Public Benefit and Privacy Panel for Health and Social Care

Application Form

Application Control *Applicants should not fill out this section*			
Application Coordinator	Fiona Campbell		
Application Number	1516-0387	Submitted Date	
Applicant Name	Anthony Chapman		
Proposal Name	Linking antenatal maternity data to non-communicable disease data in children and adults.		

Contents

Note to Applicants

Prior to completing your application form you should:

Contact the eDRIS Team, who will assist you - Nss.edris@nhs.net or by phone on 0131 275 7333

Read and understand the separate Guidance for Applicants

Your application should be typed, not handwritten. Your eDRIS application coordinator will inform you how to submit your application form and any supporting evidence. Before submitting your completed application, you should ensure that:

All relevant sections of the application are complete

Relevant supporting evidence is attached

Individuals named on the form have read and approved its submission

Please note that submitted applications may be circulated to panel members, administrative colleagues, NHSScotland information governance and information security colleagues, Caldicott Guardians, the CHI Advisory Group and, where appropriate, non-NHS Scotland colleagues from a variety of participating partner bodies, in the course of processing. You must make your eDRIS application coordinator aware of any confidential or sensitive information contained in your application which you would consider inappropriate for circulation in such a manner. Your application could be subject to disclosure or partial disclosure under the Freedom of Information (Scotland) Act, and will be retained in line with NHSScotland information policy.

Section 1 – People

1.1	**Applicant** *Please read section 1.1 of the guidance*	
1.1.01	Full Name:	Anthony Chapman
1.1.02	Title:	Mr
1.1.03	Position:	PhD Student
1.1.04	Professional Registration No.:	*If applicable*
1.1.05	Organisation Name:	Child Health, University of Aberdeen
1.1.06	Address:	Royal Aberdeen Children's Hospital, Aberdeen
1.1.07	Postcode:	AB25 2ZG
1.1.08	Telephone Number:	+44 1224 438475
1.1.09	Email:	a.s.chapman.10@aberdeen.ac.uk
1.1.10	Do you have an NHS contract/honorary contract?	No
1.1.11	Provide details of the most recent information governance training undertaken - a list of training courses is included at Appendix A, and you should particularly indicate if you have undertaken any of those listed	
	Name of course:	Medical Research Council: Research Data and Confidentiality
	Link to course content:	*http://www.mrc.ac.uk/research/facilities/regulatory-support-centre/*
	Institution:	University of Aberdeen
	Date completed:	MRC - RDC - March 20164

1.2	**Clinical Sponsor/Lead** *Please read section 1.2 of the guidance*	
1.2.01	Full Name:	Steve Turner
1.2.02	Title:	Dr
1.2.03	Position:	Senior Clinical Lecturer in Child Health / PhD Supervisor
1.2.04	Professional Registration No.o	
1.2.05	Organisation Name:	Child Health, University of Aberdeen
1.2.06	Address:	Royal Aberdeen Children's Hospital, Aberdeen
1.2.07	Postcode:	AB25 2ZG
1.2.08	Telephone Number:	+44 1224 438475
1.2.09	Email:	s.w.turner@abdn.ac.uk
1.2.10	Does this person have an NHS contract/honorary contract?	Yes

1.2.11	Provide details of the most recent information governance training undertaken - a list of training courses is included at Appendix A, and you should particularly indicate if this person has undertaken any of those listed	
	Name of course:	MRC Information Governance Training Course
	Link to course content:	"http://www.byglearning.co.uk/mrcrsc-lms/login/index.php"
	Institution:	Medical Research Council
	Date completed:	06/07/15

1.3	**Information/Data Custodian** *Please read section 1.3 of the guidance*	
1.3.01	Full Name:	Same as Section 1.2
1.3.02	Title:	
1.3.03	Position:	
1.3.04	Professional Registration No.:	
1.3.05	Organisation Name:	
1.3.06	Address:	
1.3.07	Postcode:	
1.3.08	Telephone Number:	
1.3.09	Email:	
1.3.10	Does this person have an NHS contract/honorary contract?	
1.3.11	Provide details of the most recent information governance training undertaken - a list of training courses is included at Appendix A, and you should particularly indicate if this person has undertaken any of those listed	
	Name of course:	
	Link to course content:	
	Institution:	
	Date completed:	

1.4 Others with access to identifiable or potentially identifiable data *Please read section 1.4 of the guidance*
Complete this section if applicable – for each additional person

Full Name:	To be confirmed at time of linkage	Telephone or Email:	+44 (0)1224 437046 dash@abdn.ac.uk
Organisation:	Grampian Data Safe Haven (DaSH), University of Aberdeen/NHS Grampian	Position:	Programmer/Analyst
Professional Registration No:		NHS contract/ honorary contract?	Yes

IG Training - Name of course:	All DaSH analysts have completed IG training Certificate held by eDRIS		
IG Training - Link to course:	*If applicable*		
IG Training - Institution:	SHIP – University of Edinburgh MRC	Date completed:	SHIP – March/April 2014

1.5 Others *Please read section 1.5 of the guidance*

Complete this section if applicable – for each additional person

Full Name:	Dr Wei Pang	Involvement in Proposal:	Advisor
Organisation:	University of Aberdeen	Position:	Lecturer

