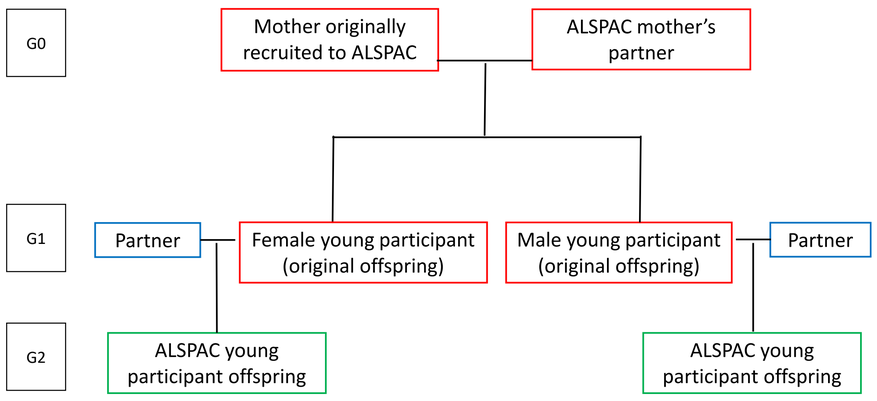
Avon Longitudinal Study of Parents and Children (ALSPAC)

A Longitudinal Birth Cohort Biobank

INTRODUCTION

- The Avon Longitudinal Study of Parents and Children (ALSPAC), also known as Children of the 90s, is a world-leading birth cohort study[1,2].
- > 14,000 pregnant women were recruited between April 1991 and December 1992.
- These women, their children and partners have been followed intensively for >26yrs.
- Recruitment of the next generation of children (ALSPAC G2) is now underway

FIGURE 1. FAMILY STRUCTURE



THE ALSPAC BIOBANK

- Biological samples have been collected from the outset of the ALSPAC study
- Samples are processed and stored in the Bristol Bioresource Laboratories, a laboratory originally set up primarily for ALSPAC, which now handles samples from 12 cohort studies. (www.bristol.ac.uk/population-health-sciences/research/groups/bblabs/)
- Samples are processed and stored in line with the laboratory's quality management system, which is ISO9001 certified by BSI under certificate number FS 651591. The laboratory is also licenced by the Human Tissue Authority (licence 12512)
- Samples collected in local research clinics are processed and frozen within 2 hours
- Multiple aliquots are produced to prevent freeze-thaw cycles
- Over 1.2 million aliquots of samples now exist
- Sample types collected at various time points are shown in **tables 1-6**

ASSOCIATED DATA

A vast array of data has been collected from the study participants – for full details see www.bristol.ac.uk/alspac/researchers/our-data/

Data includes the following – collected at many timepoints

- Questionnaires – covering a wide range of topics
- Hands-on measures from research clinics – includes anthropometry, cardiovascular (e.g. blood pressure, carotid artery scan, echocardiograph), bone (DXA, pQCT), respiratory (lung function, spirometry), vision, hearing, mental health, cognitive and social measures
- Targeted substudies - detailed phenotypes e.g. MRI scans, asthma and eczema measures
- Linkage to routine health and social records - e.g. GP, criminal, civic registration records
- Sample derived data – clinical measures, metabolomics, genetic analysis (e.g. GWAS, whole genome sequencing, copy number variation, mitochondrial copy number), expression and epigenetic (genome wide methylation) data

ALSPAC BIOBANK OBJECTIVES

ALSPAC's objective is to provide a comprehensive resource for the scientific community.

- Samples and data are available to researchers through a straightforward access process.
- Researchers apply via an online proposal system - proposals reviewed on a weekly basis.
- Laboratory team provide support for researcher before and throughout the process. A dedicated email address is provided for enquiries (bbl-info@bristol.ac.uk)
- New sample collection can be facilitated including recall by genotype or phenotype
- Users are required to return data to ALSPAC to become part of the resource
- Users are required to cover costs of supplying samples and data on a cost recovery basis.

