EGSP
Enhanced Genetics Services Project

Birmingham Women's NHS
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Enhanced Genetic Services Project

Evaluation Report

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1 Executive summary

Background

The former Heart of Birmingham Primary Care Trust (HoBtPCT) had identified in November 2008 that autosomal recessive (AR) conditions were contributing to the excess infant mortality rate in Birmingham, and in particular of that experienced by the population served by the PCT. The Enhanced Genetic Services Project (EGSP) was established by HoBtPCT to address excess infant mortality and childhood morbidity in Birmingham linked to these conditions. Compared to other ethnic groups, the Pakistani community had been identified as being at particular high risk of AR conditions. These conditions occur more frequently in communities where consanguineous partnerships are common. EGSP focused on identifying those families with a history of AR conditions, and who would benefit from individual genetic risk information, to enable couples to make informed reproductive choices. The Pakistani community was identified as the main focus of EGSP but other communities with high rates of AR conditions were also included in the Project. These activities were complemented by a primary care strand and an education strand.

The West Midlands Perinatal Institute provided data for the evaluation on infant mortality and stillbirth rates for the population of Birmingham, which were broken down by ethnic group and by cause of death. This detailed information was not available prior to the initiation of EGSP. Their analyses suggested that although infant mortality rates had decreased, the population of Birmingham continued to experience elevated rates of infant deaths and stillbirths compared to the England and Wales average and that mothers of Pakistani origin experienced higher rates compared to the White European reference group. Babies from this community were at higher risk of being affected by a congenital anomaly compared to the reference group and were at particularly high risk of being affected by an AR condition.

EGSP Components

EGSP was set up comprising three strands and an evaluation.

Strand 1 – Primary care

Strand one was located within primary care services and involved establishing opportunistic screening for haemoglobinopathies within pilot GP practices and using this as a vehicle to raise genetic literacy amongst health care staff and the patient population. Two practices participated in EGSP. Testing was offered to the practice population aged 17 and over.

Strand 2 – Clinical genetics services

Strand two consisted of an extension of the services offered by the West Midlands Clinical Genetics Services, and included the systematic identification of families appropriate for referral to genetic services. This strand involved two phases: firstly, a review of all existing families from Birmingham known to the clinical genetics department (to establish the range and number of

families with known AR conditions), followed secondly by case finding, which was then to be extended through other medical specialties. This second phase included the development of increased capacity of the local molecular genetics laboratory to provide genetic testing. There was the intention to provide outreach genetic counsellor-led clinics in local GP practices.

Strand 3 - Education

This comprised educational initiatives in the community and with health care professionals. Educational materials were developed to support the educational activities, and as a tool for individuals to approach and provide information for their extended families.

Strand 4 - Evaluation

This was an integral part of EGSP and included ongoing evaluation support for the project by an externally commissioned organisation. The evaluation was to provide iterative feedback to inform the ongoing running of the project as well as the final evaluation report. The PHG Foundation was commissioned to provide this support for EGSP and established the Evaluation Working Group.

Project objectives

Objective 1: Improved access to molecular testing for autosomal recessive disorders.

Objective 2: Improved access to genetic counselling through increased capacity within the clinical genetics service of genetic counsellors with appropriate minority languages.

Objective 3: Improved genetic literacy in families affected by a genetic disorder identified by the initiative.

Objective 4: Improved genetic literacy and understanding in the extended families.

Objective 5: Improved genetic literacy in HoBtPCT's ethnic minority communities about genetic disorders and their transmission, particularly in consanguineous families.

Objective 6: Improved genetic knowledge and competence among health professionals in HoBtPCT.

Objective 7: Carrier testing within extended family to identify high risk couples, offering genetic counselling including possibility of prenatal diagnosis and postnatal treatments.

Objective 8: Identify causative mutations in genes known to cause autosomal recessive conditions in affected family.

Objective 9: Offer carrier testing of causative mutations to the extended family.

Conclusions arising from strand activities

Primary care

- The two practices identified three patients affected by thalassaemia, 99 thalassaemia carriers, eight patients affected by sickle cell disease and 43 sickle cell disease carriers.
- Careful consideration needs to be given to the amount of information patients need in order to understand the impact of being affected by or being a carrier of a genetic disorder on themselves and the implications for other family members. Without the provision of this information the benefits of such a screening programme will not be fully realised.

Clinical strand

- EGSP achieved the delivery of services set out in the pathway documents. Two hundred and fifty sets of patient notes were reviewed, which led to the EGSP re-contacting 80 individuals and offering them genetic counselling. Of these, 60 individuals actually received genetic counselling. Thirty six individuals were offered genetic testing, of whom 26 accepted the offer.
- One hundred and eighty-eight families were reviewed ,and potentially over 700 family members were identified as 'at risk', with the potential to benefit from genetic counselling and testing. Almost 400 family members were discussed with the proband or the proband's parents resulting in the proband making known contact with 37 family members. By the end of the Project, 56 family members had been offered and had accepted genetic testing, and 169 families had been identified with eligible conditions for EGSP services.
- In practice, cascade testing was limited to immediate family members. One hundred and twenty-one children, such as siblings under the age of 16 , were identified who at a later stage may decide to take up testing. It is unclear how far cascade testing is successful in routine clinical genetics practice, or whether, as in the case of EGSP, cascade testing is usually limited to the immediate family.
- EGSP services were well received by patients. They enhanced genetic understanding and facilitated sharing of genetic information with other 'at risk' family members.
- Thirty-one genetic tests, including five diagnostic and 26 carrier tests were undertaken for individuals meeting EGSP criteria, using EGSP developed tests. In addition 185 diagnostic tests and 75 carrier EGSP developed tests were undertaken for individuals living in the West Midlands but not meeting EGSP criteria.
- Five EGSP patients received a molecular diagnosis using EGSP developed tests and 17 had carrier status confirmed. Using non EGSP developed tests, a further five molecular diagnoses were made and 29 positive carrier statuses were confirmed for EGSP patients.
- A total of 111 molecular diagnoses were made for non-EGSP patients using EGSP developed tests and 92 positive carrier status confirmed for these individuals.

- New genetic tests have been developed; they have generated sufficient income from outside of the West Midlands for the service to be sustained beyond the EGSP funding.

Education strand

- For in-depth community education on genetic risk that goes beyond awareness raising and enables specific concerns to be addressed, education is usually best delivered on a one-to-one basis. Similar programmes should incorporate both group work and the ability to work on a one-to-one basis. This highlights the importance of an interlinked clinical and education strand, so that individuals who require further information and support, and potentially genetic testing, have access to this delivered by a genetic counselling service.
- Community and professional education is a process that requires sustained efforts for educational initiatives to be delivered. Repeated contacts are often necessary following an initial approach.
- Education sessions in the community had a snowball effect when further sessions were planned on subsequent weeks. Women would return with further questions and with others that they felt would benefit.
- Consanguinity can be an emotive issue but if sensitively dealt with in a manner that is nuanced and conveys an accurate understanding of the risks, it need not be controversial. In the experience of EGSP, there were no negative responses from the community to the project. Initially some level of suspicion was often encountered, but if dealt with sensitively did not persist. Members of the community valued the services provided by EGSP, including a fuller understanding of risks.
- GP practices need to have the expertise to advise people on risks associated with consanguinity and AR conditions. Members of the community turn to their GP for such information. GPs often do not see genetics training as a priority and few had made referrals to the clinical genetics service.
- It is important to identify the approach to education that will result in most engagement and achieve best outcomes. The initial focus on genetics was less effective than focusing on high rates of infant mortality and morbidity in the locality. Once the initial interest had been developed, the audiences were more likely to engage with other aspects of education such as genetics, AR inheritance and how consanguinity can increase risk in certain families.

Recommendations

1. Autosomal recessive conditions are an important contributor to the excess stillbirths and infant mortality rates in the Birmingham Pakistani and Bangladeshi communities. This contributing factor should be considered and addressed as part of any public health efforts to address health inequalities in these populations.

2. Further work is required to establish the evidence for the best model in primary care to provide services to communities at high risk of stillbirths and infant mortality deaths due to autosomal recessive conditions.

3. Long-term enhanced public health surveillance of excess stillbirths and infant mortality rates in the West Midlands based on the systems and data generated from this Project should be established to provide the evidence base for identifying and addressing the contributory causes.

4. The learning and experience of the project should be embedded into the West Midlands Clinical Genetics Service to ensure enhanced cascade testing is available for families with identified risk of autosomal recessive diseases.

5. Genetic counsellor outreach services into general practice should be considered for a pilot, particularly in those practices with the highest population risk of autosomal recessive conditions.

6. The West Midlands Regional Genetics Laboratory should continue to develop new genetic tests, particularly for autosomal recessive conditions, building on the capacity and experience generated from EGSP.

7. Further health development work should be commissioned, building on the achievements and materials developed by the education strand including the Project website.

8. A Health Visitor (clinical genetics) lead role supported by the West Midlands Clinical Genetics Service should be established.

9. The development of patient support such as 'Patient Champions' should be considered as part of future programmes to improve both community and professional awareness and to support cascade testing.

2 Infant mortality in Birmingham: Setting up the Enhanced Genetics Services Project

The former Heart of Birmingham Primary Care Trust (HoBtPCT) had identified in November 2008 that AR conditions were contributing to the excess infant mortality rate in Birmingham, and in particular that experienced by the population served by the PCT. Reducing infant and perinatal mortality had been a key public health target. In 2008 the Department of Health charged PCTs with the objective of reducing inequalities in health outcomes by 10% by 2010, as measured by infant mortality and life expectancy at birth. HoBtPCT had highlighted in a report in 2005 that its residents experience one of the highest perinatal and infant death rates in the country. The PCT report in 2008 recommended the funding of a specific project to address this. It was acknowledged that the reduction of infant mortality is a long term goal that is unlikely to be realised within the short term timescales of a project. The following data highlight the excess in infant mortality for Birmingham compared with England & Wales during the period preceding the initiation of EGSP.

Table 1 Trends in infant mortality for Birmingham and England and Wales in 1999-2008 (3-year rolling average)

Area/years	1999 - 2001	2000 - 2002	2001 - 2003	2002 - 2004	2003 - 2005	2004 - 2006	2005 - 2007	2006 - 2008
Birmingham	8.7	9.3	10.0	9.9	9.1	8.6	8.3	8.2
England & Wales	5.6	5.4	5.3	5.2	5.1	5.0	4.9	4.8

Data supplied by Birmingham Health and Wellbeing Partnership. Data source: ONS and Birmingham Public Health Information Team 2010

Within Birmingham, the three former PCTs, Heart of Birmingham, South Birmingham and Birmingham East and North experienced differing infant mortality rates, with South Birmingham being close to the national average and Heart of Birmingham having the greatest excess of infant mortality (Table 2). This suggests that initiatives to reduce infant mortality in Birmingham need to focus on the areas covered by former Birmingham East and North and Heart of Birmingham PCTs.

Table 2 A comparison of infant death rates across the former Heart of Birmingham, South Birmingham and Birmingham East and North Primary Care Trusts.

Primary Care Trust	No. of births 2007	Infant mortality rate/ 1000 2007	No. of infant deaths	No. of deaths if national rate had applied	Excess no. of infant deaths compared to E&W
Heart of Birmingham	5710	8.7	50	28	22
South Birmingham	4601	5.0	23	22	1
Birmingham East & North	6781	7.9	54	33	21

England & Wales 2008 infant mortality rate 4.8/1000 live births

The West Midlands Perinatal Institute (WMPI) provided a breakdown of infant mortality for Birmingham by ethnic group which indicated the different infant mortality rates for different ethnic groups (Table 3). The South Asian group includes 'Asian or Asian British Pakistani', 'Asian or Asian British Bangladeshi' and 'Asian or Asian British Indian'. They also provided a breakdown of infant mortality by congenital and non-congenital anomaly cause (Table 4).

Table 3 Infant mortality rate by ethnic group for 2008 in Birmingham

Ethnic group	Live births*	Infant mortality rate	Odds ratio	95% confidence interval
British European	7547	5.3		
South Asian	6231	10.6	2.0	1.4-3.0
African-Caribbean	1049	15.3	2.9	1.6-5.2
African	1239	5.6	1.1	0.5-2.4
Other	1238	10.5	2.0	1.1-3.7

*Estimated annual births based on available data from Jan-March 2008

Table 4 Infant mortality rates for Birmingham, 2008, due to congenital anomalies and non congenital anomaly causes

Ethnic group	Live births*	Overall IMR	IMR -congenital anomalies	IMR –non congenital anomalies
British European	7547	5.3	1.5	3.3
South Asian	6231	10.6Δ	4.5Δ	5.9Δ
African-Caribbean	1049	15.3Δ	3.8	11.4Δ
African	1239	5.6	0.8	4.8
Other	1238	10.5Δ	1.6	7.3Δ

*Estimated annual births based on available data from Jan-March 2008.
Table adapted from personal communication with the West Midlands Perinatal Institute
ΔStatistically significant

Table 3 indicates that within Birmingham, the South Asian and African Caribbean groups experience elevated infant mortality, while the infant mortality figure for the British European group was close to the national average. Table 4 suggests that for the African Caribbean group this is due to non-congenital anomaly causes, while for the South Asian group both congenital and non-congenital anomaly causes result in an excess of infant deaths. Amongst the South Asian group, the increase compared to the reference British European population is particularly marked for congenital anomaly causes. The above data are not sufficient to ascertain the extent to which AR conditions, a subset of congenital anomalies, contribute to the congenital anomaly deaths among the South Asian population group.

Research in Birmingham in the 1980s suggested that 50-70% of marriages within the Pakistani community were consanguineous. Consanguinity is associated with AR conditions. Consanguinity is commonly defined as a union between a couple who are second cousins or more closely related. In many families originating in the Indian sub-continent, particularly Pakistan, marriage may be arranged within the biraderi and so couples may be related but fall outside the above definition of consanguinity. The biraderi is a kinship network of individuals who share common ancestry and the biraderi grouping may date back many centuries, resulting in multiple histories of intra-community marriages in highly endogamous communities. Thus there may be a higher degree of consanguinity in a family than is suggested by the pedigree, as a result of many generations of marriage within the biraderi.

Research undertaken by Bundey *et al* in the 1980s [1] in Birmingham found the birth prevalence of certain and probable AR conditions to be around 4% in children with consanguineous Pakistani parents and approximately 0.1% in the European group. In the Bundey study, consanguinity was identified through taking a family pedigree to the baby's great grandparents where consanguinity existed in the pedigree, or to the grandparents where no consanguinity was present in the pedigree, in order to identify related individuals in the pedigree who had married.

Stillbirth and infant death rates in Birmingham are higher than the West Midlands and England & Wales average.

Within Birmingham stillbirth and infant death rates due to congenital anomaly were significantly higher for South Asian mothers. This supports the development of a project to reduce infant mortality due to congenital anomalies specifically working with this group.

High parity within the South Asian populations further supports the potential benefits of working with families in these communities who have already had an affected birth or stillbirth.

There were no children with certain or probable AR conditions in their sample of children with non-consanguineous Pakistani parents. In this study the percentage of chronic disabilities in infants who survived their first month was 2.6% for the European reference group, 7.0% in the group with consanguineous Pakistani parents and 0.7% in the non- consanguineous Pakistani group. Chronic disabilities referred to a number of different conditions such as epilepsy, tuberculosis and cancer as well as defined AR conditions.

In another analysis of the cohort, Bundey *et al* [2] found a three fold increase in post neonatal mortality in babies of consanguineous Pakistani origin compared to the European reference group. Hutchesson *et al* [3] found that the incidence of recorded inborn errors of metabolism (IEM) in the West Midlands in the 1980s was higher in Pakistani children at 1 in 318 compared to white children at 1 in 3,760. As both of these studies are quite old, use a different ethnicity classification and do not directly relate to the Birmingham local authority area, their findings should be treated with caution in relation to health experience of the current Birmingham population.

A more recent study suggests that consanguinity continues to have an impact on infant morbidity and mortality rates. Sheridan *et al* [4] found a two fold increase in congenital anomalies in live births in Bradford, a city with a large population of Pakistani origin, compared to the national figures reported by the British Isles Network of Congenital Anomaly Register (BINOCAR). They reported that 6% of offspring of first cousin partnerships in Bradford had a congenital anomaly. This was two-fold greater than in non-consanguineous unions and was independent of deprivation level. They noted that amongst the population overall, immaturity related disorders are the leading cause of infant mortality, whilst amongst infants of Pakistani origin, congenital anomalies are the leading cause of mortality. They attributed 31% of all anomalies in children of Pakistani origin to consanguinity.

Despite the lack of recent data on AR causes of infant mortality in Birmingham, the evidence from Table 4 is clear that there is an excess of deaths due to congenital anomalies amongst the 'South Asian' groups. In order to identify whether the Pakistani community is at particular risk within this wider 'South Asian' grouping and to provide ongoing monitoring information on infant mortality, the West Midlands Perinatal Institute was commissioned to provide further information which is presented in chapter 3.

The Enhanced Genetics Services Project

The Enhanced Genetic Services Project (EGSP) was established by HoBtPCT to address excess infant mortality and childhood morbidity in Birmingham linked to AR conditions. These conditions occur more frequently in communities where consanguineous partnerships are common. The EGSP focused on identifying those families with a history of AR conditions and who would benefit from individual genetic risk information to enable couples to make informed reproductive choices. The Pakistani community was identified as the main focus of EGSP but other communities with high rates of AR conditions would also be included in the project.

EGSP comprised a number of strands and the scope and objectives of EGSP are described in the project Initiation document produced in December 2008 by HoBtPCT (see appendix 1). This document sets out the rationale for the project as well as delineating the main activities to be undertaken and deliverables to be achieved, within a specified budget and an estimated time period.

Components of EGSP

EGSP was set up comprising three strands and an evaluation.

Strand 1 – Primary care

Strand 1 was located within primary care services and involved establishing opportunistic screening for thalassaemia and sickle cell disease within pilot GP practices and using this as a vehicle to raise genetic literacy amongst healthcare staff and patients. Two practices participated in EGSP and each used different recruitment methods and so did not only use opportunistic offers of testing for haemoglobinopathies. Testing was offered to the practice population aged 16 and over. This strand also sought to identify families appropriate for referral to genetic services.

Strand 2 – Clinical genetics services

This consisted of an extension of the services offered by the West Midlands Clinical Genetics Services and included the systematic identification of families appropriate for referral to genetic services. This strand involved two phases.

The first phase was to include a review of all existing families from Birmingham known to the clinical genetics department to establish the range and number of families with known AR conditions. Part of the activity would include developing existing clinical management systems to support the systematic approach to reviewing families and using the information to provide information to the extended family. As part of this activity, baseline audits would be undertaken and evaluation measures agreed which would be incorporated into the standard procedures of the project. This first phase also included the identification of the molecular testing services to be developed to support the clinical activity as well as the appointment and training of the other EGSP funded staff; these included the laboratory staff, the genetic counsellors and educationalists. These dedicated staff would all support and extend the clinical strand activity amongst health professionals and the community.

The second phase was to focus on case finding, which was then to be extended through other medical specialties – particularly hospital and community based paediatricians. This phase included the development of increased capacity of the local molecular genetics laboratory to provide genetic testing. There was also the intention to provide outreach genetic counsellor led clinics in local GP practices.

Strand 3 - Education

The education strand was initiated during the clinical strand and comprised educational initiatives both in the community and with healthcare professionals. The aim for the community was to improve genetic literacy; for health professionals the aim was to develop educational competences to enable families to be supported with information, advice and signposting to appropriate local specialised services. In this phase educational materials would be available and used by individuals to approach and provide information for extended families.

Strand 4 - Evaluation

Integral to EGSP was ongoing evaluation support by an externally commissioned organisation. The evaluation would provide iterative feedback to inform the ongoing running of the project as well as a final evaluation.

Budget and timeframe

The EGSP budget of £1.5 million comprising £960,000 for the West Midlands Regional Genetics Service which included the clinical and education strands, £350,000 for the primary care strand, £100,000 for evaluation and £80,000 for development of educational materials.

The project initiation document was produced in December 2008 and estimated that the project would take place over three years from December 2008 – December 2011, with Dr Carole McKeown from the West Midlands Clinical Genetics Department as the Project Lead and with named Project Advisers from the HoBtPCT. The project would be managed by a steering group which would have input from HoBtPCT Public Health Department. The Project Manager would co-ordinate the four strands and be accountable to the steering group. The project commenced in April 2009 with the initiation of the primary care strand activity.

The project objectives

Objective 1: Improved access to molecular testing for AR disorders – a prerequisite for carrier testing.

Objective 2: Improved access to genetic counselling through increased capacity within the clinical genetics service of genetic counsellors with appropriate minority languages.

Objective 3: Improved genetic literacy in families affected by a genetic disorder identified by the initiative.

Objective 4: Improved genetic literacy and understanding in the extended families.

Objective 5: Improved genetic literacy in HoBtPCT's ethnic minority communities about genetic disorders and their transmission, particularly in consanguineous families.

Objective 6: Improved genetic knowledge and competence among health professionals in HoBtPCT.

Objective 7: Carrier testing within extended family to identify high risk couples, offering genetic counselling including possibility of prenatal diagnosis and postnatal treatments.

Objective 8: Identify causative mutations in genes known to cause AR conditions in affected families.

Objective 9: Offer carrier testing of causative mutations to extended family.

Evaluation of EGSP

The evaluation of EGSP was put out to tender in January 2009 and the PHG Foundation was commissioned to support the evaluation from March 2009 – November 2011. The PHG Foundation agreed to :

- Establish the Evaluation Working Group (EWG)
- Provide specialist public health consultancy to enable the Project Team to conduct its own evaluation
- Provide support for the designated EGSP Project Manager with responsibility for evaluation and the collection of data
- Provide papers for the EWG
- Chair and report on meetings and provide an interim and final evaluation report

Evaluation was built into the operation of EGSP from the start. An evaluation working group was set up to guide the evaluation process and details of its terms of reference and actions are set out in chapter 4. Evaluation findings were to be fed back to the project through biannual reports to the EWG, which includes membership from all strands of the project. Each strand of EGSP was required to provide monitoring data on its activity. The types of activity data were agreed between the PHG Foundation and EGSP team. Responsibility for the collection of the data rested with the EGSP project manager and strand leads. Reports to the evaluation working group on the activity and functioning of the strands have been the main mechanism for formative evaluation, along with regular communication between the EGSP project manager and the project manager from the PHG Foundation co-ordinating the evaluation. An interim evaluation report was produced midway through the project, which was endorsed by the evaluation working group and was submitted to the successor to HoBtPCT, Birmingham and Solihull Cluster PCT.

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3 Hutchesson AC, Bundey S, Preece MA, Hall SK and Green A A comparison of disease and gene frequency of inborn errors of metabolism among different ethnic groups in the East Midlands UK J Med Genetics (1998) 35, 5, 366-370.

4 Sheridan E, Wright J, Small N, Corry P, Oddie S, Whibley C, Petherick E, Malik T, Pawson N, McKinney P, Parslow R Risk factors for congenital anomaly in a multiethnic birth cohort: an analysis of the Born in Bradford study Lancet (2013) 328, 1350-9.

3 Congenital anomalies as a cause of infant mortality and stillbirths among different ethnic groups in Birmingham.

The West Midlands Perinatal Institute (WMPI), which closed in March 2013, contributed its expertise to the EGSP and provided high quality data on infant mortality. The data provided baseline information for ethnic groups so that the long term impact of EGSP on infant mortality and stillbirth rates could be monitored. The data also informed the education strand in its work with both health professionals and the community. A further consideration for acquiring more precise data was that access to monitoring data on stillbirth and infant mortality rates, which includes information on both causes of the mortality and analysis by ethnicity, is of relevance to the sustainability of EGSP. Such data have the potential to provide information on whether EGSP is addressing this key health inequality.

Infant mortality rates were not routinely available for ethnic groups within the 'South Asian' category, as denominator data were not available. Therefore a number of analyses were commissioned from the Perinatal Institute as part of the project to provide the level of data required.

It was also important to assess the contribution of AR conditions to infant death and stillbirths for the population of Birmingham. Since data are not collected on cause of death or stillbirth by AR conditions but are only classified by congenital anomaly, this served as a proxy for AR conditions which are a subset of the congenital anomaly data.

Infant mortality rates were not routinely available on the relevant ethnic groups within the 'South Asian' category, as denominator data were not available. Therefore a number of analyses were commissioned by EGSP from the Perinatal Institute

WMPI analyses for EGSP

The analyses were commissioned for the Birmingham Local Authority resident population. A cohort of a minimum of five years of mortality data was used due to the low frequencies of these outcomes. Due to the low frequencies of either stillbirths or infant death, the two were combined when analysing mortality rates and linkage between databases.

The following data analyses were performed:

- Mortality rates, consanguinity rates and post mortem uptake rates by ethnic group
- Distribution of all births by maternal ethnic group, corrected for Trust submission rates – this is the denominator for mortality and anomaly rates by ethnic group

- Consanguinity (first cousin, other relative) by ethnic group – this includes rates and type of consanguinity

- Mortality rates (stillbirth and infant death) by ethnic group. Subanalysis of mortality by the main congenital anomaly groups as well as cases with metabolic disorders and multiple/other anomalies

- Mortality rates for routine screened anomalies (National Screening Committee NSC Fetal Anomaly Screening Programme chromosomal and structural conditions) identifies anomalies amenable to detection. Subanalysis of prenatal diagnosis by ethnic group

- Uptake and offer of post mortem by ethnic group and by Trust

- Record linkage between mortality/anomaly registers and regional clinical genetics service medical records

- Linkage between West Midlands Perinatal Notifications, West Midlands Congenital Anomaly Register and West Midlands Clinical Genetics Database (SHIRE).This includes an examination of the proportion of deaths/anomalies referred to clinical genetics and the referral levels by Trust and by geographic area.

The full report from the WMPI is appended (appendix 4).

Additional analysis on stillbirth and infant mortality due to AR conditions

To provide information on the proportion of deaths that were due to AR conditions, the West Midlands Congenital Anomaly Register (WMCAR) and the clinical genetics department reviewed a sample of deaths. These were selected on the basis of year of death and were for the last two years of the study period between 2009-10. As cause of death within the congenital anomaly category is not routinely subcategorised into AR causes, the deaths in 2009 -10 were reviewed by the clinical geneticist managing EGSP. Summary details from the WMCAR were reviewed for all 151 congenital anomaly deaths for 2009-10, along with the SHIRE clinical genetics records in those cases that had been referred to the West Midlands Clinical Genetics Service. The likely cause of death were categorised into four groups:

1. Definite AR where there was a confirmed diagnosis of a known AR condition, made clinically, pathologically or following biochemical or DNA testing.

2. Probable AR where there was sufficient evidence of an AR condition to assess the death as being highly likely due to an AR condition but no definitive diagnosis has been reached. These deaths were likely to include more than one of the following: parental consanguinity, more than one affected child, including affected females, pedigree analysis supports AR inheritance, pattern of anomalies common in AR conditions even in the absence of diagnosis.

3. Possible AR where there was some evidence to support an AR cause, such as parental consanguinity to suggest AR inheritance, but the pattern of anomalies does not fit with current knowledge of recognised AR conditions or not enough information was available.

4. Not AR in origin, for example the condition was sporadic in origin (for example trisomy 21 or isolated structural anomaly), or inherited in other ways (*e.g.* X-linked).

Key findings from the WMPI report to the evaluation

Stillbirth and infant mortality

Stillbirth and infant mortality rates overall demonstrate a downward trend for England & Wales, the West Midland and Birmingham but in Birmingham remain consistently above those seen in the West Midlands and England & Wales. In 2010 the rate in Birmingham for stillbirths was 45% higher than the England & Wales rate and was 63% higher for infant deaths.

Table 1 Stillbirth rates (all causes): Birmingham, West Midlands, England & Wales, 2003-10

AREA	2003	2004	2005	2006	2007	2008	2009	2010
ENGLAND & WALES								
Stillbirths	3,585	3,670	3,473	3,590	3,598	3,617	3,688	3,714
rate/1,000 births	5.7	5.7	5.4	5.4	5.2	5.1	5.2	5.1
WEST MIDLANDS								
Stillbirths	393	383	406	394	396	416	426	404
rate/1,000 births	6.1	5.8	6.1	5.8	5.6	5.8	6.0	5.6
BIRMINGHAM								
Stillbirths	139	134	115	112	129	122	127	128
rate/1,000 births	9.0	8.5	7.2	6.8	7.5	7.0	7.3	7.4

Source: numerator WMPI notification (West Midlands) & ONS Vital Statistics (E & W)
denominator ONS Vital Statistics

Table 2 Infant mortality (all causes): Birmingham, West Midlands, England & Wales, 2003 10

AREA	2003	2004	2005	2006	2007	2008	2009	2010
ENGLAND & WALES								
Infant deaths	3,306	3,233	3,217	3,329	3,345	3,369	3,312	3,140
rate/1,000 total births	5.3	5.1	5.0	5.0	4.8	4.8	4.7	4.3
WEST MIDLANDS								
Infant deaths	457	427	442	439	435	458	453	404
rate/1,000 total births	7.2	6.5	6.7	6.5	6.2	6.4	6.4	5.6
BIRMINGHAM								
Infant deaths	163	130	150	137	132	137	137	120
rate/1,000 births	9.0	8.5	7.2	6.8	7.5	7.0	7.3	7.4
rate/1,000 total births	10.6	8.3	9.4	8.4	7.8	7.9	7.9	7.0

Source: numerator WMPI notification (West Midlands) & ONS Vital Statistics (E & W)
denominator ONS Vital Statistics

The following analyses are for Birmingham and do not make comparisons with the West Midlands as a whole or England & Wales. The denominator data used for these analyses were extracted from the Perinatal Episode Electronic Record (PEER); dataset version 1.7 (www.pi.nhs.uk/peer/peerdata_collection.htm).

Maternal characteristics

Over half of the maternity population (56.0%) is of non-White European ethnic origin, the largest group being Pakistani mothers (23.5%). This compares to data from the 2011 census, which estimates the size of Birmingham's Pakistani population to be 13.5% of the total population. This highlights the relatively high parity among women of Pakistani origin in Birmingham. Further details on parity by ethnic group are included in the appended full report.

Consanguinity

Data on consanguinity are routinely collected in the West Midlands at pregnancy booking and completion of this data item question is high (92% for White European and 96% for Pakistani ethnic groups). The prevalence of consanguineous unions (any relation) for all ethnic groups combined was 15.9%. There is wide geographical and ethnic variation in prevalence of consanguinity. For the White European group, prevalence is 1.3%.The majority of births in consanguineous unions were to Pakistani mothers, where the

prevalence was 49.9%. This is comparable to the Bundey data (1) and the Bradford rates (4). Other groups, such as those from the Middle East and Bangladesh, also have high rates of consanguineous unions (37% and 21% respectively). The majority of consanguineous unions were between first cousins. Among the Pakistani mothers, the consanguinity rate was 47.2% for UK born mothers and 51.9% for mothers born outside the UK. For Bangladeshi mothers, there was a higher rate of consanguineous unions among mothers who were born in the UK (24.5%) than for non-UK born mothers (19.5%).

Table 3 Father blood relation: Birmingham live births, 2010

Maternal ethnic group	Not related	Father related			Not recorded	Total births
		n	prev	(95%CI)		
White European	5,773	75	1.3	(1.0-1.6)	487	6,335
Black African	833	99	10.6	(8.6-12.6)	80	1,012
Black Caribbean	584	3	0.5	(0.0-1.1)	53	640
Indian	734	48	6.1	(4.5-7.8)	57	839
Pakistani	1,453	1,447	49.9	(48.1-51.7)	118	3,018
Bangladeshi	483	127	20.8	(17.6-24.0)	40	650
Middle Eastern	196	116	37.2	(31.8-42.5)	14	326
Other/Mixed	1,103	63	5.4	(4.1-6.7)	103	1,269
Not recorded	163	13	7.4	(3.5-11.3)	147	323
ALL ETHNIC GROUPS	11,322	1,991	15.0	(14.3-15.6)	1,099	14,412
ALL ETHNIC GROUPS ADJUSTED*	13,408	2,537	15.9	(15.3-16.5)	1,295	17,240

Source: PEER
Note: *adjusted for variation in ascertainment rates by ethnic group arising from Trust submission rates

Mortality from congenital anomalies

Stillbirth and infant mortality rates were combined to facilitate analysis by ethnicity and anomaly type (table 4). The combined rate for all causes was statistically significantly higher for Pakistani, Black Caribbean and Black African mothers than the White European reference group. For Pakistani mothers the rate was 21.4 per 1,000 births compared to the White European reference rate of 11.6 per 1,000 births.

Table 4 Stillbirth and infant death rates all causes by ethnic group: Birmingham, 2006 10

Maternal ethnic group	SB+IDs	Total births	Rate	Odds ratio	(95%CL)
White European REFERENCE	437	37,764	11.6	1.0	
Black African	102	6,264	16.3	†1.4	(1.1-1.8)
Black Caribbean	114	3,624	31.5	†2.8	(2.3-3.4)
Indian	68	4,724	14.4	1.2	(1.0-1.6)
Pakistani	431	20,117	21.4	†1.9	(1.6-2.1)
Bangladeshi	52	4,132	12.6	1.1	(0.8-1.5)
Other inc Chinese & Mixed	84	9,109	9.2	0.8	(0.6-1.0)
ALL ETHNIC GROUPS	1,288	85,734	15.0		

Source: numerator WMPI & WMCAR notification
denominator ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: rate per 1,000 births
† significantly different to reference population (*i.e.* 95% confidence limits for odds ratio exclude 1)

Stillbirth and infant mortality due to congenital anomaly was significantly higher in Pakistani (odds ratio 3.0) and Bangladeshi mothers (odds ratio 2.1) compared to the reference group (table 5). Unlike the rates for all causes, the Black African and Black Caribbean mother did not have a significantly higher rate for congenital anomaly causes of stillbirths and deaths. When subdivided by anomaly type, the most common causes of death were chromosomal, central nervous system (CNS) (including neural tube defect (NTD)), and cardiac anomalies. Compared to the White European reference group, Bangladeshi mothers had significantly higher stillbirth and infant death rates for renal and genetic/syndrome causes, Black Caribbean mothers had significantly increased rates for renal and other/tumour causes and Pakistani mothers had significantly higher rates for metabolic, NTD, renal, CNS, genetic/syndrome and other/tumour causes. It is difficult to quantify the proportion of mortality that is genetic in origin and specifically due to AR genetic conditions within the anomaly types. It is expected that AR conditions would be a significant cause for the metabolic and genetic/syndrome subdivisions of anomaly type. Cases with single structural anomalies *(e.g.* NTD and renal anomalies), and especially those with multiple anomalies, may also be due to a genetic cause.

Approximately half (49.4%) stillbirths and infant deaths had at least one anomaly that can be detected by routine fetal anomaly screening programmes. There was no significant variation in prenatal detection by ethnic group.

Table 5 Stillbirth and infant death rates from congenital anomaly: Birmingham, 2006 10

Maternal ethnic group	SB+IDs	Total births	Rate	Odds ratio	(95%CL)
White European REFERENCE	106	37,764	2.8	1.0	
Black African	21	6,264	3.4	1.2	(0.7-1.9)
Black Caribbean	16	3,624	4.4	1.6	(0.9-2.7)
Indian	18	4,724	3.8	1.4	(0.8-2.2)
Pakistani	166	20,117	8.3	†3.0	(2.3-3.8)
Bangladeshi	24	4,132	5.8	†2.1	(1.3-3.2)
Other inc Chinese & Mixed	26	9,109	2.9	1.0	(0.7-1.6)
ALL ETHNIC GROUPS	377	85,734	4.4		

Source: numerator WMPI & WMCAR notification
denominator ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: rate per 1,000 births
† significantly different to reference population (*i.e.* 95% confidence limits for odds ratio exclude 1)

Mortality from AR conditions

The two final years of data were analysed as described above to identify whether minority ethnic communities in Birmingham experienced significantly increased rates of infant deaths and stillbirths due to AR conditions. Of the 151 stillbirths and infant deaths from congenital anomalies for the two year period, 53 cases were categorised as definitely or probably AR in origin and the rate was 1.52 per 1000 births (see Table 6). The corresponding rate for infant deaths alone was 1.13 per 1000 births (see Table 7). Deaths from AR congenital anomalies accounted for 35.1% of all stillbirths and infant deaths combined due to congenital anomalies and 10.4% of stillbirth and infant mortality arising from all causes (Table 8).

The analysis further indicated that when rates of combined definite and probable AR causes of infant death and stillbirths were compared between the EGSP target ethnic groups and the White European reference group, there were statistically significant raised rates of stillbirths and infant deaths due to AR conditions for the Pakistani and Bangladeshi groups (see Table 6). The increased rates were significantly higher, with a 38 fold higher rate for the Pakistani population and a 23 fold higher rate for the Bangladeshi population. In order not to have to suppress small cell counts for the Black African, Black Caribbean, Indian and 'Other 'ethnic groups categories, these ethnic groups were combined and did not have a significantly elevated rate of deaths due to AR conditions compared to the White European reference group. Stillbirths and infant death rates for the Pakistani and Bangladeshi groups were not significantly higher than the White European reference group for non AR anomaly cause of death.

Table 6 Stillbirth and infant death rates from AR and other non-AR anomaly causes by ethnic group, Birmingham 2009-10

Maternal ethnic group	Anomaly AR inheritance			Anomaly other inheritance			Total births
	n	rate	(95%CI)	n	rate	(95%CI)	
White European REFERENCE	2	0.13	(0.00-0.31)	40	2.61	(1.80-3.42)	15,332
Pakistani	40	†4.90	(3.38-6.41)	25	3.06	(1.86-4.26)	8,167
Bangladeshi	5	†2.98	(0.37-5.59)	6	3.58	(0.72-6.43)	1,678
Other ethnic groups	6	0.62	(0.12-1.12)	27	2.80	(1.75-3.86)	9,631
ALL ETHNIC GROUPS	53	1.52	(1.11-1.93)	98	2.82	(2.26-3.37)	34,808

Source: numerator WMPI & WMCAR notification
denominator ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: AR = definite/probable autosomal recessive
rate per 1,000 births
† significantly different to reference population (*i.e.* 95% confidence limits for odds ratio exclude 1)

Table 7 Infant death rates from AR congenital anomaly by ethnic group, Birmingham 2009-10

Maternal ethnic group	Anomaly AR inheritance			Total births
	n	rate	(95%CI)	
White European REFERENCE	2	0.13	(0.00-0.31)	15,227
Pakistani	29	†3.58	(2.28-4.87)	8,111
Bangladeshi	5	†3.00	(0.37-5.63)	1,666
Other ethnic groups	3	0.31	(0.00-0.67)	9,565
ALL ETHNIC GROUPS	39	1.13	(0.77-1.48)	34,569

Source: numerator WMPI & WMCAR notification
denominator ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: AR = definite/probable autosomal recessive
rate per 1,000 births
† significantly different to reference population (*i.e.* 95% confidence limits for odds ratio exclude 1)

Among Pakistani mothers, the stillbirth rate from AR anomalies was 1.36 per 1,000 births and the infant mortality for AR anomalies was 3.58 per 1,000 live births. AR anomalies contributed to 61.5% of stillbirths and infant deaths from congenital anomaly (and 65.9% of infant mortality alone) and 26.5% of stillbirths and infant deaths from all causes (37.2% of infant mortality alone) Among Bangladeshi mothers the infant mortality rate from AR anomalies was 3.00 per 1,000 live births. AR anomalies contributed to 45.5% of stillbirths and infant deaths from congenital anomaly (50.0% of infant mortality alone) and 20.8% of stillbirths and infant deaths from all causes (29.4% of infant mortality alone for all causes) (see tables 8 and 9). However, AR anomalies contributed to less than 5% of congenital anomaly stillbirths and infant deaths in the White reference group and 1.1% of stillbirths and infant deaths from all causes.

Table 8 Stillbirths and infant deaths, proportion of mortality from AR congenital anomaly by ethnic group, Birmingham, 2009-10

Maternal ethnic group	SB+IDs from AR congenital anomalies			SB+IDs congenital anomaly	SB+IDs all causes
	n	% of mortality from congenital anomaly	% of mortality from all causes		
White European REFERENCE	2	4.8%	1.1%	42	188
Pakistani	40	61.5%	26.5%	65	151
Bangladeshi	5	45.5%	20.8%	11	24
Other ethnic groups	6	18.2%	4.1%	33	148
ALL ETHNIC GROUPS	53	35.1%	10.4%	151	511

Source: numerator WMPI & WMCAR notification
Note: AR = definite/probable autosomal recessive

Table 9 Infant deaths, proportion of mortality from AR congenital anomaly by ethnic group, Birmingham 2009-10

Maternal ethnic group	Infant deaths from AR congenital anomalies			Deaths congenital anomaly	Deaths all causes
	n	% of mortality from congenital anomaly	% of mortality from all causes		
White European REFERENCE	2	7.1%	2.1%	28	97
Pakistani	29	65.9%	37.2%	44	78
Bangladeshi	5	50.0%	29.4%	10	17
Other ethnic groups	3	20.0%	4.7%	15	64
ALL ETHNIC GROUPS	39	40.2%	15.2%	97	256

Source: numerator WMPI & WMCAR notification
Note: AR = definite/probable autosomal recessive

Pathology

The lowest post mortem rates were seen in Pakistani mothers (14.2% for stillbirths and 10% for infant deaths). This compares to a post mortem rate of 40% for stillbirths and 33% for infant deaths among the White European mothers. Post mortem offer rates vary by ethnic group and by hospital. The lowest offer rate was to Pakistani mothers (50% after stillbirths and 37.1% after infant deaths). This compares to an offer rate of 67% after stillbirths and 59% after infant deaths to the White European mothers. Uptake of post mortem varied by ethnic group, with the lowest acceptance rate being by Pakistani mothers for both stillbirths (28%) and infant deaths (15%) - this was half that of the White European mothers. More Pakistani mothers were not offered a post mortem than either accepted or declined a post mortem.

Linking deaths to clinical genetics referrals

Where possible West Midlands fetal losses or infant deaths (WMPI notifications) were matched with the West Midlands Clinical Genetics database (SHIRE). Cases could be matched by linking identifiers for mothers or baby. Not all identified links meant that a referral was made to clinical genetics for a stillbirth or infant death, as the mother may have been seen by the clinical genetics department for a previous or subsequent pregnancy, or for a condition unrelated to the fetal/infant death (*e.g.* family history of cancer). In addition some deaths may have been unlinked as there were insufficient data to match the databases.

A total of 51.2% of deaths from congenital anomaly in Birmingham from 2006-10 were linked to clinical genetics records. This was higher than the linkage rate for residents of the remainder of the West Midlands (42.7%). Linkage rates were highest in deaths to Pakistani mothers and Indian mothers (see table 10), possibly indicating a higher suspicion of a genetic cause of mortality in cases from these ethnic groups.