Section 2 – Organisations & Bodies

2.1	**Organisation or Body Leading Proposal** *Please read section 2.1 of the guidance*	
2.1.01	Organisation or Body Name:	University of Aberdeen
2.1.02	Is this organisation or body a registered data controller? If 'Yes', provide Data Protection Registration Number:	Yes, Z7266585
2.1.03	Is this a commercial organisation or body?	No
2.1.03a	If 'Yes', please provide a full explanation of the organisation or body's activity and industry sector, including any previous experience of using NHSScotland data - append supporting documentation as appropriate	*If applicable*
2.1.04	Is this organisation or body wholly funding or paying for the costs of conducting the proposal?	No

2.2	**Organisation or Body Funding Proposal** *Please read section 2.2 of the guidance*	
Complete the following section if you answered 'No' to question 2.1.4		
2.2.01	Organisation or Body Name:	Farr Scotland
2.2.02	Is this organisation or body a registered data controller? If 'Yes', provide Data Protection Registration Number:	No
2.2.03	Is this organisation or body a commercial organisation?	No
2.2.03a	If 'Yes', please provide a full explanation of the organisation or body's activity and industry sector, including any previous experience of using NHSScotland data - append supporting documentation as appropriate	N/A

2.3 Other Relevant Organisations or Bodies *Please read section 2.3 of the guidance*		
Complete this section if applicable		
Organisation Name	Nature of Business/Sector	Nature of interest in proposal

Section 3 – Overview

3.1	**Proposal Essentials** *Please read section 3.1 of the guidance*	
3.1.01	Proposal title/name:	Linking antenatal maternity data to non-communicable diseases in children and adults.
3.1.02	Is this proposal an extension or renewal of an existing approval (for example to conduct a study over a wider geographic area or for a longer period of time)? Please provide details, include the reference number of the original approval, and summarise the changes requested	No
3.1.03	Is this new proposal related to a previous application (approved or not)? Please give details, indicate if this is a resubmission, including the reference number of the original submission	No
3.1.04	What is(are) the substantive purpose(s) of the proposal? (tick all that apply)	
	☐ Patient Care	X Research
	☐ Audit	☐ Performance Monitoring/Management
	☐ Service Planning/Improvement	☐ Health/Social Care Administration
	☐ Systems Implementation/Testing	☐ Training/Education
	☐ Quality (Clinical, Educational, etc)	
	If other clearly defined purpose, please give details:	
3.1.05	Does the proposal require the use of information which can identify or potentially identify individuals?	Yes
3.1.06	Access is being requested to data from which sources? (tick as many as are relevant)	
	X A single NHS Scotland Board (excluding NSS) ☐ NHS National Services Scotland ☐ More than one NHS Scotland Board X A national NHS Scotland system/database ☐ More than one NHS Scotland system/database ☐ Community Health Index (CHI) database ☐ NHS Central Registry	

	If other, please give details:
3.1.07	Provide a full, clear concise outline of the proposal background – describe why it is needed, aims and objectives and envisaged benefits to the public and/or patients: **Background** There are several common chronic conditions of childhood which persist into adulthood of which asthma is one example. Asthma affects 5.4 million people in the UK and costs the NHS £1 billion per annum[1]. Although asthma symptoms can be palliated with inhaled steroids, there is no cure. Prevention is the most promising method for reducing the burden of asthma in Britain but better understanding of asthma pathogenesis (and a method to identify at risk individuals) is required. What is understood is that events in early life are important to asthma outcome in both childhood and adulthood. A number of observations point to important antenatal/perinatal influences on the development of asthma: (i) Reduced birth weight is associated with adult asthma suggesting that fetal growth is important to asthma aetiology[2]. (ii) Obstructed lung function, a feature of asthma, is present from one month of age in individuals who later develop asthma[3] and (iii) obstructed lung function persists from early infancy to at least 22 years of age[4]. The "fetal origins" of chronic disease hypothesis was first described in 1985[5] and suggested that physiological adaptations *in utero* alter risk for future morbidity. Only very recently has fetal ultrasound measurement been used as a surrogate for fetal wellbeing *in utero* and there is now evidence that small fetal size is associated with increased risk for morbidity in support of the fetal origins hypothesis. What is not known is whether small fetal size is the cause or is merely associated with increased risk for NCD but in the first instance any association between fetal measurements and morbidity needs to be thoroughly explored. Ours was the first group in the world to relate fetal ultrasound measurements to asthma outcomes[6-8]. We used fetal measurements as a surrogate for fetal wellbeing in a birth cohort of 2000 individuals designed to relate early life exposures to asthma outcomes. We observed an association between persistently reduced fetal size from ten weeks gestation and increased asthma and reduced lung function in five[6] and ten year old children[7]. We also observed how maternal dietary exposures[6] and smoking[8] may affect fetal growth at different gestations and these findings may be useful for future interventions. Subsequently our results have been replicated in two cohorts[9-10] but not a third[11]. Although the study which found no association between fetal size and respiratory outcomes may be flawed due to imprecise gestational estimate[12], our results require confirmation in a population which is larger and has been followed up beyond childhood. In addition to asthma, there are other chronic conditions where antenatal growth may be important to causation and these include insulin dependent diabetes mellitus (IDDM), epilepsy and attention deficit hyperactivity disorder (ADHD). In a paper currently in submission we have demonstrated an association between first trimester fetal size and a biomarker for poor IDDM control (glycosylated haemoglobin) and this is proof of concept that fetal size may be an indicator for IDDM Although there are no studies linking fetal size to epilepsy and ADHD, in one cohort fetal head circumference has been linked to language difficulties[13] which can be a surrogate for abnormal neurodevelopmental development. Given the increasing prevalence of IDDM, ADHD and the relatively high prevalence of epilepsy (1:1000) we will generalise associations we have seen between fetal growth and asthma to these other conditions.

