in epidemiological studies. Medical Research Council (New Initiative funding for MRC CAiTE Centre) (G0600705), £58,413: 2009-2011.


2008


2007

2. CAiTE fellowship, studentship or capacity building grants

2010

1 Santos AC (Postdoctoral Research Fellow), Barros H (Main Supervisor), Lawlor DA (Second Supervisor). Desenvolvimento da obesidade na infância (Development of obesity in infancy). Portuguese Research Council, €225,000: 2010-2013.

2009

2 Jago R (Research fellow), Lawlor DA (Main Supervisor), Fox K (Second Supervisor). Parental and home environment influences on youth physical activity and screen-viewing: Preventing childhood obesity. NIHR Career Development Fellowship, £379,000: 2009-2014.

3 Day I (PI), plus a consortium of supervisors. Funding to establish a capacity building doctoral training centre populations, pathways and molecules: mathematical and statistical approaches (10 four (1+3) year Ph.D. studentships (BCSBmed). Medical Research Council, £823,100: 2009-2014.


2008

5 Fraser A (Postdoctoral Fellow), Lawlor DA (Main Supervisor), Windmeijer F (Second Supervisor). Obstetric, lifestyle and genetic determinants of vascular and metabolic traits in women in early middle-age. Medical Research Council health services and health of the public research fellowship, £336,579: 2008-2012.


8 Davey Smith G (PI), Martin R, Day INM. Molecular, genetic and lifecourse epidemiology. PhD programme to provide 3 PhD students per year for 6 years. Wellcome Trust, £2.9 million: 2008-2012.

2007


10 Gregson CL (Postdoctoral Fellow), Tobias J (First Supervisor), Davey Smith G. Investigation of the epidemiology and heritability of high bone mass. Wellcome Trust, £405,008: 2007-2010.
3. Project or Programme Grants with Centre Staff as co-applicants

### 2010


### 2009


### 2008


2007


## Outputs

### 1. Awards

1. George Davey Smith received the American Psychosomatic Society Patricia R Barchas Award in Socio-physiology in 2010

### 2. Lectures

#### Named Lectures

**2008**


**2007**


#### Invited lectures to international scientific meetings

**2009**


**2008**

11. Debbie A Lawlor. Using genetic data to improve causal inference in observational epidemiology. Keynote Speaker 7th Annual Faculty Research Symposium - Frontiers in Biomedical Research, University of Hong Kong Li Ka Shing Faculty of Medicine, Hong Kong, 12 December 2008.


15 Debbie A Lawlor. Determining whether pre-adult exposures are causally and importantly related to adult chronic diseases. World Congress of Epidemiology, Porto Alegre, Brazil, 24 September 2008.


18 George Davey Smith. Understanding environmental influences on development and health from womb to tomb: can genetic epidemiology help? From Womb to Tomb: The Norwegian Mother and Child Cohort Study Recruitment of 100 000 pregnant women. Norwegian Institute of Public Health, Lovisenberg gt 8, Oslo, 15 September 2008.


2007


29 George Davey Smith. Epidemiology and the gloomy prospect: Why epidemiologists are not in the business of understanding individual risks. Laboratory for Genetic Epidemiology Annual Workshop, Yanchap, Western Australia, 19-21 November 2007.


35 George Davey Smith. Epidemiology and genetic epidemiology: convergences and divergences.

36 Debbie A Lawlor. Translating genetic and molecular information into causal inference about modifiable non-genetic risk factors in cardiovascular disease. Opening address to scientific launch of UNIKARD (a new national initiative for cardiovascular research in Norway supported by the Norwegian Medical Research Council and the 4 Medical Faculties and University Hospitals in Norway), Tromso, Norway, 1 September 2007.

3. Peer reviewed conference presentations

2009


6 Timpson NJ, C-reactive protein levels and body mass index: elucidating direction of causation through a reciprocal Mendelian randomisation design. American Society for Human Genetics 59th Annual meeting, Hawaii, USA, 20-24 October 2009.