In deaths from non-anomaly causes, 7.1% of cases were linked to clinical genetics records, amounting to 65 cases (see table 10). This suggests that this group of non-anomaly deaths may include cases with an underlying genetic disorder or congenital anomaly that was not diagnosed at the time of death or not reported to the West Midlands Congenital Anomaly Register (WMCAR). Therefore, the 65 cases were reviewed by a consultant clinical geneticist to determine if an anomaly was present. Of the 65 cases, 25 had anomalies that were ascertained by WMCAR but had died from other causes and therefore the classification as a non-anomaly death was accurate. There were 14 cases with significant anomalies that were not ascertained by WMCAR, and the congenital anomaly was likely to have been the underlying cause of death. There were a further 13 cases with anomalies that are not routinely collected by WMCAR and many of these conditions are not lethal in infancy, for example sickle cell disease or retinitis pigmentosa. So it was concluded that between 14-27 of the 65 linked 'non- anomaly' cases had been wrongly classified as deaths from non-anomaly causes at the time of death notification. Therefore ascertainment rates of stillbirths and infant deaths from congenital anomalies ascribed as a cause of death within the WMPI report were between 93.3% (377/391) and 96.4% (377/404). Of the 7.1% of non-anomaly deaths linked to genetics cases, between 21.5-41.5% had a congenital anomaly cause.

Morbidity data are equally important in understanding the impact of AR conditions on children and their families. Most non-fatal AR conditions result in ongoing health and social care needs, which cause suffering for the individual and are costly to families and to health, education and social care services. The means of obtaining such data was discussed by the evaluation working group. Due to the lack of a single depository for such data, it was agreed this area was beyond the scope and capacity of the project to gather the necessary data.

Table 10 Linkage to clinical genetics stillbirth and infant deaths by ethnic group: Birmingham, 2006-10

Maternal ethnic group	Congenital anomaly			Other causes		
	link	no link	% link	link	no link	% link
White European	43	63	40.6%	25	306	7.6%
Black African	3	18	14.3%	4	77	4.9%
Black Caribbean	8	8	50.0%	S	97	
Indian	12	6	66.7%	S	48	
Pakistani	101	65	60.8%	30	234	11.4%
Bangladeshi	13	11	54.2%	S	26	
Other inc Chinese & Mixed	13	13	50.0%	S	57	
ALL ETHNIC GROUPS	193	184	51.2%	65	845	7.1%
WEST MIDS (EXC B'HAM)	291	390	42.7%	181	2,069	8.0%

Source: WMPI & WMCAR notificationData on AR cause of death
S = suppressed count or subtotal ≤3

Conclusions

- Stillbirth and infant death rates continue to be higher in Birmingham than the West Midlands and England and Wales average, but demonstrate a downward trend.
- Within Birmingham stillbirth and infant death rates due to congenital anomaly were significantly elevated for the Pakistani and Bangladeshi mothers. For other ethnic groups with elevated stillbirth and infant death rates (Black African and Black Caribbean groups), the cause was predominantly not due to congenital anomalies. This supports the focus of EGSP in targeting cascade testing to the South Asian community rather than all groups with elevated stillbirth and infant mortality rates.
- For Pakistani and Bangladeshi mothers there is a greatly elevated rate of stillbirths and infant deaths due to AR congenital anomalies compared to the White European reference population. In contrast to the reference population the majority of congenital anomaly stillbirths and infant deaths among the Pakistani mothers were due to AR causes. This pattern also occurred for Bangladeshi mothers, but to a less marked extent.
- The high parity of Pakistani mothers supports the rationale for working with families who have had a child with an AR condition, to inform these families of the risk to subsequent pregnancies and the reproductive options available.

- Half of all Pakistani mothers are in consanguineous unions. Whether Pakistani mothers were born in Britain or outside of Britain had little effect on rates of consanguineous unions, suggesting there has been little change in the preference for cousin marriage.
- Where there are family members affected by AR conditions, they would benefit from information on the risk to future offspring and potentially to other family members who may have consanguineous marriages or have married within the biraderi. The data quantify the scope for the project targeting the groups with the highest excess of infant deaths and stillbirths and offering genetic counselling and testing, targeted to communities where there are high levels of consanguineous unions.
- Low post mortem rates are likely to result in lower rates of ascertainment of underlying cause of death and so reduce the opportunities for identifying future 'at risk' pregnancies. Offers of post mortem should be routinely made to parents and the value explained. Assumptions arising from historic low uptake of post mortems should not result in the offer not being made. This will require initiatives to raise the awareness among healthcare professionals of the value of post mortems, as well as support to professionals on how to make the offer if this support is required, particularly targeting those hospitals where offer rates are lowest.
- Investigation of non-anomaly reported cases linked to clinical genetics suggests that there is some under-ascertainment of anomaly causes of death.

4 Evaluation methodology and process

The PHG Foundation was commissioned to work with the EGSP team and support the evaluation of the programme. The first steps were to define the project's aims and detailed objectives, set out and describe the project's structures, processes and desired outcomes, quantify parameters of project quality and agree quantitative and qualitative measures of these.

A collaborative approach to the evaluation and shared responsibility was agreed between EGSP and PHG teams.

Evaluation methodology

The EWG selected the Centre for Disease Control (CDC) Framework for Program Evaluation in Public Health as a theoretical model for the evaluation of EGSP. This framework had been developed with a wide range of experts in programme evaluation and tested through the CDC's extensive public health training network.

Using this framework the evaluation addressed the following questions:

1. What is the programme that will be evaluated?
2. What aspects of the programme will be considered when judging performance?
3. What standards must be achieved for the programme to be considered successful?
4. What evidence will be used to indicate how the programme performed?
5. What conclusions are justified on programme performance by comparing the available evidence to the selected standards?
6. How will lessons learned from the enquiry be used to improve public health effectiveness?

Steps in the evaluation, as set out in the CDC Framework, include the following:

1. Engagement of stakeholders
2. Describing the programme
3. Focusing the evaluation design
4. Gathering credible evidence
5. Justifying conclusions
6. Ensuring use and sharing the lessons learned.

The interim report focused on the processes in steps 1-4 and sets out some of the findings. In November 2011 the interim report, on behalf of the EWG, was

submitted to the Birmingham and Solihull Cluster PCT, which had replaced the original commissioners of EGSP, HoBtPCT. It was considered by the Public Health Operational Group and was approved. This final evaluation report includes information on all the steps, but focuses on steps 5-6, including reporting on all available findings and drawing conclusions to enable lessons to be shared and learned.

Step 1 - Engagement of stakeholders

The main stakeholder groups were invited to be part of the EWG. These included the commissioners of the project, the managers and teams working on the three strands of EGSP and representatives from the community served by the project. Attempts were made to include lay members of the community who were part of the community advisory group. For a variety of reasons members of this group were unable to contribute directly to the EWG as stakeholders, but their contribution was provided via the community educator who was supported by this group. Appendix 2 contains the details of the membership of the EWG and their affiliations.

Step 2 - Describing the programme

The project details were set out in its initiation document. The following chapters set out more detail on the development of each component of the project . Certain aspects of the project required clearer definition after the project had started – in particular its target population and scope.

The target population for each strand differed. For the primary care strand it was the entire practice population aged 17 years or over that had not previously been screened for haemoglobinopathies. For the clinical genetics strand (clinical strand) there were a number of criteria for inclusion as being eligible for EGSP. The target population was defined as below:

For the index case

1. Those affected by or with a child with an AR condition
2. Individuals of Asian ethnicity
3. Those with a history of consanguinity
4. Being a resident of the West Midlands

For cascade testing

Ideally cascade testing would be offered to all 'at risk' individuals in the extended family. For large families this could include very many individuals. These family members might not live in the West Midlands or even in the UK and so would not be eligible for EGSP. In addition the index individual is often not in contact with wider extended family members. In practice, cascade testing focused on relatives within the nuclear family of the index patient and resident in the West Midlands. If the proband was an adult (aged over 16 years), parents and siblings in the West Midlands, and in some cases adult nieces and nephews, were discussed if the index patient provided information on these relatives. If the proband was a child, the cascade process focused on adult siblings, parents and aunts and uncles. This was set out as part of the clinical pathway.

There was a degree of flexibility on the criteria, for example a consanguineous index patient with an AR condition from an ethnic group that did not originate in Asia could be offered counselling and testing as part of EGSP. Due to the small numbers of such individuals in consanguineous unions, this applied to few individuals. The residency criteria changed during the project - when the project was initiated by HoBtPCT, only Birmingham residents were eligible for inclusion. The geographical focus broadened, in part due to the small numbers being identified for eligibility for EGSP and in part due to PCT reorganisations. HoBtPCT initially merged with the other two Birmingham PCTs (Birmingham East & North and Birmingham South) and then became part of the Birmingham and Solihull Cluster and so it was agreed in early 2011 to widen the target population to West Midlands' residents who met the criteria.

The target population for the education strand was a range of minority ethnic community groups, among whom the aim was to improve genetic literacy, and those health professionals who had a role in supporting families with information, advice and signposting to appropriate specialised services. The process of identifying the audience for the education activities is described in more detail in chapter 8.

Step 3 - Focusing the evaluation design

This involved a number of components:

1. Clarifying the scope of the evaluation
2. Clarifying the objectives of the programme
3. Specifying the information to be collected

Clarification of the scope of the evaluation

The scope aims and objectives of the evaluation were agreed by the EWG .

Aims of evaluation as set out in the CDC framework

1. To assess the merit, cost effectiveness and significance of the programme with a view to:
    a) Guiding the current and future programme management
    b) Advising funders on the continuation and shaping of the programme
    c) Advising local and national health systems on the value of implementing similar services and important aspects of their specification.

Objectives of the evaluation process

1. To clarify the goals of the overall programme
2. To decide on the scope of the programme that will be evaluated
3. To include relevant stakeholders in the evaluation
4. To decide what aspects of the programme will be considered when judging performance
5. To decide what standards (type or level of performance) must be reached before the programme is considered to be successful
6. To decide what evidence will be used for judging how the programme has performed
7. To reach conclusions about the programme performance by comparing available evidence against selected standards
8. To make recommendations about lessons to be learned from the project and to disseminate this to relevant bodies.

The EWG reported to the overall project steering group, which managed all aspects of the project. The EGSP project manager and a number of other members of the steering group were also members of the EWG. The steering group did not meet for the last two years of the programme due to significant and repeated changes in the Chair and group members.

Clarification of programme aims and objectives

An important task of the EWG was to clarify the aims and objectives of the project to ensure that they were specific, realistic and likely to be measurable.

The overall aim of EGSP was to contribute to the reduction of infant mortality in the population of Birmingham.

The project was rooted in the need to reduce infant mortality and morbidity due to AR conditions, as part of a broader priority within HoBtPCT to reduce infant mortality. EGSP was initiated as a means of reducing perinatal and infant mortality in Birmingham to the national average and this was also part of a key public service agreement (PSA) set out by the government. It was important that the EWG considered at the outset whether and how achievement or progress towards this key aim could be demonstrated over the time frame of the project or beyond. The group worked with the Perinatal Institute to refine available data and determine longer-term requirements as set out in chapter 3.

In July 2009, the project aims were discussed, refined and agreed at the initial meeting held between the project team, the representative from the commissioner of EGSP and the PHG team involved in the evaluation. This meeting preceded the establishment of the EWG. The project aims were then circulated to those invited to form the EWG prior to its first meeting, where they were discussed and agreed.

- *Project aims*

To reduce infant mortality and morbidity rates within Birmingham due to AR conditions in the Black and Minority Ethnic (BME) communities.

- *Project objectives*

To develop a multiple strand public health programme including to

1. Improve access to and acceptability of genetic services
2. Provide education to health professionals, the community and extended families of affected individuals including general genetic literacy and the genetic risks associated with consanguinity
3. Review selected general practice populations and offer carrier testing of the relevant population in the primary care trust
4. Review clinical cases and develop laboratory services to undertake molecular genetic testing where appropriate
5. Identify systematically and work with extended families to identify prevalent and incident cases of genetic disorders and provide appropriate referral and genetic counselling to individuals and couples identified as high risk for AR and other genetic disorders in the family in order to facilitate early diagnosis, better treatment and reproductive choice
6. Support and provide information for parents of affected children in the context of good clinical care
7. Develop clinical management systems for the enhanced genetics services project.

Within these overall objectives further specific evaluation objectives were agreed for each strand and are included in each chapter on the evaluation of the different strands (see chapters 5-8).

The intended deliverables, as set out in the project initiation document, were:

Deliverable 1: Mapping of the range and relative frequency of AR conditions in the Pakistani and other communities in Birmingham, particularly those contributing to perinatal and infant mortality

Deliverable 2: Adaptation of the clinical genetics IT system to allow review and recall of at risk families and to capture all activity related to the project

Deliverable 3: Improved molecular genetic testing for AR conditions associated with early childhood mortality and morbidity. Specifically this will include:

a) Identification of the mutation spectrum in a range of AR conditions including common metabolic diseases. This will enable prenatal and carrier testing to be offered to affected families and where appropriate prenatal testing to be offered to extended families

b) In most cases, molecular genetic testing will be accomplished by establishing a new diagnostic service within the West Midland Regional Genetics Laboratory (WMRGL). This will facilitate timely diagnosis of the relevant diseases in new cases

c) The identification of common founder mutations in the Birmingham population that might be suitable for population screening.

Deliverable 4: Previously seen families recontacted by genetic counsellors to offer carrier testing. Newly referred families seen to be offered genetic counselling and carrier testing. (Depends on 1)

Deliverable 5: Where appropriate running genetic counselling clinics in GP practices to increase accessibility of services.

Deliverable 6: Increased referral for genetic counselling of families from GP practices in which genetic counsellors have been based.

Deliverable 7: Training of a range of healthcare professionals in HoBtPCT in genetic competencies related to their role.

Deliverable 8: Delivery of culturally sensitive information about Genetics, AR inheritance, access to carrier testing and other genetics services, to a range of community groups in HoBtPCT.

Deliverable 9: Development and evaluation of educational material for use by affected families who will aim to convey that information to their extended families raising the genetic literacy.

Deliverable 10: The commissioning of an evaluation of the initiative.

Step 4 - Gathering credible evidence and specifying the information to be collected

Step 4 was the gathering of evidence to be used in evaluating the functioning of each strand. Information was gathered on structures, processes and activity. As a result of the differing nature of the three strands, the structures and processes involved varied for each strand. Details of the structures and processes are provided in the relevant chapters for each strand and the activity information requirements are included as appendix 5.

Evaluation processes

Evaluation can be broadly described as being formative or summative. Formative evaluation focuses on process, while summative evaluation looks at the short-term to long-term outcomes of the project and how far it has achieved its aims. Formative evaluation takes place as part of the preparation for the project, and throughout the project to improve the project design as it is being implemented. It facilitates a process of continuous improvement and is often of a qualitative nature. Summative evaluation takes place during and following the project implementation, and is usually associated with quantitative methods. Both these methods were used as part of the evaluation of this programme.

EGSP comprised three interlinked strands – a primary care strand, which focused on providing primary care screening for haemoglobinopathies in practices; a clinical strand, which provided an enhanced genetic service to those within the target population for EGSP and their families members who were resident in the West Midlands; and an educational strand which included educational initiatives amongst health professionals who were likely to have contact with those eligible for EGSP and a community focused educational work stream. The evaluation process for each of the strands differed according to the nature of the strand and is described below.

The evaluation was commissioned to start from March 2009 and formative evaluation occurred during the early stages of the project, rather than prior to its start. The initial focus of the evaluation was clarifying the aims and objectives of the project as described above.

Primary care evaluation processes

The primary care strand was active between April 2009-April 2011. This strand started operating in advance of an initial meeting to discuss the project and its evaluation held in July 2009 and prior to the establishment of the EWG. As a result the evaluation was not involved in the formative development of the strand. The activity required by the GP practices was set out in the Service Level Agreements between the practices and the PCT, leaving very limited scope for formative evaluation to modify the activities of the strand.

A priority was to establish evaluation processes for this strand, including an agreed dataset for monitoring its activity so that summative evaluation could take place. The dataset is appended as appendix 5. The dataset was specified with the lead practice, which also led on setting up a database to capture EGSP activity in order to supply the data to the evaluation. The dataset was then agreed with the second practice. In addition to ongoing monitoring of EGSP activity, the practices were asked to produce a number of monthly logs of the time spent on EGSP activities by members of the practice team.

Qualitative evaluation of both patients' experience of EGSP and that of practice staff for one of the practices also took place. The summative evaluation from both the quantitative and qualitative data are set out in chapter 5.

Clinical strand evaluation processes

For the clinical strand the formative evaluation comprised defining the target groups for case review with a view to being offered genetic counselling and then, where appropriate, offering genetic testing and cascade testing to other family members. The evaluation then focused on obtaining data so that the activity of the strand could be captured in as much detail as possible, in order to both shape the ongoing work of the clinical strand and to produce information for the summative evaluation. The dataset was agreed between the lead for the clinical strand and the evaluation team and evolved to match developments in the strand. The dataset is appended as appendix 5, and chapter 6 provides details of the evaluation findings on the strand.

Education strand evaluation processes

The education strand was designed to have two components: the development of educational materials, followed by the appointment of educators to work with the community and with health professionals. In January 2011, the evaluation team met with the education team, EGSP Project Manager, and commissioning PCT representative to agree evaluation criteria and monitoring requirements. These evaluation requirements included both formative evaluation measures and summative measures.

The EWG had stressed the importance of the educators recording formative information on how the education programme was developed. This was felt to be particularly important for this strand as, in order to be responsive to the needs of the community and health professionals, its activities were less prescribed than those of the other strands. The EWG recommended that an important part of the evaluation should be to document how such a flexible approach developed and for what reasons. The agreed information requirements for the formative evaluation are included as appendix 5. In addition, six-monthly reports were required on the activities undertaken and these reports were discussed at the EWG.

The education team were asked to evaluate each educational activity undertaken, in terms of changes to genetic literacy of those who had attended the session and attitudes to consanguinity. In practice this summative evaluation following on from sessions was often not possible and this is further discussed in the chapter on the education strand.

A third type of evaluation process for this strand was the evaluation of the educational materials developed.

Evaluation Working Group

The evaluation working group was the main mechanism for guiding the evaluation. The purpose of the EWG was to oversee the evaluation, receive reports on the progress in the evaluation of each strand and receive evaluation findings.

Membership of the EWG included representatives from the commissioners of the project, the strands of EGSP, Project Manager, lead clinicians overseeing and advising the project, the West Midlands Perinatal Institute and community representatives. The evaluation team asked for representatives from the community to advise the evaluation from the start, but such representation was only possible from 2012. The details of the membership of the group is set out in appendix 2.

The working group met in Birmingham twice a year. Meetings were chaired by the PHG Foundation and were well attended.

Steps 5 and 6 of the evaluation

The remaining chapters focus on steps 5 and 6, justifying conclusions and ensuring use and sharing the lessons learned.

Evaluation report

The PHG Foundation supported the EWG by drafting the evaluation interim and final reports. The working group contributed to and reviewed each report. The final evaluation report was endorsed by the group.

References:

http://www.cdc.gov/eval/framework/index.htm

5 Primary care strand

Background

The objectives of the primary care strand were to implement and evaluate systematic screening for haemoglobinopathy carrier status and assess family history for the presence of AR and other inherited disorders within pilot GP practices. It was active between April 2009 and April 2011.

Three GP practices intended to participate in the primary care strand. Two GP practices actively participated – those located at Balsall Heath Health Centre (with Dr Walji) and Sparkbrook Health Centre (with Dr Ramarao). The third did proceed to undertake activity as part of EGSP to screen patients for haemoglobinopathies. Different agreements were made between HoBtPCT and the practices about the services to be provided, the level of detail required and what information would be reported. This was linked to different funding arrangements for each practice.

Agreements on the activities to be undertaken by the practices

The service level agreement (dated 1 March 2009) between HoBtPCT and the two participating GP practices provides details of what each practice was expected to accomplish. The key general points are included in appendix 6.

Dr Walji's practice was funded for eight GP sessions per week and Dr Ramarao's practice for five GP sessions. In addition the practices were funded for training related to EGSP activities.

The service level agreement specified the roles and responsibilities of the practices:

The provider will:

- Deliver a prescribed programme of thalassaemia screening as defined by the agreed project plan, also identifying those families who would benefit from genetic risk information
- Work to achieve agreed objectives set out in the project plan
- Ensure that all health professionals attend appropriate training in the provision of genetics services and that the services are provided in line with current best practice
- Be expected to report exceptions and programme variance which will require prior agreement by the steering group
- Deliver regular activity reports to the steering group
- Work in partnership with the project manager and other strands of the initiative
- Be expected to work in collaboration with the organisations/individuals commissioned to undertake an evaluation of the service both in

the setting of evaluation outcomes and the implementation of data collection for those outcomes.

The pilot GP scheme was provided with £350,000 funding for 24 months.

Dr Walji's practice, Balsall Heath Health Centre

Dr Walji's practice specified their proposed activities in a study protocol which identified the following aims for their EGSP activities:

- To screen and identify all patients in the practice who are haemoglobinopathies carriers including thalassaemia (α and β), sickle cell anaemia or any other haemoglobinopathies
- To identify the prevalence of consanguineous partners in the practice populations together with their ethnic origins
- To increase genetic literacy amongst the practice population
- To identify families at risk and refer appropriately to the local genetics services.

The practice's methodology for identifying patients was through the identification of:

- Known carriers or affected individuals
- Cascade testing of known family members
- Identification of patients with symptoms or suspected carriers (for example anaemic patients)
- Opportunistic testing of patients with no known family history.

The first category of patients was classified as 'high risk', the second and third 'moderate risk' and the fourth as 'low risk'. Patients were given different lengths of appointment depending on their 'risk' categorisation.

The EWG worked closely with GP pilots to specify the activity and outcome information that should be collected for the evaluation

The EWG worked closely with GP leaders in developing information systems to specify the activity and outcome information that should be collected for the evaluation. This included basic practice demographic and ethnic origin information and information on results of the testing. The practices also provided detailed information on those identified as affected by the conditions or carriers of a haemoglobinopathy that included the various steps of offering, undertaking and reporting the results of genetic tests and the outcomes of these tests, as well as any onward referrals to the clinical genetics department. The practices were required to produce monitoring information, and data are presented on the activities of the two practices.

A number of patients were interviewed at Dr Walji's practice to investigate their understanding of the screening process and the results of their screening, as well as the implications of their results for both themselves and other family members. The practice staff who had been involved with EGSP were also interviewed to get their perspectives on both their understanding of the screening and the impact on their workload (see appendix 7). The interviews were undertaken by the community education worker for EGSP, who was independent of the practices. It was not possible to hold similar interviews with patients and staff who had been a part of EGSP at Dr Ramarao's practice.

Information from Dr Walji's practice

Dr Walji's practice had a particular interest in haemoglobinopathy screening that predated the project. He and other colleagues had undertaken screening for haemoglobinopathies among those attending a mosque in Birmingham. As a result, a number of those registered at the practice had undergone testing for haemoglobinopathies prior to April 2009; 154 patients registered with the practice had been diagnosed as carriers of a haemoglobinopathy prior to the project, and a further four individuals had been diagnosed as being affected by haemoglobinopathies rather than carriers. Since this predated the EGSP activities, these individuals are not included among the carriers and affected individuals identified during the project.

The practice population size varied over the two year period from 5215 at the start of the project to 5564 in the six month period when the practice population peaked. Only patients aged over 16 years were eligible for screening and again the numbers of this population varied over the life of the project and so the denominator varied. The lowest number of those aged over 16 registered with the practice was 4002 between October – December 2009 and the peak was 4108 between March – October 2010. The midpoint between highest number and lowest number of registered patients aged over 16 for the two year period was used as the denominator: 4055 patients.

95% of eligible patients were offered testing (3860 of the 4055 eligible patients). 56 patients declined the offer to be tested *i.e.* 1% of those approached.

Results of testing

There were conflicting data in different sections of the 'summary' data presented by the practice. Detailed review and cross-checking with anonymised individual based information confirmed the results. These were reviewed and agreed by the EWG to be an accurate report of activity.

Table 1 Numbers of carriers identified through genetic testing as part of EGSP from the 'detailed' data of individual patient data returns

Patients who consented to testing who received a positive result (carriers and affected)	90
Patients who received a positive result affected by thalassaemia	1
Patients who received a positive result for being carriers of thalassaemia	56
Patients who received a positive result affected by sickle cell disease	0
Patients who received a positive result for being carriers of sickle cell disease	33

When the above data presented in Table 1 are analysed, of the 3999 patients who consented to testing, 2.25% received a positive result and were identified as a carrier or affected by a haemoglobinopathy. It should be noted that since the practice had been involved in a mosque-based programme of testing for haemoglobinopathies prior to the start of the EGSP programme, this figure may underestimate the percentage of patients who are affected or carriers of haemoglobinopathies, as those persons who had already been tested under the mosque programme would have been excluded for the purposes of EGSP. The practice indicated that 159 patients had already had a positive haemoglobinopathy test prior to the start of the EGSP programme. Due to the changing denominator population of eligible practice population, a precise prevalence figure for affected and carrier numbers cannot be given, but if an estimated denominator of 3999 eligible practice population figure is used and the additional 159 patients with positive results prior to EGSP testing were added to the positive test results from the EGSP testing, then the carrier / affected rate would be 6.22% rather than 2.25%.

Nearly two thirds of the carriers were carriers for thalassaemia (63% of carriers), compared to a third for sickle cell disease (37%). This is not surprising since the largest ethnic group at the Practice was Pakistani/British (34%) followed by British/mixed at 13%. No other ethnic group comprised more than 7% of the practice population.

Consanguinity

Of the 90 patients identified as carriers or affected by haemoglobinopathies, 21 had consanguinity information in their notes (23%). Practices reported that they found this a sensitive subject to discuss with patients. 139 patients were reported as having pedigrees attached to their notes.

Dr Ramarao's practice, Sparkbrook Health Centre

Dr Ramarao specified his practice's activities in a project plan which set out the aims of the programme, the milestones and the patient pathways.

The practice offered screening to its patients in three ways:

1. Systematic and opportunistically, while attending the practice to see practice GPs

2. Proactively, by home visits to practice patients

3. By cascade, where other family members have had positive results or have family members with AR conditions

The project plan described these approaches in more detail. The updated project plan also described changes that were made to the screening approaches during the project – the proactive home visits were suspended as the practice felt that patients were motivated sufficiently to attend the practice for screening. It should be noted that initially testing was not undertaken at the practice; instead patients were referred to the local hospital's haematology department for the sample to be taken.

Information from Dr Ramarao's practice

Numbers tested

76% of the eligible practice population were offered testing. From the monitoring forms, 69% of eligible patients (those aged 17 years and over) responded to the offer. 48 patients declined to be tested and 1439 were tested. 516 patients were offered testing but did not respond to the offer.

Results of testing

There was conflicting data in the 'summary 'data presented by the practice. An explanation for the mismatches was found by looking at the 'detailed' anonymised information provided by the practice on each individual with a positive result for being affected or a carrier of a haemoglobinopathy.

Table 2 Genetic testing results April 2009-April 2011 Dr Ramarao's practice

Patients who consented to testing who received a positive result (carriers and affected)	63
Patients who received a positive result affected by thalassaemia	2
Patients who received a positive result for being carriers of thalassaemia	43
Patients who received a positive result affected by sickle cell disease	8
Patients who received a positive result for being carriers of sickle cell disease	10

From the testing of the 1439 patients, 63 individuals were identified by the screening as either affected or carriers of thalassaemia or sickle cell disease (4.4% of those who consented to testing). As would be expected from the ethnic breakdown of the practice population, the majority of positive tests were for carrier status for thalassaemia (68% of those with a positive result) followed by carrier status for sickle cell disease (16% of those with a positive result). If only the carrier population is considered, 81% of carriers were for thalassaemia and 19% for sickle cell disease.

Interestingly, ten individuals diagnosed through the project as being affected by haemoglobinopathies did not appear to have had a diagnosis established previously. It was agreed that the primary care commissioners should confirm with the practice if this was correct. The EWG requested that the commissioners of the primary care strand investigate and report the outcome to the group. On completion of the project this matter was still under investigation.

Consanguinity

Only three of the 63 patients who were identified as carriers or affected by haemoglobinopathies had consanguinity information in their notes. The Practice reported that clinicians found this a sensitive subject to discuss with patients. Only 14 of the 63 patients had a pedigree attached to their notes.

Other AR conditions

For both GP practices, referral of families with a rare AR condition to specialised genetics services was mentioned in the service level agreement as part of the description of the primary care strand's activities. No patients were identified by the activities within the primary care strand as being affected by other AR conditions. This was not the aim of the project activities, which were specifically focused on haemoglobinopathy screening.

Qualitative evaluation

Fourteen patients who had been offered haemoglobinopathy testing by Dr Walji's practice were interviewed by the Community Educator from EGSP. These patients, seven male and seven female patients, were selected for interview by the practice and were interviewed in English or Urdu. A separate qualitative study was undertaken with the practice staff. In that study staff who had been involved in EGSP were interviewed. Staff members included the two GPs most actively involved in EGSP and in offering testing, the practice manager and the practice receptionist. All staff and patient interviews were recorded and then transcribed and consent was sought and given by participants prior to the interviews.

Key findings from the interviews with patients

The full report of the findings from the interviews are appended as appendix 7. All respondents thought that haemoglobinopathy testing in primary care was a good idea and were positive about their experience of the testing. But there was some confusion about the concept of being a carrier and the implications both for themselves and other family members. A third of those interviewed thought that further information would be useful. Conclusions from the study

included the need for: specific types of information; appropriate information to be given to patients in an appropriate way; a process of confirming that the information provided has been understood; clear introduction to the screening programme; and an explanation of the disorders being screened for.

Most participants reported that they did not have an adequate understanding of the haemoglobinopathies that were relevant to their situation. The findings suggest that more time needs to be allocated to each patient to explain the project; this is particularly important for those patients who are found to be carriers. The findings highlight the importance of understanding that genetic test results relate to permanent states. It is therefore important that patients retain this information to use appropriately at key times during their life (for example at times when they are making reproductive choices). This may be particularly important for opportunistic screening, as in this situation the patient has not sought this information from the healthcare provider and so may require a more extensive explanation.

The following recommendations were made as a result of the qualitative interviews:

- Information needs to be given to patients at each stage of the screening process and questions asked to determine whether the patient has understood and retained the information. Genetic results often identify conditions that have an impact on children and the wider family and so it is important that the information is retained. This important fact needs to be addressed when opportunistic screening is offered.

- All the information given to patients is important for them and their understanding, not just that which the health professionals feel is most important. In order for a patient to understand risks associated with consanguinity, they need an understanding of basic genetics and its relevance for them and the wider community.

- More education/counselling time is needed if patients are to understand and retain information and share it with their families. This would also ensure that the screening programme benefits the community and makes an impact on genetic disorders and infant mortality.

- Qualitative reviews are beneficial to understanding patient experience and could be used to refine the way activities are undertaken and information is delivered. As a result, such reviews should to be carried out at intervals throughout the screening programme, to tailor explanations and so enable patients to understand the information provided by test results.

- These findings also suggest that there is a need to provide genetics education for communities and in particular those that practice consanguinity, so that they are in a better position to understand genetics test results and are more able to make informed choices for themselves and their families.

- The results would have been more meaningful if more participants were involved and were randomly selected.

A further benefit of the qualitative interviews was the increased understanding of patients' information needs, so that the community education and health professional education aspects of EGSP could be tailored accordingly.

Key findings from the interviews with practice staff

All staff noted that the workload generated by EGSP was greater than the time allocated to the project. This was due to the time taken for the administration of the project, the time taken in recontacting patients who did not attend the initial invitation for testing, and the time required for counselling the patient after receipt of results and for counselling the extended family. Developing project protocols, plans and reports were also time consuming. Interviews with staff members suggest that in their interactions with patients there was a focus by staff on the problems associated with consanguinity, rather than tailoring the information on risk to the individuals and what it meant for that individual.

All staff felt there was benefit from participating in EGSP, in terms of increasing awareness and knowledge among the staff and helping to bring genetics into primary care. It was seen as an entry point to increasing confidence in dealing with genetic disorders within primary care. All staff members said that they would recommend the project to other GP practices, especially those with a high proportion of patients from ethnic minority groups.

Other key conclusions from the staff interviews were:

- The staff members all placed a great importance on consanguinity and genetic risk, this is reflected in the participants' understanding. All the participants had an awareness of inheritance, genetic risk and how this can be passed on in families
- All the staff and participants agreed that screening was important and were grateful that the practice offered this service
- It appears that genetics education and haemoglobinopathies information may not have been provided to the patients in a structured way. This suggests that there is a need for further training for staff and or specialist genetics input for patients who need to understand genetics information and pass it onto to their families
- The staff identified that more time needs to be allocated to run projects of this type efficiently
- The staff suggested that it is important for the discipline of genetics to be understood in primary care. Structured and tailored genetics education needs to be available for staff involved in this type of screening.

Time spent on EGSP by Dr Walji's practice and Dr Ramarao's practice

The two practices estimated the amounts of time spent on EGSP over particular blocks of time. This was based on time spent by different practice team members on specific EGSP activities, recorded in half hour blocks and aggregated for monthly periods. Dr Ramarao's practice logged the time spent on the project for a three month period, while Dr Walji's practice logged the time spent on EGSP over a nine month period. Dr Walji's practice had a GP co-ordinator whose role was focused on haemoglobinopathy screening for EGSP, while Dr Ramarao's practice did not have a GP dedicated specifically to EGSP primary care activities.

The co-ordinator at Dr Walji's practice also produced a summary sheet describing the main activities undertaken by the different staff members in the practice to deliver EGSP. Dr Walji's practice spent a total of 1,125 hours (all practice staff combined) on EGSP over a nine month period. Dr Ramarao's practice spent 147.5 hours over a three month period (all practice staff combined). If this figure was tripled to estimate the time spent on a comparable nine month period to Dr Walji's practice it would amount to 442.5 hours. If these figures for time spent on EGSP activity are extrapolated to the two year time period of EGSP activity in the practices, and the time spent per patient offered testing is compared for the two practices, both practices spent very similar amounts of time per patient on EGSP activities. The figure would be 47 minutes per patient for both practices.

Other issues arising from the primary care screening

1. An issue raised by both practices was the duplication of tests for pregnant women. As results from antenatal screening for haemoglobinopathies were not passed on to primary care, women who had already been tested antenatally were retested, although their results were known to the NHS. It is unclear whether this is an issue that was specific to Birmingham or a wider communication issue between primary care and secondary care.

2. Patients from Dr Ramarao's practice initially did not have the blood sample taken at the practice but the sample was taken at the local hospital. While this pathway was operating, it is possible it may have affected the take up of screening as patients might have lost their phlebotomy forms or not wanted to expend time and money (spent on travelling to the hospital) on this extra hospital visit. Patients at Dr Walji's practice were offered testing at the surgery and so did not have to make the extra hospital visit. It was beyond the scope of the evaluation to find out if the extra visit was a barrier to taking up screening but should be considered by others planning a similar initiative. As the project developed, a change took place in the pathway followed by Dr Ramarao's practice in that an in-house phlebotomy service was established so that patients could have blood taken at the practice.

3. There was discussion between the project team and the practices about the consent process for haemoglobinopathy testing. The procedures within the practice for consent involve the clinician explaining to the patient what the practitioner is about to do and why, in a manner which is 'sufficient for the patient to understand the procedure.' This is what the

practices refer to as 'implied consent'. If the risks are seen to be significant then 'expressed consent' is sought. In such circumstances a note is made in the medical record detailing the discussion about consent and risk and a consent form may be used form the patient to express consent. After further feedback from the project team the practices moved to an explicit consent process.

Conclusions

- The two practices identified three patients affected by thalassaemia, 99 thalassaemia carriers, eight patients affected by sickle cell disease and 43 sickle cell disease carriers.
- There were challenges for the practices in data collection and addressing consanguinity in primary care consultations.
- Careful consideration needs to be given to the amount and type of information patients need in order to understand the impact of being affected by or being a carrier of a genetic disorder, both on themselves and the implications for other family members. Without the provision of this information the benefits of such a screening programme will not be fully realised.
- Undertaking haemoglobinopathy screening was more time consuming than had been anticipated and the time required to provide a high quality programme with sufficient information for patients should be carefully considered by practices before embarking on such a programme.
- EGSP activity was well received by both patients and practice staff members.

6 Clinical strand

The central component for EGSP was the clinical strand – the part of the project set up to deliver an enhanced genetics service to the target population. Although the three strands could stand alone, EGSP was designed so that the primary care and education strands would support the clinical strand through primary care and education initiatives. Arising from the activities of these strands, there would be referrals of 'at risk' individuals to the clinical strand who would be offered genetic counselling and testing by the EGSP genetic counsellor, supported by the clinical geneticists who had time allocated to EGSP.

Nine objectives were set out for EGSP and five relate specifically to the clinical strand. These objectives were:

Objective 2: Improved access to genetic counselling through increased capacity within the clinical genetics service of genetic counsellors with appropriate minority languages.

Objective 3: Improved genetic literacy in families affected by a genetic disorder identified by the initiative.

Objective 4: Improved genetic literacy and understanding in the extended families.

Objective 7: Carrier testing within extended family to identify high risk couples, offering genetic counselling including possibility of prenatal diagnosis and postnatal treatments.

Objective 9: Offer carrier testing of causative mutations to extended family.

These objectives were translated into more measurable deliverables. In all there were ten deliverables for EGSP and five relate to the clinical strand. The following deliverables were the responsibility of the clinical strand:

Deliverable 1: Mapping of the range and relative frequency of AR conditions in the Pakistani and other communities in Birmingham, particularly those contributing to perinatal and infant mortality.

Deliverable 2: Adaptation of the clinical genetics IT system to allow review and recall of at risk families and to capture all activity related to the project

Deliverable 4: Previously seen families re-contacted by genetic counsellors to offer carrier testing. Newly referred families seen to be offered genetic counselling and carrier testing. (Depends on 1)

Deliverable 5: Where appropriate running genetic counselling clinics in GP practices to increase accessibility of services.

Deliverable 6: Increased referral for genetic counselling of families from GP practices in which genetic counsellors have been based.

The laboratory and education chapters consider the performance of the project in relation to the other deliverables. This chapter will describe the activities that comprised the clinical stand and examine the evidence on the performance of EGSP on the clinical strand deliverables.

Overview of the clinical strand

The clinical strand was located within the West Midlands Clinical Genetics Department based at Birmingham Women's Hospital. It was staffed by a series of genetic counsellors with one, or at times two, genetic counsellors filling the posts at different periods of the project, with professional supervision from a consultant clinical geneticist with overall management responsibility for EGSP. There was more than one genetic counsellor working for EGSP during the periods when the genetic counsellor reduced their hours from full-time to part time, or when newly qualified genetic counsellors were appointed and supervision was required to gain the necessary experience to provide genetic counselling unsupervised. Management of the strand was shared between the EGSP Project Manager and the consultant clinical geneticist with responsibility for managing EGSP.

The focus of the strand was reviewing patients already on the Clinical Genetics' department database, followed by genetic counselling either in a clinic setting, by telephone or in the patient's home. After providing counselling and testing, where relevant, to index patients, genetic testing, genetic counselling and cascade testing of other 'at risk' family members were offered via the index patient or in cases when the index patient was a child, via the patient's parents.

As a second stage of the clinical strand, there were plans to work with other clinics in which patients, who may not have been referred to genetics, could be seen due to AR conditions . Through joint clinics, these patients could be referred to EGSP and offered EGSP review with follow-up genetic counselling and testing services. In addition, it was proposed to offer genetic counselling clinics in general practice settings.

Criteria for eligibility for the clinical strand

The eligibility criteria for individuals and their families to be included in EGSP changed during the course of the project. The initial criteria and the revised criteria are listed below. The criteria were changed in 2011 due to low numbers of patients being seen by EGSP. All criteria had to be met for eligibility as drawn up for each phase of the project.

Initial criteria:

- The index patient and/or family were affected by an AR condition. Initially the conditions targeted were those for which tests had been developed as part of EGSP that had not previously been available in-house and were developed due to being relatively common amongst minority ethnic families in the West Midlands.
- The index patients and for cascade, family members, were resident in the three Birmingham PCTS.
- The ethnicity of patients was of Pakistani, Bangladeshi, Indian and other Asian background.
- Consanguineous partnerships were present in the family. Consanguinity was defined as a union between second cousins or a closer relatedness but as the exact nature of the consanguineous union was often unknown or not recorded, families with any consanguinity in the patient pedigree or family files were included. In practice the consanguinity eligibility criteria was further extended to include families from ethnic groups where high levels of consanguinity were reported.

Revised criteria:

- The AR conditions were broadened to any AR condition for which testing was available either in-house or as send away testing.
- The residency criterion was extended to include all of the West Midlands.
- The ethnicity of patients for eligibility was of Pakistani, Bangladeshi, Indian and other Asian background. Although this remained the main target groups the ethnicity criteria was extended to other minority ethnic groups.
- The consanguinity criteria did not change.

Eligible individuals and families were then recruited into EGSP and followed the clinical pathway described below.

Description of the clinical strand pathway

The clinical pathway is presented as flowcharts in Figures 1-4. Figure 1 sets out the overall pathway covering the strand's activity from review of case notes to completion of the full pathway with the end of contact. Figures 2-4 identify in more detail the different components of the clinical pathway – the review process (Figure 2), the patient contact process (Figure 3) and the patient consultation pathway (Figure 4).

The first step involved the selection of patients appropriate for referral to EGSP. This was undertaken both by the consultant clinical geneticist and the genetic counsellors. Patients who had had no contact with the clinical genetics unit for many years were not recontacted, as it was decided that such recontact could be alarming for patients who had not been seen after such an extended period. Once suitable patients had been identified, the patient's consultant clinical geneticist was asked to check if there were any reasons for not contacting the patient. This consultant clinical geneticist could have been any member of the team of consultant clinical geneticists in the West Midlands Regional Genetics Service. If no indication was given not to contact the patient, the patient's GP was contacted to check if there were any reasons to exclude the patient from EGSP. If no reason was given, or if no reply was received within four weeks, the genetic counsellor contacted the patient in writing to invite them for a genetic counselling appointment. Up to five attempts were made to contact a patient by telephone on different days and times. If contact was made, an appointment was offered either at the clinic or at the patient's home. The pedigree was updated and genetic counselling provided, and where appropriate, genetic testing was offered. Once counselling and, where appropriate, genetic testing had been undertaken, cascade testing was offered to other family members living in the West Midlands via the index patient or the patient's parents.

For each patient, the pathway was completed at different points depending on their circumstances. For many patients the review of the patient's notes identified that they were not eligible for EGSP – for example they did not meet all of the four criteria for eligibility. For other patients, the consultant clinical geneticist that they had originally seen or the patient's GP might notify the EGSP genetic counsellor that the individual or family was not suitable for recall and the pathway would be complete. The genetic counsellor might not be able to make contact with the family, or the patient might decline the offer of an appointment, and in those circumstances the pathway would be complete. If patients were seen, the length of the pathway would be based on the patient's needs and might involve genetic counselling or genetic testing in addition to counselling.