One method to relate fetal ultrasound measurements to asthma and other non-communicable diseases would be to recruit a large birth cohort and follow this up for 25 years. An alternative, and our strategy, is to use routinely acquired fetal ultrasound measurements in Aberdeen, which have been collected since 1985, and link these to routinely acquired prescribing records in 2012. Individuals with asthma, IDDM, epilepsy and ADHD are treated with condition-specific medications and thus can be reliably identified. A smaller number of individuals with asthma, IDDM and epilepsy can also be identified from hospital admission records. The benefits of this approach, compared to recruiting a new birth cohort in 2012, are (i) results will be available in two-three years and not the 25-30 years it would take to recruit the birth cohort and for the individuals to reach adulthood (ii) the cost is a small fraction of the cost of a birth cohort (iii) drop out of a birth cohort is usually 50% over 10-15 years but our approach will ensure that fetal scan measurements can be linked to outcomes of individuals still living in Scotland (likely to be 80-90%).

Hypotheses

1. Reduced antenatal fetal size is an indicator for asthma (as evidenced by prescription of inhaled corticosteroid).
2. Reduced antenatal fetal size and growth is an indicator for type I diabetes (as evidenced by prescription of insulin).
3. Reduced second trimester fetal head circumference fetal size and growth between second trimester and birth is an indicator for epilepsy (as evidenced by prescription of anticonvulsants).
4. Reduced second trimester fetal head circumference fetal size and growth between second trimester and birth is an indicator for ADHD (as evidenced by prescription of dexamphetamine).

Aims

The aim of this project is to link fetal size and growth to non-communicable diseases in children and young adults.

1. To link fetal and maternal characteristics to outcomes in the form of dispensed medications to the specified conditions
2. To identify the key timing of growth changes relating fetal measurements to the specified conditions.

To describe the sensitivity and specificity of fetal measurements for predicting adult asthma, IDDM, epilepsy and ADHD

Objectives

1. To use the chi number to link data in the Aberdeen Maternity and Neonatal Databank (AMND) from all deliveries since 1997 to outcomes in the Prescribing Information Systems (PIS) and Scottish Morbidity Record (01).
2. To categorise individuals as every having one (or more) of the following diagnoses: asthma, type I diabetes, attention deficit hyperactivity disorder or epilepsy
3. To identify the age at which the above diagnoses were first given.
4. To use multiple imputation methods to address missingness of fetal scan data.
5. To use clustering analysis to identify growth trajectories which are linked to these four diagnoses.

Benefits to patients and the public

	This study will give a novel insight into the fetal origins of common chronic non-communicable disorders. These findings may give insight into the gestation at which intervention studies might be able to alter risk for the non-communicable conditions of interest.
3.1.08	Provide a full, clear and concise outline of the proposal design, listing: data sources; sample size; inclusion/exclusion criteria (eg involvement in trial/survey; health event, etc); relevant date range; need for identifiable or potentially identifiable data; requirement for a matched control cohort etc. *Study design.* This will be a whole population cohort study. Inclusion criteria will be a pregnancy entered into the Aberdeen Maternity and Neonatal Databank (AMND) and where there is a chi number for the infant. Exclusion criteria will include multiple pregnancies and severe congenital anomaly. Fetal measurements held on the AMND will be linked to prescribing data held by the NHS Scotland Information Services Division (ISD). ISD will also provide hospital admission details (from SMR01) which will allow hospitalisation for asthma, epilepsy and IDDM to be linked to fetal measurements. Every individual in Scotland has a community health index (CHI) number and this unique identifier means that Scotland is one of the few places in the world where the proposed linkage can take place. The CHI number is necessary to identify individuals in the three databases but governance will ensure that the researchers do not see any identifiers. The outcomes and their treatment are very common and individuals cannot be identified from either diagnosis or treatment. *Fetal measurements.* In 1985, fetal ultrasound scans became part of routine antenatal care in Aberdeen. Fetal measurements were entered into maternal case notes and we have already demonstrated that fetal measurements can be retrieved from paper records, entered onto an electronic database and linked to post natal outcomes[6-8]. The first trimester measurement will be crown rump length, and second trimester measurements will be head circumference, femur length and abdominal girth. Fetal size, i.e. crown rump length, biparietal diameter and femur length, will be expressed as an absolute measurement and also as a z score as previously[6]. Gestation at scan will be recorded. We have described the strengths and limitations of using fetal measurements as a surrogate for fetal wellbeing[14]. In one third of pregnancies, where maternal dates of last menstrual period (LMP) are uncertain, fetal gestation is determined by first trimester scan. This is an important potential confounder which we acknowledge and can address by subgroup analysis of those individuals whose maternal LMP is certain but our primary fetal measurements will be from the second trimester since we know that the gestation at these scans are more reliable than for first trimester scan. We will run our novel software which is based on multiple imputations and reduces the bias due to missing fetal scan data. *AMND*. The AMND was established in the 1950 and holds details of pregnancy, labour and delivery for each infant born in Aberdeen (http://www.abdn.ac.uk/amnd/). Permission will be sought from the AMND steering committee to access the following data from singleton term pregnancies: infant CHI number, gender, first and second trimester measurements and gestation at measurement, gestation at birth, and birth measurements (i.e. crown heel length, head circumference and birth weight), maternal age (decimal), maternal deprivation index (Carstairs), maternal smoking status, maternal chronic illness (defined as receipt of medications specific for asthma, IDDM, epilepsy and ADHD), maternal weight and height, Pregnancies where more than 10 scans were attended will be excluded; we already know that only 10% of mothers have more than five scans during a single pregnancy. Individuals with severe congenital anomalies will be excluded, e.g. trachea-oesophageal fistula, tetralogy of Fallot. *Information Services Division (ISD)*. ISD holds details of primary care prescriptions issued in Scotland since April 2009 and we know that 96% of prescriptions in Scotland have the patient's CHI number. Our primary outcome will be prescription of disease-specific medication (*see addendum for specific definitions to be used*). The secondary outcomes will be admission to hospital for asthma, epilepsy and IDDM. Additionally, and to make best use of the data collected, we will determine indices of asthma control (as evidenced by number of reliever medication inhaler/year) asthma exacerbation (as evidenced by prednisolone use/year) and asthma severity (as evidenced by British Thoracic Society treatment step ranging from 1 to 5 where treatment is stepped up and down