USAGE STATISTICS

- On average, 20 applications to access samples are received each year. The resource also receives over 200 requests for data each year
- Median time to supply samples in last 18 months was 12 days (range 0-69) once funding (when grant needed) and MTA were in place (time from approval was 69 days (0-455))
- >1,800 peer reviewed papers have been published using the ALSPAC resource. 161 have been published in 2018 and over 56% of these would not have been possible without samples from the biobank. This includes primary sample use and secondary data analysis

Case Study 1 (Existing samples + longitudinal data)

Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children.

M.P. Rayman and S.C. Bath, University of Surrey

INTRODUCTION

Iodine is essential for brain development (through the production of thyroid hormones). Severe iodine deficiency is associated with cretinism, a severe impairment of cognitive and motor system. The effects of mild to moderate iodine deficiency (seen in UK) are unknown.

OBJECTIVES

The researchers requested antenatal urine samples to test the association between maternal iodine status during pregnancy and measures of child cognition later in life.

METHODS

ALSPAC biobank staff worked with researchers to identify samples from cases with relevant longitudinal data. Iodine concentration and creatinine (to correct for urine volume) were measured in 1040 urine samples collected in the 1st trimester. Iodine-to-creatinine ratio were dichotomised to <150µg/g (mild-to-moderate iodine deficiency) and ≥150µg/g. The association between iodine status and child IQ (8yrs) and reading ability (9yrs) was assessed.

RESULTS

Children of women with iodine-to-creatinine ratio <150µg/g were more likely to be lowest quartile for verbal IQ + reading accuracy and comprehension.

CONCLUSION

Results show the importance of adequate iodine status in early pregnancy. Even mild iodine deficiency can be a risk to the developing infant. In the UK iodine deficiency in pregnant women should be treated as an important public health issue.

This work was published in The Lancet[3]

Quotes from researcher

"The application process was straightforward and easy to complete."

"Using ALSPAC was cost-effective as cognitive measures were available in the child, and samples were available from the mother"

"ALSPAC, unlike many other biobanks, had urine samples from very early in pregnancy"

IMPACT – This research has led to

- Fact sheets from British Dietetic Association[4] and Infant and Toddler forum[5]
- Citations in publications by the Dairy Council[6], Scientific Advisory Committee on Nutrition[7], EFSA dietary reference value for iodine[8], MRC impact publication[9]
- Further funding - European Commission Horizon 2020, Euthyroid (634453)

ENGAGEMENT

- 6 newspaper articles, 4 radio/television interviews and inclusion in BBC Radio4 "Awesome Iodine" as part of the In Their Element series.

ALSPAC DEMONSTRATED THROUGH THIS STUDY

- The biobank can supply samples, collected 20 years ago, which are fit for purpose with associated data to enhance use (eg gestational age when sample collected).
- Enhancement of the value of samples with decades of longitudinal data.
- Further collaboration and income generation – the data generated for this study has been supplied to 3 new projects for secondary analysis. This generated cost recovery income.

ALSPAC ENGAGEMENT ACTIVITIES

WITH RESEARCHERS VIA

- the website,
- social media,
- specific events

E.g. in Summer 2018 we held workshops for researchers asking them to contribute to the design of our 30 yr clinic

WITH PARTICIPANTS VIA

- newsletters
- the website,
- social media,
- community events
- A participant advisory panel (OCAP) of 30+ study participants provide advice on study design and acceptability for participants.
- in Summer 2018 participants were invited to a workshop to contribute to the design of our 30 yr clinic
- participants are represented on ALSPAC's independent ethics committee

WITH GENERAL PUBLIC VIA

outreach events such as

- Einstein's Garden at the Green Man Festival
- Bristol Futures event for European Researchers' Night
- Local events such as Bristol Harbour Festival

ACKNOWLEDGEMENTS

We are extremely grateful to all the families who took part in this study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. The UK MRC and Wellcome (Grant ref: 102215/2/13/2) and the University of Bristol provide core support for ALSPAC. Urine analysis was funded by European Community (FP7/2008–2013) and Horizon 2020 (634453), MRC (MR/K02132X/1), Wassen International and the Waterloo Foundation.