Figure 1 Overview of the clinical pathway

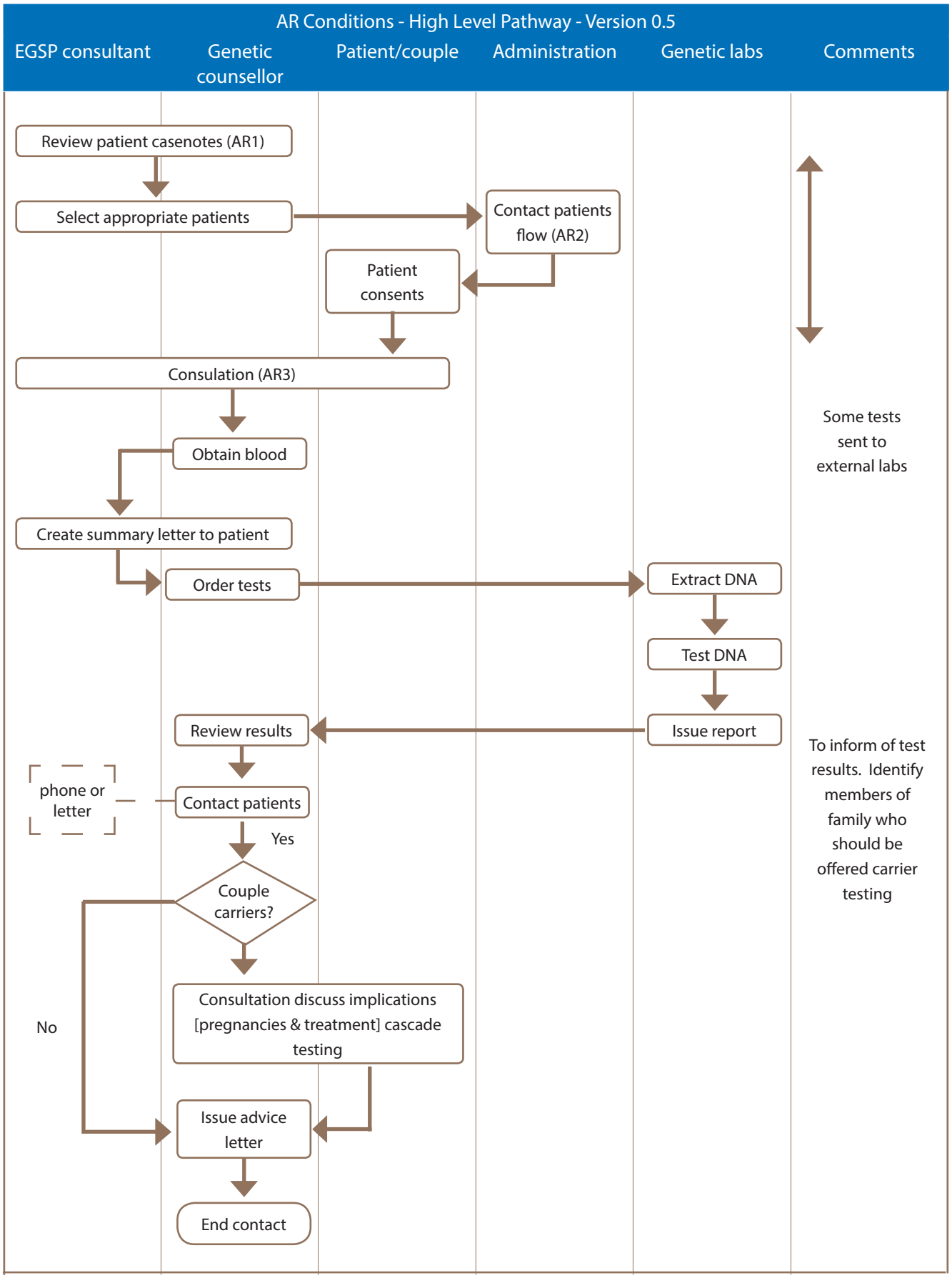


Figure 2 Review process

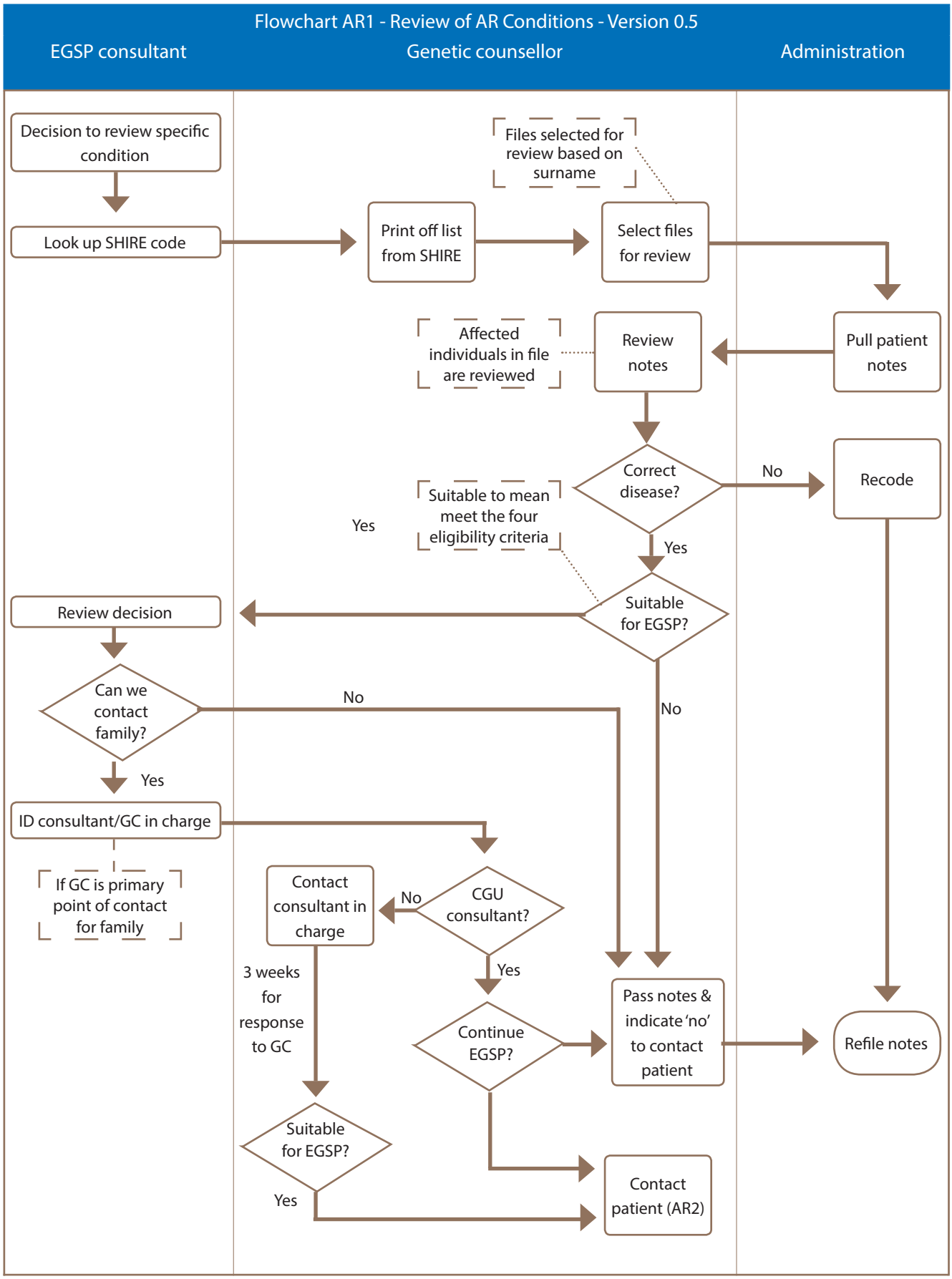


Figure 3 Patient contact process

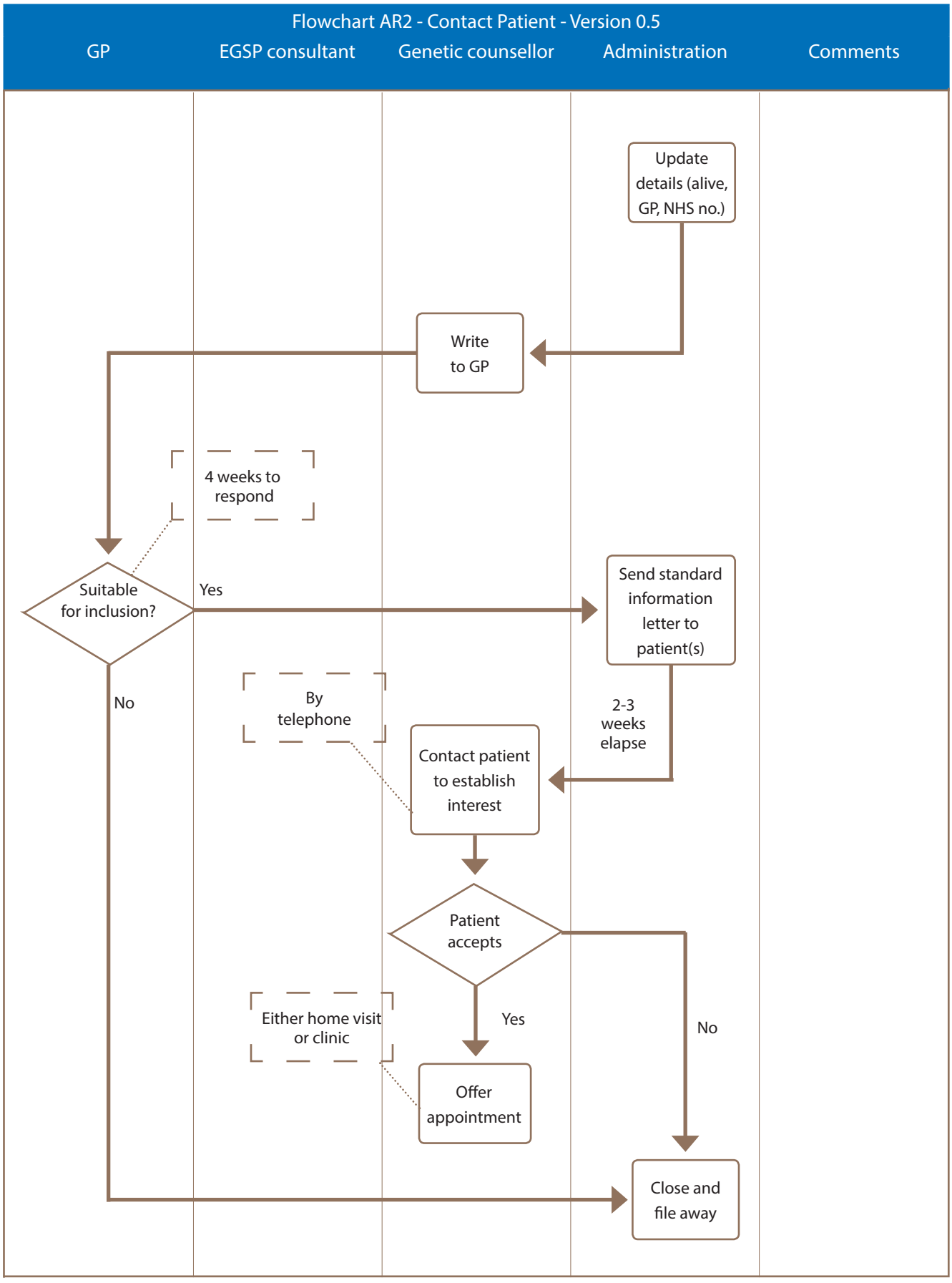
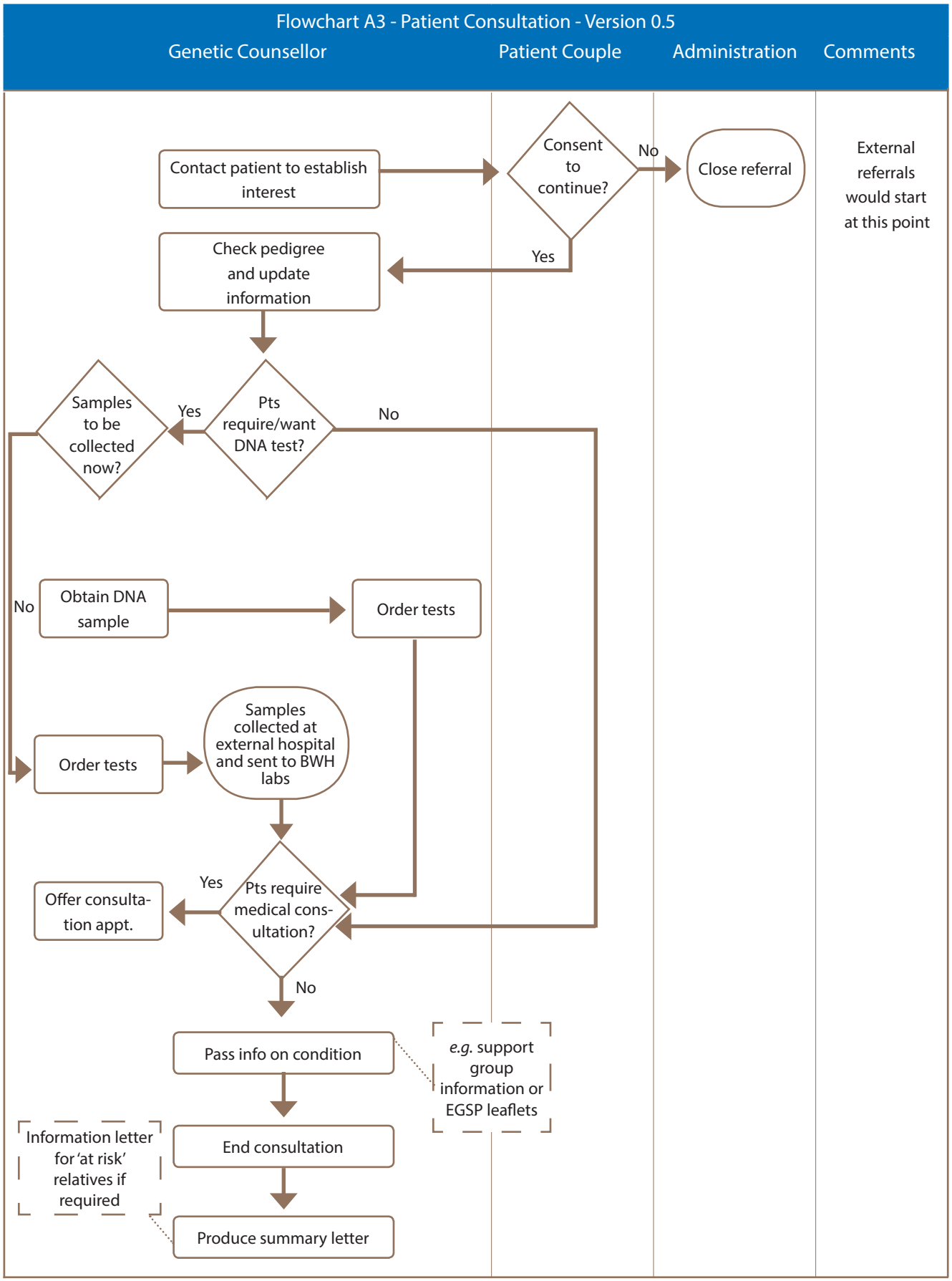


Figure 4 Patient consultation pathway



The operation of the strand in practice

The way the strand operated was modified during the course of EGSP. Through the ongoing monitoring of activity produced for the evaluation, the commissioning PCT, HoBtPCT, identified that the number of patients being seen by EGSP was lower than anticipated. As a result the eligibility criteria were widened as described.

Identification of patients for EGSP review

The initial phase for the clinical strand was to identify both the patients suitable for review and the genetic tests to be developed and offered as part of EGSP. These two activities were interlinked as reviewing the patient database of eligible patients was a means to identifying where there were gaps in genetic test availability, which could be addressed by genetic test development as part of the laboratory component.

The pathway as depicted in Figure 2 does not fully describe the complexity of identifying patients who might benefit from review. Difficulties arose due to lack of completeness of the existing clinical genetics database. In many cases ethnicity was not recorded on this database and so it could not be used to select all patients from the target communities and then identify individuals and families who would benefit from review. Since the database could not be searched using ethnicity criteria, the review was undertaken through selecting disease codes from the clinical genetics database. Within each disease code, suitable families for EGSP were then identified for review by checking names to judge whether the individual came from the target population. This was a time consuming process, as initially the diseases to be reviewed had to be selected and then case review undertaken on a disease-by-disease basis. As a consequence only a proportion of the patient database was reviewed.

In advance of the genetic counsellors coming into post, the consultant clinical geneticists attempted to map the range of diseases that EGSP review should focus on. Records grouped as 'metabolic unknown' and 'neurological unknown' were examined to see which patients could be reclassified into a diagnostic group. This involved reviewing over 1000 sets of notes of people with metabolic conditions and 800 sets of notes of those with neurodegenerative conditions who did not have a diagnosis. A diagnosis was then ascribed where possible. The list of potentially suitable patients was then ready for the genetic counsellors to continue the review process and clinical pathway.

Figure 1 indicates that case review to identify potential EGSP patients was to be undertaken by both the consultant clinical geneticist and genetic counsellor. In fact, initially the majority of the case review was undertaken by the consultant clinical geneticist, as the knowledge required to select suitable families required expertise either from a clinical geneticist or a senior genetic counsellor. It was not possible to recruit senior genetic counsellors to the EGSP posts.

The case review process was slow as there was very limited consultant clinical geneticist time allocated to EGSP, approximately seven hours per week, initially shared between three consultant clinical geneticists. As the genetic counsellors gained more experience, they took on the majority of the review process with support from a consultant clinical geneticist.

Staffing capacity and the clinical strand

EGSP activity commenced in April 2009 with the initiation of the primary care strand. Due to the recruitment difficulties, the start of the clinical strand was postponed for seven months until the first permanent Project Manager took up post in November 2009. Prior to the recruitment of the EGSP Project Manager and EGSP genetic counsellor, a genetic counsellor was seconded by the Clinical Genetics Department to EGSP for two days a week, from September 2009 to October 2010, to work on producing the educational materials required to support the clinical and educational strands. She worked at the National Genetics Education and Development Centre (NGEDC) with NGEDC staff who had been commissioned to develop educational materials for EGSP. In August 2010 the first genetic counsellor was recruited to EGSP and started to see patients in November 2010, 18 months after the commencement of EGSP.

Genetic counsellor staffing capacity to deliver the components of the pathway was an ongoing issue. This is portrayed schematically in the timeline set out below (Figure 5) which depicts the different periods of genetic counselling input provided by successive genetic counsellors recruited to EGSP.

Difficulties were encountered in both recruiting and retaining staff, resulting in low clinical activity levels for considerable periods during EGSP's operation. Initially, the ability to speak Urdu was a requirement for the EGSP genetic counsellor post. It was not possible to recruit a UK based genetic counsellor who fulfilled the language criteria and after two recruitment attempts, an Urdu speaking genetic counsellor was recruited from Canada as the first genetic counsellor to join the team. Once in post, being newly qualified, the genetic counsellor required a period of supervision before embarking on EGSP genetic counselling and so was not able to start seeing patients until November 2010. Therefore, prior to November 2010 there was no permanent EGSP genetic counsellor. As an interim measure some genetic counsellor input was provided by a seconded genetic counsellor from the clinical genetics service on a part-time basis as described above. In addition the consultant clinical geneticist managing the project saw some index patients whose families were suitable for recruitment into EGSP, but activity was piecemeal. The EGSP genetic counsellor then left the project five months later and the post remained vacant for nine months, partially filled in the meantime with up to 0.2 WTE genetic counsellor input, seconded from the clinical genetics department.

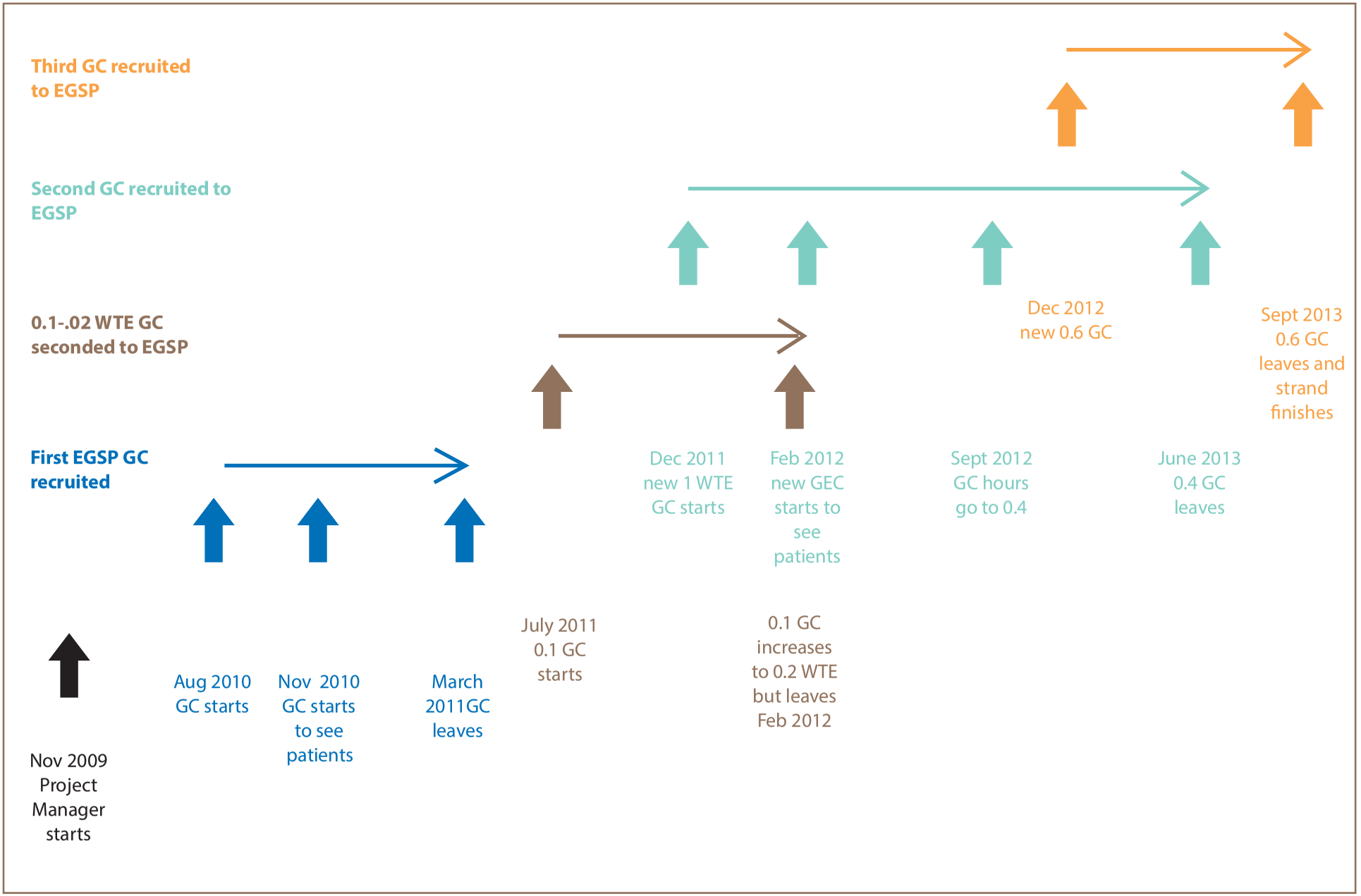
Within the limited time constraints, the genetic counsellor was able to provide some continuity for patients recruited to EGSP by the previous post holder and

provide services to some patients. Due to the difficulties outlined above, during the first 16 months of the clinical strand of EGSP (for the period November 2009- March 2011), 131 patient files had been reviewed and 79 patients had been followed up, resulting in seven patient appointments.

Prior to December 2011, the main activity by the consultant clinical geneticist and part-time seconded genetic counsellor had been undertaking file review in order to identify patients for clinical review by the full-time EGSP genetic counsellor once in post. The consultant clinical geneticists also had consultations with index patients whose families were eligible for EGSP services and identified these families for follow up by EGSP. This was in addition to the previously mentioned initiation of the pathway for 79 patients and appointments with seven patients.

The clinical strand was able to function fully for eight months starting from February 2012, once the replacement genetic counsellor recruited to EGSP was in post, and had undergone the supervision period (during this time she did not counsel EGSP patients), as the postholder was also newly qualified. Capacity continued to be an issue with the postholder reducing hours allocated to EGSP and the subsequent genetic counsellor working part-time and both then leaving the project to join the West Midlands genetic counselling service. The result of this was that the clinical strand was only fully staffed with the equivalent of one WTE genetic counsellor for 15 months of the EGSP's four and a half years of operation.

Figure 5 Clinical strand timeline – genetic counsellor input to providing genetic counselling to EGSP patients



GC = Genetic Counsellor

Patient numbers seen by the clinical strand

There were concerns over the number of patients being seen by the clinical strand. This in part stemmed from different expectations of patient numbers by the commissioners, compared with those of the consultant clinical geneticists and genetic counsellors. From the consultant clinical geneticists' perspectives, the AR conditions that EGSP focused on were rare conditions, and so the numbers of people 'at risk' for these conditions and resident in the three Birmingham PCTs would be few. The commissioners had anticipated greater numbers being reviewed and provided with enhanced genetic services. The differences in expectations between the project commissioners and the clinical genetics providers may not have been apparent to both parties at the start of the project.

Another reason for the low numbers of people being seen was that the decision-making process to undergo genetic testing, and in particular cascade testing, is a lengthy one for many individuals and families. The decision to take up cascade testing is often dependent on a number of factors such as the age of 'at risk' relatives. If a child is 'at risk' of being a carrier, in line with UK professional guidelines, parents often decide to postpone testing until the child is of an age to participate in the decision-making. Deciding whether to share genetic information with other family members is often a complex process depending on family relationships, timing as to when to share sensitive information and considerations connected to impact on the wider family. In families where marriages are arranged, stigma associated with genetic conditions may impact on whether such marriages proceed. As a result, it is often many years after the initial contact with the clinical genetics department to discuss cascade testing that families decide to proceed, and this would not take place within the timescale of EGSP. The EGSP clinical strand did note that during the last year of the project some individuals who originally did not want a genetic counselling appointment were making contact with the service. As a result it is likely that the impact of EGSP will extend beyond the time period captured by the activity monitoring data.

Deciding whether to share genetic information with other family members is often a complex process depending on family relationships, timing as to when to share sensitive information and considerations connected to impact on the wider family

Monitoring of the strand activity

As with the other strands, monitoring requirements were agreed between the evaluation team, the EGSP Project Manager and genetic counsellors.

A database to collect the data from the clinical strand was developed by the IT department at Birmingham Women's Hospital. Due to the small number of patients seen for the first year of EGSP, little patient data was entered for this period and only related to initial steps of the pathway. The database was only tested for its functionality at a much later stage, At that later point the limitations of the database became apparent.

Once patients started to be seen in greater numbers and the EGSP team tried to enter data, they found the system did not meet their needs. Problems with the database, and the decision to collect additional data items to better reflect the patient pathway necessitated changes to the database. The EGSP Project Manager requested support from the IT department but was unable to obtain it in the timeframe required. A system of monitoring the activity using a number of manual spreadsheets was adopted, so that in the absence of a database,

evaluation data could be submitted. This made data collection laborious and producing monitoring data required a high level of familiarity with the spreadsheets. Staffing changes in the strand resulted in multiple people using the spreadsheets, often in relation to patients seen by their predecessor. Despite these difficulties, the project was able to supply data for the period from November 2011 until the end of September 2013, which was the main period of activity of the clinical strand. This activity is reported in the section below.

Clinical strand activity November 2011- end September 2013

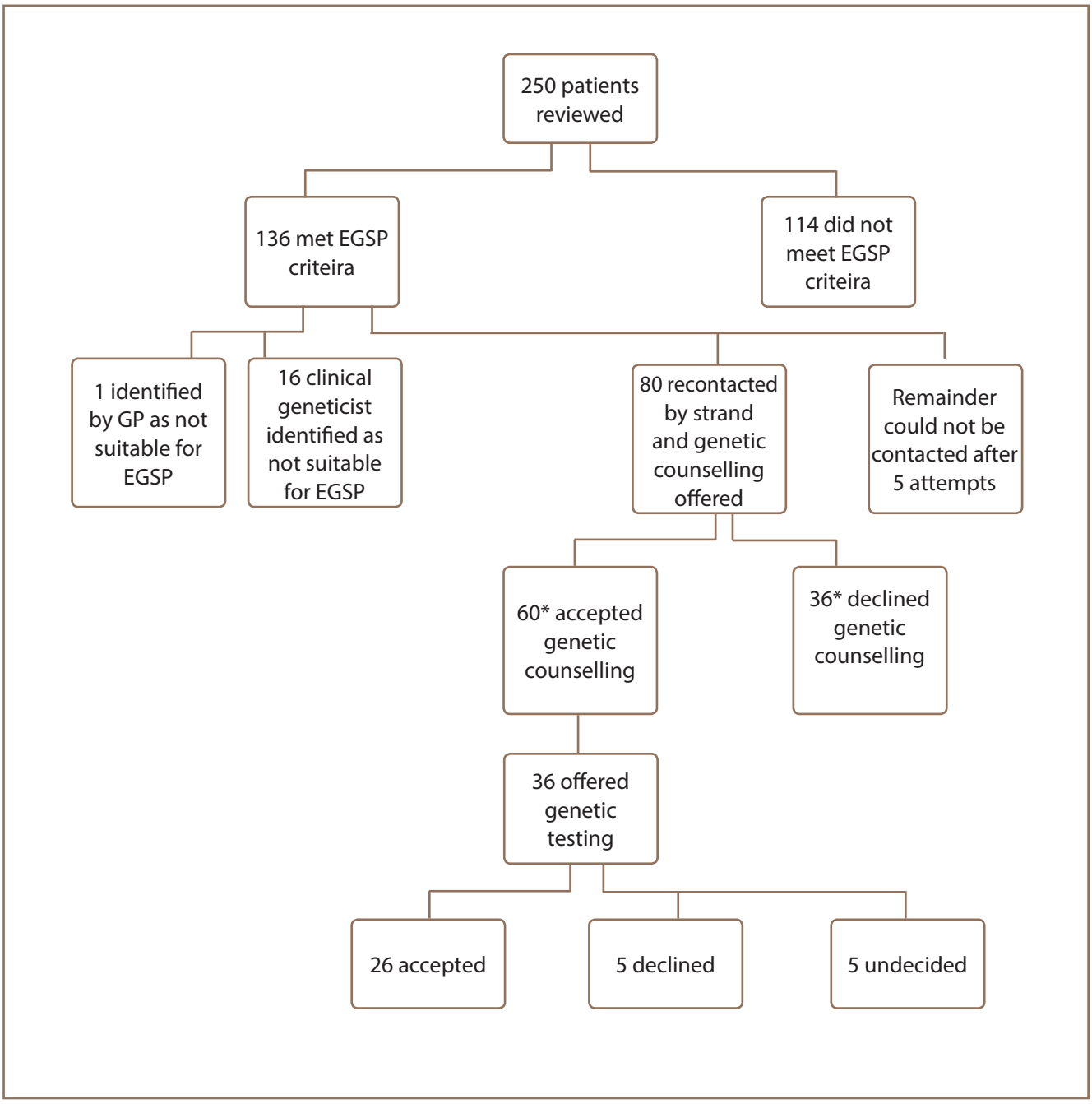
Individual patient review

The figures for activity undertaken as part of the clinical strand, encompassing the process from patient review to the offer of genetic testing, are set out in Figure 6. Two hundred and fifty sets of patient notes were reviewed and of these 114 (46%) were found not to meet the EGSP criteria. In a few cases molecular testing was still being developed and was not available to the patients during the time period of the clinical strand's activity. One hundred and thirty-six patients were suitable for EGSP (54%). For sixteen of the eligible patients (12%), the consultant who had been approached to confirm whether patients should be offered EGSP services advised they were not suitable for EGSP follow up – this could be for a variety of reasons such as recent bereavement, or that they were currently being seen by another member of the clinical genetics department. In only one case did the GP advise that the patient should not be approached by EGSP. In all, 80 patients were recontacted by EGSP and offered genetic counselling, which was about a third of the reviewed patients. The remaining patients were not offered genetic counselling as they could not be contacted.

Of the patients who were offered genetic counselling, 36 declined the offer (37%) and 60 (63%) accepted. Some of those who accepted included partners who were not the index case, and so the total number who both declined and accepted counselling is greater than the number of eligible patients who were recontacted.

Thirty-six patients were then offered genetic testing, 26 of whom accepted (72%) and five declined (14%). The remainder were undecided. 143 patients completed the full clinical pathway to the endpoint that was relevant to each individual. This number represents more patients than had been originally identified as eligible for EGSP - and so had embarked on the pathway - as some partners of the index patient were also offered EGSP genetic counselling or testing.

Figure 6 Numbers of patients reviewed and offered genetic counselling and/or testing



* Some of those who accepted genetic counselling included partners of the index case and so the total number who both declined and accepted counselling is greater than the number of eligible patients who were recontacted.

Cascade testing

As well as providing information on individual patient review, the clinical strand provided data on the numbers of individuals who had been offered cascade testing and the potential numbers for whom cascade testing might be relevant. Due to sensitivities that affect discussion of the wider family, the genetic counsellors felt they often only received partial information as patients were willing to speak only about parts of the family or certain family members. Therefore, numbers relating to the potential for cascade testing can only be estimates and are likely to be an underestimate.

Discussions relating to cascade testing did extend to siblings, and in some cases, adult nieces and nephews. When discussing siblings of the affected child who might benefit from genetic testing, information was provided on how to contact the genetics service in the future as these siblings were usually too young to be tested at the time of contact. In some cases, after discussion with the parents, the siblings were registered in the family file and the genetic counsellor wrote to the child's GP so that a reminder to offer genetic counselling at the appropriate time could be placed in the child's notes. Although the offer of cascade genetic counselling and testing was made to wider family members, other than in a very few cases it was only taken up by immediate family members during the time-frame of the project. The immediate family members were adult children of the index case living in the family home, or a parent of the index patient who had not previously been tested.

In all 188 families were reviewed. This was undertaken by reviewing the case notes. In addition, there were a few referrals to EGSP. 129 of the reviewed families were recontacted either by telephone, or in the clinic or through a home visit. The family pedigree was updated for 72 of these families. In 77 families 'at risk' family members were identified. To assess the number of potentially 'at risk' family members that could benefit from a project such as EGSP, the genetic counsellors were asked to estimate the number of families with different numbers of 'at risk' family members, most of whom were resident in the West Midlands and so could have been eligible for EGSP. This was undertaken for 68 of the families. In about half of the families (54%) there were 1-10 potentially 'at risk' family members that could have benefited from EGSP. For a third (32%) of families, there were 11-20 potentially 'at risk' family members; five families (7%) had approximately 21-30 'at risk' family members; and four families (6%) had 31+ family members with members who would have been mostly eligible for EGSP review. In all, the genetic counsellors identified approximately 786 family members who were eligible for genetic counselling through EGSP and who could have been contacted by the index patient or the index patient's parents. Such offers of cascade testing are made to family members via the index patient and, as discussed earlier, there are a variety of reasons why the index patient may not make this offer to family members or not in the timescale of EGSP.

In all 188 families were reviewed. 129 of these families were recontacted either by telephone, or in the clinic or through a home visit. The family pedigree was updated for 72 of these families. In 77 families 'at risk' family members were identified

Of the 786 family members who might be eligible for EGSP review, 395 were discussed with the proband or proband's parents by the genetic counsellors with a view to the proband contacting them. For 260 of these family members, the proband agreed to contact the family members. For 37 of these family members there was known contact by the proband. This resulted in 48 offers of genetic counselling, as in some cases more than those discussed with the proband were offered counselling. Forty-five of the 48 accepted genetic counselling.

Fifty-four family members were then offered genetic testing. The number was greater than those who received genetic counselling (45), as sometimes the partner of the individual who had received genetic counselling had been counselled in the past, or had received written information from the service, and felt they had sufficient information to decide that they wanted to undergo genetic testing without a counselling session. In all such instances, a genetic counselling session had been offered to the partner. A total of 56 genetic test offers were accepted. This included some individuals who were referred to EGSP having already had genetic counselling, and so no offer of counselling was made. For a small number of individuals it was relevant to offer more than one genetic test and so two genetic tests were offered. Thus there were more genetic tests accepted by family members than family members offered genetic tests after genetic counselling. Nine family members were still considering the offer and were undecided at the time the clinical strand ended. An additional 121 'at risk' children were identified by family members as potentially wanting to take up the offer of genetic testing on reaching the appropriate age for testing.

As part of their interaction with EGSP, 35 individuals reported that they had decided not to marry within the family. Marriage intentions were not specifically asked about by the genetic counsellors but in some instances were raised by the person being counselled and noted by the genetic counsellor. In all, 169 families with eligible conditions were identified by the clinical strand of EGSP.

Figure 7 Cascade process and potential numbers of patients generated by cascade

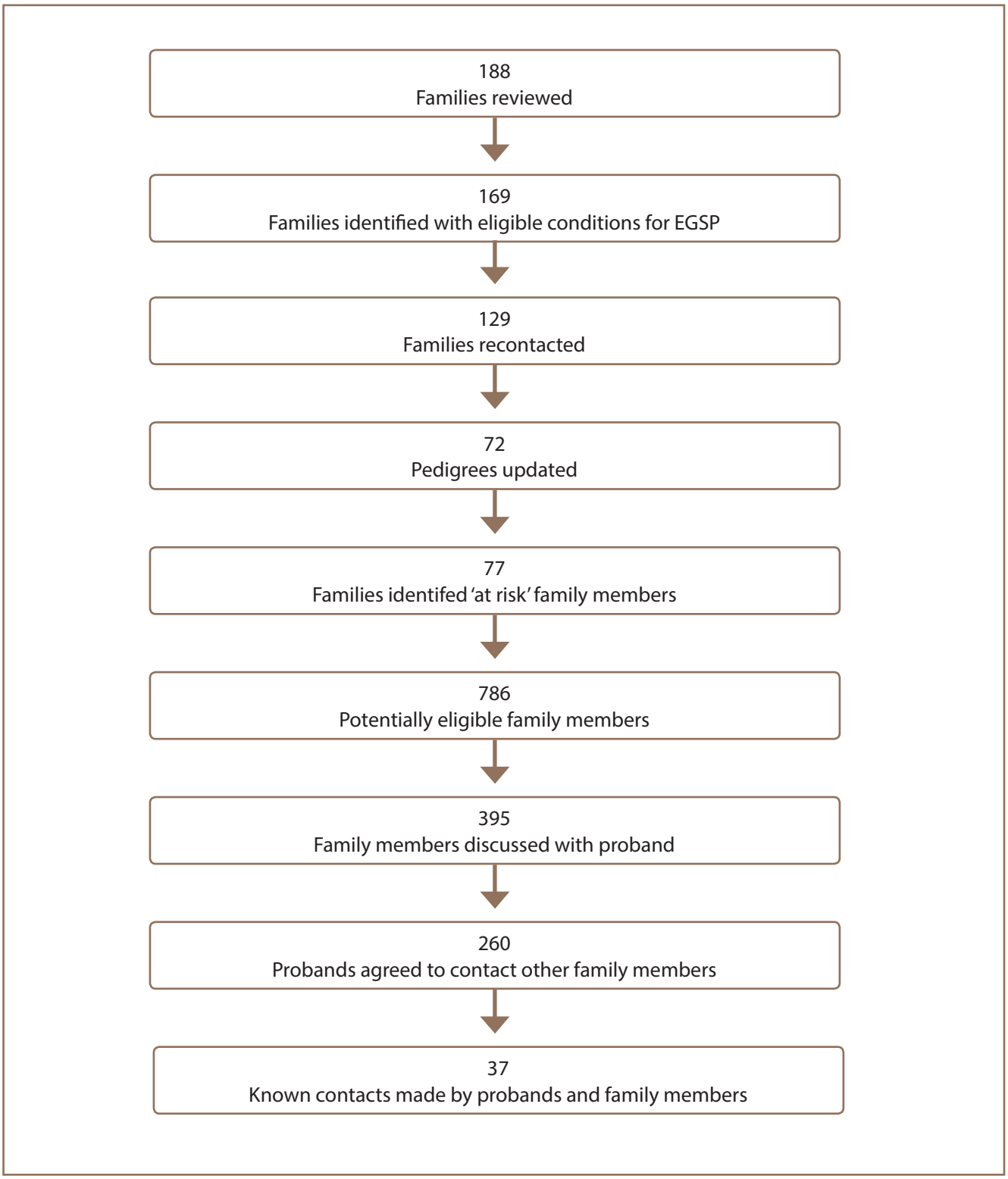
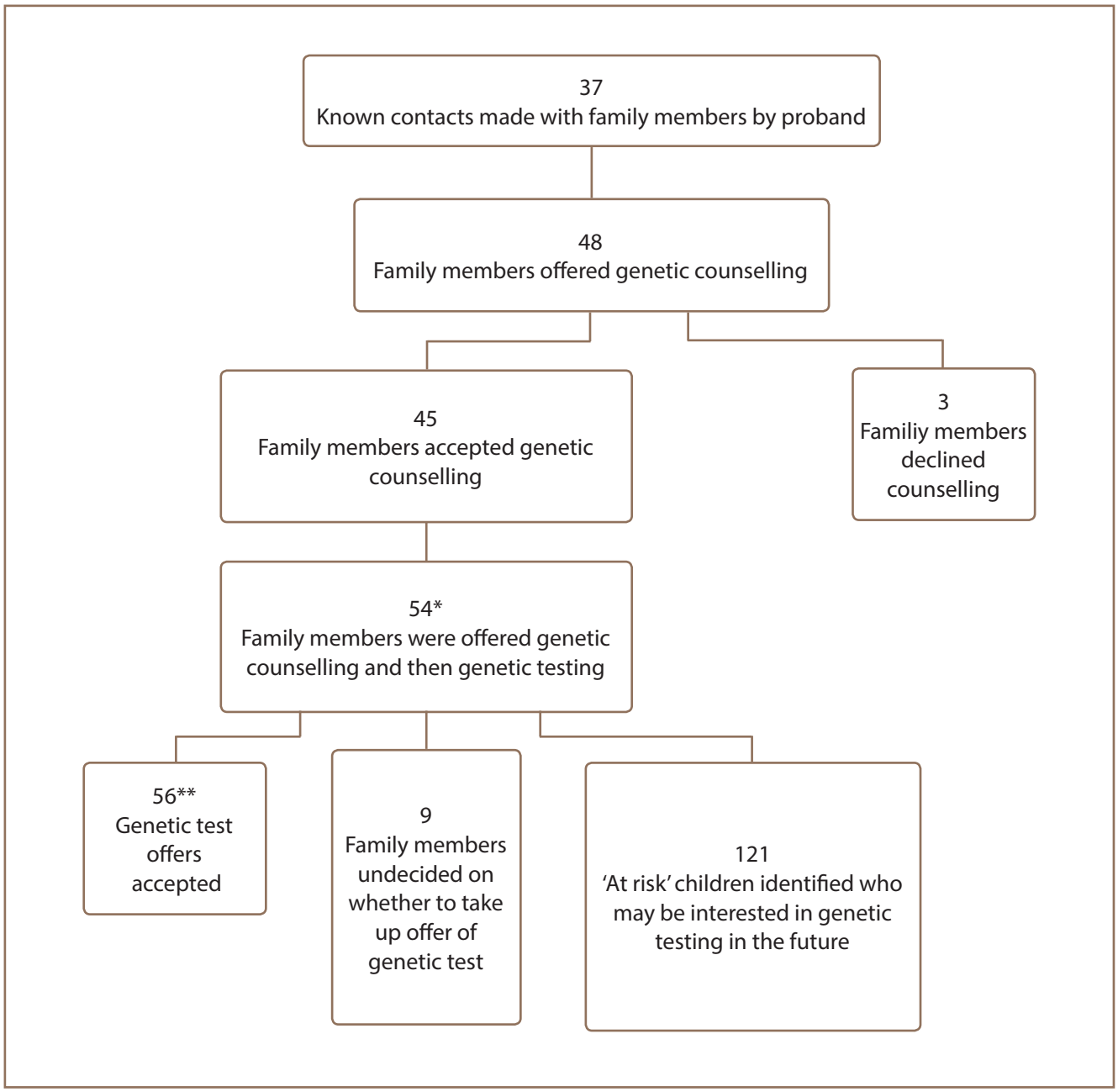


Figure 8 Offers of genetic counselling and genetic testing to family members via the cascade process



*More people were offered genetic testing than accepted genetic counselling as other family members may be offered genetic testing (such as the patient's partner) following the original family member's genetic counselling session and felt they had sufficient information and so refused the offer of genetic counselling.