16 Palmer TM, Lawlor DA, Sterne JAC. Including
multiple instrumental variables in Mendelian randomization analyses. 30th Annual Conference of the International Society for Clinical Biostatistics, Prague, Czech Republic, August 2009.


2008


25 Freathy RM, Bennett AJ, Ring SM, et al (18 authors including Timpson NJ and Davey Smith G), Type 2 Diabetes Risk Alleles at the CDKAL1 and HHEX-IDE Gene Loci Reduce Birth Weight, Providing Direct Evidence to Support the Fetal Insulin Hypothesis. 68th Scientific Sessions of the American Diabetes Association, San Francisco USA, 6-10 June 2008.

26 Bell JT, Timpson NJ, Rayner NW, Morris AP, Zeggini E, McCarthy MI, (for the UKT2D Consortium), First Generation of Scan of Genome Wide Association Data Allowing for Epistasis Prioritizes Multiple Interacting Candidate Loci in Type 2 Diabetes. 68th Scientific Sessions of the American Diabetes Association, San Francisco USA, 6-10 June 2008.

27 Rayner NW, McCarthy MI, Frayling TM, et al (11 authors including Timpson NJ), Genome Wide Association Analyses Reveal Differences in Genetic Susceptibility Profiles between Obese and Lean Type 2 Diabetes. 68th Scientific Sessions of the American Diabetes Association, San Francisco USA, 6-10 June 2008.


2007


36 Freathy RM, Timpson NJ, Lawlor DA, et al (20 Authors including Davey Smith G), Analysis of 16784 individuals shows that BMI-altering FTO genotypes are associated with obesity-related quantitative traits in the general population. American Society for Human Genetics 57th Annual meeting San Diego, California, USA, 23-27 October 2007.


4. Peer reviewed research journal publications

2010


15. Dupuis J, Langenberg C, Prokopenko I, et al (306 authors, including Lawlor DA, Davey Smith G and


Jokela M. Common mental disorder and obesity — Insight from 4 repeat measures over 19 years in the prospective Whitehall II cohort study. British Medical Journal 2009; 339:b3765 doi.10.1136/bmj.b3765.


41 Dennison EM, Syddall HE, Jameson KA, Sayer AA, Gaunt TR, Rodriguez S, Day IN, Cooper C,


69 Ferreira MAR, Zhao ZZ, Thomsen SF, James M, Evans DM, Postmus PE, Kyvik KO, Backer V, Boomsma DI, Martin NG, Montgomery GW and Duffy DL. Association analysis of eight genes under asthma linkage peaks. Allergy, 2009; 64:1623-8, PMID: 19824886.


2008


85 Chen L, Davey Smith G, Harbord RM, Lewis SJ. Alcohol Intake and Blood pressure: A Systematic


109 Evans DM, Barrett JC, Cardon LR. To what extent


123 Lewis SJ, Lawlor DA, Nordestgaard BG,


139 Hillsdon M, Lawlor DA, Ebrahim S, Morris JN. Physical activity in older women: associations with area deprivation and with socioeconomic position over the life-course. Observations in the British


2007


151 Wellcome Trust Case Control Consortium (Including Evans D, one of lead statisticians & Timpson N on behalf of type 2 diabetes group). Genome wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature 2007; 447: 661-678, PMID: 17594300.


Davey Smith G. Refining associations between TAS2R38 diplotypes and the 6-n-propylthiouracil (PROP) taste test: findings from the Avon Longitudinal Study of Parents and Children. BMC Genetics, 2007; 8:51.


5. Journal reviews, commentaries or editorials


15 Davey Smith G. Assessing intrauterine influences on offspring health outcomes: can epidemiological findings yield robust results? (Commissioned review) Basic and Clinical Pharmacology and Toxicology 2008; 102:245-256.


20 Batty GD, Alves JG, Correia J, Lawlor DA. Examining lifecourse influences on chronic disease: the importance of birth cohort studies from developing countries (Commissioned review). Brazilian Journal of Medical and Biological Research 2007; 40:1277-1286, PMID: 17876486.