TABLE 1 G1 – CHILDREN MAIN COHORT COLLECTION

AGE	Whole cohort	Blood	Urine	saliva	Milk teeth	Hair	placenta	DNA	Cell line	RNA
Birth	yes	x					x	x		
6-18m	yes					x				
31 m	10%	X								
3yrs	yes					x				
43 m	10%	x						x		
4yrs	yes					x				
61 m	10%	x								
5-7 yrs	yes				x					
7yrs	yes	x						x		
7-8yrs	10%	X -fasting								
9yrs	yes	x						X	x	
10yrs	yes		x							
11yrs	yes	x		x					X (subset)	
12yrs	yes			x						
13yrs	yes	X							X (subset)	
15yrs	yes	X -fasting	x			x		x	X (subset)	
17yrs	yes	X -fasting	x			x		x	X (subset)	
24yrs	yes	X -fasting	x					x	X (subset)	x

TABLE 2: G0 MOTHERS SAMPLES

timepoint	Participant group	blood	urine	Hair and nails	DNA	Cell lines
Antenatal (various gestations)	Whole cohort	x	x		x	
1993	Whole cohort			x		
2004-2008	Whole cohort	x			x	x
FOM1	5000	X fasting			x	X (subset)
FOM2	3000	X fasting			x	X (subset)
FOM3	3000	X fasting			x	X (subset)
FOM4	3000	X fasting			x	X (subset)

TABLE4: G2 CHILD

Sample type	7-15 days	6 months	12 months	24 months	36 months	48 months	60 months	72 months	84 months	9 years	11 years
Meconium	X										
Cord blood	X										
Placenta	X										
Blood					x			x		x	x
Saliva (if refuses blood)					x			x		x	x
Stool	x	x	x				X				
Urine										x	x

TABLE 3: G0 PARTNERS

timepoint	Participant group	blood	urine	Hair and nails	DNA	Cell lines
1993	Whole cohort			x		
2004-2008	Whole cohort	x			x	x
2010	Whole cohort	x			x	X(subset)
FOF	Whole cohort	x	x		x	X(subset)

TABLE 5: G1 MOTHER

Sample type	Early pregnancy	Late pregnancy	7-15 days	1 month	3 months	6 months	12 months	24 months	36 months	48 months	60 months	72 months	84 months
Blood		X							X			x	
Breast milk				x	x	x	x						
Saliva (if refuses blood)		X							x			X	
Stool		X	x			X							
Urine		X											

TABLE 6: G1 PARTNERS

timepoint	Blood	Saliva (if refuses blood)	Stool
Antenatal	x	x	x
24m-36m	x	x	x
72m-84m	x	x	x

1. Boyd A et.al 2013. Cohort Profile: The 'Children of the 90s'; the index offspring of ALSPAC. International Journal of Epidemiology 2013; 42: 111-127. **2.** Fraser A, et.al 2013 Cohort Profile: The ALSPAC mothers cohort. International Journal of Epidemiology 2013; 42:97- 110. **3.** Bath SC, et al. 2013 Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children. Lancet 382, 331-337. **4.** www.bda.uk.com/foodfacts/Iodine.pdf **5.** www.infantandtoddlerforum.org/media/upload/pdf-downloads/5.1_Pregnancy_Factsheet_FINALa.pdf **6.** www.milk.co.uk/publications/default.aspx **7.** www.gov.uk/government/publications/sacn-statement-on-iodine-and-health-2014 **8.** EFSA 2014 Scientific Opinion on Dietary Reference Values for iodine. EFSA Journal 12, 3660. **9.** https://mrc.ukri.org/publications/browse/outputs-outcomes-and-impact-of-mrc-research-2013-14/