**Some individuals were offered genetic testing without having been offered genetic counselling, as they had already received genetic counselling before being referred to EGSP. In addition, due to their clinical presentation, some individuals, were offered more than one genetic test and so overall the total of tests accepted and undecided individuals is greater than the number offered testing.

Self- referrals to EGSP

Access to clinical genetics services is via GP referral or via other clinicians. Members of the public had the opportunity to self-refer into EGSP services. This option taken up in only ten instances. Two arose from use of the Talking Genetics website, one of which was from a person not residing in the West Midlands, and so was guided to another regional genetics service. Nine of the ten self- referrals were suitable for EGSP and were offered genetic counselling, eight of whom took up the offer. Six of the eight were then offered genetic testing and all took up the offer. Of these, five had completed the pathway by the end of the clinical strand's period of operation. In addition four children were identified who may be interested in carrier testing once they reach an appropriate age to decide whether to take this up.

Work with GPs and other clinics

In addition to providing counselling to patients known to the clinical genetics department, the project attempted to reach out to patients who might be eligible, but had not been referred to the department. Genetic counselling sessions were planned to take place in GP surgeries. Although attempts were made to set this up, it proved difficult to achieve. For example the GP practice approached asked for the project to pay for use of its surgery for the genetic counselling clinic.

Another initiative was to work jointly with clinics where there were likely to be a number of patients with AR conditions who may not have been referred to Clinical Genetics. These clinics included the paediatric metabolic disease and adult renal clinics. In the case of the metabolic clinic, this approach was limited by lack of access to consulting rooms where genetic counselling could take place. It was not appropriate to use waiting room space to approach patients due to confidentiality issues. As a result it was agreed that leaflets about EGSP would be left with the specialist nurses to be handed out to patients.

A number of sessions took place in the renal clinic, and the following provides an example of the benefits of such an approach.

Since April 2012, five families have accepted genetic counselling as part of EGSP whilst attending a follow-up appointment in the renal clinic. Of these families, four had previous input from the clinical genetics department to varying degrees. The final family who were not previously known to the department have since undergone genetic testing. Genetic testing involved a mutation screen in the index case, in addition to genetic testing to confirm the carrier status of both parents. This process has successfully identified the gene alteration in the family, which will enable carrier testing for a future partner of the index case and if they wish, prenatal testing and cascade testing in the wider family. If this family had not been identified through EGSP, it is possible that they may not have had the opportunity to benefit from this new information and the associated options.

Referrals from GPs and other clinical services (including the clinical genetics department)

There were eight referrals from GPs in the period from November 2011 – September 2013. None of these referrals came from the practices that had participated in the primary care strand of EGSP. Four referrals were made from renal clinics, and two from obstetrics and gynaecology clinics as a result of the joint clinics. Twenty-six of the people seen by EGSP were as a result of referrals from the clinical genetics department, mostly from the consultant clinical geneticist who managed EGSP. Half of these referrals occurred in the last six months of the project. Arising from these referrals, 19 individuals were offered genetic counselling, 12 took up the offer and eight were offered genetic testing. Thirteen of the 40 referrals to EGSP had completed the pathway by the end of September.

At the close of the clinical strand there were six couples still on the pathway – they were contacted by letter with the option of making an appointment if they wished to proceed with genetic counselling and / or testing, as relevant for their situation.

In addition to offering genetic counselling and genetic testing, the clinical strand provided support to the project as a whole, and to the educational strand in particular, through contribution to the Talking Genetics website content, the development of the educational materials, referral guidelines and referral sheets. The clinical strand also undertook some teaching of health professionals, primarily in the period when there was not a professional educator in post. These activities took up a considerable amount of time that was additional to the core work of the clinical strand.

Achievement of the deliverables

Deliverable 1: Mapping of the range and relative frequency of AR conditions in the Pakistani and other communities in Birmingham, particularly those contributing to perinatal and infant mortality

The deliverable was achieved in that AR conditions were selected for patient review and through delivery of genetic counselling and genetic testing services.The range and frequency of different AR could not be mapped for Pakistani and other minority ethnic communities due to ethnicity fields being incomplete, and so they could not be used to select the conditions for this process. As a result the conclusions on the range and frequency of AR conditions were based on professional judgement of the consultant clinical geneticist arising from working with patients' representative of the target ethnic groups. To supplement this, a mapping exercise was undertaken prior to the selection of the conditions, through examination of 1800 sets of notes of patients with metabolic and neurological disorders where previously a diagnosis had not been possible and, where possible, ascribing a diagnosis. Hence, this deliverable was partially achieved.

In addition, attempts were also made to ascertain the cause of death for still births and perinatal deaths within the 'congenital anomalies' category in the West Midlands Perinatal Institute's registry. Full details are presented in chapter 3.

Deliverable 2: Adaptation of the clinical genetics IT system to allow review and recall of at risk families and to capture all activity related to the project.

The clinical genetics IT system was unable to capture all the activity related to the project and spreadsheets were used.

Deliverable 4: Previously seen families re-contacted by genetic counsellors to offer carrier testing. Newly referred families seen to be offered genetic counselling and carrier testing. (Depends on 1)

This deliverable has been achieved. It could have been achieved more fully if more families had been re-contacted by the EGSP genetic counsellors. This was limited by staffing capacity issues that have been discussed. Carrier testing beyond immediate family members was very limited. In addition, very few families were referred to EGSP from the clinical genetics department or from other specialties. Clinics did not take place in the community or in primary care, further limiting the scope for identification of suitable families for EGSP activity.

Deliverable 5: Where appropriate running genetic counselling clinics in GP practices to increase accessibility of services.

Consultant specialists conducted two clinics which took excessive investment of time and effort (time spent on organising clinics, finding suitable venues, agreeing locations and finding suitable space). These factors were recognised as being a major issue and hindered any further development, particularly as these health centres could not provide an ongoing regular commitment to use of the venue without payment. Such payment had not been anticipated and budgeted for. Therefore, deliverable five was not met on this basis.

Deliverable 6: Increased referral for genetic counselling of families from GP practices in which genetic counsellors have been based.

This deliverable was very much dependent on the outcome of deliverable 5, and finding suitable venues and accessibility and was therefore not achieved.

Patient views

The clinical strand genetic counsellors identified five patients who had agreed to be interviewed about their experience of receiving EGSP genetic counselling and testing. Four patients were interviewed by the community educator – a member of the EGSP team who had not been involved in providing genetic counselling and testing services to the patients. The fifth patient could not be contacted. Patients were asked whether they had understood why they had been invited for genetic counselling and testing; whether they understood what would be involved and the information that the testing would provide; and whether they understood the results and what the implications of being a carrier was for themselves and other family members. They were also asked about their overall experience of EGSP services; whether any improvements could be made to enhance their experience of the services received; whether they required further information; and if they felt able to discuss risks and carrier testing with other family members as a result of their contact with EGSP. The questions were designed to be as comparable as possible to the interview questions used to assess patients' experience of the primary care strand.

The small number of patients interviewed and the fact that patients were not randomly recruited for interviews means that the interviews can only provide an indication of patients' experience of the clinical strand of EGSP. Nonetheless, all responses were very positive in terms of patients' understanding of the reasons for being invited for counselling and testing; the information that the testing would provide; the accuracy of their explanation of the significance of being a carrier for themselves and for other family members; and their confidence in being able to talk about risks with other family members. They all felt that their experience of contact with EGSP had been very good and there were no suggestions of improvements that would be beneficial. One patient noted that she had not understood what would be involved in the genetic counselling and testing process until she saw the genetic counsellor. The interviewer also explained that genetics education was being offered in the community as part of EGSP, and asked whether prior understanding of genetics and carrier testing would have been helpful. All four of the interviewees felt that this would have been helpful, suggesting an educational need. The views of this very small sample of patients suggested that EGSP services were well-received and that they enhanced both genetic understanding and the ability to share this understanding with other 'at risk' family members.

Discussion and conclusions

The clinical strand was the key component of EGSP. The primary purpose of EGSP was to deliver an enhanced genetics service. EGSP was partially successful in delivering this. The clinical strand did not function at full capacity for most of the period that EGSP was active. More conditions could have been selected for review and more patients could have been seen had the strand been fully staffed. Since the anticipated patient numbers to be seen during the project were not set at the outset, it is not possible to quantify the extent to which the clinical strand met its primary objective.

The mapping of AR conditions in order to focus the rest of the activity within the clinical strand could not be achieved, due to limitations and completeness of the clinical genetics database regarding the coding of ethnicity. As a result, at best a partial mapping of the AR conditions affecting the target groups was achieved, based on professional judgement. Clinical expertise from working with the target communities, along with the identification of which genetic tests would bring most benefit in identifying causal mutations, were the basis for patient review and EGSP services. This allowed identification of patients who could benefit from EGSP services.

There was limited referral from other medical disciplines and from within the clinical genetics department service. This limited the potential for EGSP services to be offered to the target population. It is likely that patients seen by non-clinical genetics specialists could have also benefited from a consultation on the genetic aspects of their condition. EGSP had the potential to meet this need, but did not do so for a variety of reasons, including staffing capacity issues within EGSP and a lack of consulting rooms. Private consulting rooms are a pre-requisite, as confidentiality needs to be maintained when discussing genetic conditions. The joint clinic model should be explored further if clinic space can be found.

Outcomes

Patient review

250 patients records reviewed

60 patients participated in genetic counselling

36 patients offered genetic testing

26 patients took up genetic testing

Family based outcomes

188 families reviewed

169 families identified with conditions eligible for EGSP review

72 pedigrees updated

77 families identified with 'at risk' members

37 known contacts made by proband with family members regarding cascade genetic counselling and testing

45 family members took up the offer of genetic counselling

56 family members took up the offer of genetic testing

121 'at risk' children identified who may take up genetic testing at an appropriate age.

EGSP achieved the delivery of services as set out in the pathway documents. Two hundred and fifty sets of patient notes were reviewed, leading to 80 individuals being recontacted by EGSP and genetic counselling being offered. This resulted in 60 individuals receiving genetic counselling. Thirty-six individuals were offered genetic testing, of whom 26 accepted the offer.

One hundred and eighty-eight families were reviewed and potentially over 700 family members were identified who may be 'at risk' and could benefit from genetic counselling and testing. Almost 400 family members were discussed with the proband or the proband's parents, resulting in the proband making known contact with 37 family members. By the end of the project, 56 family members had been offered and had accepted genetic testing, and 169 families had been identified with eligible conditions for EGSP services.

There are limits to what can be achieved in terms of uptake of genetic testing in the time period of a Project such as EGSP. This is particularly true of cascade testing, where a range of factors influence the decision of whether families take up the offer of genetic testing. Intentions regarding genetic testing are often acted upon at a later time - as children reach an age to make such decisions or when couples face reproductive choices. It is likely that the impact of EGSP will extend beyond the timeframe of EGSP, as families make contact with clinical genetic services in the future according to their needs at different points in their lives.

In practice, cascade testing was limited to immediate family members. One hundred and twenty one children (such as siblings) under the age of 16 were identified, who at a later stage may decide to take up testing. It is unclear how far cascade testing is successful in routine clinical genetics practice or whether, as in the case of EGSP, cascade testing is usually limited to the immediate family. This was not an issue that the evaluation explored, and so is not in a position to make a judgement on the extent of the success of EGSP on the cascade testing criterion.

Family dynamics, and in particular stigma associated with AR conditions, which may be particularly important in families who practice arranged marriages, are likely to impact on the extent to which genetic information is communicated within families and in turn the uptake of cascade testing.

EGSP services were well received by the small group of patients who were surveyed about their experience of receiving genetic counselling and genetic testing services as part of EGSP.

The adapted clinical genetics IT system was not able to support the collection of data intended to monitor the review and recall of 'at risk' families and to capture all patient pathway activity related to the project. A manual spread sheet was used instead. This was cumbersome and did not track the progress of individual patients and families through the pathway, and so required interpretation from those who had entered the data. A commissioned external database would have been an alternative to an in-house system, and could have met the needs of EGSP if specified so that ongoing support was provided to cater for adaptations as the project developed.

The establishment of genetic counselling clinics in GP practices was attempted but not achieved. There was no increased referral activity from primary care. One of the reasons for not setting up these clinics was the request for payment to use surgery space which had not been anticipated and so not specifically budgeted for. Since genetic counselling clinics were not set up in primary care, it is still unclear whether AR conditions are too rare for general practice-based clinics to be an appropriate setting for EGSP genetic counselling and testing.

Case studies

The case studies outlined below demonstrate the application of molecular testing for conditions for which testing was developed through the EGSP. These case studies focus on the processes and outcomes for some of the families who have utilised the EGSP genetic clinical services.

Case study 1: EGSP activity with a family with two different autosomal recessive conditions in the same family

Background

In some families consanguinity increases the risk of two (or sometimes more) autosomal recessive conditions. For these families, genetic counselling is extremely important as the genetic risks are complicated and the information needs to be accurately and clearly portrayed to the family. These risks are a 1 in 16 chance of having a son or daughter affected by both AR conditions; a 3 in 16 chance of a child inheriting the first, but not the second condition; a 3 in 16 chance of a child inheriting the second, but not the first condition; and a 9 in 16 chance of having a child who has neither condition.

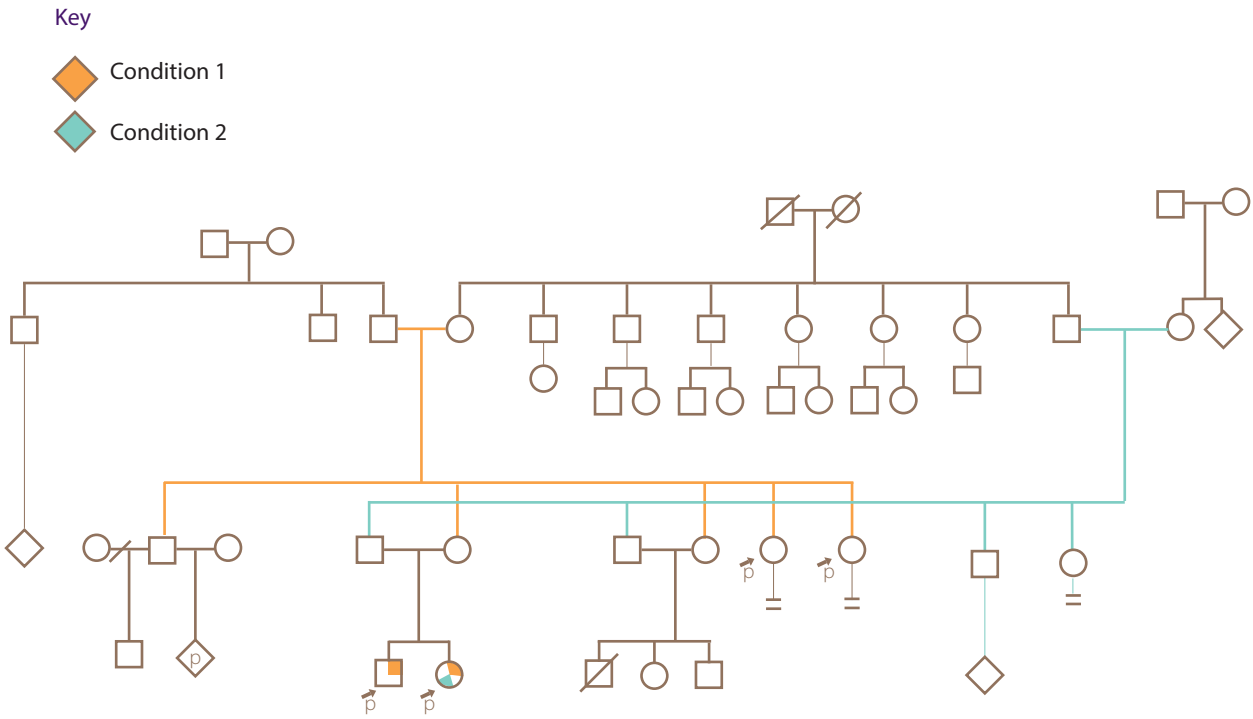
Genetic counselling process

This family has been known to the clinical genetics department since 2006 - following the referral of the couple's one year old daughter with a number of complex medical problems, including severe visual impairment, microcephaly and significant learning difficulties. The couple are first cousins. Their first child also has microcephaly and learning difficulties, but no visual symptoms. Initial assessment suggested two different autosomal recessive conditions in the daughter. For one of these conditions routine DNA testing was available, and the diagnosis was confirmed a few months after the first clinic appointment. Testing for the second condition was not routinely available. The oldest child was assessed and thought to have this second condition, though this could not be confirmed by genetic testing.

Testing for the second condition in this family was developed as part of the laboratory initiatives of the EGSP. The parents were subsequently re-contacted by the clinical team, both children underwent testing, and the second diagnosis was confirmed by DNA testing. The couple were already aware of their own genetic risks, but were now in a position to be offered accurate pre-implantation genetic diagnosis for both conditions, for which they have been referred.

The couple have also discussed the availability of genetic testing with the wider family. Four other family members have now received genetic counselling, undergone genetic testing and had their own risks of having affected children defined. In all cases we have been able to reassure very close family members that they are not at risk of having children affected by either autosomal recessive condition. This would not have been possible without the development of genetic testing for the second recessive condition as part of EGSP.

This is a highly motivated family who are keen to understand the genetic risks in the family, and further individuals have indicated to us that they will come forward for carrier testing prior to starting their own families. The family have built up a trusting relationship with the genetic counsellor and have contacted her on several occasions for informal advice.



Case study 2: EGSP activity with a family where there was no DNA is available from the affected index case

Background

Mucopolysaccharidoses are a group of autosomal recessive metabolic conditions which arise due to a deficiency in one of several enzymes involved in complex carbohydrate metabolism in the body. As a result of this deficiency there is a build-up of complex carbohydrates known as mucopolysaccharides, which affect several organs, leading to a significantly reduced life expectancy for affected individuals. At present, clinical treatment is limited to symptom relief and supporting the needs of patients.

Genetic counselling process

This family have been known to the department since 2001, when they were referred by their midwife during their fourth pregnancy as they wished to discuss prenatal diagnosis. The couple had recently lost their eldest son due to a metabolic condition involving mucopolysaccharidosis, which had been diagnosed on a biochemical basis. Ten years later this file was reviewed as part of EGSP, and we offered the family an appointment to discuss the option of genetic testing for this condition in the family.

We met with the parents on two occasions at their home to discuss the developments in genetic testing for this condition, and to explore this option for the family. Having the opportunity to visit the family in their home, where they are most comfortable, facilitated developing a rapport with the family. We were also not constrained by time or resources, therefore we were in a position to offer extended counselling sessions and multiple appointments where required to support the family. We recapped the genetic basis of the condition, and the family were keen to learn about updates in research into treatment possibilities

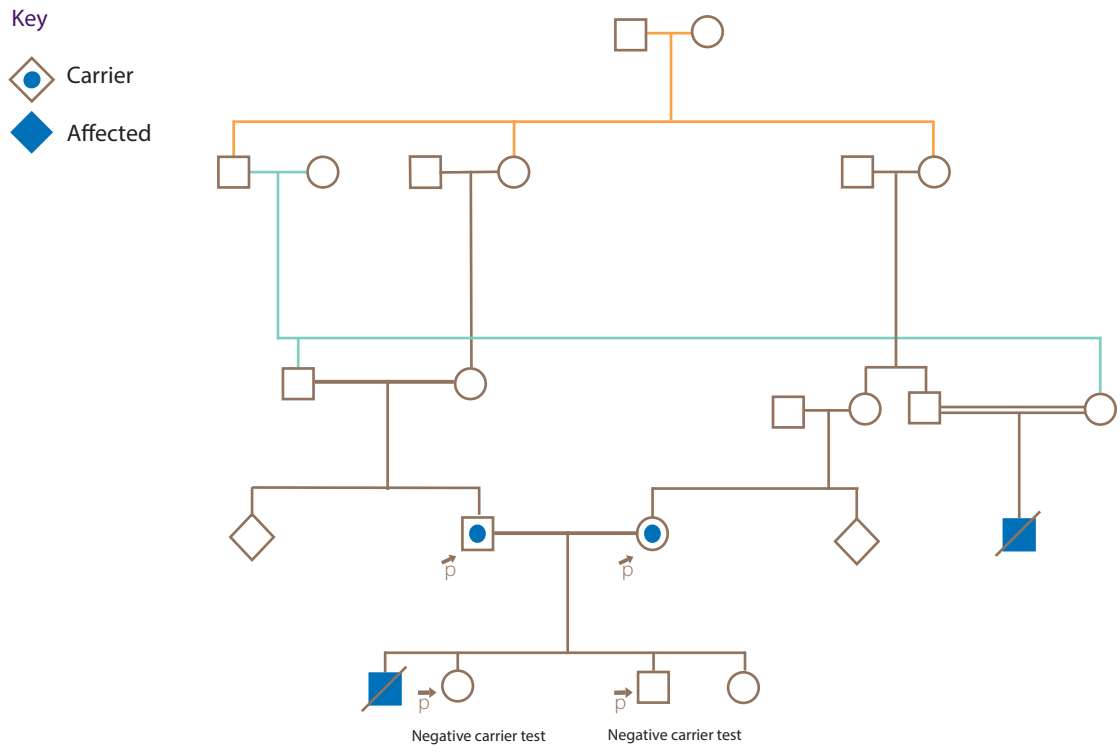
Outcome

The couple chose to pursue genetic testing for the benefit of their other children; however, we had no DNA stored from their deceased son. We explored the possible testing options with our laboratory, and we were in a position to offer genetic testing to the parents directly, which was initiated in one parent. Sequence analysis of the coding regions of the relevant gene using a DNA sample from this parent detected heterozygosity for a pathogenic nonsense mutation. Subsequent testing of the second parent's sample confirmed the presence of the same heterozygous nonsense mutation. These results successfully identified the gene alteration responsible for the metabolic condition which affected their son, and confirmed that this couple are both

carriers of this condition. Based on this result it was possible to offer carrier testing to other family members.

We were subsequently contacted by this couple, as two of their older children wished to discuss carrier testing. We arranged a further home visit to provide genetic counselling to both siblings regarding carrier testing. They chose to undergo genetic testing and, reassuringly, they were not carriers of of the familial condition, which they were both pleased by.

This successful and cost-effective method of identifying pathogenic mutations in consanguineous couples where DNA from the index case is not available has facilitated offering carrier testing for this family. Furthermore, as we have now identified the molecular cause for the metabolic condition in this family, the option of pre-implantation genetic diagnosis is possible, which would not have been the case prior to genetic testing. The family are keen to pursue carrier testing for their younger child in the future and at the appropriate age, demonstrating that the impact of the EGSP project is longitudinal rather than short-term.



Case Study 3: EGSP activity with a family considering their reproductive options

Background

The condition in this family arises due to a deficiency of propionyl-CoA carboxylase, and usually presents shortly after birth. Clinical signs include ketoacidotic coma, hyperammonemia and convulsions. Later presentations are also observed and include hypotonia, intellectual impairment and recurrent coma. Complications that patients with this condition may encounter include: cardiomyopathies, pancreatitis and neurological disorders affecting the grey matter.

Dietary restrictions surrounding protein intake are key to the management of affected patients. Therefore, timely testing at birth is critical to ensure that appropriate advice is provided and that treatment is implemented if required. Carrier testing on a molecular basis enables the clarification of a couple's carrier status ,and thus identifies couples who are at risk of having an affected baby prior to the birth. This ensures that newborn testing is only offered to couples who have been confirmed as 'at risk', thus reducing financial and time resources whilst alleviating unnecessary anxiety in couples not 'at risk'.

Whilst typically diagnosed biochemically, the availability of molecular testing for this recessive condition enables the identification of carrier couples, thus providing them with the opportunity to explore their reproductive options. This relates particularly to pre-implantation genetic diagnosis, which requires molecular confirmation of the gene alteration in the family, and molecular confirmation of the couple's carrier status. Further to this, clarification of a couple's carrier status reduces the need for unnecessary invasive prenatal diagnosis. This is particularly relevant to 'at risk' couples who may have undergone biochemical prenatal testing in the past due to a family history of this recessive condition, where it was not previously possible to clarify if they were carriers or not.

Patient A (indicated on the pedigree) was reviewed as part of the EGSP as she has a biochemical diagnosis of a known metabolic condition. The family were known to the clinical genetics department following their initial referral in 2002, and had previously received genetic counselling, including information regarding recurrence risks and the option of biochemical prenatal diagnosis. The family were regularly seen by the department for follow-up in the period 2002 - 2012.

Genetic counselling process

Having met the recruitment criteria for EGSP, the parents of patient A were contacted as per the contact pathway outlined in Figure 3. The mother of patient A, having received our letter, telephoned the department and wished to arrange an appointment to discuss the available options. The couple were offered a clinic appointment or a home visit, and opted to meet with the genetic counsellor in their home. Genetic counselling was provided which included updating the family history, providing refresher information on recessive inheritance and establishing the couple's needs.

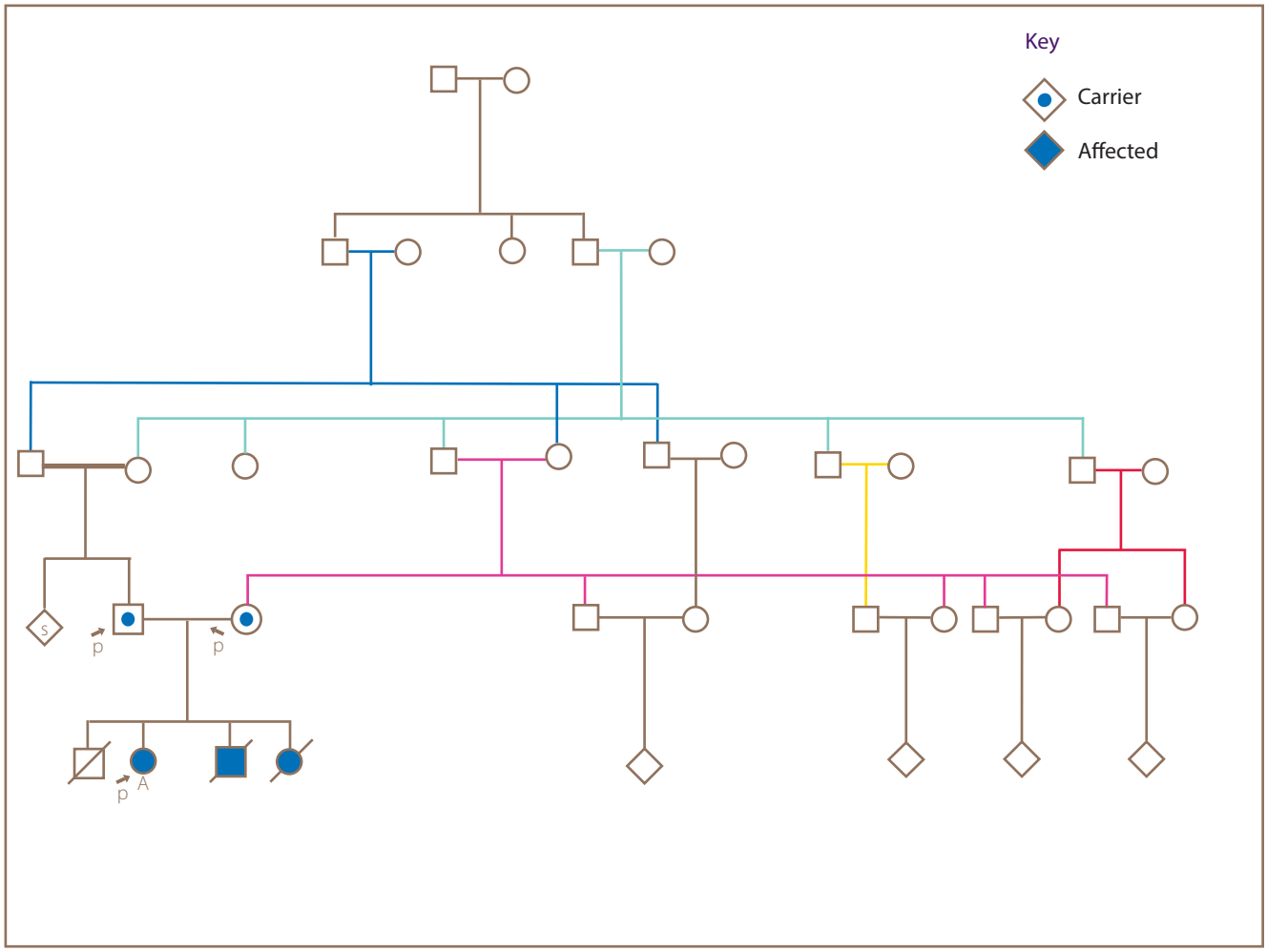
The couple were not keen to pursue invasive prenatal testing during a future pregnancy. Therefore, the option of molecular testing was explored for the couple's affected daughter, which would widen the reproductive choices available to the family to include pre-implantation genetic diagnosis (PGD). Further to this, a molecular diagnosis would enable carrier testing for the wider family.

Outcome

As the couple were open to discussing carrier testing with their relatives and were keen to explore reproductive avenues which did not involve invasive prenatal diagnosis, they chose to proceed with genetic testing for their child. Following analysis of the coding exons of the genes associated with this metabolic condition, a homozygous C to T base substitution at nucleotide position +2 (c.1498+2C>T) was identified in one gene. This was considered to be pathogenic and was consistent with a diagnosis of the familial condition. Furthermore, it made it possible to offer carrier testing to patient A's parents and family members. Following confirmation of the gene alteration responsible for their daughter's condition, both parents had their carrier status confirmed.

This couple benefitted from a follow-up appointment to explain their results and to discuss their reproductive options further. Currently this couple are in the process of deciding whether to attempt to conceive naturally and have testing at birth, or to pursue PGD which has been made technically feasible through testing as part of the EGSP service.

As carrier testing is now possible for the wider family, information letters regarding this option have been provided to the couple for the benefit of their extended family members.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7 Laboratory component of the clinical strand

The improved availability of molecular testing for AR conditions in the target population of EGSP was an important component of the clinical strand.

Objective 1 of EGSP, as set out in the project initiation document, was:

'Improved access to molecular testing for AR conditions – a prerequisite for carrier testing.'

Objective 8 of EGSP was also relevant to the laboratory component:

'Identify causative mutations in genes known to cause AR conditions in affected family.'

The two are interdependent, as achievement of the first objective is in part dependent on the identification of the causative mutations, particularly when new genetic tests are developed.

One of the ten deliverables focused on the laboratory aspect of EGSP. Deliverable 3 required:

'Improved molecular genetic testing for AR conditions associated with early childhood mortality and morbidity. '

This was to include:

1. The identification of the mutation spectrum in a range of AR disorders, including common metabolic diseases to enable prenatal and carrier testing to be offered to affected families and, where appropriate, prenatal testing to be offered to extended families

2. In most cases molecular genetic testing will be accomplished by establishing a new diagnostic service within the West Midland Regional Genetics Laboratory (WMRGL). This will facilitate timely diagnosis of the relevant disease in new cases

3. The identification of common founder mutations in the Birmingham population that might be suitable for population screening.

Identification of the mutation spectrum in a range of AR conditions to enable prenatal and carrier testing to be offered.

It was agreed between the WMRGL and the clinical strand that as part of EGSP there was scope for developing genetic testing for 30 genes not previously available in-house. The following criteria were utilised to choose which AR genetic conditions should be selected for test development:

1. Condition is relatively common amongst families from ethnic minorities in the West Midlands

2. Testing was not previously available in-house

3. Genetic counselling and antenatal diagnosis allow potential treatment from birth for subsequent pregnancies in extended families, or management decisions will be influenced by definite diagnosis.

Genetic tests (see Table1) were developed for 21AR conditions and covered 29 genes. The table indicates which of the three criteria were met as part of the process of selecting the genetic tests to be developed.

The analytical strategy for all of the tests was Sanger sequencing. The reason for using Sanger sequencing was that all of the diseases are caused by mutations that cause a loss of protein function. As a result, the mutation can occur in any part of the gene (and so there are no particular common mutations in 'hotspots').

Two of the 21diseases have common deletion mutations that would not be picked up by Sanger sequencing, and so required additional tests to be developed to detect these (Pompe and Krabbe disease). A further two diseases had MPLA kits already available, which can detect large deletions and duplications – these kits were validated so that they could be used for testing as part of EGSP (for *NPC* and *PFIC3*).

Table 1 Genetic tests selected for development as part of EGSP

Disease	Genes	UKGTN gene dossier	Critieria	Diagnosis or confirmation of biochemical diagnosis
Niemann Pick disease type C	NPC1	Y	1,2,3	D/C
	NPC2	Y	1,2,3	D/C
Gaucher disease	GBA	N	1,2,3	C
Progressive familial intrahepatic cholestasis	ATP8B1	Y	1,2,3	D
	ABCB11	Y	1,2,3	D
	ABCB4	Y	1,2,3	D
Citrin deficiency	SLC25A13	Y	1,2,3	D/C
Pompe disease	GAA	N	1,2,3	C
Metachromatic leukodystrophy	ARSA	N	1,2,3*	C
Saposin	PSAP	N	2	D/C
Krabbe disease	GALC	N	1,2,3*	C
Sanfilippo syndrome	SGSH	N	1,2,3*	C
	HGNSAT	N	1,2,3*	C
	NAGLU	N	1,2,3*	C
	GNS	N	1,2,3*	C
Fowler syndrome	FLVCR2	Y	1,2,	D
Propionic acidaemia	PCCA	Y	1,2,3	C
	PCCB	Y	1,2,3	C
Glutaricacidaemia type I	GCDH	N	1,2,3	C
Morquio A syndrome	GALNS	N	1,2,3*	C
I-cell disease	GNPTAB	Y	1,2	C
Argininosuccinicaciduria	ASL	N	1,2,3	C
ASPM microcephaly	ASPM	Y	1,2,	D
Isovalericaciduria	IVD	N	1,2,3	C
Citrullinaemia type I	ASS1	N	1,2,3	C
Succinic semialdehyde dehydrogenase deficiency	ALDH5A1	N	1,2	C
Niemann Pick disease type A/B	SMPD1	N	1,2,3*	C
Homocystinuria	CBS[1]	N	1,2,3	C
	MTHFR[1]	N	1,2,3	C
Trichohepatoenteric syndrome	TTC37[2]	Y	1,2,3	D

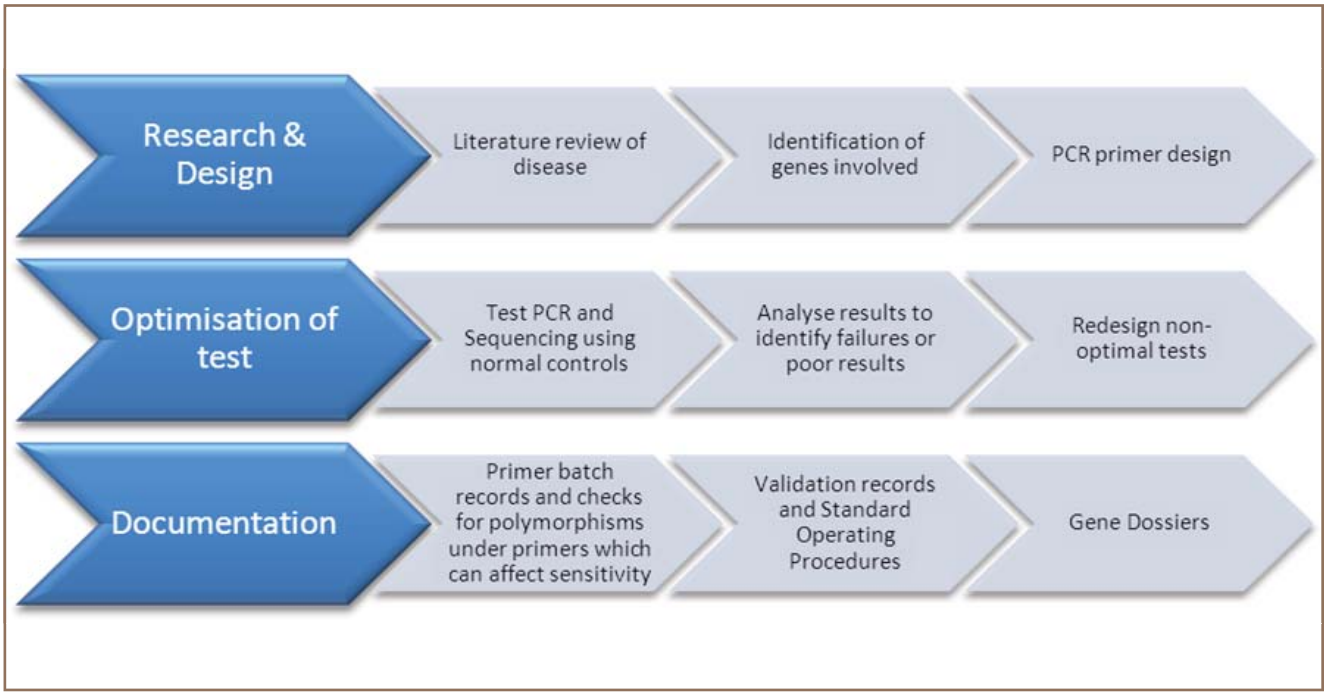
*The asterisks indicate disorders where treatment trials are in progress

1 These genetic tests were developed after EGSP's clinical strand ceased and so were not offered to patients as part of EGSP.

2 In addition a genetic test for Trichohepatoenteric syndrome was commissioned by EGSP. This genetic test was not developed during the course of EGSP but is planned as a new assay using targeted next generation sequencing to sequence many genes at the same time. This assay was in the design phase when the clinical strand of EGSP concluded operation and as a result TTC37 testing was not offered as part of EGSP.

The steps involved in the development of the new genetic tests are outlined below.

Steps involved in developing new tests



Achievement of the objectives and deliverables

The laboratory activities combined with the clinical strand's activities resulted in improved access to molecular testing for AR conditions. This was achieved through identifying the causative mutations in genes that are known to cause AR conditions (objective 8), developing the specified number of genetic tests, and finally, delivery of testing by the WMRGL to the target population and to the wider population (objective1).

The first two components of the laboratory deliverable were achieved: (i) the identification of the mutation spectrum so that genetic testing could be offered to EGSP patients, and (ii) the development of a laboratory service to deliver the testing.

The third part of the deliverable, the identification of common founder mutations in the Birmingham population that might be suitable for population screening, was not achieved. The reasons for not achieving this deliverable were that insufficient mutations have been tested to identify whether any founder mutations have been identified. For a founder mutation to be identified, the same mutation would need to be found in several unrelated individuals.

Activity from the laboratory strand

The genetic tests developed as part of EGSP were offered to:

- EGSP patients, ie. those individuals who met the criteria of EGSP eligibility
- Those living in the West Midlands who did not meet the criteria for EGSP and
- Those living elsewhere and so by definition did not meet EGSP eligibility criteria.

Activity undertaken for each of the three categories of genetic testing using EGSP-developed tests is examined in turn, as well as genetic testing offered to EGSP patients using non-EGSP developed tests.

In addition, as a result of developing testing for EGSP patients, EGSP funding enabled a new area of activity for the WMRGL to be developed. The WMGRL has become a centre for molecular testing for rare liver diseases based on these activities.

1. Genetic testing using EGSP developed tests for patients meeting EGSP criteria

   Thirty-one tests for patients fulfilling EGSP criteria were performed using the newly developed EGSP tests. The majority of testing was for carrier testing (26 of the 31). The remaining five were for diagnostic referrals. All five of the results of the diagnostic tests were positive and 17 of the 26 carrier tests (65%) were positive.

   Prenatal testing was excluded from EGSP activity. However, EGSP genetic counsellors and education staff did advise patients of the information provided by prenatal testing and the reproductive options available. EGSP patients will therefore have the option of prenatal testing in future, if clinically appropriate.

2. Genetic testing undertaken using EGSP developed tests for non- EGSP patients living in the West Midlands

   Some of the testing using EGSP developed tests was offered to patients who were residents in the West Midlands, but did not meet the other EGSP criteria. Such testing would have not been income generating for the laboratory as it would come within the laboratory contract for the West Midlands resident population. A total of 260 tests were performed – of these 33% of the tests arose from referrals by the clinical genetics department, 43% from Birmingham Children's Hospital and 24% from other referrers. The majority for the tests were for molecular diagnosis (71%) and the remaining tests were for carrier status. Of the tests undertaken, seven were for prenatal testing. Twenty-nine percent of the diagnostic tests yielded a positive result, while 70% of the carrier tests yielded a positive result. Of the seven prenatal tests, one identified an affected fetus and four identified carriers of the condition.

EGSP-developed tests provided improved access to specific genetic testing for the West Midlands population and met a national need for access to specific genetic testing.

EGSP-developed tests provided improved access to specific genetic testing for the West Midlands population.

3. Genetic testing undertaken using EGSP-developed tests for non- EGSP patients living outside the West Midlands

EGSP-developed tests were also performed for those living outside of the West Midlands and so by definition were not for EGSP patients. Such tests generated income for the WMGRL. A total of 243 patients were provided with EGSP-developed genetic tests but were not residents of the West Midlands. 45 (18%) were referred from clinical genetics departments, 97 (40%) from the Birmingham Children's Hospital and 104 (42%) from other centres. 194 (80%) were referred for diagnostic tests and 49 (20%) for carrier testing, three of these tests were performed prenatally. Of the diagnostic tests, 30% were positive and of the carrier testing, 82% were positive. Of the prenatal tests, one identified a fetus as being affected and the remaining two fetuses were identified as being carriers.

The EGSP supported genetic testing service also met a national need for access to specific genetic testing.

4. Genetic testing of patients referred by EGSP using non EGSP developed tests

By their nature most AR genetic conditions are rare, and so affect small numbers of individuals. This is even more apparent when testing is offered in a restricted geographical area, as in the case of EGSP eligibility. As the EGSP-developed tests would only be appropriate for a small number of criteria-fulfilling patients, testing using non-EGSP developed tests was also included as part of EGSP activity to improve clinical care and maximise the beneficial impact of EGSP.

Forty-eight genetic tests were requested, and 42 were performed for patients meeting the EGSP eligibility criteria using genetic tests other than those developed as part of EGSP. As expected, all referrals were from the West Midlands Clinical Genetics Department. Five (12%) of the tests were performed for diagnostic purposes and 37 (88%) for carrier testing. As explained above, there were no prenatal tests requested. Of the diagnostic tests performed, five (100%) were positive. Of the carrier testing, 29 (78%) of the results were positive for being carriers, and the remaining eight were negative (22%).