22 Batty GD, Alves JG, Correia J, Lawlor DA. Examining lifecourse influences on chronic disease: the importance of birth cohort studies from developing countries (Commissioned review). Brazilian Journal of Medical and Biological Research 2007; 40: 1277-1286, PMID: 17876486.

6. Books – Authored


7. Books – Edited

8. Book Chapters


9. Audio-visual publications

Training

1. PhD Studentships

In addition to four PhD studentships awarded for the first 5 years as part of the central MRC CAiTE funding, Professor George Davey Smith (PI) was successful in his bid for a Wellcome Trust programme of PhD students (18 studentships over 6 years) in genetic and lifecourse epidemiology. The MRC CAiTE and Wellcome Trust programme PhD studentships are all for 4-year studentships and we have just completed (academic year 2008-09) the first year of the first set of students appointed to these 4-year studentships. During this first year all students (irrespective of final PhD thesis) have completed post-graduate short courses and mini-projects aimed at providing them with basic skills in epidemiology, statistics, molecular-genetics and bioinformatics. A focus of the training is on interdisciplinary work and translation of research. This first year of training is currently being evaluated.

Professor Ian day (PI), together with a number of potential PhD supervisors from across the University has been awarded an MRC grant for 10 4-year PhD students concerned with mathematical and statistical approaches in studies of populations, pathways and molecules. Students for this programme will start in October 2010 with the next intake of CAiTE and Wellcome Trust 4-year PhD students (see above). CAiTE staff also supervise students (usually on 3 year studentships) funded from a variety of other sources. The table lists current PhD students who are being supervised by CAiTE staff.
<table>
<thead>
<tr>
<th>Student</th>
<th>Title of project</th>
<th>Main supervisor</th>
<th>2nd supervisor</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dylan Williams</td>
<td>The causal effect of vitamin D on cardiovascular risk factors in adolescents</td>
<td>DA Lawlor</td>
<td>A Fraser</td>
<td>Wellcome Trust 4-year programme</td>
</tr>
<tr>
<td>Ruth Kipping</td>
<td>Feasibility and pilot study to evaluate a primary school based intervention to prevent obesity</td>
<td>DA Lawlor</td>
<td>R Jago</td>
<td>NHS Public Health training scheme</td>
</tr>
<tr>
<td>Jane West</td>
<td>Explaining differences in birth size and adiposity between Pakistani and white babies</td>
<td>J Wright</td>
<td>DA Lawlor</td>
<td>MRC population science fellowship</td>
</tr>
<tr>
<td>Rita Patel</td>
<td>Socioeconomic position and childhood health in Belarus</td>
<td>R Martin</td>
<td>DA Lawlor</td>
<td>UoB Staff Bursary</td>
</tr>
<tr>
<td>Corrie MacDonald-Wallis</td>
<td>Maternal blood pressure change in pregnancy and offspring health</td>
<td>DA Lawlor</td>
<td>K Tilling</td>
<td>Wellcome Trust grant</td>
</tr>
<tr>
<td>Amy Taylor</td>
<td>The Measurement of whole body and abdominal adiposity in Indian Populations</td>
<td>G Davey Smith</td>
<td>N Timpson</td>
<td>Wellcome Trust 4-year programme</td>
</tr>
<tr>
<td>Neil Davis</td>
<td>Identification of causal treatment effects in observational studies</td>
<td>R Martin</td>
<td>F Windmeijer &amp; G Davey Smith</td>
<td>CAITE 4-year programme</td>
</tr>
<tr>
<td>Anya Burton</td>
<td>Identification and assessment of markers of progression of localised prostate cancer</td>
<td>R Martin</td>
<td>K Tilling</td>
<td>CAITE 4-year programme</td>
</tr>
<tr>
<td>John Kemp</td>
<td>Genome wide association study of osteoporosis</td>
<td>D Evans</td>
<td>J Tobias</td>
<td>Wellcome Trust 4-year programme</td>
</tr>
<tr>
<td>Ghazaleh Fatemir</td>
<td>Methylation studies of bone mineral density</td>
<td>D Evans</td>
<td>J Tobias</td>
<td>Wellcome Trust 4-year programme</td>
</tr>
<tr>
<td>Chris Raistrick</td>
<td>Bioinformatics of splice-translational efficiency polymorphisms</td>
<td>I Day</td>
<td>T Gaunt</td>
<td>MRC Bioinformatics Capacity Building 4 year standalone studentship/project 2007</td>
</tr>
<tr>
<td>Osama Alghamdi</td>
<td>Genetic basis of extreme values in clinical chemistry analytes</td>
<td>S Rodriguez</td>
<td>I Day</td>
<td>Saudi Arabian Department of Education 2009</td>
</tr>
<tr>
<td>Chris Boustred</td>
<td>Population Studies of Genetic Variation in KCNH2 and other ECG-relevant ion channel genes</td>
<td>I Day</td>
<td>J Hancox</td>
<td>Wellcome Trust 4 year programme 2008</td>
</tr>
<tr>
<td>Hashem Shihab</td>
<td>Genomic aspects of common disease genetic effects</td>
<td>T Gaunt</td>
<td>J Gough</td>
<td>MRC Systems Biomedicine 4 year programme 2009</td>
</tr>
<tr>
<td>Tamuno Alfred</td>
<td>Genetics of ageing NDA Programme PhD studentship 2009</td>
<td>I Day</td>
<td>Y Ben Shlomo</td>
<td>Cross-Research Councils</td>
</tr>
</tbody>
</table>
2. Post-graduate short courses
CAiTE staff have developed an integrated portfolio of short courses covering causal analyses, Mendelian Randomization, Genetic Epidemiology and Bioinformatics. These include:

- An Introduction to Human Genetics (3 days, organizer Dr Philip Guthrie): an introduction to basic genetic concepts for use in genetic epidemiology. This course is intended to provide epidemiologists and statisticians with the foundation knowledge necessary to understand genetic epidemiology.

- Genetic Association Studies (2 days, organizers Drs Santi Rodriguez & Sarah Lewis): a course on basic issues related to the design, analysis and interpretation of genetic association studies. This course emphasizes the application of genetic association data in Mendelian Randomization for causal analyses.

- Introduction to Bioinformatics (2 days, organizer Dr Tom Gaunt): this course provides epidemiologists with a basic introduction to aspects of bioinformatics relevant to genetic epidemiology. The course places a particular emphasis on analysis of genome-wide association study and next generation sequencing data in genetic epidemiology.

- The Complex Genome (2 days, organizer Professor Ian Day): this course covers aspects of genomic complexity other than SNPs addressing the wider structure and function of the genome relevant to genetic epidemiology. The emphasis is on describing the molecular mechanisms causing disease, with the intention of highlighting both the similarities and differences in causation between common (multifactorial) and rare (Mendelian) disorders.

- Causal Analysis. March/April 2008 Course organisers: DA Lawlor & J Sterne. Teaching Faculty: Profs Jamie Robins & Miguel Hernan (from Harvard University, USA); Profs J Sterne & DA Lawlor and Dr K Tilling (from University of Bristol, UK). This was a one-off short course with a teaching faculty of international experts. It aimed to bring CAiTE staff, affiliate members, collaborators and the wider scientific community up to date with the latest methods relating to making causal inference in observational studies. A follow-up short course is planned for 2011.

These complement the existing portfolio of short-courses that were developed and running in the Department of Social Medicine prior to September 2007. All CAiTE staff contribute to the development and teaching of the new courses outlined above and existing courses relevant to CAiTE aims in the Social Medicine portfolio (http://www.epi.bris.ac.uk/shortc/shortc.htm).

3. Research Seminars
We have organised a number of varied and very well attended research seminars since CAiTE opened. The following list completed and currently programmed seminars:

**2010**

1. 5 October - Dr John McBeth: University of Manchester – Chronic widespread pain – explaining the unexplained.

2. 22 July - Dr Sarah Garnett of The Children’s Hospital at Westmead, Sydney, Australia - Secular trends in the waist to height ratio in Australian young people.