according to symptoms and also age, http://www.sign.ac.uk/pdf/qrg101.pdf). The combined database containing fetal and maternal details will be merged with the ISD database holding prescribing and admission data (a process called "cross-warehouse analysis") within the ISD safe haven. To assure confidentiality, the CHI will then be stripped out of the database, rows sorted randomly and the database returned to Aberdeen securely via SFTP. The database will be stored in the Aberdeen safe haven.

Ethical concerns/Governance. Our team has expertise in undertaking large data linkage projects such as we propose whilst protecting the individual's identity. We will seek approval from the AMND steering committee. We will also seek approval from the North of Scotland Research Ethics Committee. Data management, linkage and linkage validation will be undertaken with the support of experienced data linkage research co-ordinators and data managers in ISD and carried out within the governance arrangements of the ISD. The linked dataset will be stored in the Grampian Data Safe Haven (DaSH). Data management and data linkage plans will be prepared by DaSH in conjunction with the research team and submitted as part of the approvals process above.

Analysis. The primary outcome will be receipt of >1 prescription of disease specific medication between 2009 and 2015. The secondary outcome will be admission to hospital with an ICD-10 code which corresponds to one of the four outcomes of interest from 1997 to date. Data collected on all participants will be described using number or percentage in each category or mean and standard deviation for normally distributed continuous variables (or median and inter-quartile range if skewed). Logistic regression will be use to relate outcome to absolute fetal size with adjustment for gestation at scan and covariates including gender, maternal smoking, deprivation and maternal asthma. We will use mixed linear models to study the relationship between changes in fetal size and outcomes; this approach considers the co-linearity of fetal measurements within an individual, provides a magnitude of association between change in growth and risk for outcomes and increase the power of the analysis by imputing missing variables. We will explore the potential for applying Frequentist and Bayesian models to the dataset. We have developed software which will use computational approach to clustering analysis. A receiver operated characteristic curve will be used to determine the CRL z score with best sensitivity and specificity for outcomes. For asthma severity (measured on ordinal scale of 1-5 and based on treatments prescribed) we will use ordinal logistic regression.

Power. This calculation is based on asthma since this is where we have robust data to inform a power calculation. Assuming 5000 deliveries per year and scans available between 1985 and 1996, there will be as many as 60,000 scan results to enter into the database; our experience is that the actual figure will be closer to 55,000 as some mothers do not have ultrasound scans and some scan results will be misplaced. On a *pro rata* basis we will expect 20,350 (37%) to have persistent high growth, 16,500 (30%) persistent low growth, 11,000 (20%) growth acceleration and 7,700 (14%) growth deceleration between the first and second trimesters[8]. We shall assume that the prevalence of asthma (as evidenced by receipt of more than one inhaled corticosteroid prescription in 6 months) is 10% in the persistently low group and 5% in the persistently high group. Using a two group chi-squared test with a 1% two-sided significance level will have greater than 90% power to detect the difference between a Group 1 proportion of 0.100 (persistent low group) and a Group 2 proportion of 0.050 (persistent high group) (odds ratio of 0.474) suggests samples of at least 824 in each group indicating that the sample sizes of 16500 and 20350, respectively will be sufficient.