Discussion

It is unclear how systematic the process was for identifying which conditions should be prioritised for genetic test development. The approach taken utilised expert opinion to select the tests to be developed. The selection of tests is a crucial step as the clinical strand then focused patient review and its consequent activity with families affected by those conditions for which the new tests had been developed. Although this approach was not the only approach used, it was the main means of identifying families to work with. Few (less than 10) or no referrals were received for 10 of the 21 conditions for which the genetic tests have been developed. This was regardless of whether patients were West Midlands residents or were living outside of the West Midlands. For two of the conditions no testing had been undertaken. These were tests developed during the latter part of the laboratory test development phase and so it may require longer to evaluate whether the tests developed were the most appropriate ones. Thirty-one genetic tests using the newly developed tests for a total of nine of the 21 conditions were performed for EGSP patients. No EGSP patients had genetic testing for 12 of the 21 conditions.

The number of tests requested for EGSP patients was not within the control of the laboratory but depended on the level of activity within the clinical strand. As a result this limited the amount of testing undertaken for EGSP patients. For much of the life of the project there was limited activity within the clinical strand. In addition genetic testing tends to occur towards the end of the patient pathway and by November 2013 a number of the patients had not reached that end point. The laboratory noted that a substantial proportion of its activity had taken place in the last six months of its EGSP funded operation with 37% of the tests being performed for EGSP patients requiring EGSP developed tests in that period and 69% of the testing for non-EGSP developed tests.

The experience of the clinical strand was that some patients initially decided not to take up testing and at a later point recontacted the genetic counsellors to request testing. This is explored further in chapter 5. As a result some of the genetic testing arising from EGSP activity has not been captured.

All prenatal testing was excluded from EGSP and was undertaken as requests from the clinical genetics department. As a result it is not possible to accurately quantify the number of prenatal tests that arose from EGSP education and genetic counselling activities. There were two positive prenatal test results using EGSP developed tests, one of which was to a mother living in the West Midlands but it is not possible to link prenatal testing with EGSP activity.

Benefits of genetic testing

A molecular diagnosis provided by genetic testing will make accurate diagnosis and prediction of the course of the disease possible. In some conditions, appropriate treatment can be provided following diagnosis which may otherwise have been delayed or not given, resulting in serious clinical consequences. For example, testing for Propionic acidaemia allows early diagnosis of this condition which means that treatment by dietary restriction and antibiotics can begin. This can often prevent brain damage from occurring.

Molecular genetic testing may also prevent repeated testing for other conditions, and will provide valuable information to parents and family members on the cause of illness and disability in the family.

Molecular diagnosis allows accurate cascade screening in the family. Family planning options of pre-implantation genetic diagnosis, invasive and non-invasive prenatal diagnosis can only be carried out if the mutations in the family are known.

Costs of testing and income generated

The income generated by the 243 EGSP-developed tests ordered by services outside the West Midlands was £182,000. As a result the WMRGL was able to make a successful business case to their funding Trust to continue to employ a clinical laboratory scientist, so that the enhanced genetic testing service could continue beyond the funded period (July 2009 - April 2013), and maintain the improved access to genetic testing for the West Midlands population.

Strategy developed for carrier screening in consanguineous couples

EGSP funding enabled a new strategy to be introduced for testing consanguineous couples when a sample from the affected child was not available, such as after the death of a fetus or child, and when DNA had not been banked. The strategy comprised testing the full gene in one parent and then confirming the mutation in the other parent. Without the funding from EGSP this would have been considered too costly a strategy. This strategy works well for conditions which have distinctive phenotypes and only a limited number of genes are involved, so there is a high chance that the parents will have a mutation. Fowlers syndrome is an example of such a condition where the strategy was used successfully. EGSP-developed testing was used to identify that parents were carriers in a number of cases; in one case, parents were subsequently offered prenatal diagnosis.

Legacy of the laboratory component of the clinical strand

Funding from EGSP facilitated the development of a new series of genetic tests, which focused on AR conditions more common amongst families with consanguineous partnerships. The availability of these tests generated sufficient income from outside of the West Midlands for this to be a sustainable service beyond the life of the EGSP. As a result,testing for these conditions will be available for patients who would have met the EGSP criteria beyond the period that EGSP is operational.

Gene dossiers were produced for 12 of the 21 conditions, enabling these tests to be evaluated by the NHS UK Genetic Testing Network (UKGTN) and then, when approved, to be listed on the UKGTN directory. The directory is the main UK resource and is used by clinicians and laboratory scientists to identify which laboratories offer testing - either for specific conditions or for particular genes - and to access tests. It is also a means of evaluating the quality of genetic tests.

In time it is likely that more of the tests will have gene dossiers produced and submitted to the UKGTN. Due to the time consuming nature of developing a gene dossier, priority was given to developing dossiers for those tests where there was no test offered by UK laboratories. The laboratory strand noted that there was an increase in demand for tests once they were listed on the UKGTN website.

The WMRGL has developed a new specialist genetic testing area due to referrals from local liver units. An analysis of the numbers of referrals by disease highlighted that the diseases PFIC, Citrin and NPC elicited the most referrals. The six genes involved in these three conditions are now included on a next generation sequencing panel, which allows simultaneous screening for all six conditions at a reduced cost to the clinician. This has enabled the WMRGL to become a centre for molecular testing for rare liver diseases, a specialist field not covered by other regional genetics laboratories. The development of this genetic test panel would not have been possible without EGSP support.

EGSP-developed genetic tests and funded genetic testing service provided 534 genetic tests for NHS patients, resulting in molecular genetic diagnoses for 116 patients and confirmation of carrier status for 109 individuals.

Conclusions

- The laboratory component of the clinical strand met its objectives of identifying causative mutations in genes known to cause AR conditions and developing new genetic tests for AR conditions.
- Two of the three components of deliverable 3 were fulfilled; this was the only deliverable specifically for the laboratory strand.
- Thirty-one genetic tests, including five diagnostic and 26 carrier tests were undertaken for individuals meeting EGSP criteria using EGSP developed tests. In addition 185 diagnostic tests and 75 carrier EGSP developed tests were undertaken for individuals living in the West Midlands not meeting EGSP criteria.
- Five EGSP patients received a molecular diagnosis using EGSP developed tests and 17 had carrier status confirmed. Using non-EGSP developed tests, a further five molecular diagnoses were made and 29 positive carrier statuses were confirmed for EGSP patients.
- A total of 111 molecular diagnoses were made for non-EGSP patients using EGSP developed tests and 92 positive carrier status confirmed for these individuals.
- New genetic tests have been developed and have led to sufficient income from outside of the West Midlands for the service to be sustained beyond the duration of the EGSP funding.
- Improved genetic testing service and access to genetic testing to address local population need has been demonstrated.
- The success of the genetic testing service developed has also met a national genetic testing need which has resulted in the new developments being embedded as standard provision for the West Midlands population.

8 Education strand

The purpose of the education strand was to support the educational and outreach activities of the project as a whole, as important aspects of the other strands involved delivering education to the target community. The educational activities with health professionals and in the community aimed to promote the clinical strand, encouraging health professionals to refer patients to EGSP and informing members of the community of the services of EGSP genetic counsellors. The education strand also had its own specific educational objectives.

Objectives and deliverables

Four of the nine objectives of EGSP relate to the educational strand:

Objective 3: Improved genetic literacy in families affected by a genetic disorder identified by the initiative.

Objective 4: Improved genetic literacy and understanding in the extended families.

Objective 5: Improved genetic literacy in HoBtPCT's ethnic minority communities about genetic disorders and their transmission, particularly in consanguineous families.

Objective 6: Improved genetic knowledge and competence among health professionals.

Objectives 3 and 4 were largely the focus of the clinical strand but required some support from the education strand, while the education strand focused primarily on objectives 5 and 6.

Three of the nine deliverables were specific to the education strand. These include:

- Training of a range of healthcare professionals in HoBtPCT in genetic competences related to their role (deliverable 7)
- Delivery of culturally sensitive information about genetics, AR inheritance, access to carrier testing and other genetic services, to a range of community groups in HoBtPCT (deliverable 8).
- Development and evaluation of educational material for use by affected families who will aim to convey that information to their extended families raising genetic literacy (deliverable 9).

The PHG Foundation evaluation lead and the education team agreed objectives for the education strand against which the evaluation could assess the success

of the project. The objectives of the education strand had only been very broadly laid out in the project initiation document (see appendix 1), and required greater specification as to how the objectives should be achieved.

Description of the strand

The education strand had two major components:

- Community education to improve genetic literacy in the EGSP target populations
- A professional education component to enhance genetic literacy amongst health professionals.

The professional education focused on health professionals who work with the target populations (as described in chapter 6), and whose role could include providing information relevant to understanding risks associated with consanguineous partnerships and of AR conditions.

Each component had a dedicated member of staff to deliver the educational activities. The staff came into post in May 2010.

A third part of the strand, the educational materials project, was to produce the materials required by the education team.

Educational materials

The purpose of the materials was to enhance understanding of genetic risk associated with AR conditions, and to support communication of that understanding within families in the target 'at risk' communities.

The National Genetics Education and Development Centre (NGEDC) was commissioned by EGSP to develop validated educational materials on inheritance and familial implications of AR conditions. The NGEDC planned to hold a series of focus groups to identify the content areas for the materials. The NGEDC sought ethical approval for four focus groups – one with health professionals and three with family members. Only the focus group for health professionals was approved and went ahead. As a result, when the education team took up their posts in May 2010, the materials had not been developed. It then became a focus of the education team and clinical team to develop the materials, and they received support from the NGEDC in doing this. Therefore for the initial phase, the education team focused on producing educational materials rather than delivering education.

The education team produced three leaflets in English, Urdu, Bengali and Arabic entitled Understanding *Genetics and Inheritance, Genetics Explained for Parents who are Consanguineous* and *Sharing Genetics Information with the Family* (see appendix 8). The first two leaflets were produced and were available by March 2011. The third leaflet was available from July 2013. In addition to written materials, the education and clinical teams produced a DVD in Urdu and English to explain basic concepts of inheritance, genes, family history, the role of genetics in health and disease and information on the West Midlands

Clinical Genetics Service, including the referral pathway to clinical genetics. The production of the leaflets and DVD were the main focus of the community education strand for much of the first year, and the strand was guided by a Community Advisory Group in producing these materials. Finally a website www.talkinggenetics.co.uk was developed with the clinical team, which signposted users to EGSP as well as providing links to the educational materials developed - including the leaflets and DVD. It also contained additional materials on genetics, consanguinity and the clinical genetics services, which was provided by the West Midlands Regional Genetics Service.

Education strand activities

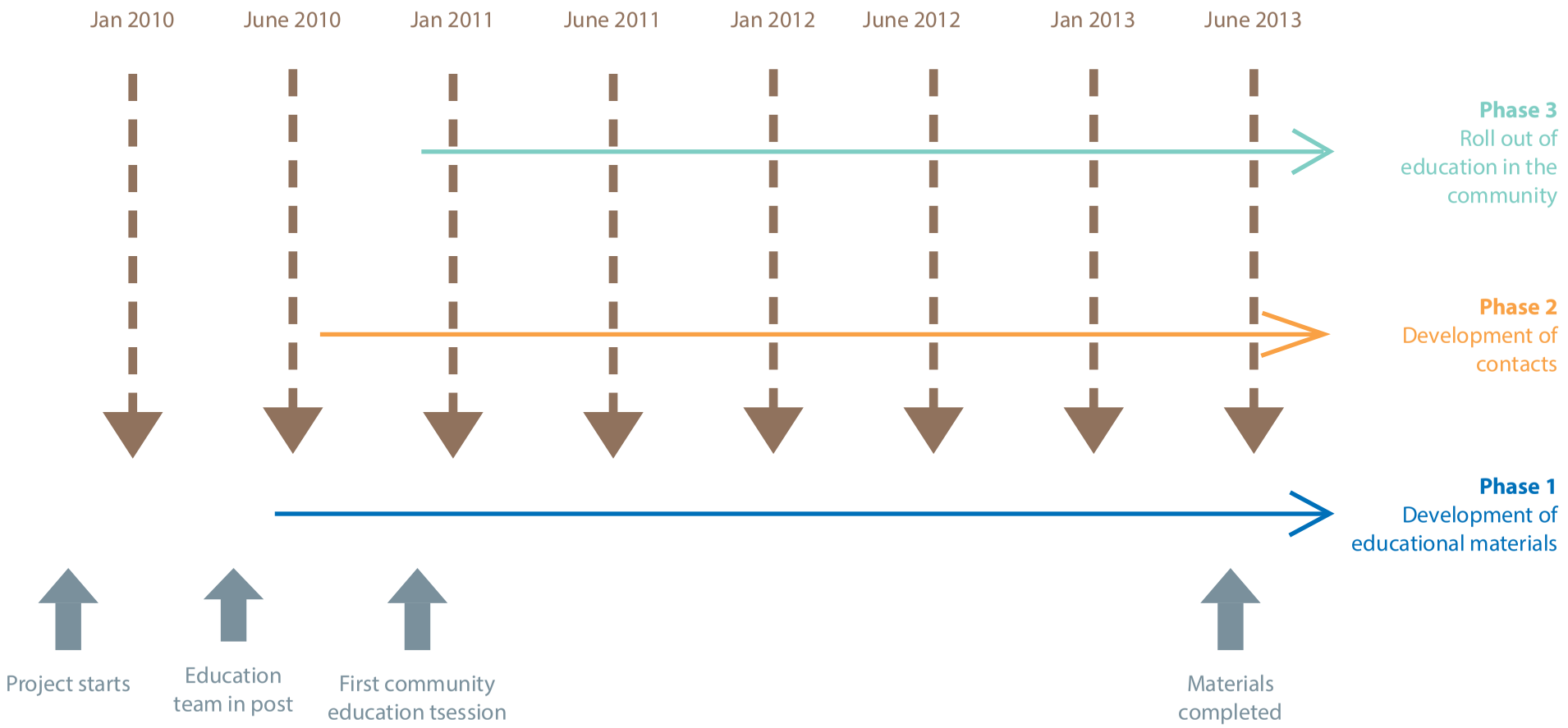
The strand's activities involved developing educational initiatives through making contacts, then organising educational activities with the contacts and evaluating the educational activity. These phases were iterative, so that certain contacts made at early stages resulted in initiatives at much later stages, and often it took several approaches to a community-based organisation or an organiser of professional education for the education to take place. For purposes of the evaluation and to support the iterative process, both parts of the strand kept a log of contacts made, the context of that contact (for example a community health fair), the educational outcomes and the follow-up actions. This enabled contacts made at different time points to be followed up, and information on the process of developing the educational initiatives to be monitored. It also provided continuity when there were staff changes.

Community education

The community educator came into post in May 2010, and it was decided to divide this part of the project into three phases. Phase one focused on developing educational materials. The second phase focused on developing contacts with community leads and raising awareness of EGSP. The third phase comprised the roll-out of the education to community groups.

A community advisory group was set up in July 2010 to guide the educational activities and review the materials produced. This group met three times. Outcomes from their guidance included making a shortened version of the DVD to inform people of EGSP, with the original longer version for use with those who required further information. They also guided the community educator on the key groups to be targeted, including parents' groups at children's centres, young adults in schools and colleges, and community members that attend workshops in mosques and classes for learning English. The community advisory group noted that some women were only allowed to leave the house to attend English classes, and so this was an important focus for EGSP. The community advisory group also suggested that a male advisory group should be convened. This was established and met at a mosque.

Figure 1 Community education timeline



Community education using the media

EGSP team members intended to use the Asian media such as Noor TV, an Islamic TV channel to publicise the messages of EGSP. They were approached by a presenter from Noor TV and Unity Radio, which hosts health shows. These are media that broadcast in minority languages, cater for members of the community that have poor English and cannot access other sources of information including those provided by the NHS. The EGSP team were keen to take this forward but this initiative was not progressed due to concerns of possible negative consequences arising from media involvement.

Evaluation

Educational sessions in mosque settings

For the first 18 months the focus of the community education was in mosques. The community educator met with those imams who were happy to work with EGSP. The imams expressed the view that the health consequences of consanguinity was not a sensitive issue, but became a sensitive issue if health professionals blamed the community for the disability arising in children born to consanguineous families

The community educator noted that for many of the educational sessions, it was not appropriate to evaluate the learning in a formal way using written questionnaires. This is because educational sessions took place in mosques and in such instances women usually did not have enough time to complete a formal evaluation before they had to leave to collect children or attend to other priorities. Women attended the mosques to pray rather than to participate in an educational session. For some women, completing a written evaluation form was not appropriate due to their level of language skills in English or in written Urdu. EGSP was also invited to address the congregation before Friday prayers, and in this context asking for formal evaluation to take place would have been inappropriate where the primary purpose for attendance was to pray.

Quotations from verbal feedback illustrated the impact of the educational activities.

Comments from the men at the mosques indicated a level of suspicion initially with comments such as:

'*Have you come here to tell us to stop marrying our cousins?*'

'*If genetic conditions occur because you marry a cousin , then why do English people who don't marry relatives have genetic disabilities?*'

The EGSP community educator noted that after discussion of mortality data and explanation of recessive mode of inheritance, the group agreed that it was a public health issue and the community should be educated about the topic. They also agreed that the role of consanguinity should be discussed so the community can understand the message rather than feel that they are being criticised for their culture.

The male community advisory group felt that most men would not attend workshops, but that the Friday congregation should be addressed and information made available, with contact details of where further information and help can be obtained. A major concern was regarding the ability of GPs to offer support:

'Once the community are aware and they go to their GPs, can you assure us that the GPs will know how to provide the genetic help they need? If not this will further alienate the community'.

Workshops were run at the mosques before and after Friday prayers. The community educator noted that great interest was shown by the women attending, but most women felt more comfortable when discussing genetics on a one-to-one basis. Many of those attending the sessions were defensive initially, but after the teaching session felt that this was a problem that the community needed to be aware of. Initial comments included:

'*So there is real scientific evidence that genetic risk is increased in consanguineous marriages*?'

After the session the following views were expressed:

' *I am beginning to understand what you are saying, you are not telling us to stop cousin marriages but it can be a problem if there is a genetic condition in the family, this makes sense and we should think about. '*

'The health professionals should help couples and families to understand genetic risk without being critical about cousin marriages.'

'It's important that you tell the community the figures about infant mortality and genetics so they understand that it is a health issue and not just a criticism of the custom of cousin marriages.'

There was also concern expressed that risks associated with consanguinity were being used by the younger generation to evade cultural practices such as consanguineous marriages:

'*You need to teach all the generations so they understand otherwise the older generation will think it is an excuse that the younger generation is using to break a tradition.*'

The interest in the sessions was highlighted by the community educator's observation that most of the women came back the following Friday with more questions, and invited other women interested in learning about genetics to attend. As a result, key contacts from the community offered to distribute the genetics literature and organise meetings.

Educational sessions in children's centres

From 2012, in order to increase the opportunity for educational sessions to take place, the focus of community-based education shifted from mosques to children's centres. Children's centres have extensive experience of providing services and support to families. The children's centres are often based within areas of Birmingham with high populations of Black and Minority Ethnic (BME) families, are orientated to delivering education for the whole family and are proactive in working with EGSP to provide genetics education to their staff and to families using the centres. Washwood Heath Children's Centre was identified as a key children's centre, as it serves a predominantly Muslim Pakistani area, and is part of a partnership of all the centres in the area and it therefore enabled work to take place with the other children's centres serving the locality.

EGSP was contacted by Washwood Heath Children's Centre, and teaching sessions were initiated in early 2011. Feedback from the sessions was very positive and included the following comments:

'*Very important, it affects day to day life and family issues. Gets you thinking a lot about genetics and your children and family inheritance.'*

'The way you have explained inheritance and link to cousin marriages is easy to understand and also made me understand that you are not telling us what to do but be aware of the risks.'

The community educator noted that a number of the women that attended said that there was a genetic condition within their family and wanted further information of risks, both for them and the wider family. The link to the genetic counsellors in the clinical strand was important for this need to be addressed.

Following from the change in focus to children's centres, further educational activities with the Washwood Heath Children's Centre were initiated. This involved teaching sessions with staff and with clients of the centre. All the staff at Washwood Heath Children's Centre attended a session.

In addition sessions were held at Apna and Summerfield Centres. In the context of educational sessions in the children's centres, some more formal evaluation was possible. Of the 100 members of the community attending a total of 11 sessions, all reported that they felt the session had explained inheritance and genetics adequately. No-one indicated that they did not understand any aspect of the genetics teaching or would like further explanation. All but one participant in all of the groups felt that it is important to raise awareness of the risks of genetic disorders within families, and all felt that the session had been a useful way of doing this. The community educator noted that evaluation of teaching sessions had been problematic, in that respondents tended to only provide yes/no answers in an attempt to complete the forms quickly.

Cascade education on the community

The community educator highlighted the value of training others so that they could signpost members of the community to EGSP. This was in recognition of the limitations of the impact that a single community educator could have in raising the profile of EGSP and its messages in the community. The community educator focused on health trainers, whose role is to work within the community to support individuals, families and groups in taking actions to improve their health. Twelve health trainers attended the training, 8 of whom were of Pakistani or Bangladeshi ethnicity. After the session all the health trainers felt that the training had been useful in raising awareness, and that it was important to raise awareness of the risks of genetic disorders within families. Comments included:

'*You can't change arranged marriages to cousins but it's worth talking to them about the risks to their children.*'

The manager of the scheme attended the training and was keen for such training to be rolled out to other areas.

Other community education settings

In addition to working with children's centres and mosques, the community educator utilised a number of community events to publicise EGSP and its educational messages. These included a stall at a community health fair; a children's centre locality event; a forced marriages event that targeted professionals working in the community of most relevance to EGSP; a women's day event; a diabetes awareness event; a primary care conference and a showcase of family health visiting and family nurse partnership event.

An example of feedback from these events included:

'I speak to many families who are unable to cope with children with special needs, a lot of whom have genetic conditions and practice consanguinity and continue to have many children, I didn't know where they could get help specifically for this to help prevent future problems. I will definitely point them in your direction now that I have all the details in the pack.'

The community educator also noted that at an event that attracted teenagers there was interest in how to become a genetic counsellor. In the longer term, increased recruitment into the genetic health professional groups from members of 'at risk' communities would be an excellent way of promoting genetic literacy in these communities.

Health professional education

The health professional educator came into post in May 2010. This part of the strand was active until June 2012 when the health professional educator left EGSP. From June 2012 – December 2012 the post was vacant and little education took place targeted at health professionals. In December 2012 a new post-holder was appointed and activity resumed.

Health professional education objectives

The following objectives for the health professional component of the strand were agreed:

- Undertake education needs assessment/formative evaluation for health professionals
- Develop educational materials for health professionals
- Set up and deliver educational courses for health professionals
- Set up and deliver training for identified link workers for cascade training
- Act as educational resource for health professionals in clinical practice
- Evaluate all educational materials and delivery
- Raise awareness about EGSP, this in turn will inform a sustainable stream of referrals, particularly from primary care.

Launch event

One of the first initiatives was organising a launch of EGSP in order to promote EGSP amongst health professionals, primarily GPs. It also aimed to raise awareness on the impact of genetic conditions on levels of infant mortality in Birmingham, raise awareness of the clinical genetics service, publicise educational resources and develop relationships with healthcare professionals, so that further activities could be initiated. In addition to GPs, the main audience was healthcare professionals, including midwives, health visitors, practice nurses, practice managers, staff from the children's hospital, GP educators, members of the deanery, community paediatricians and school nurses. These groups had been identified as the main target audiences for EGSP's professional education. The launch took place on the 6th October 2010.

Seven hundred GPs were invited from the three Birmingham PCTs. The initial response to the invitation letters was very low with 13 positive responses. So a targeted campaign of telephone calls, emails and personal visits to GP surgeries was initiated. Thirty-seven delegates attended, of whom 13 were GPs. The remainder were EGSP-linked staff (11 attendees), and one or two of the following: practice nurses, health visitors, paediatricians and representatives from Birmingham Children's and Birmingham Women's hospitals.

Feedback from the launch

Sixteen evaluation forms were returned – all indicated that they had found the event enjoyable, interesting and informative. In addition, respondents suggested ways of improving awareness of genetics within the BME communities in Birmingham. They also indicated whether they would be interested in participating in genetics education, and in what form they would like that education (lectures, study days, GP meetings).

The team concluded that while attendance was lower than anticipated, the launch did provide a valuable opportunity to get feedback on how to develop the professional education part of EGSP. It indicated the challenges that lay ahead with engaging GPs in education on genetics. The team learnt that attempting to approach other members of the primary healthcare team, such as health visitors and midwives through GP surgeries, would not be effective and these groups would need to be targeted separately.

Education needs assessment

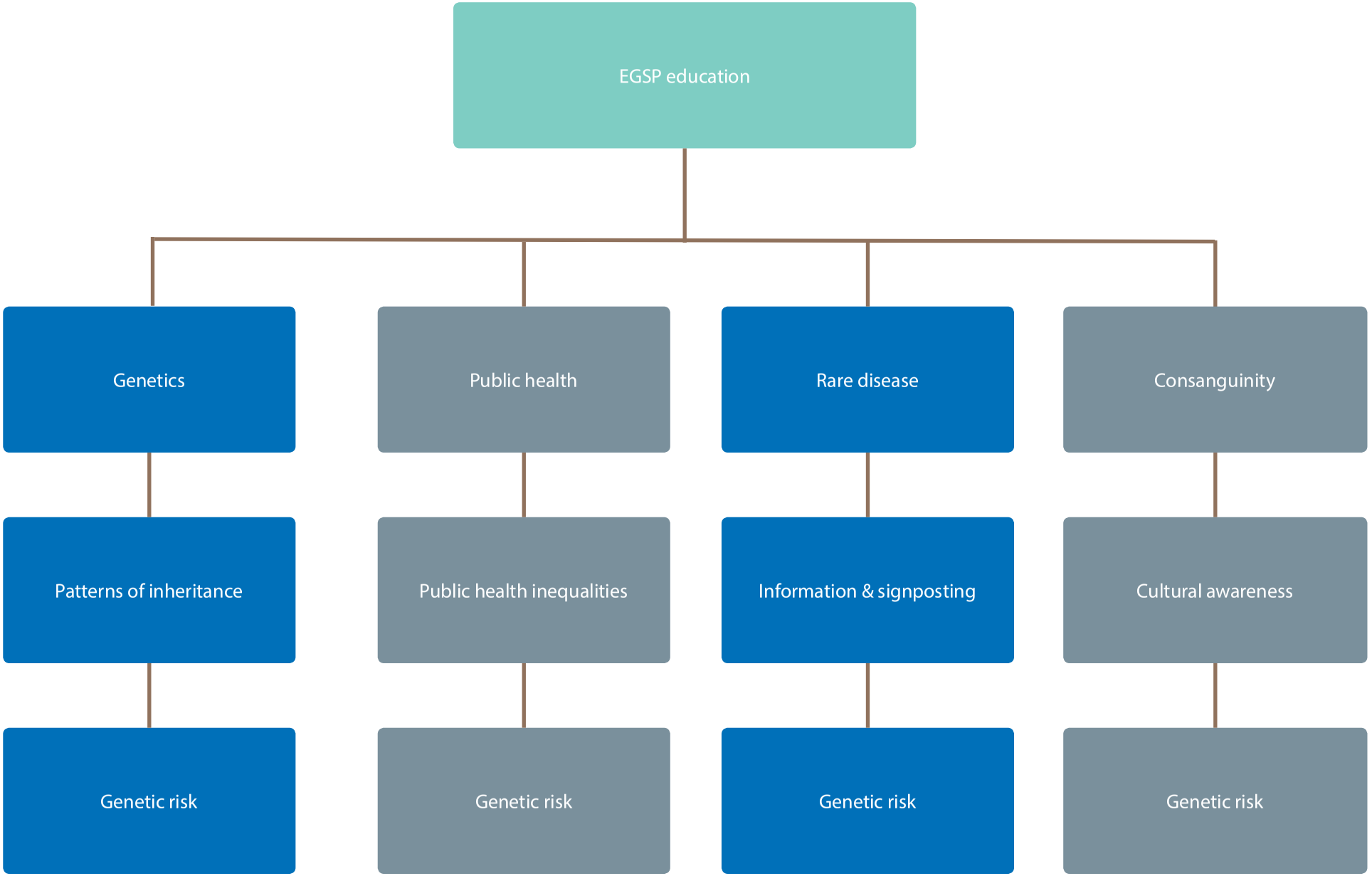
This was undertaken through the launch event and as part of delivering the education. Feedback from these activities was used to modify the focus of the education, for example from an initial focus on genetics to a focus on high rates of infant mortality and morbidity in Birmingham as detailed below. Another example of the impact of the education needs assessment was the way that rare disease was discussed. Many GPs had not heard of many of the rare genetic diseases mentioned and so did not feel the topic was relevant to their everyday practice. So the team initially focused on the more common recessive conditions such as thalassemia, sickle cell disease and cystic fibrosis. On understanding the inheritance for these conditions, it was more acceptable to introduce rare diseases, and how some of these diseases may be more common in certain BME groups and in particular those with high rate of consanguineous unions. This approach was well received and many GPs asked for further information on specific rare diseases. The Department of Health initiative on rare disease, which provided a higher profile for rare diseases during EGSP, may have contributed to the interest in rare diseases.

The educational model (Figure 2) for the professional education was developed as a result of the educational needs assessment and the evaluations from a six month period of the educational sessions. This illustrates the four main components of the professional education teaching, and the topics covered within each component.

Development of educational materials for health professionals

By working with the NGEDC, suitable materials for use with health professionals were identified, used to support the education, and to signpost their availability to the health professionals so that the health professionals in turn could use them. A gap in community-focused materials was identified and was given a higher production priority than materials targeted at health professionals.

Figure 2 **Model for health professional sessions**



Set up and deliver educational courses for health professionals

This was achieved by a variety of educational sessions. To support the educational activities the professional educator developed:

- an education presentation covering the aims and objectives of EGSP
- data on infant mortality and morbidity
- AR genetic conditions and patterns of inheritance
- rare disease including data on increased incidence in certain communities
- identification of individuals with or at risk of genetic conditions
- what the project could offer clinically and educationally
- how to refer into the project

This is set out schematically in Figure 2. The health professional educator noted that groups often had to be repeatedly approached regarding setting up activities, and that she often met with a low level of interest.

Set up and deliver training for identified link workers for cascade training

This aspect of the strand was not achieved, although attempts were made to initiate cascade training. The initial concept was to use the model provided by the PEGASUS programme that supported the national thalassemia and sickle cell disease screening programmes. The intention was to use this model to develop cascade professional training as part of EGSP. The interest in and uptake of cascade testing was poor and so the model was not followed. The professional educator noted that attempts to develop this was hampered by instability across the target professional groups, due to high levels of uncertainty and change taking place during a period of health service reforms. As a result, enthusiasm to commit to cascading training was absent. Lack of time and lack of educational credits attached to the training were also cited as reasons for why this objective was not achieved.

Act as educational resource for health professionals in clinical practice

The health professional educator worked with other health professionals, for example those working in the renal clinics and inherited metabolic disease clinics, and acted as a resource for genetic information for those staff. Educational resources were provided for these teams to help them in supporting patients.

Evaluation of educational materials and delivery

This was part of the education activities, and summaries of the evaluations are presented below. Evaluation of teaching sessions was undertaken using questionnaires. Initially questionnaires were included in packs containing educational resources given out at the beginning of the educational sessions but this yielded a poor response rate. The approach was modified to giving out the packs in exchange for completed questionnaires. While this improved the numbers of forms returned, many were handed back partially completed or not completed at all. The following figure shows the numbers of evaluation forms completed in the first year compared to the number distributed. Some GPs

found the time commitment to stay for the full session challenging, and left before the session finished, and so did not complete evaluation forms.

An evaluation of attitudes pre and post education measured whether there had been a change in attitudes following the delivery of the education. This was a complicated process and was not possible to achieve in large groups, but worked well for small groups. The questionnaires were anonymously completed and so it was possible to show that there had been a shift in attitudes overall, but not that a particular individual had changed his or her attitude.

Initially evaluation focused on attitudes to the teaching session and materials. This was broadened to also include the evaluation of change in confidence in relation to understanding of genetics, whether consanguinity was thought to be a cause of genetic conditions and whether patients should be advised not to marry their cousins.

Figure 3 Return of questionnaire in the first year of education strand activity

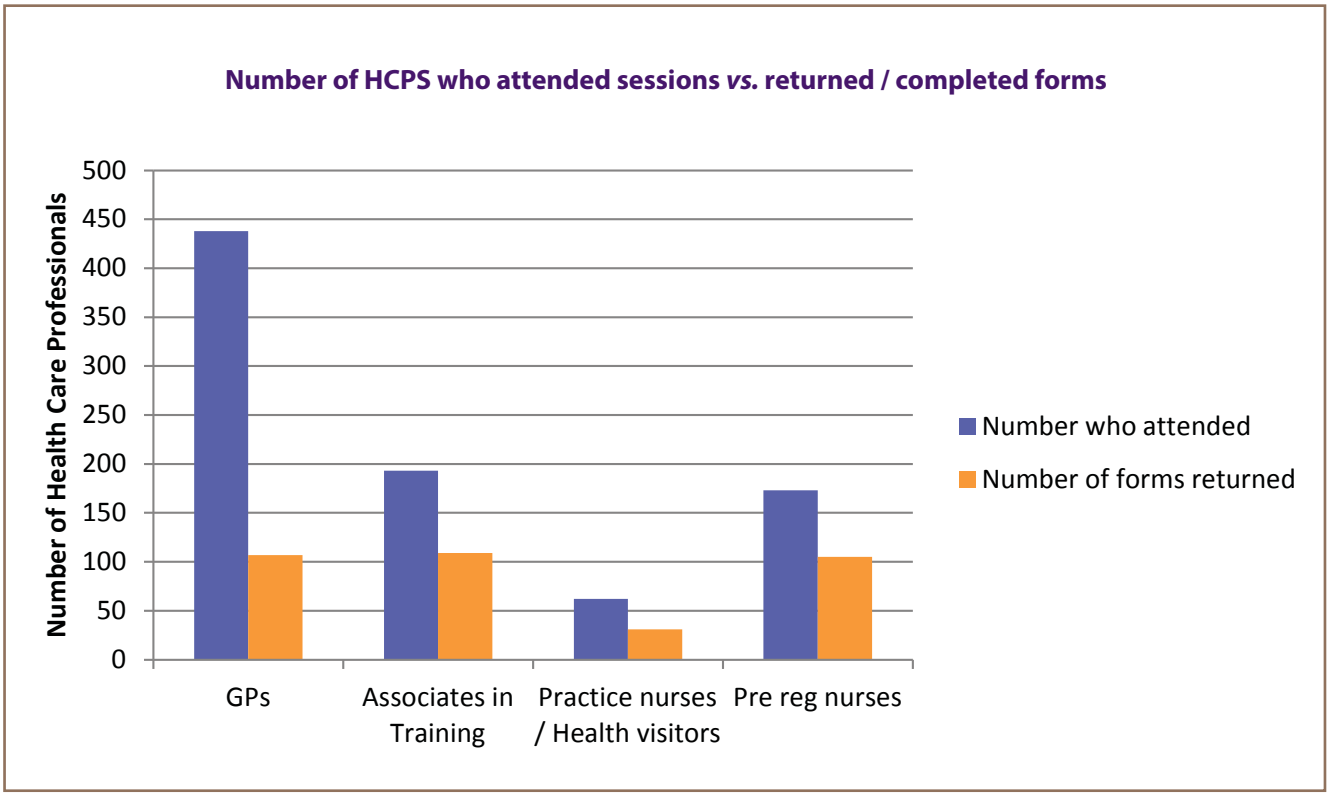
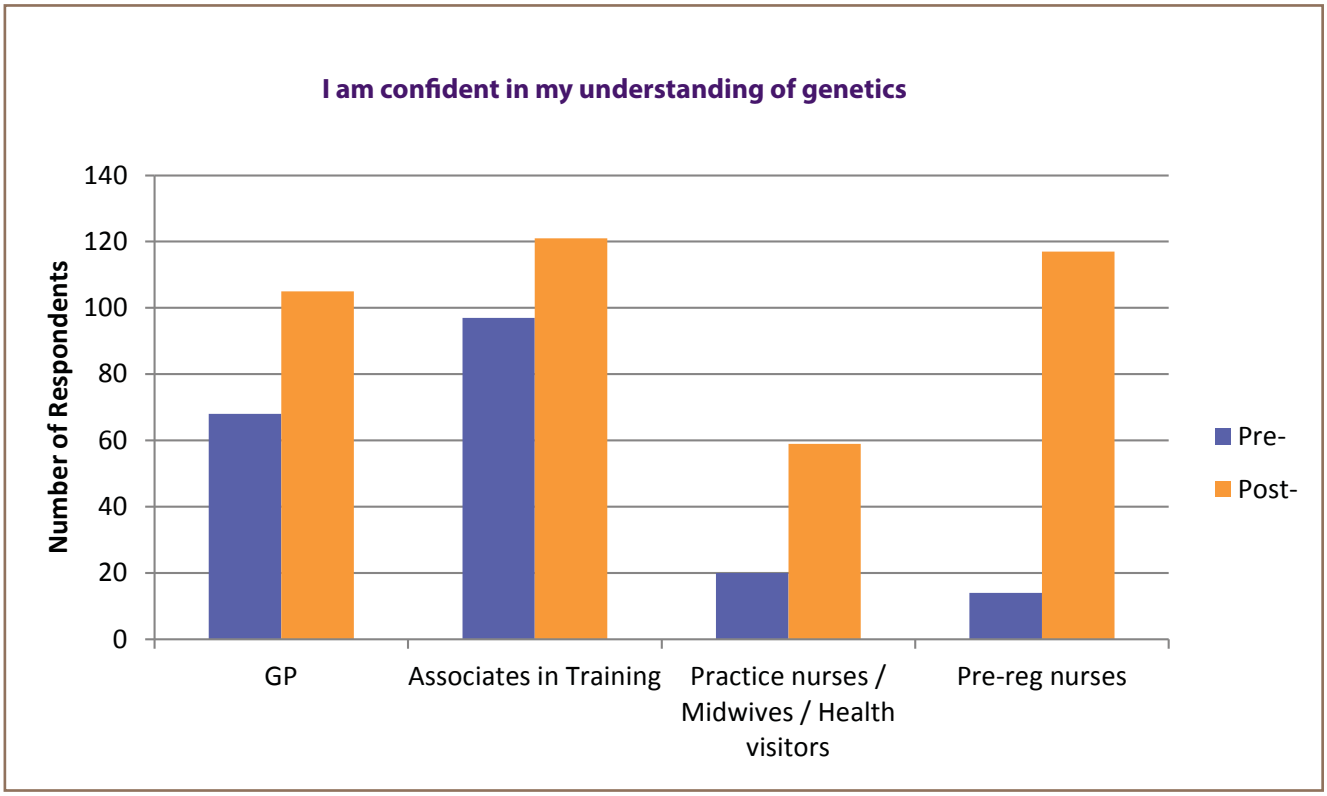


Figure 4 Understanding of genetics pre- and post-educational session



Changes in confidence regarding understanding of genetics

All groups stated that they had an increased understanding and confidence post session.

Changes in attitudes to consanguinity pre and post education session

There was variation in how well the term consanguinity was understood. Definitions were broadly correct and focused around cousin marriage, marrying in the family and so on, but more extreme and misinformed terms such as inbreeding and incest were sometimes used. Some were aware of the cultural and historical background to consanguinity. Following education, some modified their views on the risks associated with consanguinity, to a more subtle understanding of the increased risk being substantially higher in those consanguineous families where a rare recessive condition exists (Figure 5).

Pre-education, it was generally felt that cousin-to-cousin marriage should be advised against. This changed somewhat post-education. However a number of health professionals continued to believe that consanguinity is a risk factor, and as such should be discouraged (Figure 6). Understanding the likelihood of being affected by a rare disease was helpful to contextualise the significance of rare recessive conditions and of consanguinity, and to help healthcare professionals gain an accurate estimation of risk for consanguineous families compared with the rest of the population. This approach made it more acceptable to introduce issues around consanguinity. Consanguinity became an additional predisposing risk factor for these inherited conditions and not the cause of them, putting the issue into a more realistic and less 'victim blaming' perspective. The educators concluded that more resources need to be developed to successfully demonstrate the actual increased risk

for consanguineous families, as opposed to the perception, so that health professionals understand the risks and can correctly support families.

Figure 6 suggests that across the range of professional groups, the teaching sessions resulted in an attitude change to consanguinity, so that fewer professionals felt that patients should be advised against cousin marriage. The aim of the education was to provide a more nuanced understanding of the health effects of consanguinity and it appears to have been successful in doing this.

To raise awareness about EGSP, to inform a sustainable stream of referrals, particularly from primary care

Awareness raising on EGSP was part of all the educational activities but did not result in referrals from primary care or from other professionals (see chapter 6).