3. 10 June - Professor Tim Cole of UCL Institute of Child Health - SITAR - a useful instrument for growth curve analysis.

4. 14 April - Professor Sander Greenland: UCLA, Meaninglessly small P-values: A new statistical plague?

5. 17 November - Dr Niels Keiding: Department of Biostatistics, University of Copenhagen (Visiting MRC Biostatistics Unit Cambridge) Analysis of Time to Pregnancy.

6. 27 October - Professor Chris Holmes: Department of Statistics, University of Oxford – Metabolomics and common complex disease.

7. 13 October - Dr Miranda Geelhoed: Generation R Rotterdam - Hypertensive disorders during pregnancy are associated with offspring blood pressure and adiposity measures: the Avon Longitudinal Study of Parents and Children.

8. 19 June - Professor Els Goetghebeur: University of Ghent - On estimating the causal odds ratio using instrumental variables.

9. 9 June - Professor Marc Schuckit: Department of Psychology, University of California, San Diego - Factors for alcoholism in adolescents: An update on the ALSPAC-UCSD Collaboration.
10 12 May - Dr Duncan Baird: Department of Pathology, Cardiff University - Telomere dynamics.

11 28 April - Dr Anna Murray: Lecturer in Human Genetics, Peninsula Medical School - Frax/premature ovarian failure.

12 7 April - Dr Jonathan Wells: University College London - Metabolic capacity and metabolic load; an evolutionary perspective on the aetiology of the metabolic syndrome.

13 10 March - Professor Sir David Cox: Honorary Fellow, Nuffield College, Department of Statistics, University of Oxford - Randomization.

14 24 February - Professor Alistair Poole: Department of Physiology and Pharmacology, University of Bristol - Functional analysis of genes involved in platelet biology and thrombosis using mouse and zebrafish model systems.

15 17 February - Dr Ellen Aadaard Nohr: Institute of Public Health, Aarhus University, Denmark – Weight gain in pregnancy: Does it matter and how should we guide? Epidemiological studies based on the Danish National Birth Cohort.

16 10 February - Dr Frederick Pettersson: Wellcome Trust Centre for Human Genetics, Oxford - Multivariate approaches for the analysis and visualisation of dense genotypic and phenotypic datasets: A practical demonstration using Gs2 and Evince.

17 3 February - Dr James Hodge: Department of Physiology and Pharmacology, University of Bristol - Modelling human gene function in Drosophila.

18 19 January - Professor Gordon Lowe: Professor of Vascular Medicine, University of Glasgow - What can circulating biomarkers tell us about cardiovascular disease and death?

2008

19 16 December - Prof John Whittaker from the London School of Hygiene and Tropical Medicine - Meta-Analysis of Genetic association studies with different sets of marker from summary data.

20 15 December - Dr Ewan Birney from the European Bioinformatics Institute - Molecular genetics meets big biology.

21 2 December - Dr Richard Anney from the Institute of Molecular Medicine, St James Hospital Dublin - Genome-wide association studies in childhood psychiatric disorders.

22 15 October - Dr Paul Brennan from the International Agency for Research on Cancer - Lessons from Candidate gene and genome-wide studies of lung cancer.

23 9 September - Dr Hugh Montgomery from the Centre for Cardiovascular Genetics, University College London - Genetics and athletic performance.

24 12 September – Dr Steven Walker of the ALMAC group.

25 17 July – Dr Michael Meaney from McGill University - Maternal care alters neuroendocrine function through epigenetic programming of gene expression: Does mom really know best?

26 19 June - Dr Brendan Keating, Institute for Translational Medicine and Therapeutics, University of Pennsylvania - Concept, design and implementation of a gene-centric 50K SNP array for CVD studies: peering into gene-phenotype relationships in >200,000 individuals.

27 5 June – Dr Julie Marsh from the Laboratory for Genetic Epidemiology, Western Australian Institute for Medical Research - The relationship between inter-uterine growth trajectories and the FTO genetic polymorphism.