References

1. Asthma UK. http://www.asthma.org.uk/news-centre/facts-for-journalists/
2. Shaheen et al. Birth weight, body mass index and asthma and young adults. Thorax 1999;54:396-402

	3. Turner SW, et al. The relationship between infant airway function, childhood airway responsiveness and asthma. Am J Respir Crit Care Med 2004;169:921-927 4. Stern DA. Poor airway function in early infancy and lung function by age 22 years: a non-selective longitudinal cohort study. Lancet 2007; 370: 758–764. 5. Barker DJ. Fetal origins of coronary heart disease. Br Med J 1995;311:171–174 6. Turner SW, et al. Associations between fetal size, maternal α-tocopherol and childhood asthma. Thorax 2010;65:391-397 7. Turner S, et al. First and second trimester fetal size and asthma outcomes at age ten years. Am J Respir Crit Care Med 2011; 184:407-413 8. Prabhu N, et al. First trimester maternal smoking habits and fetal growth. Thorax 2010;65:235-40 9. Pike KC, et al. Patterns of fetal and infant growth are related to atopy and wheezing disorders at age 3 years. Thorax 2010;65:1099–1106 10. Hall G, et al. Increased fetal growth protects against early wheeze, airway hyper-responsiveness (AHR) and current asthma in early mid-childhood: Results from the Raine birth cohort (abstract). Eur Respir J 2011;38:S569 11 Sonnenschein-van der Voort AM. Fetal and Infant Growth and Asthma Symptoms in Preschool Children: The Generation R Study Am J Respir Crit Care Med 2012; 185: 731-737 12. Turner S, Devereux G. Fetal Ultrasound: Shedding Light or Casting Shadows on the Fetal Origins of Airway Disease. Am J Respir Crit Care Med 2012 185: 694-695 13. RAINE fetal measurements and language delay 14. Turner S. Perinatal Programming of Childhood Asthma: Early Fetal Size, Growth Trajectory during Infancy, and Childhood Asthma Outcomes. Clin Dev Immunol 2012; 2012, Article ID 962923
3.1.09	Does the proposal have implications for, or target, sensitive groups or vulnerable populations? Please give details
	Non
3.1.10	Does the proposal seek to use information exclusively about deceased persons? Please give details
	No
3.1.11	Have any members of the public/lay representatives been involved in the proposal design? Please give details
	No
3.1.12	Has any peer review of the proposal been undertaken? Please give details (for example formal review by a peer organisation or funding body, informal internal review, review by a third party)
	Yes. By anonymised internal-peer review.
3.1.13	Is there *any* commercial aspect or dimension to the proposal or its outcomes? Please give details
	No

3.2 Proposal Geography *Please read section 3.2 of the guidance*
X Local/Regional (relating to one or more specific areas within Scotland)
☐ National (relating to the whole of Scotland)
☐ UK-wide (relating to the whole of the UK, or to UK regions outside Scotland)

☐ International (relating to areas within the EEA) ☐ International (relating to areas beyond the EEA)

3.3	**Proposal Duration and Frequency** *Please read section 3.3 of the guidance*	
3.3.01	What is the proposed duration of the proposal?	3 years
3.3.02	Does the proposal require updates of information at regular intervals? Please give details	No
3.3.03	Are you seeking approval to iterate the proposal (ie the *whole* project, audit or study) at regular intervals? Please give details	No, the study will only be run once

3.4	**Statutory and Regulatory Context** *Please read section 3.4 of the guidance*	
3.4.01	Does your proposal have a statutory or regulatory justification - is the proposal responding to a statutory or regulatory instruction, duty or order? Please give details	No
3.4.02	Which Data Protection Act schedule 2 and schedule 3 conditions are relevant? (a list of conditions can be found at Appendix B)	Condition 6 of schedule 2 Condition 8 Schedule 3
3.4.03	Are there any relevant information sharing agreements, protocols or contracts in place which support your proposal? Please give details and attach as supporting documentation if available	Approval from the AMND steering committee will be sought.
3.4.04	Has a Privacy Impact Assessment been carried out which supports your proposal? Please give details and attach as supporting documentation if available	A data linkage plan will be created with DaSH.
3.4.05	Has local Caldicott approval been given for your proposal at a local level? Please give details	Yes. The AMND steering committee is the Caldcott for AMND. This decision was made in 1950 by Sir Dugald Baird.
3.4.06	Are approvals from Caldicott Guardians outside Scotland pending or received? Please give details	No

3.5	**Research and Ethics Governance** *Please read section 3.5 of the guidance*	
3.5.01	Has your proposal sought research/ethics approval?	No, but this will be sought from the North of Scotland Research Ethics Committee
3.5.01a	If yes, please provide committee details and status of	

	approval (ie pending, approved, etc). Please attach as supporting documentation if available	
3.5.01b	If no, please explain why research/ethics approval is not sought:	

3.6	**Safe Havens** *Please read section 3.6 of the guidance*	
3.6.01	Do you intend to access the data requested exclusively through a safe haven listed at Appendix A? Please provide details of which safe haven/s	Yes, the data will be accessed via the Grampian Data Safe Haven (DaSH)
3.6.02	If you applying to use NHS NSS data and you do not intend to do this through the National Safe Haven, please explain why	AMND is held by the University of Aberdeen and the ISD analysts are very familiar with the data having undertaken many linkages. We would like to be able to make use of their database specific knowledge and expertise.