Figure 5 Number of reposondents who felt that consanguinity causes genetic conditions pre- and post-educational session

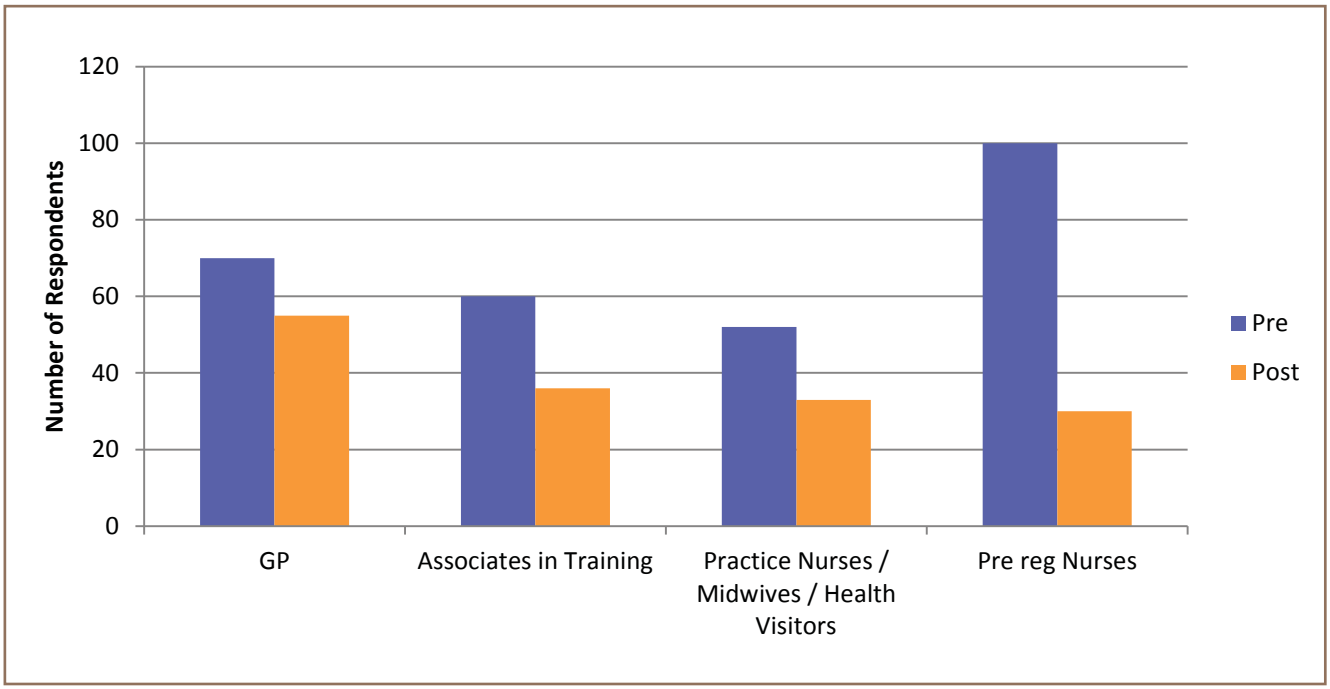
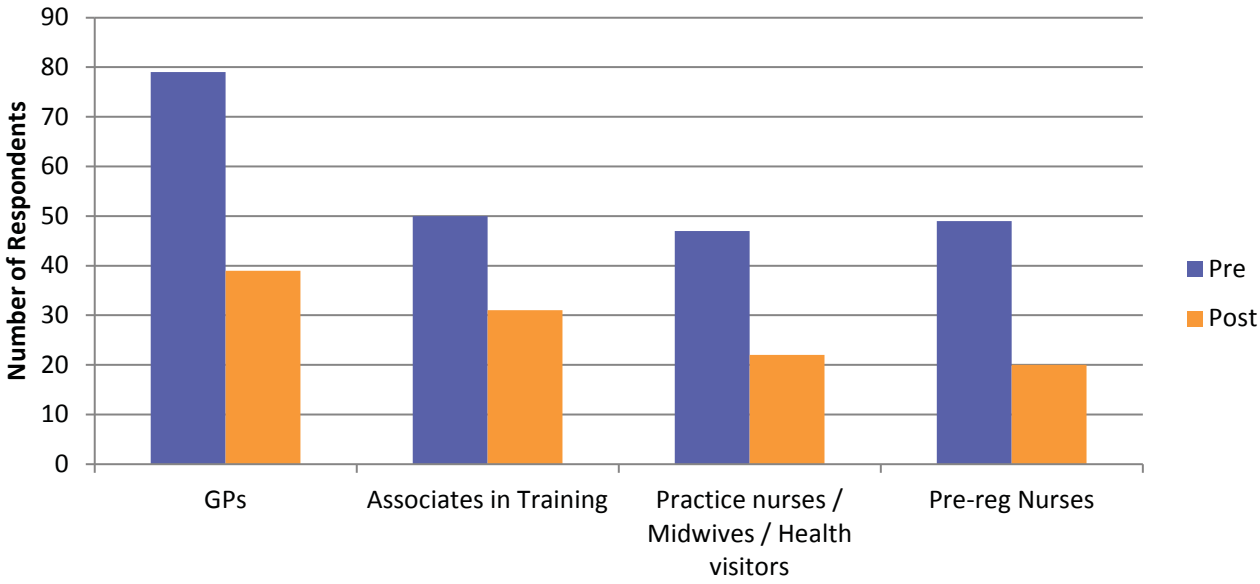


Figure 6 **Number of attendees who felt that patients should be advised not to marry their cousins pre- and post-educational session**



Education activities with GPs

GPs, as the first point of access to specialist services, were still seen as the priority for the educational activities and the fact that the community educator was from the target community, and had links to a number of practices was recognised as being invaluable in gaining access to a number of practices.

The regional GP tutors were key contacts as they enabled the team to participate in the training programmes for GPs and GP trainees (Associates in Training (AiTs)). The education presentation was delivered to a number of large groups of GPs and GP trainees and was well received. For example, a session was held by HoBtPCT as part of GP-protected learning time, and was attended by 150 GPs.

The following number of professionals attended educational sessions during the first year of the project and for its final six months. The project was unable to supply information on the numbers who had attended training during its second year, and subsequent to that period, the professional educator post was vacant for six months until the final six months of the project.

The majority of these sessions were carried out using existing educational schedules and programmes such as GP lunchtime meetings, protected learning time and Associates in Training (AiT) training days. The GP tutors particularly, were very supportive in inviting EGSP to present at the Associates in Training training meetings. This led to a good cascade effect, with many AiTs then asking their own GPs to invite EGSP to do sessions at their local practice. These sessions provided a good platform, both to meet and to establish a

Table 1 Types and number of health professionals attending educational sessions during the first year of the education strand

GPs	GP trainees (AiTs)	Health visitors	Mid-wives	GP Practice nurses	Student nurses	Renal doctors and other specialist doctors and specialist nurses	Children's centres staff	Conference workshops and others	Total
580	190	248	35	38	198	70	74	155	1588

communication link with healthcare professionals which may not have existed before.

The protected learning time co-ordinator was able to provide some evaluation feedback. For example, of the 30 responses received on the teaching, 0 rated their response as 'dissatisfied', 5 rated it as 'satisfied', 15 as 'good' and 10 as 'excellent.' Despite the generally positive evaluation of the limited number of returned evaluations, the EGSP education team noted that for a significant proportion of GPs, genetics was not a clinical priority.

The team found that focusing the message on infant mortality and morbidity resulted in more successful engagement with GPs and other health professionals. The impact of morbidity in particular was an issue that health professionals related to well, as most were in contact with families who are living with inherited conditions and they were enthusiastic to develop their skills to support these families more effectively. As a result the training sessions were modified to start with this topic to generate interest, which resulted in a more positive approach to the education.

Examples of feedback:

'Don't focus on talking about a new genetics service - focus on the high infant mortality rate that will make GPs take notice- we all need to do something about that.' (GP)

'I have at least three families who have affected children being treated at BCH (Birmingham Children's Hospital). It has never occurred to me to have a discussion with them about the implications for the wider family or to ask whether they have had carrier testing etc.' (GP).

Educational activities with other health professionals

Specialist nurse groups, health trainers, further education colleges as providers of education for health and social care students, health trainers and special schools were all contacted and offered educational sessions. As time went on, it became apparent that although there was good engagement in formal education sessions, it was more challenging to work at the individual practice level to provide educational sessions and the most receptive group was health visitors. This may be because many health visitors were actively involved in supporting families who have a child or children affected by long term conditions, many of which will be genetic in origin. EGSP was invited to attend a health visitor academy and run sessions for 170 health visitors. These sessions were well received and there was a lot of interest in the project. The majority of the health visitors who returned the evaluation forms indicated that they found the sessions relevant (95%) and could incorporate learning from the sessions into their practice (86%). They also felt that the resources provided would be useful (77%).

Once the professional education post was filled in December 2012, after the 6 month period when the post was vacant, the opportunities for the professional education were reviewed. GPs were prioritised initially, through the protected learning time (PLT) and continuous professional development (CPD) opportunities and GP practice meeting sessions. The rationale for prioritising GP education is that they are key figures as information sources and the means to access genetic services. There was a low level of response to the offer of education.

The educator concluded this was for a variety of reasons:

- Timing of offer coinciding with a period of major NHS changes and much of the education focused on GP commissioning
- Many GPs felt that there are other clinical priorities such as cancer, obesity and cardiovascular disease
- Some could not see the relevance of genetics to primary care
- GPs who had already had contact with EGSP did not see the need to attend further educational activities

When it had been possible to arrange sessions, the response from GPs who had attended was positive and many GPs expressed a desire to attend further sessions on genetics.

Specialist doctors were also targeted for educational input including community paediatricians and renal specialists.

Health visitors were the group who responded most enthusiastically to offers of educational sessions. This was also noted by the previous post holder. Offers were made via nurse leads and tutors and also through children's centres.

Completed evaluation forms indicate high levels of satisfaction with the teaching, along with low levels of awareness of EGSP. Many of the health professionals had consanguineous families among those they served, had families with genetic conditions and had patients for whom a referral to the clinical genetics department or EGSP would be beneficial.

Key issues identified from the evaluation of the healthcare professionals education activities

1 There was a lack of knowledge and understanding among many health professionals of all groups regarding basic genetic concepts.

2 There was a lack of understanding among many health professionals regarding cultural issues. For example, many attitudinal assumptions were observed among healthcare professionals, *i.e.* that the cultural issues related to consanguinity are impenetrable and that approaching families with information was a waste of time.

3 There was a lack of awareness regarding rare diseases and the increased risk of these conditions within consanguineous families.

4 Both parts of the education strand engaged with support groups to identify potential partnerships to raise awareness with patients, families and health professionals. They worked collaboratively with support groups to use their existing resources, or worked with them to develop resources to inform and educate health professionals.

5 There was an assumption by some GPs that affected families within their practices would have been offered carrier testing by other agencies, *i.e.* the Children's hospital, and that discussion with families regarding risk of genetic diseases was not within their remit.

6 There were many other health issues within primary care that GPs see as a greater priority.

7 Specialist services such as renal and inherited metabolic disease services were enthusiastic to work collaboratively to identify and meet patient needs.

8 Health care professionals were reluctant to commit to ongoing education, such as a cascade model of delivering training.

9 Some genetic skills such as taking a pedigree were considered unnecessary and too time-consuming within the context of clinical practice in primary care.

10 Recent NHS organisational change was making engagement in the short term more difficult as health professionals were prioritising workloads and were less inclined to respond to issues outside of their current practice.

Work with patient organisations

The education strand engaged with a number of patient organisations, particularly the Polycystic Kidney Disease charity, and as part of this they attended an Autosomal Recessive Polycystic Kidney Disease family day. In general the experience was of low representation by the target minority ethnic groups in patient organisations.

Evaluation of the educational materials

The leaflets were evaluated by community members, primarily using the children's centres. Leaflet 1 was also evaluated in a mosque setting by a women's group. The three leaflets developed by EGSP are found in appendix 8.

Leaflet 1: Understanding genetics and inheritance

In all 85 people evaluated leaflet 1 including groups who met at children's centres and in mosques. This included 74 female and ten male evaluators aged between 17-50 years. Comments included:

'*Important information because families need to know where to go for help.*'

Before reading the leaflet the male attendees commented that they did not think genetic disease and marrying within the family were connected and it was just a way to stigmatise cousin marriages. After reading the leaflet they all accepted the information in the leaflet as factual.

Leaflet 2: Genetic risk explained for parents who are blood relatives

This was evaluated by 38 people attending three community based groups, including two groups who met at children's centres. Those evaluating the materials comprised a total of 34 women and four men aged 20-50 years and they commented that:

'*This information is important for us otherwise we think it is just that they don't approve of cousin marriages.*'

'*Families need to know of risks before marriage.*'

All the attendees said that they would go to their GP first for advice if they had concerns about a genetic condition and then look on the internet. It is therefore important that the genetics services work closely with primary care health professionals so that they can provide the information patients need.

Leaflet 3: Sharing genetic information

This leaflet was evaluated in six locations, three were children's centres and the other three were community centres. In all 63 attendees evaluated the leaflet, 49 of whom were female and 14 male, and were within the age range of 20-63 years. All said that the leaflet explained the information clearly and that there were no words used that they did not understand. Reading the leaflets resulted in an increase in confidence in sharing genetic information with other family members as depicted in Figure 7.

When asked where the attendee would go to get further information on genetics, the two most common responses were to the GP or the internet/a website (see Figure 8). Respondents could give more than one answer.

A main objective of producing the leaflets was to facilitate the sharing of genetic information within families. There had been a lack of such resources to help family members share information, which is the key process needed for cascade testing to take place. So an important part of the evaluation of the leaflet was to ascertain whether it would be used for such purposes. Figure 9 shows the different ways attendees indicated that they would share genetic information with other family members. The most commonly given response was to show the relative the leaflet and talk to the relative; the second most common response was to talk to the relative. Sixteen said they would talk to the relative and show them the EGSP website. Thus those evaluating the leaflet indicated that the leaflet would fulfil its purpose – the sharing of genetic information within families.

Website usage

The EGSP developed a website 'Talking Genetics' http://www.talkinggenetics.co.uk/ and content was added throughout the project. It could be accessed through links on the West Midlands Regional Genetics Service webpages. The website featured interactive learning tools, the three leaflets produced by EGSP, links to other educational resources including those produced by the NGEDC, information on clinical genetics services and clear contact links to the EGSP team. Only two emails were received via the website, enquiring about risk information and providing feedback on EGSP resources posted on the website. In addition two telephone calls were received from prospective patients enquiring about genetics services.

Figure 7 **Number of people who felt confident levels regarding sharing genetic information with family members before and after reading the leaflet**

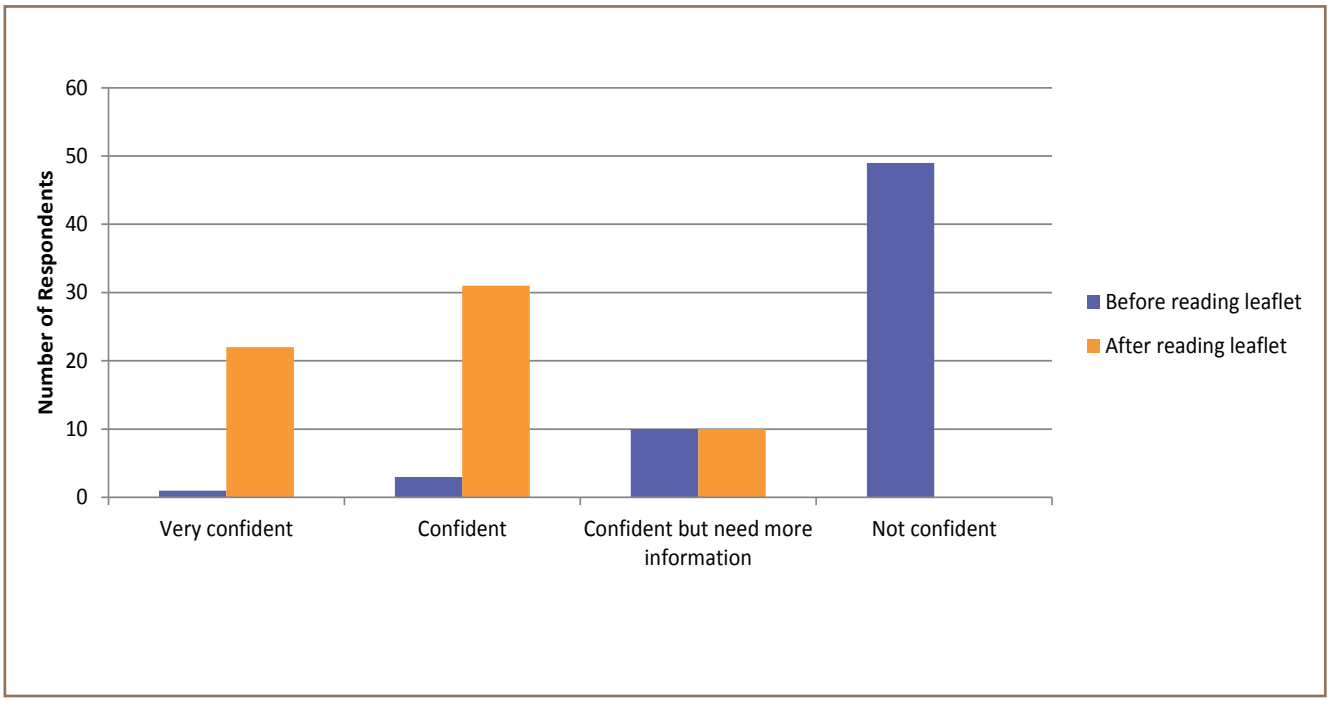


Figure 8 Number of responses to where to obtain further information on genetics

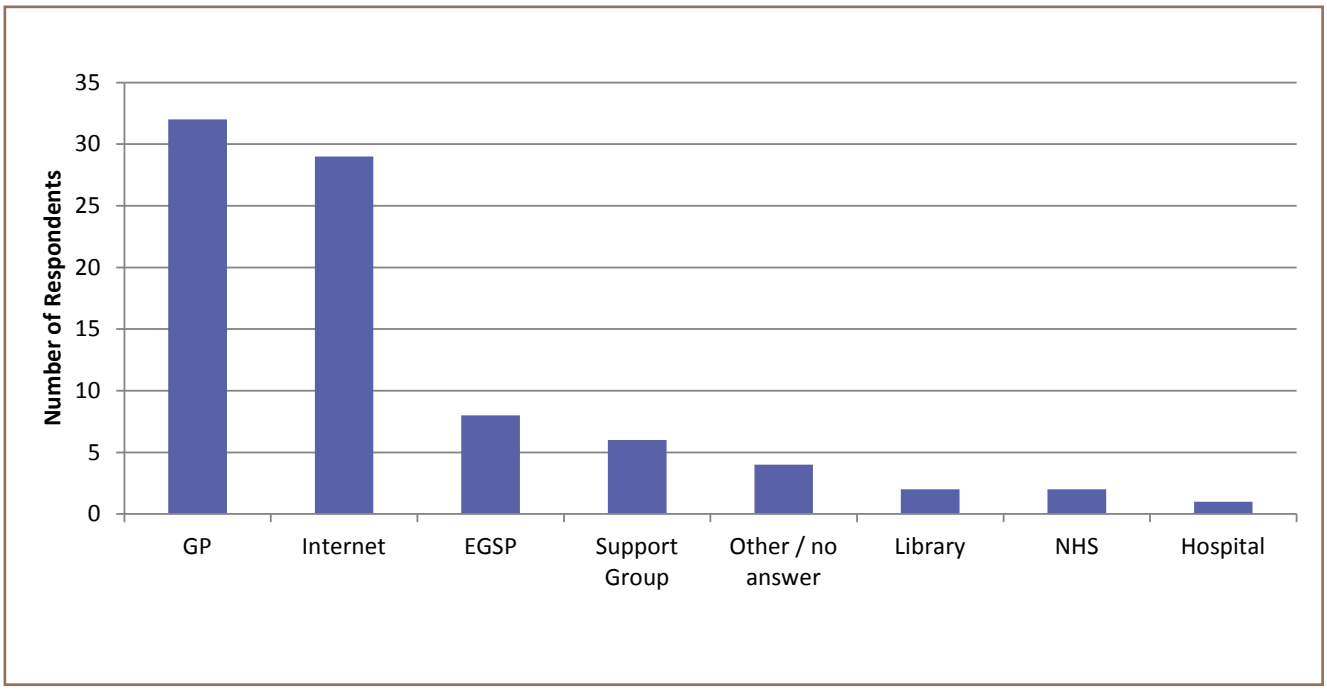
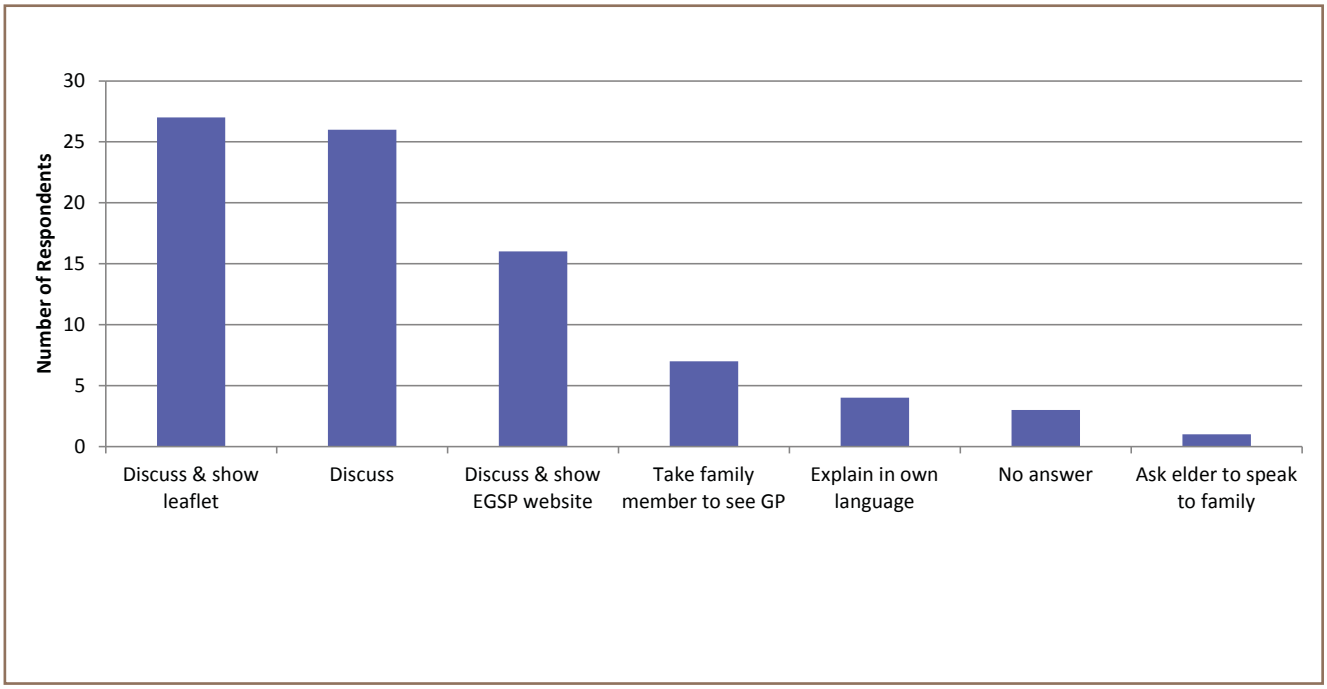


Figure 9 Number of people responding to how they would share genetic information within the family



Conclusions

Achievement of educational objectives

Broadly all of the seven objectives were achieved, other than the fourth and seventh ones. The fourth objective aimed to set up a cascade approach to training using link workers. Some progress was made on this in the community education part of the strand with the training of health trainers. There is little evidence that the seventh professional education objective has been achieved in relation to increasing referrals from primary care or from other professionals. In part this may be due to the longer timescale required for the increased awareness to result in referrals. Some referrals may have taken place as a result of education activities, but if these were made to the clinical genetics department rather than directly to EGSP it would be difficult to identify that they arose from the educational activities. Initially there were discussions as to how to capture such referrals, but this would have required specific enquiry when referrals were received by the clinical genetics department, and the team felt that this would not have been feasible. A referral form was developed by EGSP for use by GPs, but the team felt that in practice it was unlikely that GPs would use a different method of referral from their standard one.

Achievement of the education strand deliverables

- The three deliverables for the education strand were achieved. The materials were developed and evaluated, although the second leaflet was evaluated by only a small number of people; there had been plans for further evaluation of leaflet 2 with more individuals, but this did not take place. It was recognised that there was a tension between allocating limited time to delivering educational activities and evaluating the educational materials. This balance was further influenced by a decrease in the hours of the community educator prior to her leaving EGSP in December 2012.
- The educational materials were not ready in advance of the education team coming into post as had been the intention. As a result, instead of being able to focus on delivering the educational materials the team spent considerable time developing a series of three leaflets. This reduced the time available for delivering educational initiatives.

Community education

- For indepth community education which enables specific concerns to be addressed, the education is usually best delivered on a one to one basis. This is due to the potentially sensitive nature of information relating to a person's family being affected by an AR condition, compounded by the stigma associated with genetic disorders in communities where arranged marriages are common. In such communities it may disadvantage the family's ability to arrange a marriage if the family is known to be affected by genetic conditions. Hence, both group work and the ability to work on a one-to-one basis should be incorporated into similar programmes.
- The importance of an interlinked clinical strand is highlighted by the need for one-to-one education, so that individuals who require further information and support, and potentially genetic testing, have access to this delivered by an expert genetic counselling service.

- Community and professional education is a process that requires sustained efforts for educational initiatives to be delivered. The community educator noted that many centres required repeated contacts, and it often took a long time for contacts to respond to the initial approach.
- Education sessions in the community had a snowball effect when further sessions were planned on subsequent weeks. Women would return with further questions and with others who they felt would benefit from sessions.
- Community education is much easier when the objectives of the community centre and the project are aligned. This is likely to be the explanation for why the initiatives with the children's centres were more productive than those with the mosques, where attendees were attending to pray rather than to take part in an educational session.
- EGSP community education staff found it difficult to engage with Muslim men. The mosques had been selected for educational sessions as a means to make contact with men. The community educator noted that Muslim men are usually the head of the family and normally have the final say in family decision-making. As a result, this difficulty in delivering education and information to men was felt to be a barrier that needed to be overcome. Once attempts to set up educational sessions with the mosques met with limited success, approaching fathers' groups in the children's centres became a possible way forward. A further opportunity that was not fully explored was father groups and sessions for parents at the madrasahs (Islamic schools).
- Consanguinity can be an emotive issue, but if sensitively dealt with in a manner that is nuanced, conveying an accurate understanding of the risks, it need not be controversial. In the experience of EGSP there were no negative responses from the community to the project. Initially some level of suspicion was often encountered. If dealt with sensitively this did not persist, and members of the community valued the services and information provided by EGSP, including a fuller understanding of risks.

Professional education

- All seven professional education objectives (page 96) were met, except for the objective relating to the setting up of cascade training. Some progress was made on this within the community setting through the training of health trainers. There was little evidence of the impact of the community or professional education on referrals into EGSP, but this may be in part due to the limited timescale of EGSP and available alternative referral pathways.
- Time is required to set up professional education. The professional educator noted that she had re-contacted the same groups on multiple occasions to offer education sessions, but perseverance usually led to sessions taking place.
- The experience of EGSP underlined the importance of having pre-existing contacts in the community, including with GP practices, to increase the likelihood of sessions taking place.

- GP practices need to have the expertise to advise people on risks associated with consanguinity and AR conditions, as it was found that members of the community would turn to their GP for such advice and information. GPs themselves often do not see genetics training as a priority, and few had made referrals to the clinical genetics service.
- It is important to identify the approach to education that will result in most engagement and achieve best outcomes. The initial focus on genetics was found to be less effective than focusing on high rates of infant mortality and morbidity in the locality. Once the initial interest had been established, both community and professional audiences were more likely to engage with other topics necessary for a fuller understanding of how to reduce risks. These topics included basic genetics, AR inheritance and how consanguinity can increase risk in certain families.

9 Views of the EGSP staff

Process evaluation

A key aim of the evaluation was to disseminate learning arising from the experience of EGSP. This would enable commissioners and clinical providers, who are considering the future of EGSP, to learn from EGSP's experience and to inform any future direction of the project. It would also guide other similar service provision. An important source of information for the evaluation was the experience of members of the EGSP team. They were particularly well positioned to provide insights on organisational issues. Their views are based on their experience of what had been successful, and with hindsight what could have been improved.

Members of the EGSP team were interviewed in order to gain insight into organisational issues - what had been successful and what had not worked so well.

To gain this information, semi-structured interviews were undertaken with key EGSP team members and managers. The team members included the genetic counsellors, the community and professional educators, the project manager and the consultant clinical geneticist project lead. The plan was to interview these individuals twice, midway through the project and again towards the end of the project, using a similar set of questions. An initial set of interviews was carried out two years into the project, in November 2011 and a final set undertaken in September 2013, prior to the end of the EGSP's funding in November 2013. Due to staff changes only one member of the team, the consultant clinical geneticist manager, was in post at both time points. Where possible, exit interviews were undertaken with the team members who left in the intervening period.

The interviews focused on how far the interviewee thought that the objective of their part of the project had been achieved; what had been the main successes; what had been the main challenges; what would the individual have changed about the project; for the mid-term interviews, what should be the main objectives for the second half of the project; what recommendations the individual would make to others setting up a similar service; and some very specific questions clarifying particular aspects of the strand.

All interviews were undertaken by the PHG Foundation evaluation project lead and were recorded. The recordings were examined so that key themes could be extracted. These are divided into the main themes that were identified in most interviews, and subsidiary themes that the evaluation considered to be important, but were mentioned in a third or fewer of the interviews. The questions were open-ended and so the following themes, with the exception of point 1, arose spontaneously rather than as a result of interviewer prompts.

Main themes

1. EGSP was seen as a worthwhile and important project by all members of the team. It was seen as having an important role to play in reducing the burden of Autosomal Recessive (AR) conditions among the target communities. Once the public health impact of AR conditions linked to consanguineous unions was understood, it was welcomed by the community. EGSP staff were committed to improving access to genetic services for the target community in light of the high burden of congenital anomalies experienced by the target population.

2. Overall, staff felt that most of EGSP's objectives had been met. There was a consensus that the education strand in particular, but also the laboratory component, had been notably successful elements of EGSP.

3. The perception of the team was that for a variety of reasons the clinical strand had struggled to meet its anticipated activity levels, in terms of patient numbers and take–up of cascade testing. The reasons for the lower than anticipated activity of the clinical strand are explored further in the following key themes, and recommendations for other projects are made.

4. The overriding theme that came out from the interviews was the failure to integrate EGSP into the clinical genetics department. This was mentioned in 10 of the 12 interviews and by eight of the nine members of staff interviewed. It was seen to have hampered the effectiveness of the clinical strand. EGSP staff felt that the clinical genetics department viewed EGSP as a separate entity rather than as an opportunity to provide an enhanced genetics service. This view was reflected by the low numbers of referrals received by EGSP, both from the genetic counsellors and clinical geneticists from the clinical genetics department. EGSP had the potential to provide additional time for the genetic counselling of all families affected that met the EGSP entry criteria and to use this time to explore and provide cascade testing. Although cascade testing is offered by the clinical genetics service to all patients where relevant, within the 45 minute clinic appointment there are time constraints on how far this can be discussed with patients. Referrals to EGSP would have allowed this indepth discussion, but depended on the referrals being made. EGSP staff members suggested that this could have been resolved by making the clinical strand of EGSP a part of the clinical genetics department. The additional resources provided by EGSP could have been ring-fenced to provide an enhanced genetic counselling service focusing on supporting cascade testing within the target communities.

5. Some interviewees suggested that the education of health professionals could have been incorporated into the role of the genetic counsellors. In addition the project could have benefited from greater integration between the community education and genetic counsellor roles, with the genetic counsellors providing clinical support in some of the community settings.

6. The full EGSP team were not located together. The education team were based with the NGEDC, while the rest of the team were based in a separate building in the clinical genetics department. Locating the two together would have created a more a unified team.

7. EGSP's effectiveness was hindered by recruitment and retention difficulties, particularly in relation to the clinical strand. Many of these difficulties could have been improved by integrating EGSP into the clinical genetics department. For EGSP to have functioned optimally, experienced genetic counsellors would have been required to manage the patient review process as patients entered EGSP. Periods of supervision were required for newly qualified counsellors which impacted on the capacity of a short term project. Secondment of genetic counselling staff to EGSP would have brought experienced genetic counselling staff to EGSP. In addition, secondment of genetic counsellors from the clinical genetics department could have aided staff retention, as being a short-term project, the genetic counsellor would have had a post to return to when EGSP's funding ceased, and so would have been less likely to leave the project during the course of EGSP.

8. Consanguinity is less contentious a subject when dealt with sensitively than had been anticipated. This was mentioned in most interviews and by six of the nine team members. There had been concerns, based on the PCT's experience prior to the setting up of EGSP, that a project concerned with the effects of consanguinity would provoke a hostile response from minority ethnic groups locally. Although there was often much discussion about consanguinity in the context of the community education sessions, no hostility to EGSP was experienced by members of the team when discussing consanguinity. In the context of the professional education, health professionals welcomed the opportunity to gain more information on consanguinity and how to approach the subject with patients. The only situation in which EGSP's approach to consanguinity was met with criticism was where a non-health professional felt that EGSP was not strongly enough dissuading members of minority ethnic communities from marrying within the family. The community educators noted that during the educational sessions in the community, attendees started to understand that consanguinity was a public health issue and that education about the potential health impact was not an attack on cultural values.

9. The concerns of the host Trust and PCT around consanguinity and the media resulted in a reluctance to allow EGSP to engage with the media. There was no communications plan. As a consequence, a number of approaches made to EGSP by a variety of Asian media could not be taken forward by the team. EGSP team members felt this reduced the reach of EGSP and so its potential to provide services to the local community.

10. The lack of a project steering group for much of the EGSP's life was seen as reducing both the effectiveness of EGSP and its sustainability. This was mentioned by five of the nine interviewees. The steering group met sporadically and was poorly attended other than by EGSP team members. Steering group members with membership comprising key senior health professionals and community leaders could have provided focus for the team, and made EGSP accountable in the way it prioritised its activities. Staff changes meant that at times there was a lack of continuity in project management and staff felt that this impacted on the focus of EGSP. The steering group could have ensured that the focus was maintained and their expertise could have also provided support to overcome challenges and to provide guidance. They could have become champions for EGSP,

increasing the likelihood of ongoing funding for the project being secured.

11. Unrealistic time expectations were mentioned in a variety of contexts by interviewees. Firstly, there were unrealistic timeframe expectations in the initial objective set to reduce infant mortality. Secondly, the time that individuals and families take for decision-making when deciding whether to take up genetic testing, and in particular cascade testing, were felt not to have been adequately recognised by EGSP commissioners. It was anticipated by members of the team that the effects of EGSP will be realised well after the time of EGSP's operation. It also took time to refine the messages of EGSP, particularly in the context of rare diseases, where many of the target professional groups for education did not initially view AR conditions as a priority for their education.

Subsidiary themes

12. The lack of community representation to provide guidance to EGSP was also highlighted, particularly by the educators and project manager. Team members felt that greater prominence should have been put on developing this prior to initiating the project.

13. There was inadequate IT support for the project and this should have been more of a priority. Having IT commissioned from within the clincal genetics service was seen as a missed opportunity. This was because competing demands on IT expertise resulted in it not being available at periods when it was required. IT support needed to be ongoing if it was to be fully responsive to the different phases of the project. The staffing retention difficulties added to the need for ongoing IT support.

14. The community educators noted how valuable the process monitoring exercise had been. It provided continuity when there were staff changes and facilitated their ability to reflect on how to develop the education and maintaining contacts.

15. Finally, a couple of novel ideas were suggested during the interviews that the project did not have time to pursue. A different approach to the patient review process and pathway might have resulted in more patients being seen by the clinical strand, through focusing on 'champion families'. These families are those already known to the genetics department who are enthusiastic about pursuing cascade testing within their family. The number of individuals taking up testing could have been higher, compared to the return from following the pathways as set out in chapter 6, if the focus of testing had been to cascade through such families. In addition, such families might interest other families with AR conditions in their communities in investigating cascade testing.

16. A second suggestion involved seconding a health visitor for regular sessions to work alongside EGSP. The health visitor would be a resource for other health visitors, raising awareness of genetic services and their

potential to provide reproductive choices to families both among other health visitors and the families they see. This 'cascade' educational approach could have provided a degree of continuity to the education components of EGSP, beyond the life of EGSP.

Conclusions

- EGSP would have benefited from greater integration with the clinical genetics department. It is likely that greater involvement with the department would have achieved higher rates of patient review and cascade testing. It could have also alleviated the recruitment and retention problems that had a major impact on the success of the clinical strand.
- A genetic counsellor with a particular interest in education could have undertaken the educational role with health professionals and worked closely with the community educator. Co-location of the full team could have helped foster better team work.
- Approached sensitively, consanguinity was not a contentious issue in communities with high levels of AR conditions.
- A communications strategy supported by training in working with the media should have been developed and adopted to guide use of the media. The media could have been a powerful force for raising awareness of a project like EGSP that encouraged members of the target communities to self-refer to the project or make contact via their GP.
- Projects such as EGSP benefit from being supported by and being accountable to an effective steering group. Involvement of key individuals would have also helped efforts to secure ongoing sustainability.
- Community representation on the steering group or as a separate advisory group, should have been established before the project was initiated to help the project meet the community's needs. It is recognised that this might have required considerable effort.
- IT support should have been available at all stages of the project. It was identified as a key component to enable a project such as EGSP to provide services to its target population and to provide evaluation data.

10 Discussion

The Enhanced Genetics Services Project was established to provide a better understanding of the contributory causes to the excess stillbirth and infant mortality rates in the Birmingham population, and to pilot interventions to address the specific cause of AR conditions.

Through the detailed analyses and linkage of regional datasets, the project successfully confirmed the contribution of AR conditions to the excess mortality rates experienced by the Pakistani and Bangladeshi communities. In addition, further information was obtained through clinical audits. This evidence highlighted the need for additional support to be provided for these communities; to reduce their risks, and for the provision of care to address the health inequalities identified. The work undertaken illustrated the importance of timely enhanced surveillance of perinatal and infant mortality data for ongoing health and social care activities to address the excess mortality rates experienced by some communities in the West Midlands. As was acknowledged from the outset of this project, interventions to address these excess mortality rates will need to be long-term and sustained to be successful.

The primary care strand was focused on haemoglobinopathy screening in primary care. The results from the two practices involved indicate that this service can be successfully provided in primary care and could be a useful model of care for high risk populations. However, further work is required to establish the optimum specification of such a service, the level of additional training for the primary care team, the level of specialist clinical support necessary and evidence of cost-effectiveness of this model. This should include specifically the time and expertise required within the consultation to provide information on carrier status, so that this information can be understood fully and appropriately shared with other family members or future partners. The primary care strand was established in advance of the start of the project and this resulted in less integration of this strand into the overall project. This prevented the development of a longer-term and sustained contribution from the other project strands to the two practice teams and their populations.

The clinical strand has demonstrated that an enhanced clinical genetics service for family support and cascade testing of family members can be implemented and provide the intended clinical care. Within this project, the clinical strand was not able to achieve the expected capacity of referrals due to insufficient clinical staffing and frequent changes in staffing. There were also lower than expected referrals from within the clinical genetics service, primary care and other hospital departments. The reasons for this remain unclear, particularly as there was evidence from the laboratory strand of a larger number of EGSP eligible patients seen by other hospital clinical departments. Lack of suitable IT and database support also prevented the clinical strand from achieving its full potential in identifying eligible families. The project has identified a clear population health need to address the risk of AR conditions in the West Midlands population and the enhanced clinical genetics service pilot has shown an approach to addressing this. It is likely that the full benefits of the clinical service established will not have been achieved in the limited timescales of the project. These are expected to accrue in the future, assuming

the clinical genetics service will proceed to follow up EGSP activity. Further consideration needs to be given on how to embed the learning and experience of the clinical strand pilot into the West Midlands Clinical Genetics Service, to ensure enhanced cascade testing is available for families with identified risk of AR conditions.

There was no opportunity to test the provision of genetic counsellor outreach services into general practice, particularly in those practices serving populations within the West Midlands with the highest risk of AR conditions. This should remain an option for future investigation.

EGSP-funded development of new genetic tests and the genetic testing service provided a significant improvement in healthcare provision for the NHS population. 534 patients received genetic tests which resulted in molecular genetic diagnoses for 116 patients and confirmation of carrier status for 109 individuals. Testing for 12 conditions as part of this activity was not available in the UK and the benefits achieved from this genetic testing are directly attributable to EGSP. These benefits included the correct treatment for some patients who were diagnosed, and the opportunity of cascade testing in affected families. The additional benefit of the project is that the West Midlands Regional Genetics Laboratory has been able to generate income from providing these testing services to the population outside of the West Midlands. This has enabled it to continue to provide the new genetic testing service at the conclusion of the project to the benefit of the West Midlands population.

A major area of activity for EGSP was community and professional education. For both education activities, considerable understanding of the target audiences' needs was achieved, and different approaches to deliver education were attempted. Feedback indicates that positive impacts were achieved in both groups and the strand was successful in its objectives. However, to achieve longer term outcomes these activities will need to be sustained and developed further based on the experience and learning obtained. Specific education materials were developed and evaluated as part of the project and these should continue to be used by health development services. The project-specific website, whilst underutilised, could also be reviewed and maintained to provide additional support to health development activities, particularly in the target communities. There is a risk that the community-specific approaches and tools developed by the education strand could be lost if these are not incorporated into mainstream health development activities.

The project initiation process did not include outcome measures to define the clinical effectiveness and cost-effectiveness of the new services piloted as part of the project. This has prevented the analysis and provision of such evidence for service development and implementation purposes. The morbidity impact of AR conditions can be significant but this could not be investigated as part of this project. Further work is needed to describe and quantify the morbidity caused by these diseases.

Overall the project with all its strands and components required careful and integrated programme management. This proved challenging due to the separate nature of the primary care strand - in how it was established, insufficient dedicated management time for the lead clinician, lack of support

EGSP-funded development of new genetic tests and the genetic testing service provided a significant improvement in healthcare provision for the NHS population.

from an established Project Steering Group, continuous personnel changes within the project team for the duration of the project and lack of clinical capacity within the West Midlands Clinical Genetics Service. It was also identified that the project would have benefited from being integrated into the clinical genetics service, with the project team being co-located. Despite these significant challenges, and through the considerable efforts of the project team and partner services, most of the deliverables were achieved. In doing so, there have been successful pilots of new services for patients and professionals in the West Midlands which improved the quality of healthcare for patients.

11 Recommendations

1. Autosomal recessive conditions are an important contributor to the excess stillbirths and infant mortality rates in the Birmingham Pakistani and Bangladeshi communities. This contributing factor should be considered and addressed as part of any public health efforts to address health inequalities in these populations.

2. Further work is required to establish the evidence for the best model in primary care to provide services to communities at high risk of stillbirths and infant mortality deaths due to autosomal recessive conditions.

3. Long-term enhanced public health surveillance of excess stillbirths and infant mortality rates in the West Midlands, based on the systems and data generated from this Project, should be established to provide the evidence base for identifying and addressing the contributory causes.

4. The learning and experience of the project should be embedded into the West Midlands Clinical Genetics Service to ensure enhanced cascade testing is available for families with identified risk of autosomal recessive diseases.

5. Genetic counsellor outreach services into general practice should be considered for a pilot, particularly in those practices with the highest population risk of autosomal recessive conditions.

6. The West Midlands Regional Genetics Laboratory should continue to develop new genetic tests particularly for autosomal recessive conditions building on the capacity and experience generated from EGSP.

7. Further health development work should be commissioned building on the achievements and materials developed by the education strand including the Project website.

8. Development of a Health Visitor (clinical genetics) lead role supported by the West Midlands Clinical Genetics Service should be established.

9. The development of patient support such as 'Patient Champions' should be considered as part of future programmes, to improve community and professional awareness, and to support cascade testing.

Appendices

Appendix 1	Project Initiation document
Appendix 2	Evaluation Working Group membership
Appendix 3	EGSP Project Team
Appendix 4	West Midlands Perinatal Institute Report May 2012 and appendices
Appendix 5	Activity data requirements for primary care, clinical and education strands
Appendix 6	Key points from Primary Care Strand Service Level Agreement
Appendix 7	Patient and primary care staff experience of primary care strand
Appendix 8	Leaflets developed by EGSP

Appendix 1 Project initiation document

Project name	A focused approach to reducing infant mortality and morbidity attributable to autosomal recessive disorders within Birmingham. The provision of a comprehensive package from primary to secondary care.
Release	Draft Date:

Author:	Tom Fowler SpT in Public Health Carole McKeown Consultant Clinical Geneticist Ghazala Rafiq
Owner:	Carole McKeown
Client:	Heart of Birmingham Primary Care Trust & Birmingham Wellbeing Partnership
Document Number:	001

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Approvals This document requires the following approvals.
Signed approval forms are filed in the project files.

Name	Signature	Title	Date of Issue	Version
Jacky Chambers		Director of Public Health		
Project Steering Group				

Distribution This document has been distributed to:

Name	Title	Date of Issue	Version
Project Steering Group			
Womens Hospital (Management Team)			
PEC			
PCT Contracts Department			

Project Initiation document

Project executive summary

The objective of the project is to address the issue of autosomal recessive disorders causing an excess of infant mortality and childhood morbidity within Birmingham. This is also a major contributor to the high levels of infant mortality and morbidity of England. Research suggests there is a high prevalence of autosomal recessive genetic disorders amongst the Pakistani community compared to other ethnic groups. Where the genes for an autosomal recessive disorder is present in extended families, where consanguinity is common this will increase the chances of people marrying within the family of both being carriers for the autosomal recessive disorder (i.e. having one copy of the gene that codes for the autosomal recessive disorder). However, this is not the only reason for congenital disorders and couples marrying outside families may also both be carriers for autosomal recessive disorders.

