FOOD-CT-2005-007036

EARNEST

EARly Nutrition programming- long term follow up of Efficacy and Safety Trials and integrated epidemiological, genetic, animal, consumer and economic research

Instrument: Integrated Project

Thematic Priority 5.4.3.1: Food Quality and Safety

Final public report on activity 2.2.3:
Analyse and write up data collected on blood pressure and body composition

Period covered from 15.04.2005 to 14.10.2010

Start date of project: 15.04.2005 Duration: 5,5 Years

Organisation Name of Lead Contractor for this report: University of Bristol

Avon Longitudinal Study of Parents and Children

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a geographically-based birth cohort investigating the health and development of children, which is described in detail elsewhere (Golding J, Pembrey M, Jones R, 'ALSPAC--the Avon Longitudinal Study of Parents and Children. I. Study methodology.', Paediatric and Perinatal Epidemiol 2001; 15 (1): 74-87) and on the study website (www.alspac.bris.ac.uk**)**. Briefly, all pregnant women living in three health districts of Bristol (formerly known as the Avon Health Area), England with expected delivery dates between April 1st 1991 and December 31st 1992 were eligible to take part in the study. A total of 14,541 were enrolled, and 13,678 had a singleton, live born child. Detailed data have been collected by self-completed questionnaires (relating to the mother, her partner, and her offspring) from pregnancy onwards. From the age of seven, all children have been invited to regular research clinics. Ethical approval was obtained from the ALSPAC Law and Ethics Committee and the three Local Research Ethics Committees.

Aim of Activity 2.2.3

The aim of activity 2.2.3 was to use data on offspring blood pressure and body composition at age 15 years (see Activity 2.2.2), and explore associations with early life factors.

Blood pressure data

Findings relating to the early life factors and offspring blood pressure at age 15 analyses were presented in a talk given by Andy Ness at the Earnest meeting held in Cracow in September 2009 ("Beyond birthweight: modifiable maternal exposure and offspring blood pressure"). They have also been written up as a paper which will be submitted to the American Journal of Epidemiology within the next few weeks; here is the abstract:

Background: A recent review found little evidence for substantial effects of modifiable maternal exposures on offspring blood pressure, but this may have been because almost all the studies reported on blood pressure in early and mid childhood.
Methods: We used data from the Avon Longitudinal Study of Parents and Children to look at associations between smoking during pregnancy, age at childbirth and prenatal diet on offspring blood pressure at age 15 in 4723 mother-child pairs.
Results: None of the maternal exposures were associated with offspring blood pressure, after adjusting for gender, offspring age and maternal energy intake (prenatal diet variables only).
Conclusion: Our findings suggest that associations between modifiable maternal exposures and offspring blood pressure do not emerge with age.

Body composition data

Findings relating to the early life factors and offspring body composition at age 15 analyses were presented in a talk given by Andy Ness at the Earnest conference held in Munich in May 2010 (**"**Early life risk factors for obesity in childhood**")**. The findings are currently being written up for publication. The main findings are summarised below (note that we have used DXA fat mass and lean mass as measures of body composition):

1) ***Parental smoking and offspring body composition at age 15***

	Fat mass (z score)		Lean mass (z score)	
	β	95% CI	β	95% CI
Maternal smoking				
minimal adj.*	0.15	0.08, 0.21	0.08	0.04, 0.12
full adj.**	0.15	0.08, 0.22	0.09	0.05, 0.13
Partner smoking				
minimal adj.*	0.15	0.09, 0.20	0.03	0.004, 0.06
full adj. **	0.10	0.04, 0.17	0.03	-0.01, 0.06
Simultaneous				
mother minimal adj.*	0.10	0.02, 0.17	0.09	0.05, 0.12
partner minimal adj.*	0.13	0.07, 0.19	0.01	-0.02, 0.04

* age, sex, height, height squared
** age, sex, height, height squared, maternal/partner size and age in pregnancy, parity, social class, maternal education, birthweight, gestation