Section 4 – Data & Data Subjects

4.1 Data yet to be collected *Please read section 4.1 of the guidance*		
None. The data are already collected from routine historical NHS activity		
Dataset/source Name	Collection by (whom)?	Explicit consent sought? If Yes, describe how explicit consent being sought – provide copies of participant consent/registration forms, etc. If No, explain why consent is not being sought (eg impractical, risk associated with seeking consent, etc)

4.2 All Other Dataset*s / sources Please read section 4.2 of the guidance*			
Dataset/source Name	Data Controller (Organisation)	Original purpose compatible with proposal?	
AMND	AMND steering committee	yes	
PIS	Information Services Division	yes	
SMR01	Information Services Division	yes	
How were individuals originally informed of the use of their data? (if known)			For the AMND data - posters are displayed in the antenatal clinics and in information leaflets in patients' antenatal books, with information about the use of these data and the option to opt out. NHS patient data - NHS Scotland produces information leaflets and posters describing the use of routine health data which are made available to the public at NHS facilities.
For existing dataset/sources for which the data controller is not an NHSScotland board, please append evidence of the data controllers permission to use the data			The current Caldicott for the AMND is Dr Asha Shetty. We provide the current approval from an ethics committee for the AMND steering committee to administer the AMND.

4.3 Data Variables *Please read section 4.3 of the guidance*

Dataset/source Name	Variable	Time Period/Range	Processing only?
Prescribing (PIS)	Y/N flag indicating whether the patient has been prescribed the medication in BNF category of interest (see below*) in the calendar years 2009, 2010, 2011, 2012, 2013, 2014 and (if available) 2015. (A single flag is adequate for ADHD, epilepsy and diabetes but for asthma we'd like a flag for 3.1.1, 3.1.3, 3.2, 3.3.2 and 3.4) i.e. medications specific for asthma, epilepsy, ADHD and type I diabetes Asthma medications listed in the BNF include 3.1.1 (short and long acting bronchodilators), 3.1.3 (theophylline), 3.2 (inhaled steroids), 3.3.2 (LTRA) and 3.4 (antihistamines) Epilepsy medications 4.8.1 (preventer) 4.8.2 (status treatment) ADHD 4.4 Type 1 diabetes 6.1.1.1 and 6.1.1.2	All children born at Aberdeen Maternity Hospital who have a CHI number (mostly complete for deliveries post 1996) will be linked to PIS where available (1st Jan 2009).	No
AMND (specific terms used in the AMND are described in the adjacent column)	Gender Year_of_delivery	Children born after routine introduction of CHI number (mid-late 1990s) to date.	Yes

	MatHyper Smoking PatOcc AMND_height AMND_weight AgeDel Depcat Parity Gestn BabyWt CHLength BabyOFC MatGestBooking ScanGest_1 ScanGest_Weeks_1 To save space, ScanGest and Scangest_Weeks with suffix 2 through to 10 will also be provided		
SMR01	Disease-specific (ICD-10) codes i.e. J45.0 and J45.9 for asthma G40.0 through to 40.919 inclusive and R56.9 for epilepsy F90.9 for ADHD E10.1 through to E10.9 for type 1 diabetes	1st Jan 1996 to date	No
Please justify your need for identifiable or potentially identifiable variables:			
CHI number is required for linkage. Researchers will not have sight of the chi number or any identifiable variables.			

4.4	**NRS/NHSCR Data Sources** *Please read section 4.4 of the guidance*	
Complete this section if access to NHSCR is required, or if there is any National Records of Scotland involvement		
4.4.01	Does the proposal require access to NHS Central Registry as a sampling frame for cohorts?	No
4.4.02	Does the proposal involve flagging of individuals on the NHSCR for long term follow up?	No
4.4.03	If yes, is flagging necessary:	
	☐ To trace and contact individuals throughout the UK?	
	☐ To be informed of fact and cause of death?	
	☐ To be informed of the incidence of on-going cancers?	
	☐ To be informed of emigrations prospectively and retrospectively?	
4.4.04	Is any other NRS involvement required? Please provide details	

4.5	**Making Contact with Individuals** *Please read section 4.5 of the guidance*				
4.5.01	Is any direct contact with any group of individuals required? If Yes, please provide details below				No
	Contact Group and Method of contact				Contact by (whom)
	☐ Hospital Consultants	☐ Letter	☐ Phone	☐ Other	
	☐ Other NHSS Staff	☐ Letter	☐ Phone	☐ Other	
	☐ General Practitioners	☐ Letter	☐ Phone	☐ Other	
	☐ Patients/Public	☐ Letter	☐ Phone	☐ Other	
	☐ Relatives of participants	☐ Letter	☐ Phone	☐ Other	
	☐ Others (please specify):	☐ Letter	☐ Phone	☐ Other	
4.5.02	Please explain why contact is being made – append copies of relevant correspondence as supporting evidence				
	If applicable				

4.6	**Community Health Index (CHI) Database** *Please read section 4.6 of the guidance*	
Complete this section if access to CHI Database is required		
4.6.01	What monitoring and audit of the use of CHI is planned? Please provide details	N/A
4.6.02	What technical method will be used to access CHI (online read-only, download, other extract, anonymised extract, etc)? Please provide details	N/A
4.6.03	Have any risks been identified in the proposal which relate specifically to CHI?	N/A