28 4 June - Dr Felix Burden from the Heart of Birmingham Teaching PCT - Prevention of premature death from coronary heart disease (CHD) in men: the Deadly Trio project.

29 3 June - Dr Fredrik Karpe from the Oxford Centre for Diabetes, Endocrinology and Metabolism - Recruit-by-genotype to investigate complex intermediary phenotypes for diabetes and cardiovascular risk genes.

30 20 May - Professor Dongfeng Gu, Chair of Epidemiology, Medical Genetics and Medicine at the Fuwai Hospital and Cardiovascular Research Institute in Beijing, China, - An overview of epidemiology and genetic epidemiology in China.

31 3 April - Professor James Robins, Harvard School of Public Health - Estimation and extrapolation of optimal treatment and testing strategies.

32 2 April - Professor James Robins, Harvard School of Public Health - Direct and Indirect Effects.

Details of future seminars can be found on the Centre website (http://www.bristol.ac.uk/caite/). If you would like to receive e-mails of future CAiTE seminars, please inform us by emailing: info-caite@bristol.ac.uk.
4. Research Workshops

The centre has also hosted larger scale research meetings/workshops:

1. 4th June – 5th June 2009 Colston Research Society Symposium “The New Genomics: Public Health, Social and Clinical Implications”. In celebration of the University’s Centenary, this year’s Colston Research Society Symposium was organised by Professor George Davey Smith of The Department of Social Medicine. The meeting brought together a range of speakers from those working at the forefront of many areas of medical research and clinical practice relating to Genetics, Society and Public Health. The Public Lecture was delivered by Professor Sydney Brenner of Salk Institute. Some of the talks were recorded by special consent and available to only those who attended the symposium to borrow and return on disk.

2. 2nd -3rd March 2009 MRC CAiTE Research Symposium The aim of this symposium was to show case completed and on-going research projects of CAiTE members, affiliate members and collaborators. The symposium was organised by Professor Debbie Lawlor and Ms Bhavna Mistry and had participants from across UK, Europe and Australia. Copies of the presentations are available from our website.www.bristol.ac.uk/caite.

3. April 2008 - Birth Cohorts Collaboration - This meeting aimed to bring together researchers from birth cohorts across Europe in order to explore future potentials for collaboration in causal epidemiology and translational research. The meeting was organised by Professor D A Lawlor, Professor G Davey Smith and Ms Marie Elmhirst*, and had representatives from a number of birth cohorts. Slides are available through our website from this meeting. As a result of this meeting several collaborative projects including the award (April 2009) of an FP7 grant to explore ways of collaborating across European birth cohorts and influencing health and social policy, have been established. The plan is to repeat the meeting on a 2-yearly basis at different European venues.

4. March/April 2008 - Use of Instrumental variables in epidemiology and health services research workshop. This workshop aimed to examine current use and future potential for genetic and non-genetic instrumental variables analyses in epidemiology and health services research. It was organised by Prof D A Lawlor and funded by a small grant from the MRC Population Health Sciences Research Network. A summary of the meeting can be found on our website. www.bristol.ac.uk/caite.
Public Engagement

As well as translating research findings into next stage research and clinical/public health policy we are committed to engaging with the public and explaining our research findings to them. Ms Bhavna Mistry is the Centre’s public engagement lead; over the coming years she will take on an active role in communicating key research findings from the Centre to the public.

**CAiTE staff have attended a number of public engagement training sessions and have contributed to a number of public engagement activities since the centre opened:**

6 March 2010
Dr Philip Guthrie and Mr Dylan Williams (PhD student) volunteered on the MRC Stand at the Oxfordshire Science Festival.

4 March 2010
Dr Nicolas Timpson organised a seminar for the department by Dr Helen Jamieson of Science Media Centre whose talk was “Science and the Media: Experience from the front line”.

20 January 2010
Ms Bhavna Mistry attended the MRC Communications Management Team Open Meeting at MRC Head office.

2009-2010
Professor Ian Day contributed to a film documentary being made by Dan Lewis, 3rd year student at UWE for Media and Cultural Studies on the subject of ‘Science, Ideology and Society’; Prof Day’s input was about human genetics.