2) Breastfeeding and offspring body composition at age 15

Adjustment	Fat mass (z score)		Lean mass (z score)	
	β	95% CI	β	95% CI
Minimal*	0.08	0.04, 0.12	0.01	-0.01, 0.03
Full**	0.03	-0.01, 0.07	-0.002	-0.02, 0.02

* age, sex, height, height squared
**age, sex, height, height squared, maternal size and age in pregnancy, parity, social class, maternal education, birthweight, gestation

3) Infant sleep and offspring blood pressure at age 15
Exposure: ≥ 10.5 hours sleep per night at age 30 months

Adjustment	Fat mass (z score)		Lean mass (z score)	
	β	95% CI	β	95% CI
Minimal*	-0.09	-0.16, -0.01	-0.02	-0.06, 0.02
Full**	-0.08	-0.16, -0.01	-0.01	-0.05, 0.03

* age, sex, height, height squared
**age, sex, height, height squared, maternal size and age in pregnancy, parity, social class, maternal education, birthweight, gestation

Therefore maternal (but also paternal) smoking, and reduced infant sleep are both associated with higher offspring fat mass at age 15, but the association with breastfeeding is lost after adjustment for potentially confounding factors. Maternal smoking is the only factor of those explored that is associated with offspring lean mass at age 15.

Epidemiology and Statistics workshop

In addition to our original aims for Activity 2.2.3, we ran a workshop entitled "Introduction to Critical Appraisal for Early Life Epidemiology" in Crawcow, September 2009. the workshop lasted three hours, and was led by Andy Ness, Sam Leary, Alex Griffiths, and Laura Howe, all from the University of Bristol. The aim of this workshop was to introduce participants to

the skills required for critical appraisal of epidemiological research, with a particular emphasis on early life research. These skills included an understanding of study design and interpretation of statistical analysis. There was a mixture of formal teaching to cover the main issues, and interactive exercises based on early life data examples to aid understanding. There were four sessions: the first two which introduced basic epidemiological and statistical issues respectively. Then the second two dealt with specific challenges faced by early life researchers regarding epidemiology and statistics. Issues such as bias and confounding, interpretation of p values, loss to follow up, and missing data were covered in these later sessions. The workshop was open to all involved in Earnest. The workshop was attended by 28 people, and feedback was very positive: 95% thought the content and format of the Basic Epidemiology session was good/excellent, 96% thought the Basic Statistics session was good/excellent, 88% thought the Early Life Epidemiology session was good/excellent, and 79% thought the content/50% thought the format of the Early Life Statistics session was good/excellent. Podcasts of the sessions will be available on the web shortly.

The content of the workshop has been summarised in a paper which is currently being reviewed for the American Journal of Clinical Nutrition; this is the abstract:

Observational studies can describe associations between early life exposures and subsequent outcomes in human populations. Drawing causal inferences from these associations is challenging as exposures often occur many years before the outcome and are related to other early life exposures. An approach is required that combines traditional epidemiological and statistical principles with the use of novel and sophisticated analytic methods. To minimise bias in longitudinal studies of early origins, researchers need to do all they can to reduce losses to follow up and to describe those that are lost to follow up. To reduce the play of chance researchers should concentrate on effect sizes and the strength of the evidence to support these effect sizes, and they should be cautious in their interpretation of sub group analyses. More complex analytic approaches can and should be used to handle missing data and repeated measurements. Addressing the issue of confounding is not straightforward. Statistical adjustment for the confounders measured in a study may help, but lack of attenuation does not guarantee that the association is not confounded. Ecological studies, observational studies in populations with a different confounding structure and follow up of randomised trials (where these exist) can be informative. Genetic and non genetic instrumental variable approaches (such as Mendelian randomisation) may also provide causal insights. These approaches to confounding often require comparison of data from different populations or combination of studies, to ensure adequate power to provide robust estimates of the causal effect.