In a community with a cultural preference for consanguineous marriages, the formulation of a public health program with a multi-approach strategy, including education about the anticipated genetic consequences, prenatal diagnosis, neonatal screening, and genetic counseling, is a necessity.

It has been estimated that 8-10% of consanguineous couples are at high (1 in 4 per pregnancy) risk of having a child with a autosomal recessive genetic disorder, while the remaining 90% are at general population level risk i.e. just as likely to have a child with congenital problems as any couple in the population. Recessive disorders occur when a child inherits two copies of an identical mutation; cousins are more likely to inherit an identical mutation because of sharing a pair of grandparents, one of whom might carry a mutation that they could pass on to their children and grandchildren. Adverse outcomes occur for a number of reasons not just genetic disorders.

The current project seeks to identify those families/extended families identified as carriers of an autosomal recessive genetic disorder and who would benefit from individual genetic risk information to help couples make informed reproductive choices. Family history information is a necessary beginning step in determining the underlying etiology of the disorder.

The project will take a multifaceted approach comprising of a number of strands, to identify families who would benefit from genetics services input as well as raising the genetic literacy of the community and relevant Health Care Professionals.

The first strand will consist of undertaking opportunistic screening for Thalassemia (inherited autosomal recessive blood disease) within pilot GP practices and using this as a vehicle to raise genetic literacy within the population. It will also seek to identify families appropriate for referral to genetic services (see below). This aspect of the project is subject to a separate project implementation plan.

The second strand will consist of an extension of current services within the West Midlands Clinical Genetics Services to allow systematic identification and enhancement of services to families at high risk of genetic disorders (particularly autosomal recessive disorders). This will be split into two phases:

Phase 1

A review of all existing families from Birmingham known to the Clinical Genetics department will be undertaken to establish the range and number of families known with autosomal recessive disorders. This will be supervised by Consultant Clinical Geneticists and the results will help to inform the molecular laboratory aspects of the project. It will include further development of the existing clinical management systems to offer a systematic approach to reviewing of families at risk of autosomal recessive disorders and using known families as a conduit to provide information to extended families. As a part of this, relevant baseline audits will be undertaken and key evaluation measures will be agreed upon and incorporated into the standard procedures of the project.

This phase will also include the appointment of a laboratory technician/scientist to start developing molecular testing services and the appointment and training of relevant educationalists and genetic counsellors or genetic field workers.

Phase 2

The case finding approach will be extended through hospital and community based paediatricians and other relevant health professionals. This will include the consolidation of capacity for local laboratories to provide carrier testing within families so that information regarding individual genetic risk can be provided. The development of Outreach Genetic Counsellor led clinics based in local GP practices where possible, will also be initiated/extended in this phase.

The third strand will be rolled out in phase 2 and consist of an educational initiative in both the community and with health care workers. In the community this will be to raise the genetic literacy of the Pakistani population. The educational initiatives with health care professionals will seek to improve their genetic competence to ensure they are able to support families with information, advice and signposting to appropriate specialised services. It is also intended that the educational material will be used by families as a conduit when approaching and providing information to their extended families.

The final strand will be an ongoing evaluation of the project by an externally commissioned organisation. This will provide both iterative feedback to improve the ongoing running of the project and a final evaluation.

There are a number or risks associated with this project, the two main risks being an adverse public reaction to addressing this issue and the lack of uptake of services by the extended families, (though this may be hard to assess within the timeframe of the project).

Although the project will have an emphasis on the Pakistani community, other communities who also show a prevalence of the autosomal recessive disorder will benefit from the services offered.

The funding available for this project circa £1.5 million, of which £960,000 has been allocated to the WMRG service, £100,000 for evaluation, £80,000 for development of educational material and £350,000 to the primary care initiative.

Project overview

Reducing perinatal and infant mortality in Birmingham to the national average is a key Public Service Agreement target. But data provided by the West Midlands Perinatal Institute, shows that infant mortality in Birmingham rose from 8.5 per 1000 live births in 1998-2000 to 9.7 per 1000 live births in 2002-04. The rate for England and Wales fell from 5.7 per 1000 live births to 5.2 per 1000 live births over the same period, so the gap between Birmingham and the national average has increased rather than reduced over this period.

Infant mortality and congenital malformation amongst the Pakistani community has been an area of cause for concern in the west midlands for many years (see table 1). This can be partly attributed to autosomal recessive genetic disorders particularly for those in consanguineous marriages. Nationally, of the estimated 2,300 children born annually with severe autosomal recessive disorders at least 690 (30%) are born to parents of Pakistani origin. About a third of the affected children die before five years of age. Most of the survivors suffer chronic disability, and they are cared for by their families posing tremendous emotional and financial strain. Paediatricians provide specialist services.

Table 1 Early Neonatal Deaths (END) (i.e. death in first week of life) due to Congenital Abnormality and other causes by Ethnicity (HOBtPCT)

Average Annual (2002-2004)	European	Indian	Pak/Ban	Bca/Baf	Other	Total
No. New Births	717	469	2535	495	594	4810
Total no. of END due to all causes	1.3	2.3	19.6	9.0	4.0	41.0
No. of END due to Congenital anomaly (will include single gene, chromosome and multi-factorial conditions)	0.3	0.7	10.3	1.3	1.0	13.7
Total excess no. of END due to all causes (c/f European rate)	----	1.5	10.5	8.1	2.9	32.1
Excess no. of END due to Congenital anomaly (c/f European rate Source: Director of Public Health Report of PCT 2006	----	0.4	9.2	1.1	0.7	11.4

Despite many attempts to address this issue locally, success has been hampered by the lack of an overarching strategic approach incorporating primary care and specialised services, appropriate materials with which to improve genetic literacy and explain risk (both to those at highest risk and to health care professionals) and a fully resourced and integrated genetic service to provide specialised support.

Key Facts:

- Previous work in the Birmingham area (Birmingham Birth Study; reported in Modell & Darr, 2002) suggests the prevalence of congenital and genetic disorders is 4.3% in North European children and 7.9% among British Pakistani children (almost double). ***This difference in risk is almost entirely due to greater prevalence of autosomal recessive-inherited disorders through consanguineous marriages.***
- Couples at risk for autosomal recessive disorders (i.e. both carriers) have a 1-in-4 risk of an affected child in

each pregnancy. This means that 8-10% of consanguineous couples are at high (1 in 4) genetic risk, whilst the remaining 90% are at general population risk.

- Local surveys suggest the prevalence of consanguineous marriages in mothers giving birth from the Pakistani community currently is around 50-70%.
- 61% of 5 year old children on SEN register in Birmingham are Asian/British Asian (Pakistani and other). (Dr Moy, Trends in the Epidemiology of Childhood Disability in Birmingham).
- British Pakistani children in Birmingham are 10 times more likely to have an inherited metabolic disorder than North European children. Collectively metabolic disorders are more prevalent than Down syndrome in the West Midlands. (Dr Moy, Trends in the Epidemiology of Childhood Disability in Birmingham)
- Birmingham BME communities account for 29.6% (England 9.1%), however 50% of under 16 year olds are from ethnic minorities and this proportion is predicted to grow. The implication of this is that the number of infant deaths and childhood disability due to genetic disorders is likely to increase over the next 10 years (Dr Moy, Trends in the Epidemiology of Childhood Disability in Birmingham).
- Many extended Pakistani families at risk of autosomal recessive conditions will already have had an affected child. These families can be contacted and information disseminated on the risks to the health of children born to parents who are both carriers of a recessive disorder. Encouraging early diagnosis and treatment options in addition to offering support in making the decisions they feel morally right for themselves.
- Ideally, genetic information and counselling should be offered to families most likely to benefit, if they can be identified as having a rare autosomal recessive disorder. Informing families with individualised risk information according to the social context and circumstances of their lives will help them understand probabilistic risk information and is likely to motivate them to change their behaviour to reduce the risk as opposed to providing them with statistical data on a population at risk.
- Over a 10 year period a multidisciplinary strategy including an organised programme of genetic counselling is likely to bring about a 50% reduction in deaths and disability due to consanguineous marriages. (Dr Darr and Professor Modell, personal communication).

Rationale for Multidisciplinary Intervention

- It is important to identify and prioritise those families most likely to benefit from this project. A sensitively combined and focussed approach in providing them with information will allow them to make informed decisions.
- Where Individuals have responded to information on individual genetic risk (e.g. carrier status) behavioural change has resulted in affected families working with health services to ensure they reach the minimum family size of healthy children they desire. There is likely to be less motivation and behavioural change in responding to information on population at risk.
- Most Pakistani families where the problem is present will have had an affected child within the UK extended family. This allows:-

    1. The identification of families for whom it would be appropriate to approach.
    2. The ability to access the extended family through the immediate family of the affected child who, previous experience suggests, will often act as a champion to encourage uptake of genetic services.

Impact of the proposed Multidisciplinary strategy

Table 2. illustrates the estimated impact of the multidisciplinary approach including a focused genetic counselling programme and an integrated primary care approach to Heart of Birmingham teaching Primary Care Trust (HobtPCT) residents.

Individual genetic risk is effective at motivating individuals in changing behaviour. Other outcomes include:-

1. An increase in informed choice about options in pregnancy
2. A reduction of the immense personal cost to families when an infant death or child with severe disability occurs,
    - This project addresses an area of need that is unlikely to be able to be effectively met in any other manner.
    - The approximate average cost per annum of care packages for Severe Learning Disability is £70,000. These are ongoing cost, suggesting the intervention is likely to be *Cost Saving* in the long-term due to its impact on Severe Learning Disabilities alone (potential annual saving £2,000,000).

Table 2. Expected rates and costs of infant death and disability due to consanguineous marriages in HOBtPCT.

Outcome	British Pakistani Births				
	Yearly Rate per 1000 Births			Yearly Number attributable to consanguineous marriages	Yearly reduction in affected children due to intervention (assuming 50% efficacy)
	Total	Attributable to Congenital/ Genetic	Excess attributable to consanguineous marriage		
Genetic abortion	4	4	0.1	0.21	0.1
Death 1st month	21.9	8.5	5.9	12.1	6.1
Death 1 month-5yrs	13.9	7.5	4.8	9.8	4.9
Severe Chronic Disability	49.9	41.3	27.3	56.0	28.0
Corrected congenital malformations	15.8	15.8	0	0.0	0.0
Total	105.5	77.1	38.1	78.1	39.1

Additional benefit.

- Increased genetic literacy of healthcare professionals will lead to greater utilisation and more appropriate referral to services of all individuals (Pakistani and other) for autosomal a variety of genetic disorders (e.g. cancer genetic services).

Key Facts: Cultural Sensitivity

Recent qualitative work in Pakistani community residents of Springfield ward (Understanding Inter-Generational Attitudes towards Consanguineous Marriages in Birmingham), commissioned by the Health and Well Being Partnership, strongly suggests that the model of identifying families through affected children is likely to be most effective. Findings included:

- Considerable lay confusion regarding the role of genetics in understanding inherited diseases and an

emphasis on the need to improve genetic literacy to enable informed decisions.

- A general belief that still births and disabilities were not significantly higher among the Pakistani community compared to other ethnic groups and suspicion of evidence to the contrary.
- A strong value placed on the benefits of arranged marriages, including consanguineous marriages, coupled with a feeling that the debate around the issue represented an attack on the Islamic and cultural way of life.
- A perceived need and enthusiasm for more information regarding genetic risk in a format that was culturally sensitive and does not pathologies cousin marriages

Thus a programme focusing on improving genetic literacy and providing information on genetic risk focusing on those Pakistani extended families (*Biraderis*) identified at high risk is likely to avoid the backlash that may occur by solely addressing the issue of cousin marriages at the community level. The programme is intended to benefit the population as a whole with initial focus on those who will benefit most. Providing adequate and relevant information and support on making the right reproductive choice for them.

Project objectives

The project will meet the following objectives:

Objective 1: Improved access to molecular testing for autosomal recessive disorders – a prerequisite for carrier testing.

Objective 2: Improved access to genetic counselling through increased capacity within the Clinical Genetics Service of Genetic Counsellors with appropriate minority languages.

Objective 3: Improved genetic literacy in families affected by a genetic disorder identified by the initiative.

Objective 4: Improved genetic literacy and understanding in the extended families.

Objective 5: Improved genetic literacy in HoBtPCTs ethnic minority communities about genetic disorders and their transmission, particularly in consanguineous families

Objective 6: Improved genetic knowledge and competence among health professionals in HoBtPCT.

Objective 7: Carrier testing within extended family to identify high risk couples, offering genetic counselling including possibility of pre-natal diagnosis and postnatal treatments.

Objective 8: Identify causative mutations in genes known to cause autosomal recessive conditions in affected family.

Objective 9: Offer carrier testing of causative mutations to extended family.

Project objectives will need to be evaluated throughout and at the conclusion of the project in order to validate its success.

Deliverables Intended

Deliverable 1: Mapping of the range and relative frequency of autosomal recessive disorders in the Pakistani and other communities inBirmingham, particularly those contributing to perinatal and infant mortality

Deliverable 2: Adaptation of the Clinical Genetics IT system to allow review and recall of at risk families and to capture all activity related to the project

Deliverable 3: Improved molecular genetic testing for autosomal recessive disorders associated with early childhood mortality and morbidity. Specifically this will include:

- Identification of the mutation spectrum in a range of autosomal recessive disorders including common metabolic diseases. This will enable prenatal and carrier testing to be offered to affected families and where appropriate prenatal testing to be offered to extended families.
- In most cases, molecular genetic testing will be accomplished by establishing a new diagnostic service within the West Midland Regional Genetics Laboratory (WMRGL). This will facilitate timely diagnosis of the relevant diseases in new cases.
- The identification of common founder mutations in the Birmingham population that might be suitable for population screening.

Deliverable 4: Previously seen families re-contacted by Genetic Counsellors to offer carrier testing. Newly referred families seen to be offered Genetic Counselling and carrier testing. **(Depends on 1)**

Deliverable 5: Where appropriate running Genetic Counselling clinics in GP practices to increase accessibility of services.

Deliverable 6: Increased referral for Genetic Counselling of families from GP practices in which Genetic Counsellors have been based.

Deliverable 7: Training of a range of health care professionals in HoBtPCT in Genetic competencies related to their role.

Deliverable 8: Delivery of culturally sensitive information about Genetics, autosomal recessive inheritance, access to carrier testing and other Genetics services, to a range of community groups in HoBtPCT.

Deliverable 9: Development and evaluation of Educational material for use by affected families who will aim to convey that information to their extended families raising the genetic literacy.

Deliverable 10: The commissioning of an evaluation of the initiative.

Project scope

The scope of this project includes and excludes the following items.

In scope:

- Scoping the range and relative frequency of autosomal recessive disorders in the Pakistani and other communities in Birmingham.
- Working with selected GP practices to provide regular experienced Genetic Counsellor's presence within the practice for several months
- Offering counselling and carrier testing to affected families and extended families living in Birmingham.
- Regular review of clinical activity to optimise use of resources for molecular testing in light of specific gene and/or family circumstances (depends on evaluation of Phase 1 – molecular testing and case review).
- Genetic education of health care professionals and community.

Out of scope:

Molecular testing for every autosomal recessive disorder where causative genes have been identified.

Families where affected family member not Birmingham based.

Primary care and community, educational initiatives outside HoBtPCT.

The implementation planning of the primary care strand of the initiative, which is the subject of a separate document.

Outcomes:

Organisation:

- Data on process and activity will be available which can be used to base future commissioning of ongoing specialised Genetics Services for this high risk community.
- More timely referral (pre-pregnancy) will ensure informed choice for families and a more efficient use of clinical and laboratory resources.

- The initiative will also contribute to a sustained reduction in perinatal and infant mortality in the longer term.

Satisfaction: Patient satisfaction will improve with:

- Greater genetic awareness, competence and cultural sensitivity of the health care professionals with whom they come in contact.
- The wider availability of timely Genetic Counselling and carrier testing close to home and by Genetic Counsellors with minority languages

Clinical Effectiveness: A specification will be in place to ensure the service identifies families at a high (1:4) risk for autosomal recessive disorder pregnancies (i.e. both carriers) and provides them with adequate information so they can make informed decisions.

Activity: A systematic approach to identifying families, offering genetic testing, and genetic counselling via a genetic education programme to raise the literacy of the population.

ORGANISATIONS OR SUBSTRUCTURES AFFECTED

The impact of this project on other organisations needs to be determined to ensure that the right people and functional areas are involved and communication is directed appropriately.

Organisation or Substructure	How are they affected, or how are they participating?
HoBtPCT	Funding the Initiative, Residents for which they have responsibility will be offered services
Birmingham Women's Hospital	Hosting the project
Primary Care Team	Education initiatives and development of genetic competencies
Families	Development of enhanced genetic understanding to allow informed choice for affected and extended families
Community	Awareness to be raised through education initiatives
South Birmingham PCT	Residents for which they have responsibility will be offered services
Birmingham East and North PCT	Residents for which they have responsibility will be offered services
Birmingham Children's Hospital	Recruiting families from metabolic and other specialist departments

Project estimated effort/cost/duration

Estimated cost of delivery: £1,500,000 (£960,000 WMGS, £350,000 Primary care initiative, £100,000 evaluation, £80,000 development of education tools)

Breakdown of costs:

GP Based Initiative, 3 GP practices	A separate document
Evaluation Costs	£33,333 per annum
West Midlands Regional Genetics Service	£275,599 per annum
West Midlands Genetics laboratory	£47,568 per annum

The above costs include on-costs.

Estimated duration:

Three years

Project milestones

Project Estimated Dates: Dec 2008 – Dec 2011

The project will fall under three distinct phases, below lists milestones to be accomplished within each phase. Phase's may run parallel to each other.

Phase 1

Evaluation tender: Dec 08

Evaluation Report, appoint a body to undertake the evaluation.

Start: April 09

Input and Review from

Start: May 09

Yearly report: May 010 and May 011

Thalassemia Screening: Working with 2 or 3 appointed General Practices within Birmingham, accessing their database of patient list, approaching for Thalassemia testing, widening to congenital disorder testing.

Start: July 09

A Separate Document

National Genetics Centre: Development of educational tool (genetic literacy)

Start: April 09-July 09

Validation of educational tool (1 year ongoing evaluation) combined with delivery of tool (phase 2).

Start: July 09 (with patients) – July 010

Recruitment of Genetic Professionals and Health Care Educational Professionals. Linked to Phase 2

Start:April 09, appoint by June-Aug 09

Recruitment of Laboratory Scientist: Creation of Job Spec/banding. Vacancy to be placed:

Feb/March 09, appoint by May/June 09

Setting up of Laboratory Systems: To assist in analysis of consanguineous families.

Start: May/Jun 09

Recruitment of IT Person: IT system to record project activity.

Start: appoint by March 09

Metabolic Unit, West Midlands Genetic Services: Existing IT database of consanguineous patients. Working with the IT unit, genetic and health care professionals and the laboratory services.

Asap – June 09

Project Management appointment.

Start: Job to advert by Dec 08/Jan 09 - appoint by March 09

Phase 2

Development of Education Programme: by Genetic professionals and Health Care Educational professionals delivered to GP's

Start: May 09

Delivery of Educational Programme

Start: Sept 09

Initial 6 month review then yearly reviews.

Genetics Counselling: Working with Patients, in collaboration with Genetic Professionals and Health Care Education Professionals. 6 monthly reviews. Extend contact to extended families.

Start: July 09—ongoing

Analysis of Case finding data from West Midlands Genetic Services

Start: Aug 09, Development of strategy for case finding in Birmingham Childrens Hospital, working with Paediatricians.

Duration: 1 ½ years.

9 month review.

Phase 3

Evaluation

Project assumptions

In order to identify and estimate the required tasks and timing for the project, certain assumptions and premises need to be made. Based on the current knowledge today, the project assumptions are listed below. If an assumption is invalidated at a later date, then the activities and estimates in the project plan should be adjusted accordingly.

Assumption 1: The interventions identified will have an impact in reducing **the risk factors** associated with perinatal and infant mortality.

Assumption 2: Genetic Counselling capacity – recruitment of staff with languages and good at genetic skills and knowledge.

Assumption 3: Suitable project manager appointed to develop detailed project plan.

Assumption 4: Families with affected children taking part and acting as a conduit to the extended family encouraging participation.

Assumption 5: Community on a whole will participate and find this an acceptable approach benefiting therein.

Project rists

Project risks are characteristics, circumstances, or features of the project environment that may have an adverse affect on the project or the quality of its deliverables. Known risks identified with this project have been included below. A plan will be put into place to minimize or eliminate the impact of each risk to the project.

Risk Area	Likelihood	Consequence	Risk	Risk Plan
Recruitment of Staff	4	3	12	Staggered recruitment and secondment
GPs – not signing up to education	1	3	3	Genetic counsellor offered to practice
Capacity – lab costs	1	4	4	Flexibility to budget to divert extra funds
Extended Families not interested	2	4	8	Ongoing evaluation will provide feedback and adaptation required
Affected Families not interested	1	4	4	Ongoing evaluation will provide feedback and adaptation required
Lack of interest from Pakistani Community	4	1	4	Ongoing evaluation will lead to adaptation of programme
Antagonism	2	4	8	Contingency plan to be developed by Project Manager.

Project approach

This project will need to be signed up by the West Midlands Genetics Services, West Midlands Laboratory Services, National Educational Centre.

It will also need to engage Health Education Professionals and GP practices in Birmingham.

Project organisation

An appropriate project organisation structure is essential to achieve success. The following diagram depicts the proposed organisation.

Project executive lead: Dr McKeown

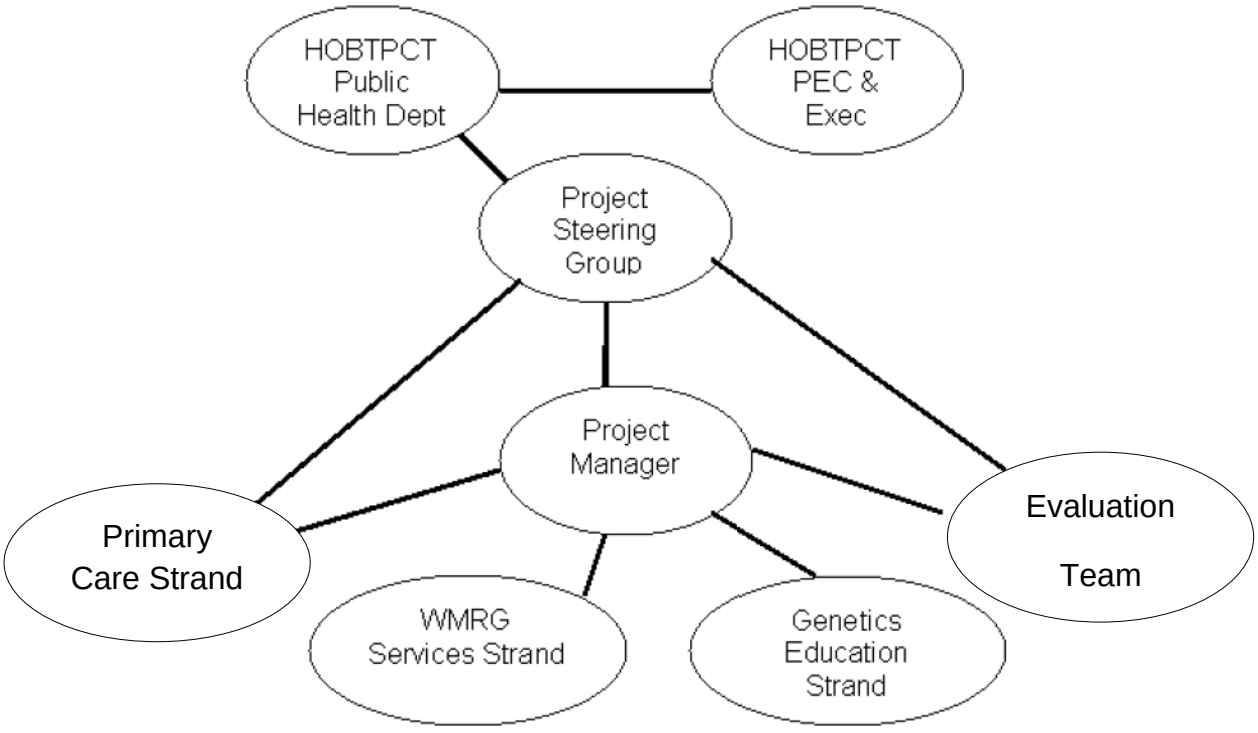
Project sponsor: Dr Chambers

Project Manager: TBC

Project advisors: Tom Fowler, Annette Williamson

Steering Group: Birmingham Rare recessive genetics group

Organisation chart:



Project approvals

Executive Lead	Date
Project Manager	Date

Appendix 2 Membership of the Evaluation Working Group (EWG)

Not all the individuals below were members of the EWG throughout the project. Those with an * attended most meetings.

Name	Designation	Organisation
Corinna Alberg*	Project Manager	PHG Foundation, Cambridge
Dr Rizwan Alidina	Salaried GP	Balsall Heath Health Centre
Liz Altay	Consultant in Public Health	Birmingham Public Health
Uruj Anjum	Genetic counsellor	EGSP
Chris Baggott	Lead for NHSE, PHE & CCG Liaison and Assurance	Birmingham Public Health
Beverley Batchelor	Family Work Co-ordinator	Washwood Heath Nursery School/ Children's centre.
Nicola Benge*	Director of Public Health	Birmingham East and North PCT
Dr Catherine Bennett	Education Specialist	National Genetics Education and Development Centre
David Brownhill	Information Officer	West Midland Regional Genetics Service
Dr Hilary Burton*	Director	PHG Foundation, Cambridge
Dr Jacky Chambers	Director of Public Health	HoBtPCT
Yasar Eltaf*	Project Manager	EGSP
Professor Peter Farndon	Director	National Genetics Education and Development Centre
Alasdair Firth	Data Analyst	Washwood Heath Children's Centre
Dr Tom Fowler*	Specialty Registrar/Consultant in Public Health	HoBtPCT
Claire Giffney*	Genetic Counsellor	EGSP
Dr Wayne Harrison	Consultant in Public Health	Birmingham Public Health, Birmingham City Council
Barry Henley*	Non-Executive Director	HoBPCT
Heena Jabbar	Project Manager	EGSP
Dr Kannan	GP	Sparkbrook Health Centre

Name	Designation	Organisation
Chris Kotara	Chief Technology & Information Officer	West Midland Regional Genetics Service
Dr Mark Kroese*	Programme Director	PHG Foundation, Cambridge
David Latham	Associate Director	National Genetics Education and Development Centre
Dr Fiona Macdonald*	Head of Molecular Genetics / Deputy Director	West Midlands Regional Genetics Laboratory
Zahira Maqsood*	Community Educator	EGSP
Kirsten McKay Bounford*	Clinical Scientist in Molecular Genetics	West Midlands Regional Genetics Laboratory
Dr Carole McKeown	Consultant Clinical Geneticist	West Midland Regional Genetics Service
Maarya Modan*	Community Educator	EGSP
Dr Amal Muflahi*	Health Professionals Educator	EGSP
Mary Anne Preece*	Consultant Biochemist & Director of Laboratory IMD	West Midlands Metabolic Laboratory
Dr M V RamaRao	GP	Sparkbrook Health Centre
Marie Richards*	Health professionals educator	EGSP
Shazia Quereshi	Family Liaison Worker	Washwood Heath Nursery School/ Children's Centre
Dr Helen Robertson*	Community Paediatrician	South Birmingham PCT
Dr Saba Sharif	Clinical geneticist	West Midland Regional Genetics Service
Ann Tonks*	Project Manager	West Midlands Congenital Anomaly Register/West Midlands Perinatal Institute
Sonia Ward	Genetic Counsellor	EGSP
Dr Denise Williams*	Clinical geneticist	West Midland Regional Genetics Service
Annette Williamson	Programme Manager	West Midlands Perinatal Institute

Appendix 3 Enhanced Genetic Services Project team

Administrative support was provided to EGSP by Elizabeth Browning, Lyn Yeung, Claire Rooney and a number of other administrators on temporary contracts.

Name	Role	Period of time member of EGSP Team
Asfa Ahmed	Genetic counsellor	July 2011-February 2012
Uruj Anjum	Genetic counsellor	August 2010– March 2011
Pooja Desani	Genetic counsellor	September 2009- October 2010
Yasar Eltaf	Project manager	November 2009-December 2012
Claire Giffney	Genetic counsellor	December 2011-June 2013
Heena Jabbar	Project manager	January 2013-November 2013
Zahira Maqsood	Community educator	May 2010-March 2013
Kirsten McKay Bounford	Laboratory scientist	July 2009-April 2013
Dr Carole McKeown	Project lead, Consultant clinical geneticist	Retires from West Midland Regional Genetics Service November 2010
Maarya Modan	Community educator	December 2012 - end of project
Dr Amal Muflahi	Health professionals educator	December 2012-December 2013
Marie Richards	Health professionals educator	May 2010-June 2012
Dr Saba Sharif	Consultant clinical geneticist	Start of project - December 2012
Sonia Ward	Genetic counsellor	December 2012-September 2013
Dr Denise Williams	Project lead, Consultant clinical geneticist	Part of team throughout Project

Appendix 4 West Midlands Perinatal Institute Report

Congenital anomaly, mortality, and maternal risk factors in Birmingham

Ann Tonks

Annette Williamson

Jason Gardosi

May 2012

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INTRODUCTION AND BACKGROUND

The Perinatal Institute (PI) has been commissioned by the Birmingham Enhanced Genetics Services Project to undertake an analysis of stillbirth and infant mortality associated with congenital anomalies and population characteristics in Birmingham's multi-ethnic population.

The City of Birmingham represents a highly diverse population, offering a rich mixture of cultures and commerce. Such diversity creates specific needs and challenges within maternity care:

- Two thirds of mothers in the Birmingham local authority live in the most deprived quintile of social deprivation[1].
- There is a wide range of inequalities across the City[1].
- Birmingham's birth rate has been increasing, following the national trend[2].
- There is a high proportion of migrants and asylum seekers with specific needs, requiring sufficient time and resources from care providers to engage the required health and social services and interpreters.

This analysis utilises multiple data sources, including the Institute's perinatal mortality and congenital anomaly registers, the clinical genetics database, and the Perinatal Episode Electronic Record (PEER). PEER is a unique, quality assured database consisting of over 100 data items sourced at patient level. Denominator data from 2010 were used in this analysis; dataset version 1.7 was in use (www.pi.nhs.uk/peer/peerdata_collection.htm) at the time. Whilst PEER data collection is continuing in most other West Midlands units, it has ceased in Birmingham and Solihull from early 2011 because of lack of funding.

The linking of datasets has allowed sub analysis of mortality by maternal ethnic group, and accurate estimates of consanguinity, early booking, parity, and folic acid supplementation. The contribution of congenital mortality, including recessive disease, towards infant mortality is quantified, as is the scope of primary (folate supplementation) and secondary (fetal anomaly screening) prevention strategies.

While the focus of this report is infant mortality, morbidity is also of great significance, in terms of number of children affected, the impact upon their families, and direct and indirect costs.

SUMMARY FINDINGS

Stillbirth and infant mortality

- Stillbirth and infant mortality rates in Birmingham remain consistently above those seen in the West Midlands and England & Wales. While overall stillbirths as well as infant deaths demonstrate a downward trend, the rate for mortality associated with congenital anomalies has not been decreasing.

Maternal characteristics

- Over half of the maternity population (56.0%) are from non-British European ethnic origin, the largest group being Pakistani mothers (23.5%).
- The prevalence of consanguineous unions (any relation) for all ethnic groups combined was 15.9%. There is wide geographical and ethnic variation in prevalence. The majority of births in consanguineous unions were to Pakistani mothers, where the prevalence was 49.9%.
- Compared to White European mothers, the prevalence of antenatal folate use is low in all minority ethnic groups except Indian mothers.

Mortality from congenital anomalies

- When stillbirth and infant mortality rates were subdivided by anomaly type, the most common causes of death were chromosomal, central nervous system (including neural tube defect), and cardiac anomalies.
- Stillbirth and infant mortality from congenital anomaly was significantly higher in Pakistani (odds ratio 3.0) and Bangladeshi mothers (odds ratio 2.1).
- Approximately half (49.4%) stillbirths and infant deaths had at least one anomaly that is amendable to detection by routine fetal anomaly screening programmes. There was no significant variation in prenatal detection by ethnic group.
- It is difficult to quantify the proportion of mortality that is genetic in origin. Deaths from metabolic disorders and non-chromosomal syndromes do not represent all deaths with a genetic cause. Cases with single structural anomalies (e.g. neural tube defects and renal anomalies), especially those with multiple anomalies, may have a genetic origin.

Pathology

- The lowest postmortem rates were seen in Pakistani mothers. Postmortem offer rates vary by ethnic group and by place of death. Uptake of postmortem varied by ethnic group.

Linking deaths to clinical genetics cases

- 51.2% of deaths from congenital anomaly were linked to clinical genetics records. This was higher than the linkage rate for residents of the remainder of the West Midlands (42.7%).
- Linkage rates were highest in deaths to Pakistani mothers and Indian mothers, possibly indicating a higher suspicion of a genetic cause of mortality in cases from these ethnic groups.
- In deaths from non-anomaly causes, 7.1% of cases were linked to clinical genetics records. This suggests that a proportion of death not ascribed to congenital anomaly, are genetic in origin.

1. STILLBIRTH AND INFANT MORTALITY

Methods

Annual mortality rates are presented for Birmingham (Local Authority or 3 PCTs combined) for 2003-10. Regional and national rates are provided for comparison. Populations were selected using maternal postcode at delivery (i.e. resident population) and annual rates are presented for calendar year of birth.

Key findings

- Stillbirth rates (all causes) in Birmingham remain consistently above those seen in the West Midlands and England & Wales (Table 1).
- Stillbirth rates (all causes) for all areas have decreased since 2003 (Figure 1). Stillbirth rates (all causes) for Birmingham have dropped significantly from 8.2 (CI 7.4-9.0), in 2003-05, to 7.2 (CI 6.5-7.9), in 2008-10. Conversely, stillbirths with congenital anomalies have seen a recent increase, as illustrated in Figure 2.
- Infant mortality rates (all causes) for Birmingham (7.6, CI 6.8-8.3 2008-10) are significantly higher than rates for the West Midlands (6.1, CI 5.8-6.5) and England & Wales (4.6, CI 4.5-4.7 2008-10), Table 2.
- Infant mortality rates (all causes) for all areas show a consistent downward trend from 2003 to 2010 (Figure 3). Infant deaths due to congenital anomalies have not shown such downward trend (Figure 4).

Table 1 - Stillbirth rates (all causes): Birmingham, West Midlands, England & Wales, 2003-10

AREA	2003	2004	2005	2006	2007	2008	2009	2010
ENGLAND & WALES								
Stillbirths	3,585	3,670	3,473	3,590	3,598	3,617	3,688	3,714
rate/1,000 births	5.7	5.7	5.4	5.4	5.2	5.1	5.2	5.1
WEST MIDLANDS								
Stillbirths	393	383	406	394	396	416	426	404
rate/1,000 births	6.1	5.8	6.1	5.8	5.6	5.8	6.0	5.6
BIRMINGHAM								
Stillbirths	139	134	115	112	129	122	127	128
rate/1,000 births	9.0	8.5	7.2	6.8	7.5	7.0	7.3	7.4

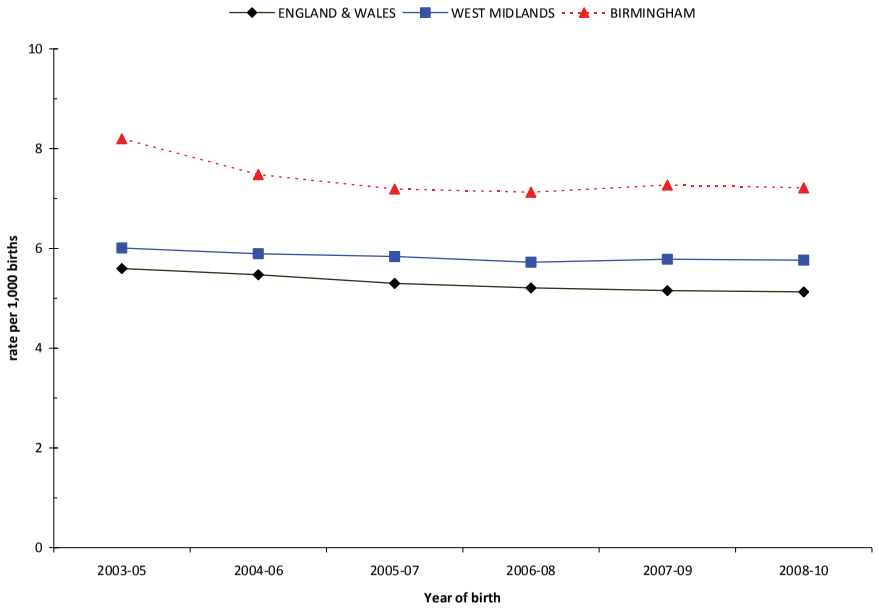
Source: numerator - PI notification (West Midlands) & ONS Vital Statistics (E & W)
denominator - ONS Vital Statistics

Table 2 - Infant mortality (all causes): Birmingham, West Midlands, England & Wales, 2003-10

AREA	2003	2004	2005	2006	2007	2008	2009	2010
ENGLAND & WALES								
Infant deaths	3,306	3,233	3,217	3,329	3,345	3,369	3,312	3,140
rate/1,000 total births	5.3	5.1	5.0	5.0	4.8	4.8	4.7	4.3
WEST MIDLANDS								
Infant deaths	457	427	442	439	435	458	453	404
rate/1,000 total births	7.2	6.5	6.7	6.5	6.2	6.4	6.4	5.6
BIRMINGHAM								
Infant deaths	163	130	150	137	132	137	137	120
rate/1,000 total births	10.6	8.3	9.4	8.4	7.8	7.9	7.9	7.0

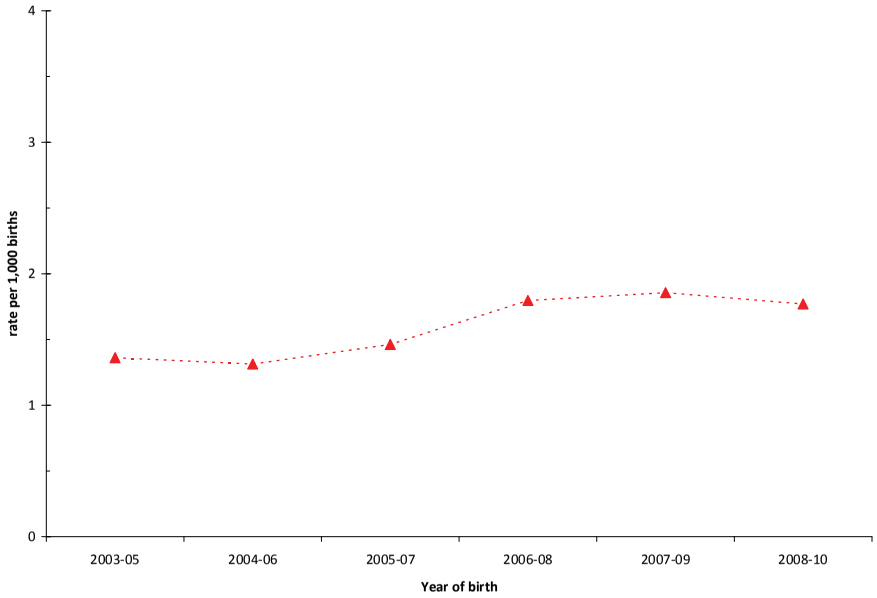
Source: numerator - PI notification (West Midlands) & ONS Vital Statistics (E & W)
denominator - ONS Vital Statistics

Figure 1 - Stillbirth rate trend (all causes): Birmingham & comparative areas 2003-10 (3 yr moving average)



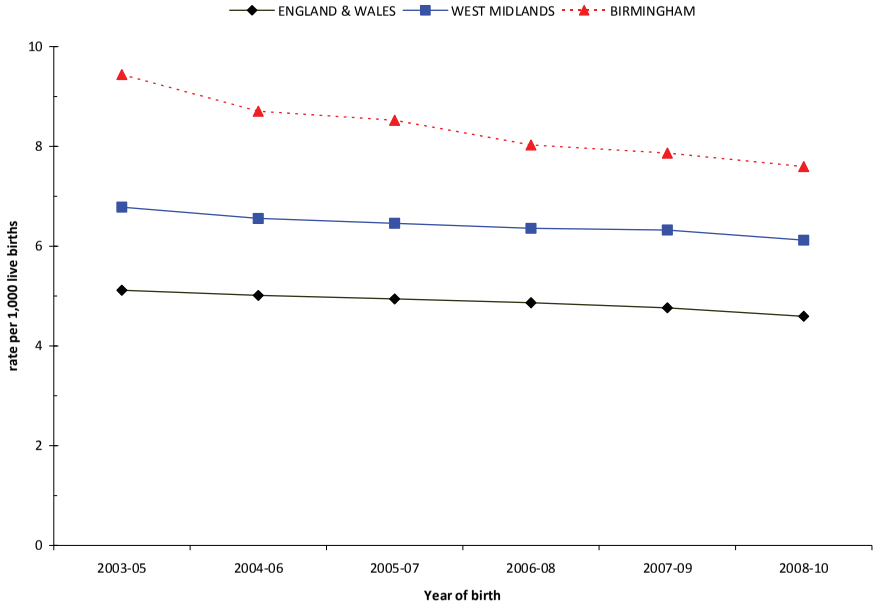
Source: numerator - PI notification (West Midlands) & ONS Vital Statistics (E & W)
denominator - ONS Vital Statistics

Figure 2 - Stillbirth rate trend (cong anomaly): Birmingham 2003-10 (3 yr moving average)



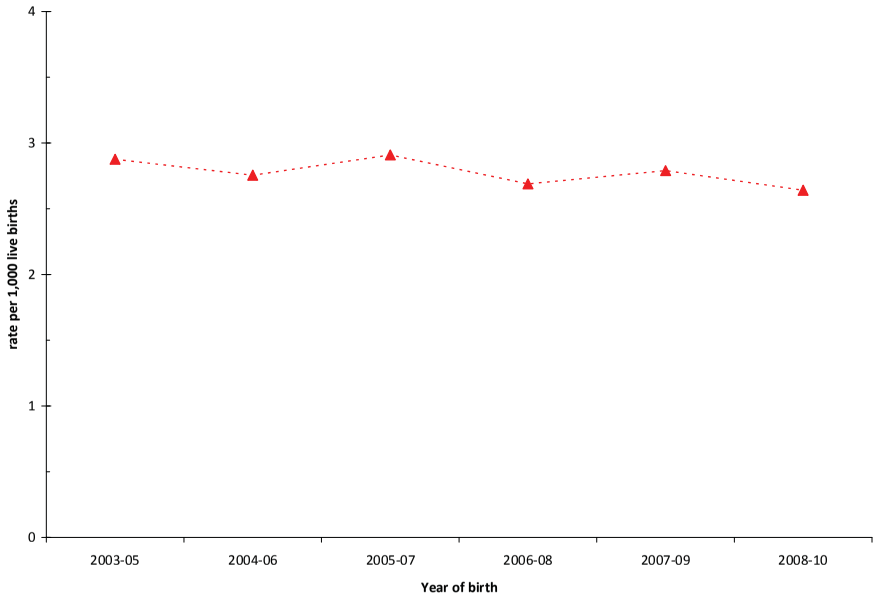
Source: numerator - PI notification
denominator - ONS Vital Statistics

Figure 3 - Infant mortality trend (all causes): Birmingham & comparative areas 2003-10 (3 yr moving average)



Source: numerator - PI notification (West Midlands) & ONS Vital Statistics (E & W)
denominator - ONS Vital Statistics

Figure 4 - Infant mortality trend (cong anomaly): Birmingham 2003-10 (3 yr moving average)



Source: numerator - PI notification
denominator - ONS Vital Statistics

2. MATERNAL CHARACTERISTICS

Denominator data on births can be used to calculate mortality rates for subgroups (e.g. ethnic group, maternal age, etc) and to describe the maternal population within Birmingham.