Section 5 – Methodology & Data Processing

5.1	**Methodology** *Please read section 5.1 of the guidance*		
5.1.01	Does the proposal require any of the following:		
	X Data matching/linking ☐ Use of matched controls	☐ Single anonymised data extract	
	Other (please specify):		
5.1.02	Who is carrying out any indexing/ linkage/anonymisation, and where?		Linkage will be carried out by analysts in ISD using CHI number. After linkage the dataset will be anonymised in ISD and transferred to the Grampian Safe Haven
5.1.03	Which data sources listed at section 4.1 and 4.2 will NSS/NRS receive identifiers for linkage purposes?		AMND
5.1.04	What variables will be provided for linkage?		
	X CHI Number	☐ Forename	☐ Surname
	☐ Date of Birth	☐ Address or Postcode	☐ NHS Number
	Other Please Specify:		

5.2	**Access** *Please read section 5.2 of the guidance*	
Complete the following section if you answered 'No' to question 3.6.1		
5.2.01	At what location is identifiable or potentially identifiable data being accessed?	
5.2.02	Please provide details of security policy/procedure governing access to this physical and technical environment – append supporting documentation	
5.2.03	Does this policy/procedure cover password policy in detail? Please provide details/ append supporting documentation	
5.2.04	Does this policy/procedure cover user account management, including review or removal of access to sensitive/personal data, in detail? Please provide details/ append supporting documentation	
5.2.05	Will individuals with access to data have individual or shared accounts?	
5.2.06	Will the data be accessed by staff working off site eg staff working from home at any time during the duration of the proposal?	Choose an item.

5.2.06b	If yes, are policies/procedures in place to facilitate, monitor and audit this access? Please provide details/ append supporting documentation	*If applicable*
5.2.07	Provide any additional detail of how data is protected from unauthorised access	*If applicable*

5.3	**Store & Use** *Please read section 5.3 of the guidance*	
Complete the following section if you answered 'No' to question 3.6.1		
5.3.01	Where is data being stored and used? (location, organisation, address – refer to addresses in previous sections if appropriate)	
5.3.02	Data Protection Registration Number	*If applicable*
5.3.03	ISO 27001 Cert. No.	*If applicable*
5.3.04	Please provide details of security policy/procedure governing storage and use of data within this physical and technical environment – append supporting documentation	
5.3.05	Does this policy/procedure cover the implementation of up-to-date controls for the detection and prevention of malware? Please provide details/ append supporting documentation	
5.3.06	Does this policy/procedure cover access control and auditing of system administrator activity? Please provide details/ append supporting documentation	
5.3.07	Does this policy/procedure cover the production of backups and the controls in place around these? Please provide details/ append supporting documentation	
5.3.08	Does this policy/procedure describe the controls in place to prohibit unauthorised copying of data? Please provide details/ append supporting documentation	
5.3.09	Does this policy/procedure describe physical and site controls? Please provide details/ append supporting documentation	
5.3.10	Does this policy/procedure cover hardware repair, replacement or disposal and protection of data from inappropriate access during such procedures? Please provide details/ append supporting documentation	
5.3.11	Describe the systems, software and security used to store and use data - please provide details/ append supporting documentation	
5.3.12	Is outsourced IT in use? Please give details	
Please repeat section 5.3 above for each relevant location in the proposal – see guidance		

5.4	**Transfer** *Please read section 5.4 of the guidance*

5.4.01	Please provide details of security policy/procedure to ensure that data will be transferred in such a way that it is protected from inappropriate or unauthorised access (mention email encryption, secure file transfer protocols SFTP, device encryption, physical controls, etc, as appropriate) - append supporting documentation	Data will be securely transferred via the SFTP application which is part of the NSS national safe haven
5.4.02	At what intervals/ trigger points will data transfer take place?	To be determined
5.4.03	Will any identifiable or potentially identifiable data be transferred outside of the UK?	No
5.4.03b	If yes, please provide details of the country of destination, the method of transfer, the proposed location and method of storage outside of the UK, and details of any further onward transfer	*If applicable*
5.4.04	Other than initial transfers from source systems, is there any copying of data required within the proposal? Please give details	No

5.5	**Dissemination** *Please read section 5.5 of the guidance*	
5.5.01	Will proposal findings be published or disseminated beyond the proposal team?	Yes
5.5.01a	If yes, how will proposal findings be published or disseminated, to what audience and in what format? Please give details	Through a research publication, conference or seminar paper.
5.5.01b	If yes, what steps will be taken to ensure that persons cannot be identified in published findings (eg disclosure control procedures (safe haven), use of aliases, numbers, avoidance of small geographical areas, avoidance of small numbers , etc)? Please give details	No identifiable data will be reported. In accordance with DaSH governance, researchers are not provided with any identifiable data.
5.5.01c	If yes, are there any circumstances where a living or dead individual would be cited? (eg where a person consented to their data being used as a case study)? Please give details	No
5.5.01d	If yes, were any permissions to publish data required or sought (for example from data controllers)? Please provide details	No