8 October 2009
Professor Ian Day gave a lecture to Bristol Enterprise Network (local business leaders) ‘The potential of genetics to enable personalization of healthcare’ in an evening themed The personalised health care revolution.
Venue: The Garden Room, Clifton Pavilion, Bristol Zoo Gardens, College Rd., Clifton, Bristol, BS8 3HH BEN: ‘connecting technology businesses in the Bristol & Bath region’.

1 August 2009
Dr Nic Timpson became a Science Media Centre scientist.

30 June 2009
Ms Bhavna Mistry attended Engage 2009 – University of Bristol public engagement workshop hosted by the Centre for Public Engagement.

13-14 June 2009
Dr Tom Palmer and Ms Bhavna Mistry helped at the ALSPAC stand at the Cancer Research UK Race for Life.

31 March 2009
Ms Bhavna Mistry attended the MRC Communications day “Introduction to News Media Event” by the Science Media Centre held at Cardiff University.

July–August 2008
Professor Ian Day hosted a school student (Devon Buchanan) from Wessex Setpoint during the Summer of 2008 and attended and made input to the Wessex Setpoint presentation day event in Bath in September 2008. At this event, many school students who have had experience attachments meet to present and discuss their work with each other and their hosts. Devon learned about genocopy/phenocopy effects and applied this to analysis of pigmentation effects in age-related macular degeneration and to effects of smoking or nicotine across a wide range of diseases. Devon obtained a Nuffield Bursary with us; and will in March 2009 be presenting at the national UK Young Scientists' and Engineers' Fair 2009 which will further spread understanding of the work of our Centre to a bright and ambitious national cadre of school students.
July 2008
Professor George Davey Smith agreed to act as a consultant to the Science Museum as they are updating the Epidemiology section of the Health Matters modern medicine gallery.

30 June 2008
Professor Debbie Lawlor gave a talk entitled “Detective Work in Medical Research” as part of the University of Bristol annual residential summer school for potential future university students from under-represented groups. The University of Bristol hosted 200 plus students from years 11 and 12 (15 to 17 year olds) for one week at the university. The summer school aimed to provide an opportunity for students from under-represented groups across the UK to access the world-class facilities at the University. It was hoped that it would encourage young people to think about higher education as an option once they finish school or college.

4–8 June 2008
Dr Philip Guthrie and Ms Marie Elmhirst* took part in the Cheltenham Science Festival by helping out on the MRC stand in the Discover Zone. It is estimated that around 8,000 adults and children came through into the Discover Zone over the 5 days of the festival.

4 June 2008
Professor Debbie Lawlor’s work was featured in a two-page spread in the Bristol Evening Post. This was on the two-year study to understand the causes, development and prevention of obesity, diabetes and heart disease in women.

29 May 2008
Ms Marie Elmhirst* attended the MRC Communication Workshop at the SAID Business School in Oxford.

29 April 2008
Ms Marie Elmhirst* attended the SPark in the Science City conference at the HP Labs, Bristol. SPark is the new £300 million science park for Bristol and Bath.

31 March and 1 April 2008
Dr Philip Guthrie attended the two-day Public Engagement skills session, which was led by Ecsite-UK, the UK’s science centre and museum co-ordination network.

7–8 March 2008
Ms Marie Elmhirst* took part in Science Alive. This was organised by the University of Bristol’s Centre for Public Engagement as part of National Science and Engineering Week. Broadmead and the Mall Galleries hosted demonstrations of the University’s research enabling shoppers and schoolchildren to explore a variety of activities.

29 November 2007
Professor George Davey Smith took part in a public debate on “The Future of Genomics” held, together with an exhibition at Explore @ Bristol. The exhibition called “Inside DNA: A genomic revolution” was the UK’s first major touring exhibition on genomics.

* Ms Marie Elmhirst was the Centre Administrator, Public Engagement and Training Co-ordinator prior to Ms Bhavna Mistry, who is currently in post.
Who caused the boat to sink?