5.6	**Retain/Dispose** *Please read section 5.6 of the guidance*	
5.6.01	Which information/data/records retention policy will you be applying to the proposal data (details of the policy and the organisation to which it belongs)?	The institutional policy at the University of Aberdeen/Grampian DaSH is for data to be retained for 5 years following the study completion date. University of Aberdeen Records Retention Schedule:"http://www.abdn.ac.uk/central/records-

		management/retention-schedules.pdf"http://www.abdn.ac.uk/central/records-management/retention-schedules.pdf (Section 2.9) "http://www.abdn.ac.uk/central/records-management/retention-schedules.pdf"
5.6.02	How long do you intend to retain identifiable or potentially identifiable data after the conclusion of the proposal (including archive/backup copies)?	5 years after the project completion date the project will be reviewed with the data custodian(s) to determine whether the data (including identifiable data) should be deleted or retained in the archives
5.6.03	Who will retain the data and where?	DaSH safe haven
5.6.04	What is the purpose for retaining the data for the specified time?	To have capability to check analysis prior to appropriate dissemination. Additionally, many journals insist that data are held for at least 5 years after publication (the Lancet requests 10 years)
5.6.05	What method of disposal or destruction will be used when this period has expired (including archive/backup copies)?	Data will be erased from central file store and from backup tapes.
5.6.06	What evidence will be obtained that destruction has occurred (eg IT supplier certificate of destruction, etc)?	University of Aberdeen IT Services will send confirmation to the data owner that data destruction has been completed.

5.7	**Review** *Please read section 5.7 of the guidance*	
5.7.01	Describe how the mechanisms which safeguard data security will be audited and reviewed at regular intervals to ensure their continued efficacy	Standard project specific internal and NHS R&D auditing will occur for any project in DaSH. DaSH facility will be externally audited as part of the National Safe Haven accreditation process from 2016 onwards.
5.7.02	Describe any resource implications to any of the proposed measures for the protection of physical or technical security of information which are	None

	unresolved at the time of this application? (for example encryption of devices is an intention not yet fulfilled, training is not yet undertaken, etc)	
5.7.03	Describe the breach reporting mechanisms to be invoked in the event of any inappropriate access to data or other information security incident	DaSH records (within a specified time frame) and investigates any situation that either could or does lead to a breach of data security for any research project being handled by DaSH. Initial investigations are used to classify the severity of the incident. The incident is flagged up as a priority to the whole DaSH team. Actions required to be undertaken to rectify the situation and their progress are logged in the DaSH project management dbase. The Clinical and Technical leads are updated within 24 hours however in the event the breach is serious they are contacted directly immediately. Actions may involve recommendations for procedural changes or training requirements. The DaSH steering committee is kept up to date with all breaches. Serious incidents will be reported to the NHS Grampian Caldicott Guardian and the UoA Institute of Applied Health Sciences Director/Deputy Director.

Section 6 – Declaration

I DECLARE THAT this application is accurate, and that, should it be successful, any health data made accessible will be used for no other purpose, and in no other way, than as described above.

I UNDERTAKE TO notify the Public Benefit and Privacy Panel of any future changes to the purpose or manner in which data is processed in accordance with this application.

I UNDERSTAND THAT any future applications by me, or my employing or sponsoring organisation, may be refused should any health data made accessible be used for any other purpose or in any other way than that described above.

I CERTIFY THAT all those who have access to health data in this proposal are aware of the requirements of confidentiality and understand that any breach (eg disclosure of confidential information to a person not authorised to receive it) will be reported to the data controller, and in the case of NHS Scotland originated data to Scottish Government eHealth division.

I GUARANTEE THAT no publication will appear in any form in which an individual may be identified without the written permission of that individual, and that I will apply appropriate disclosure control when planning publications involving the data requested.

I UNDERSTAND THAT the Data Controller, and agents acting on its behalf, reserves the right to inspect the data on the sites where it is being processed.

To be signified by the APPLICANT

Name (in Capitals): ANTHONY CHAPMAN	Date: 29 April 2016

I DECLARE THAT (the applicant named above) is a *bona fide* worker engaged in a reputable project and that the data he/she asks for can be entrusted to him/her in the knowledge that he/she will conscientiously discharge his/her obligations, including in regard to confidentiality of the data, as stated in the declaration above.

To be signified by the INFORMATION CUSTODIAN named in Section 1.3 above (where the Information Custodian is not the applicant).

Name (in Capitals): DR STEVE TURNER	Date:29 April 2016

Section 7 - Supporting Evidence

Supporting Evidence *Please read section 7 of the guidance*

Please list each piece of supporting evidence which you have included with your application in the box below – the name of each should clearly indicate what the document/file/reference is about
Approval from the North of Scotland Ethics Committee for the AMND research database team to administer the AMND.

Appendix A – Reference lists for applicants

1. Examples of Existing Datasets and Data Sources	
SMR 00 Outpatients	SMR 04 Mental Health
SMR 01 Inpatients and Day Cases	SMR 06 Cancer Registration
SMR 02 Maternity	SMR 11/SBR Neonatal/Scottish Birth Records
Scottish Drugs Misuse Database (SDMD)	Birth Registrations
A&E – Accident & Emergency	Stillbirth Registrations
PIS Prescribing Information	Death Registrations
CHSP-PS/CHSP-S/SIRS – Child Health Surveillance and Immunisation	SCI-DC
NHS National Service Scotland's Information Services Division (ISD) maintains a National Dataset Catalogue (NDC) containing details of all health and health related datasets that are held by ISD. The Administrative Data Liaison Service (ADLS) publishes further information on key NHSScotland datasets	