PI datasets record maternal ethnic group using codes that map to 2011 Census ethnic groups. The paucity of national perinatal mortality data by maternal ethnic group means that comparative rates for the rest of England and Wales by ethnic group are not available. The statutory notification system (birth registration) is the standard source for mortality statistics across the UK, but country of birth of mother is collected and not ethnic group. The Census is another source of demographic (self-assigned) ethnic information, however a birth cohort cannot accurately be defined within it. Maternal ethnic group is recorded routinely within Hospital Episode Statistics (HES) but the quality of the birth/delivery subset is poor. Baby's ethnic group is available in most Child Health Systems.

Methods

Data on live births (Jan-Dec 2010) was extracted for Birmingham PCT residents from the West Midlands Perinatal Episode Electronic Record (PEER). PEER provides standardised patient level data on all births across the West Midlands (http://www.pi.nhs.uk/peer/peerdata_collection.htm).

For the period Jan-Dec 2010, rates of PEER submission for Birmingham hospitals were high (BWH 93%, City 89%), however, submission rates for Heartlands Hospital were lower (55%). An estimate of the distribution of Birmingham births across ethnic groups was made by applying the ethnic distribution for individual Trusts (Source PEER) to the total number of Birmingham births at each Trust (Source ONS). This adjustment ensures appropriate levels of statistical representation of ethnic groups.

In the later sub analysis of PEER data (e.g. parity, folate use), no adjustment was made within ethnic groups for lower submission rates from Heartlands Hospital. It was assumed that the missing cases do not suffer from any selection bias and have the same characteristics (e.g. parity, folate use) as those with the same ethnic group captured elsewhere, i.e. Pakistani women delivering at Heartlands Hospital are similar to those delivering at Birmingham Women's Hospital. There was evidence that some ethnic groups were under-reported in the total births for Birmingham (all ethnic groups) due to low submissions from Heartlands Hospital. Te measures for all ethnic groups combined were therefore adjusted by applying the total rates (e.g. consanguinity) for each ethnic group to the total births for Birmingham (Source ONS) using the estimated Birmingham maternal ethnic group distribution 2010.

2.1 Maternal ethnic group distribution

The estimated Birmingham maternal ethnic group distribution 2010 was generated and used in later analyses of mortality rates by ethnic group.

Key findings

- The completeness of maternal ethnic group within the PEER data was 97.9%
- In Birmingham 2010, 23.5% of births were to Pakistani mothers (Table 3). Data from the 2001 Census estimate the size of the Birmingham Pakistani population to be 9.7% of the total population (all ages).
- The differences between the ethnic distribution of births (Table 3) and the total population (Table 4) reflect variations in fertility rates between ethnic group and potential under-reporting of some minority ethnic groups within the Census data.

Table 3 - Estimated Birmingham maternal ethnic group distribution: Birmingham live births, 2010

Maternal Ethnic Group	Submissions	Estimate Adjusted for Trust submission levels	
		All submissions	Known ethnic group
White European	44.0%	43.1%	44.0%
Black African	7.0%	7.2%	7.0%
Black Caribbean	4.4%	4.1%	4.4%
Indian	5.8%	5.4%	5.8%
Pakistani	20.9%	23.0%	20.9%
Bangladeshi	4.5%	4.7%	4.5%
Middle Eastern	2.3%	2.1%	2.3%
Other/Mixed	8.8%	8.3%	8.8%
Not recorded	2.2%	2.1%	2.2%
ALL ETHNIC GROUPS	**100.0%**	**100.0%**	**100.0%**

Source: PEER
ONS Vital Statistics 2010

Table 4 - Total population ethnic group distribution: Birmingham all ages, 2009

Ethnic Group	Submissions
White European	68.0%
Black African	2.0%
Black Caribbean	4.0%
Indian	5.8%
Pakistani	9.7%
Bangladeshi	2.5%
Other/Mixed	8.0%
ALL ETHNIC GROUPS	**100.0%**

Source: ONS National Statistics Experimental estimates of the population by Ethnic Group, May 2011

2.2 Consanguinity

Data surrounding rates of consanguinity are routinely collected at booking within the standardised, hand held maternity record ('Pregnancy Notes'). The data are collected using the question, "Is the baby's father a blood relation?" The question has been asked routinely at the booking assessment and recorded within the hand-held pregnancy notes since their introduction across the West Midlands in 1993. Responses are recorded as first cousin, second cousin, or other blood relation and completion rates to this question are consistently high. Previous analyses by Modell[3] assessed the impact of first cousin unions only and, therefore, underestimated the true levels of genetic risk within some communities. Increased genetic risk is apparent outside first cousin marriage when unions occur within the same "Biraderi," a practice that is favoured amongst the Pakistani community, e.g. within Birmingham where migration occurred from the Miripuri district of Pakistan.

Comparative data on consanguinity are not available within any other national maternity/birth datasets. Local data may be available from the Born in Bradford project, but are currently unpublished.

Key findings

- The completeness of the data on consanguinity within the PEER data was 92.4% (White European 92.3%, Pakistani 96.4%).
- The total prevalence of consanguineous unions (any blood relation) for all ethnic groups combined was 15.9% (CI 15.3-16), Table 5.
- The majority of consanguineous unions were in births to Pakistani mothers, where the prevalence of consanguinity was 49.9% (CI 48.1-51.7). *Note:* This consanguinity rate is comparable to the analysis by Bundey[4] and Griffin in 2008[5], which site the prevalence of consanguineous marriages in mothers giving birth from the Pakistani community currently as 50-70%. Evidence from Ali[6] also suggests that assisted marriages are a central foundation within Pakistani culture and, whilst the arranged marriage system has changed over time, it continues to be valued regardless of gender or age.
- Consanguineous unions were also common in births to Middle Eastern and Bangladeshi mothers, prevalences of 37.2% and 20.8% respectively.
- The father was a first cousin in 54.4% of consanguineous unions (8.1% births) in Birmingham and second cousin in 20.7% (3.1% births), Table 6. The proportions in the Pakistani ethnic group were 57.5% first cousin and 22.9% second cousin.
- Consanguineous unions were nearly three times more prevalent in non-UK born mothers (26.7%) compared to UK born mothers (9.5%), Table 7. Within the largest minority ethnic group (Pakistani), the preference for consanguinity was significantly higher in non-UK born mothers (51.9%) compared to those born in the UK (47.2%, p=0.01).
- Overall 62.6% of Birmingham mothers were born in the UK. Middle Eastern, Black African, and Bangladeshi groups had the lowest proportions of UK born mothers.

- The highest prevalence of consanguineous unions was seen in central and eastern wards of Birmingham (Figure 5).

Table 5 - Father blood relation: Birmingham live births, 2010

Maternal Ethnic Group	Not related	Father related			Not recorded	TOTALS BIRTHS
		n	prev	(95%CI)		
White European	5,773	75	1.3	(1.0-1.6)	487	6,335
Black African	833	99	10.6	(8.6-12.6)	80	1,012
Black Caribbean	584	3	0.5	(0.0-1.1)	53	640
Indian	734	48	6.1	(4.5-7.8)	57	839
Pakistani	1,453	1,447	49.9	(48.1-51.7)	118	3,018
Bangladeshi	483	127	20.8	(17.6-24.0)	40	650
Middle Eastern	196	116	37.2	(31.8-42.5)	14	326
Other/Mixed	1,103	63	5.4	(4.1-6.7)	103	1,269
Not recorded	163	13	7.4	(3.5-11.3)	147	323
ALL ETHNIC GROUPS	**11,322**	**1,991**	**15.0**	**(14.3-15.6)**	**1,099**	**14,412**
ALL ETHNIC GPS ADJUSTED*	**13,408**	**2,537**	**15.9**	**(15.3-16.5)**	**1,295**	**17,240**

Source: PEER

Note: *adjusted for variation in ascertainment rates by ethnic group arising from Trust submission rates

Table 6 - Father blood relation: Birmingham live births consanguineous unions, 2010

Maternal Ethnic Group	1st cousin		2nd cousin		Other/undoc relation	TOTAL RELATED
	n	%	n	%		
White European	16	21.3	4	5.3	55	75
Black African	35	35.4	18	18.2	46	99
Black Caribbean	0	-	0	-	3	3
Indian	15	31.3	4	8.3	29	48
Pakistani	832	57.5	331	22.9	284	1,447
Bangladeshi	76	59.8	18	14.2	33	127
Middle Eastern	79	68.1	26	22.4	11	116
Other/Mixed	29	46.0	9	14.3	25	63
Not recorded	2	15.4	3	23.1	8	13
ALL ETHNIC GROUPS	**1,084**	**54.4**	**413**	**20.7**	**494**	**1,991**

Source: PEER

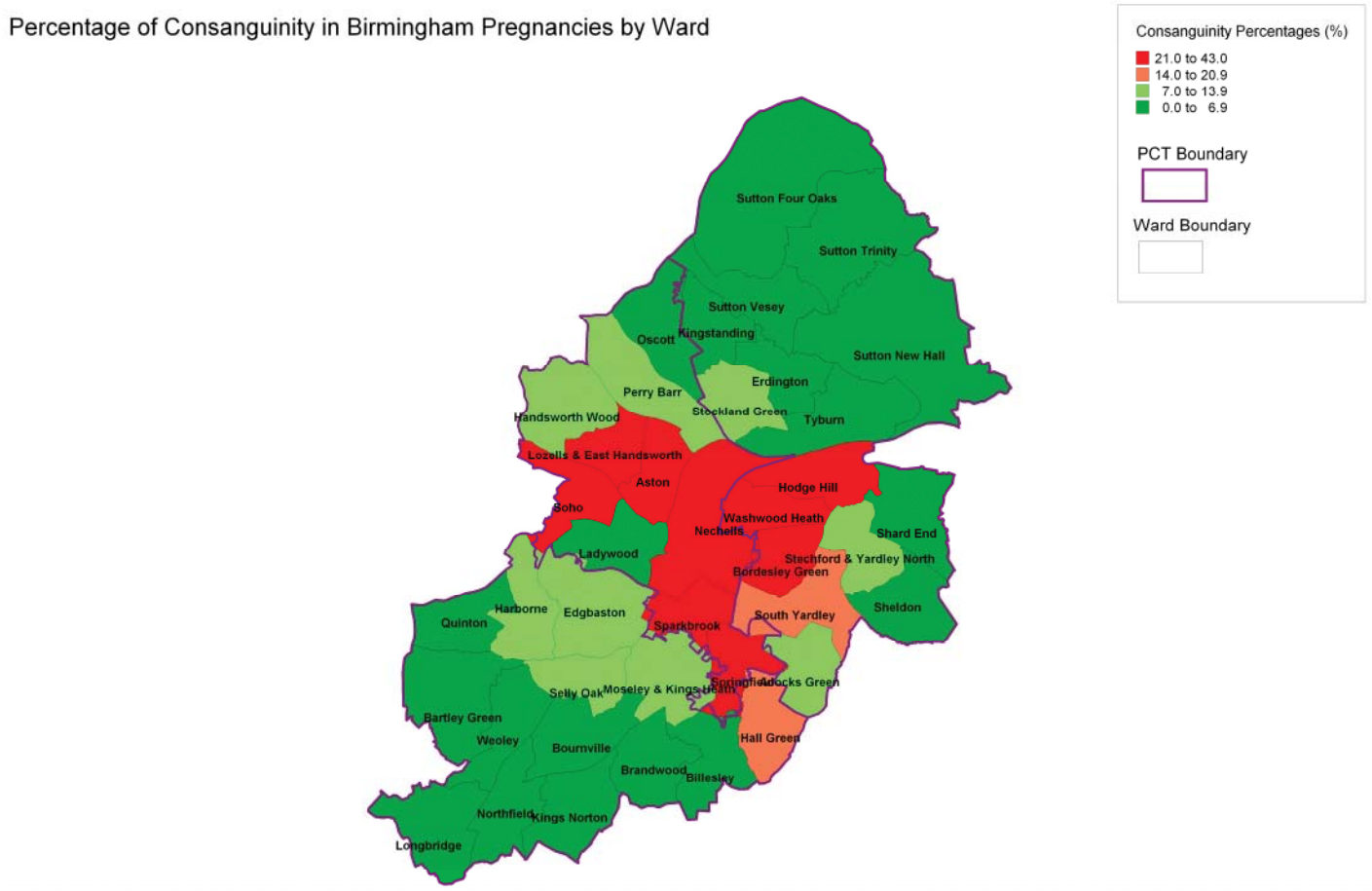
Table 7 - Father blood relation: Birmingham live births consanguineous unions, 2010

Maternal Ethnic Group	UK born			Non-UK born			Missing data	UK born %	ALL BIRTHS
	n	N	%	n	N	%			
White European	49	5,337	0.9	22	407	5.4	591	92.9	6,335
Black African	0	44	-	99	879	11.3	89	4.8	1,012
Black Caribbean	3	414	0.7	0	160	-	66	72.1	640
Indian	15	397	3.8	33	373	8.8	69	51.6	839
Pakistani	595	1,260	47.2	829	1,597	51.9	161	44.1	3,018
Bangladeshi	38	155	24.5	87	446	19.5	49	25.8	650
Middle Eastern	3	31	9.7	113	279	40.5	16	10.0	326
Other/Mixed	12	512	2.3	47	629	7.5	128	44.9	1,269
Not recorded	7	104	6.7	2	34	5.9	185	75.4	323
ALL ETHNIC GROUPS	**722**	**8,254**	**8.7**	**1,232**	**4,804**	**25.6**	**1,354**	**63.2**	**14,412**
ALL ETHNIC GPS ADJUSTED*	**930**	**9,793**	**9.5**	**1,560**	**5,850**	**26.7**	**1,597**	**62.6**	**17,240**

Source: PEER

Note: *adjusted for variation in ascertainment rates by ethnic group arising from Trust submission rates

Figure 5 - Father blood relation by ward: Birmingham live births, 2010



Source: PEER

2.3 Early booking and parity

National policy and guidelines recommend that all women have seen a midwife or a maternity healthcare professional, for a full health and social care assessment of needs, risks, and choices by 12 completed weeks of pregnancy. Early booking is necessary in order to access screening programmes for fetal anomaly.

Key findings

- Overall 39.0% of births were to nulliparous mothers and 6.1% were to mothers with four or more previous births (Table 8).
- Parity appeared to vary significantly by maternal ethnic group. Pakistani, Black African, Bangladeshi, and Middle Eastern groups had the largest proportion of multiparous and grand multiparous mothers.
- In 5.1% of Birmingham births, the first booking appointment took place at 20 weeks or more (Table 9). In Black African mothers, 10.9% were late bookers and all minority ethnic groups booked later than White European mothers.
- Mothers with parity 1 book no later than primips. The median gestation, however, increases with each pregnancy. Mothers with four or more previous births book, on average, 12 days later than primips (Figure 6).

Table 8 - Parity: Birmingham live births, 2010

Maternal Ethnic Group	Primiparous		Multiparous					Not recorded	ALL BIRTHS
	n	%	1	2	3	4+ (n)	4+(%)		
White European	2,888	45.9	1,945	881	347	225	3.6	49	6,335
Black African	273	27.1	296	180	103	154	15.3	6	1,012
Black Caribbean	252	39.6	189	117	49	29	4.6	4	640
Indian	387	46.4	308	91	34	14	1.7	5	839
Pakistani	805	26.9	862	666	390	269	9.0	26	3,018
Bangladeshi	176	27.4	166	162	74	65	10.1	7	650
Middle Eastern	92	28.6	85	62	33	50	15.5	4	326
Other/Mixed	592	47.0	410	151	63	44	3.5	9	1,269
Not recorded	94	34.1	84	49	36	13	4.7	47	323
ALL ETHNIC GROUPS	**5,559**	**39.0**	**4,345**	**2,359**	**1,129**	**863**	**6.1**	**157**	**14,412**
ALL ETHNIC GPS ADJUSTED*	**6,583**	**38.6**	**5,185**	**2,855**	**1,378**	**1,053**	**6.2**	**186**	**17,240**

Source: PEER
Note: *adjusted for variation in ascertainment rates by ethnic group arising from Trust submission rates

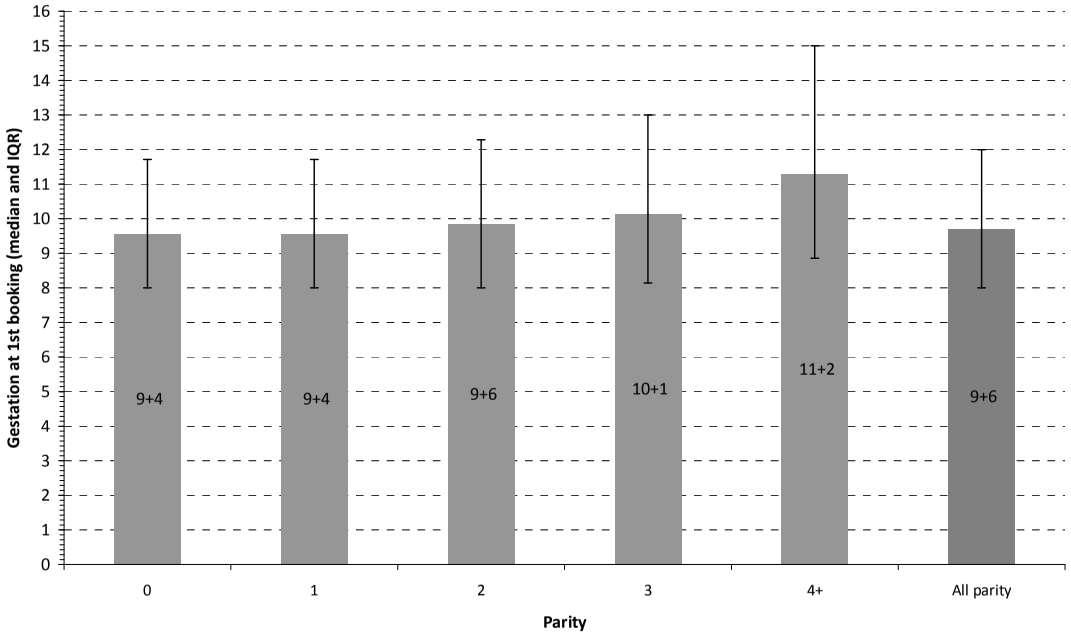
Table 9 - Gestation at first booking: Birmingham live births, 2010

Maternal Ethnic Group	< 13 wks		13-19 wks	20+ weeks		Not recorded	ALL BIRTHS
	n	%		n	%		
White European	5,343	86.6	608	221	3.6	163	6,335
Black African	603	61.4	272	107	10.9	30	1,012
Black Caribbean	472	74.9	125	33	5.2	10	640
Indian	677	82.7	106	36	4.4	20	839
Pakistani	2,361	80.7	432	132	4.5	93	3,018
Bangladeshi	463	73.3	138	31	4.9	18	650
Middle Eastern	239	75.4	59	19	6.0	9	326
Other/Mixed	947	76.4	194	98	7.9	30	1,269
Not recorded	164	66.4	50	33	13.4	76	323
ALL ETHNIC GROUPS	**11,269**	**80.7**	**1,984**	**710**	**5.1**	**449**	**14,412**
ALL ETHNIC GPS ADJUSTED*	**13,475**	**80.7**	**2,382**	**847**	**5.1**	**536**	**17,240**
ALL ETHNIC GROUPS primip	**4,561**	**83.8**	**614**	**270**	**5.0**	**114**	**5,559**
ALL ETHNIC GROUPS multip	**6,660**	**78.9**	**1,351**	**426**	**5.0**	**259**	**8,696**

Source: PEER

Note: *adjusted for variation in ascertainment rates by ethnic group arising from Trust submission rates

Figure 6 - Gestation at first booking (weeks and days) by parity: Birmingham live births, 2010



Source: PEER

2.4 Folic acid supplementation

Pre-conceptional folate supplementation is a primary prevention tool in reducing the prevalence of neural tube defects (anencephaly, spina bifida, encephalocele). Women are routinely asked about folate supplement use, including start date, at booking and this information is recorded within the Pregnancy Notes.

Key findings

- The completeness of information on folate use within the PEER dataset was 96.4%. Data on mothers' start date of folate use was available in 47.4% of mothers (5,632/11,880).
- Compared to White European mothers, the prevalence of antenatal folate use is low in most minority ethnic groups (Black African, Black Caribbean, Pakistani, Bangladeshi and other/mixed maternal ethnic groups), Table 10.
- Of the 85.5% of mothers who report using folate supplements antenatally, only 19.9% (17.0% of all women) did so pre-conceptionally (Table 11). Only 6.3% (5.4% of all women) took folate supplements for over 3 months before conception, corresponding to previous DH advice. The uptake of any pre-conceptual advice/care will be limited to proportion of pregnancies that are planned.

Table 10 - Antenatal folate supplementation: Birmingham live births, 2010

Maternal Ethnic Group	No folate use	Antenatal folate			Not recorded	TOTAL BIRTHS
		n	prev	(95%CI)		
White European	702	5,499	88.7	(87.9-89.5)	134	6,335
Black African	241	726	75.1	(72.4-77.8)	45	1,012
Black Caribbean	96	520	84.4	(81.6-87.3)	24	640
Indian	74	728	90.8	(88.8-92.8)	37	839
Pakistani	465	2,458	84.1	(82.8-85.4)	95	3,018
Bangladeshi	114	504	81.6	(78.5-84.6)	32	650
Middle Eastern	53	265	83.3	(79.2-87.4)	8	326
Other/Mixed	213	1,020	82.7	(80.6-84.8)	36	1,269
Not recorded	56	160	74.1	(68.2-79.9)	107	323
ALL ETHNIC GROUPS	**2,014**	**11,880**	**85.5**	**(84.9-86.1)**	**518**	**14,412**
ALL ETHNIC GPS ADJUSTED*	**2,421**	**14,203**	**85.4**	**(84.9-86.0)**	**616**	**17,240**

Source: PEER
Note: *adjusted for variation in ascertainment rates by ethnic group arising from Trust submission rates

Table 11 - Timing of antenatal folate supplementation: Birmingham live births, 2010

Maternal Ethnic Group	Pre-conception use					Post-conception use			TOTAL KNOWN START
	12+ wk		<12 wk	Subtotal		<5 wk	5-10wk	10+ wk	
	n	%	n	n	%				
White European	217	8.0	430	647	24.0	914	1,002	136	2,699
Black African	11	3.5	31	42	13.3	72	152	49	315
Black Caribbean	5	2.1	10	15	6.4	65	134	22	236
Indian	27	8.4	66	93	29.1	94	116	17	320
Pakistani	37	3.2	120	157	13.7	346	549	96	1,148
Bangladeshi	5	2.3	16	21	9.9	58	105	29	213
Middle Eastern	2	1.4	10	12	8.3	46	74	13	145
Other/Mixed	51	10.3	70	121	24.4	147	198	29	495
Not recorded	1	1.6	10	11	18.0	21	26	3	61
ALL ETHNIC GROUPS	**356**	**6.3**	**763**	**1,119**	**19.9**	**1,763**	**2,356**	**394**	**5,632**

Source: PEER

3. MORTALITY AND CONGENITAL ANOMALY DATA

Methods

Data on stillbirths and infant deaths (2006-10) were extracted from the West Midlands database of fetal losses and infant deaths (PI notifications). Cases are notified by maternity and tertiary paediatric units and are routinely matched with statutory notifications, pathology, safeguarding boards, and HES data to ensure high ascertainment.

Cases were selected using maternal postcode at birth (Birmingham PCT residents) and date of death. This dataset includes information on maternal ethnic group, cause of death, place of death, and postmortem. Stillbirth and infant deaths were combined to facilitate analysis by subgroups of anomaly/ethnic group.

Mortality rates by ethnic group were generally calculated per 1,000 births but mortality rates for specific anomaly groups were expressed per 10,000 births. The denominator for mortality rates (total births by ethnic group 2006-10) was generated using the estimated Birmingham maternal ethnic group distribution 2010 (Table 3) applied to the total births for Birmingham (ONS Vital Statistics 2006-10). This assumes that the ethnic distribution of Birmingham births has not changed between 2006 and 2010. If this assumption is not valid, and there has been an increase in births to particular ethnic groups, then the denominator for these ethnic groups 2006-10 (derived from the 2010 distribution) will be over-estimated. A consequence may be that the corresponding mortality rates are underestimated.

West Midlands mortality data are routinely classified and coded using a variety of methods including the hierarchical fetal and neonatal classification[7]. Deaths from congenital anomalies are classified in groups 1-6. As group 6 “other malformation” is large and heterogeneous, cases classified in this group have been further split into the following subgroups: central nervous system, skeletal malformation, abdominal/respiratory, syndrome (non-chromosomal), multiple anomalies, and other malformation/tumour.

3.1 Mortality by ethnic group

Key findings

- The combined stillbirth and infant mortality rate from all causes for Birmingham 2006-10 was 15.0 per 1,000 births (Table 12). This rate was significantly higher in Black African (OR 1.4, CI 1.1-1.8), Black Caribbean (OR 2.8, CI 2.3-3.4), and Pakistani mothers (OR 1.9, CI 1.6-2.1) compared the reference/largest ethnic group (White European).

- Deaths from congenital anomaly comprise 29.3% of stillbirth and infant mortality (Table 13). Stillbirth and infant mortality from congenital anomaly was significantly higher in Pakistani (OR 3.0, CI 2.3-3.8) and Bangladeshi mothers (OR 2.1, CI 1.3-3.2).

- When stillbirth and infant mortality rates were subdivided by anomaly type, the most common causes of death were chromosomal, central nervous system (including neural tube defect), and cardiac anomalies (Table 14).

- Stillbirth and infant mortality for specific anomaly types varied by maternal ethnic group (Table 15). Black Caribbean mothers had significantly higher mortality rates from renal and other anomalies/tumours. Pakistani mothers had significantly higher mortality rates from metabolic disorders, neural tube defects, renal anomalies, syndromes, and other anomalies/tumours. Bangladeshi mothers had significantly higher mortality rates from renal anomalies and genetic (non-chromosomal) syndromes.

- It is difficult to quantify the proportion of stillbirths and infant deaths that are genetic in origin. Stillbirths and infant deaths from metabolic disorders and genetic (non-chromosomal) syndromes occurred at a rate of 2.3 and 1.9 per 10,000 births. Whilst these subgroups are genetic in origin, they do not represent all deaths with a genetic cause. Some of the deaths from other single structural anomalies (e.g. neural tube defects and renal anomalies), especially those with multiple anomalies, will have a genetic origin.

- The type of anomaly causing stillbirth and infant mortality from congenital anomaly is shown for all mothers (Figure 7) and Pakistani mothers (Figure 8).

Table 12 - Stillbirth and infant death rates all causes by ethnic group: Birmingham, 2006-10

Maternal Ethnic Group	SB+IDs	Total births	Rate	Odds ratio	(95%CI)
White European REFERENCE	**437**	**37,764**	**11.6**	**1.0**	
Black African	102	6,264	16.3	†1.4	(1.1-1.8)
Black Caribbean	114	3,624	31.5	†2.8	(2.3-3.4)
Indian	68	4,724	14.4	1.2	(1.0-1.6)
Pakistani	431	20,117	21.4	†1.9	(1.6-2.1)
Bangladeshi	52	4,132	12.6	1.1	(0.8-1.5)
Other inc Chinese & Mixed	84	9,109	9.2	0.8	(0.6-1.0)
ALL ETHNIC GROUPS	**1,288**	**85,734**	**15.0**		

Source: numerator - PI & WMCAR notification
denominator - ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: rate per 1,000 births
† significantly different to reference population (i.e. 95% confidence limits for odds ratio exclude 1)

Table 13 - Stillbirth and infant death rates from congenital anomaly: Birmingham, 2006-10

Maternal Ethnic Group	SB+IDs	Total births	Rate	Odds ratio	(95%CI)
White European REFERENCE	**106**	**37,764**	**2.8**	**1.0**	
Black African	21	6,264	3.4	1.2	(0.7-1.9)
Black Caribbean	16	3,624	4.4	1.6	(0.9-2.7)
Indian	18	4,724	3.8	1.4	(0.8-2.2)
Pakistani	166	20,117	8.3	†3.0	(2.3-3.8)
Bangladeshi	24	4,132	5.8	†2.1	(1.3-3.2)
Other inc Chinese & Mixed	26	9,109	2.9	1.0	(0.7-1.6)
ALL ETHNIC GROUPS	**377**	**85,734**	**4.4**		

Source: numerator - PI & WMCAR notification
denominator - ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: rate per 1,000 births
† significantly different to reference population (i.e. 95% confidence limits for odds ratio exclude 1)

Table 14 - Stillbirth and infant deaths rates by anomaly type: Birmingham, 2006-10

Maternal Ethnic Group	Chromo-somal	Meta-bolic	NTD	Cardiac	Renal	CNS	Skeletal	Abdo/ Resp	Multiple	Syndrome	Other/ Tumour	ALL ANOMALIES
White European REFERENCE	**9.5**	**0.8**	**2.6**	**7.4**	**1.9**	**2.4**	**-**	**1.6**	**0.8**	**0.5**	**0.5**	**28.1**
Black African	16.0	-	4.8	3.2	3.2	-	1.6	-	1.6	1.6	1.6	**33.5**
Black Caribbean	8.3	-	2.8	5.5	11.0	5.5	-	2.8	2.8	-	5.5	**44.2**
Indian	12.7	2.1	6.4	10.6	-	4.2	-	-	2.1	-	-	**38.1**
Pakistani	12.4	7.5	8.0	11.4	5.5	12.4	7.5	3.0	6.5	5.5	3.0	**82.5**
Bangladeshi	12.1	2.4	-	9.7	12.1	7.3	4.8	-	2.4	4.8	2.4	**58.1**
Other inc Chinese & Mixed	11.0	-	3.3	4.4	2.2	2.2	1.1	-	3.3	-	1.1	**28.5**
ALL ETHNIC GROUPS	**11.1**	**2.3**	**4.2**	**7.9**	**3.6**	**5.0**	**2.2**	**1.5**	**2.7**	**1.9**	**1.5**	**44.0**

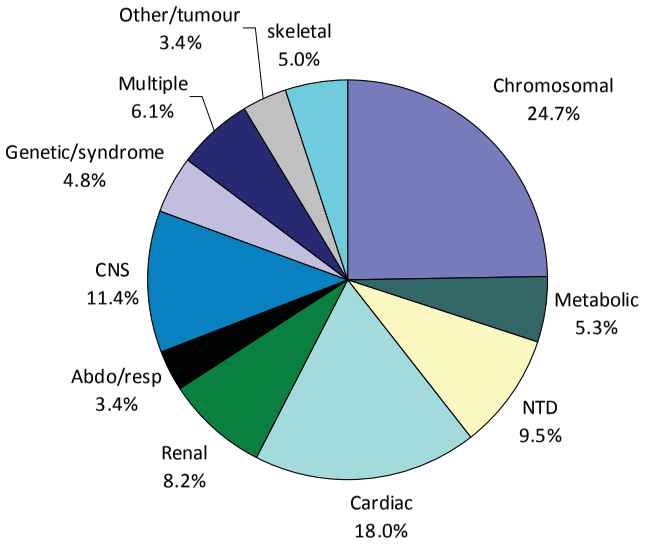
Source: numerator - PI & WMCAR notification
denominator - ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: rate per 10,000 births

Table 15 - Odds ratios for ethnic groups stillbirth and infant deaths rates from congenital anomaly types: Birmingham, 2006-10

Maternal Ethnic Group	Chromo-somal	Meta-bolic	NTD	Cardiac	Renal	CNS	Skeletal	Abdo/ Resp	Multiple	Syndrome	Other/ Tumour	ALL ANOMALIES
White European REFERENCE												
Black African	1.7		1.8	0.4	1.7				2.0	3.0	3.0	**1.2**
Black Caribbean	0.9		1.0	0.7	†6.0	2.3	*	1.7	3.5		†10.4	**1.6**
Indian	1.3	2.7	2.4	1.4		1.8			2.7		0.0	**1.4**
Pakistani	1.3	†9.4	†3.0	1.5	†3.0	†5.2	*	1.9	8.1	†10.3	†5.6	**†3.0**
Bangladeshi	1.3	3.0		1.3	†6.5	3.0	*		3.0	†9.1	4.6	**†2.1**
Other inc Chinese & Mixed	1.2		1.2	0.6	1.2	0.9	*		4.1	0.0	2.1	**1.0**

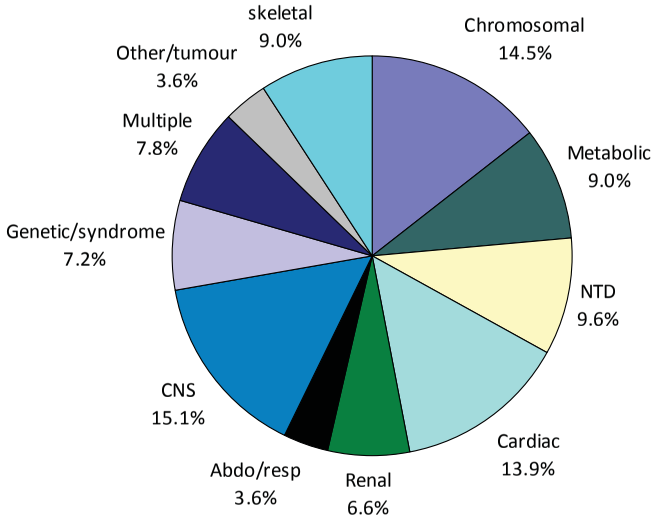
Source: PI & WMCAR notification
Note: rate per 10,000 births
† significantly different to reference population (i.e. 95% confidence limits for odds ratio exclude 1)
* unable to calculate OR as no occurrences in reference populations

Figure 7 - Stillbirth and infant deaths by anomaly type - all ethnic groups: Birmingham, 2006-10



Source: PI & WMCAR notification

Figure 8 - Stillbirth and infant deaths by anomaly type - Pakistani mothers: Birmingham, 2006-10



Source: PI & WMCAR notification

3.2 Mortality by ethnic group FASP anomalies

In January 2010, the NHS Fetal Anomaly Screening Programme (FASP) published a set of National Standards and Guidance for the 18^{+0} to 20^{+6} Fetal Anomaly Scan[8]. The standards list nine structural and two chromosomal anomalies that are detectable at the fetal anomaly scan along with their prenatal detection rates. There is a separate screening programme for trisomy 21.

Key findings

- Approximately half (49.4%) of stillbirths and infant deaths had at least one anomaly that is amendable to detection by routine fetal anomaly screening programmes (Table 16).
- The prenatal detection rate for chromosomal anomalies (trisomies 21, 13, and 13) was 54.4% and 88.2% for structural anomalies (Table 17). There was no significant variation by ethnic group.

Table 16 - Stillbirth and infant deaths from congenital anomaly proportion with FASP anomalies: Birmingham, 2006-10

Maternal Ethnic Group	Chromosomal		Structural		non-FASP		ALL
	n	%CA deaths	n	%CA deaths	n	%CA deaths	ANOMALIES
White European	25	23.6%	41	38.7%	40	37.7%	**106**
Black African	9	42.9%	4	19.0%	8	38.1%	**21**
Black Caribbean	3	18.8%	4	25.0%	9	56.3%	**16**
Indian	S	S	S	S	9	50.0%	**18**
Pakistani	18	10.8%	52	31.3%	96	57.8%	**166**
Bangladeshi	S	S	S		20	83.3%	**24**
Other inc Chinese & Mixed	9	34.6%	9	34.6%	8	30.8%	**26**
ALL ETHNIC GROUPS	**68**	**18.0%**	**119**	**31.6%**	**190**	**50.4%**	**377**

Source: PI & WMCAR notification
Note: S = suppressed count or subtotal ≤3

Table 17 - Detection rates for stillbirth and infant death with FASP anomalies: Birmingham, 2006-10

Maternal Ethnic Group	Chromosomal		Structural	
	%PND	(95%CI)	%PND	(95%CI)
White European	60.0%	(40.8-79.2)	90.2%	(81.2-99.3)
Black African	44.4%	(12.0-76.9)	75.0%	(32.6-100.0)
Black Caribbean	66.7%	(13.3-100.0)	100.0%	
Indian	50.0%	(0.0-100.0)	100.0%	
Pakistani	55.6%	(32.6-78.5)	84.6%	(74.8-94.4)
Bangladeshi	0.0%		100.0%	
Other inc Chinese & Mixed	55.6%	(23.1-88.0)	88.9%	(68.4-100.0)
ALL ETHNIC GROUPS	**54.4%**	**(42.6-66.2)**	**88.2%**	**(82.4-94.0)**

Source: PI & WMCAR notification
Note: PND prenatally diagnosed

3.3 Pathology

The PI mortality dataset includes information on the offer and uptake of postmortem. Fetal pathology is classified as "PM done full/partial" (offered and accepted), "not offered," "declined" (offered), "coroner postmortem," and "unknown pathology."

- The rates of postmortem (all causes) were 30.8% for stillbirths and 22.6% for infant deaths (Table 18). The lowest postmortem rates were seen in Pakistani mothers (stillbirth 14.2% and infant death 10.0%).
- Excluding coroners postmortems, postmortems were offered in 63.0% of stillbirths and 47.6% of infant deaths (Table 19). Offer rates vary by ethnic group. The lowest offer rates were to Pakistani mothers (stillbirth 50.0% and infant death 31.7%), these were significantly lower than for White European mother ($p<0.01$).
- Postmortem offer rates varied by place of death (Table 20). Offer rates were low at Heartlands Hospital for stillbirth (21.2%) and infant deaths (23.0%) and at Birmingham Children's Hospital for infant deaths (7.1%).
- The uptake/acceptance of postmortem (when offered) was 48.8% for stillbirths and 27.9% for infant deaths (Table 21). Uptake varied by ethnic group from 28.4% (Pakistani, sig $p<0.01$) to 69.4% (Black Caribbean) for stillbirths and 10.0% (Bangladeshi) to 46.9% (Black Caribbean) for infant deaths.

Table 18 - Rates of postmortem by ethnic group all causes: Birmingham, 2006-10

Maternal Ethnic Group	Stillbirths				Infant deaths			
	Done	PM rate	Not done	Not known	Done	PM rate	Not done	Not known
White European	84	39.8%	127	S	73	33.2%	147	6
Black African	21	42.0%	29	S	12	24.0%	38	S
Black Caribbean	25	48.1%	27	S	23	39.0%	36	S
Indian	16	44.4%	20	S	4	12.9%	27	S
Pakistani	29	14.2%	175	S	22	10.0%	198	6
Bangladeshi	0	0.0%	17	S	5	15.6%	27	S
Other inc Chinese & Mixed	14	31.8%	30	S	8	20.5%	31	S
ALL ETHNIC GROUPS	**189**	**30.8%**	**425**	**5**	**147**	**22.6%**	**504**	**18**

Source: PI notification
Note: numerator = PM done + coroner PM; denominator = all known pathology
S = suppressed count or subtotal ≤3

Table 19 - Offer rates of postmortem by ethnic group all causes: Birmingham, 2006-10

Maternal Ethnic Group	Stillbirths				Infant deaths			
	Offered	Offer rate	Not offered	Not known/other	Offered	Offer rate	Not offered	Not known/other
White European	141	66.8%	70	S	106	58.6%	75	45
Black African	40	80.0%	10	S	24	51.1%	23	4
Black Caribbean	36	69.2%	16	S	32	62.7%	19	11
Indian	26	72.2%	10	S	18	62.1%	11	S
Pakistani	102	50.0%	102	S	66	31.7%	142	18
Bangladeshi	10	58.8%	7	S	10	35.7%	18	6
Other inc Chinese & Mixed	32	72.7%	12	S	20	55.6%	16	S
ALL ETHNIC GROUPS	**387**	**63.0%**	**227**	**5**	**276**	**47.6%**	**304**	**89**

Source: PI notification
Note: numerator = PM done (excluding coroner PM) + PM declined; denominator = all known pathology (excluding coroner PM)
S = suppressed count or subtotal ≤3

Table 20 - Offer rates of postmortem by place of death (excluding deaths at home/elsewhere) all causes: Birmingham, 2006-10

Place of death	Stillbirths				Infant deaths			
	Offered	Offer rate	Not offered	Not known/other	Offered	Offer rate	Not offered	Not known/other
Birmingham Women's	200	93.0%	15	S	164	90.6%	17	6
Heartlands	46	21.2%	171	S	40	23.0%	134	22
City	90	84.9%	16	S	33	64.7%	18	7
Good Hope	40	81.6%	9	S	20	66.7%	10	4
Birmingham Children's					7	7.1%	92	30
Other Hospital (outside B'ham)	10	41.7%	14	S	10	27.8%	26	12
Home/elsewhere							7	
ALL TRUSTS	**386**	**63.2%**	**225**	**5**	**274**	**48.0%**	**297**	**81**

Source: PI notification
Note: numerator = PM done (excluding coroner PM) + PM declined; denominator = all known pathology (excluding coroner PM)
S = suppressed count or subtotal ≤3

Table 21 - Uptake rates of postmortem by ethnic group all causes: Birmingham, 2006-10

Maternal Ethnic Group	Stillbirths				Infant deaths			
	Accept	Accept rate	Decline	Not offered/other	Accept	Accept rate	Decline	Not offered/other
White European	84	59.6%	57	70	34	32.1%	72	120
Black African	21	52.5%	19	11	10	41.7%	14	27
Black Caribbean	25	69.4%	11	16	15	46.9%	17	30
Indian	16	61.5%	10	11	S	S	16	13
Pakistani	29	28.4%	73	103	10	15.2%	56	160
Bangladeshi		0.0%	10	8	S	S	9	24
Other inc Chinese & Mixed	14	43.8%	18	13	5	25.0%	15	19
ALL ETHNIC GROUPS	**189**	**48.8%**	**198**	**232**	**77**	**27.9%**	**199**	**393**

Source: PI notification

Note: numerator = PM done (excluding coroner PM); denominator = PM done + PM declined (excluding coroner PM)
S = suppressed count or subtotal ≤3

4. RECORD LINKAGE BETWEEN MORTALITY/ANOMALY REGISTERS AND CLINICAL GENETICS

Where possible, West Midlands fetal losses or infant deaths (PI notifications) were matched with the West Midlands Clinical Genetics Database (SHIRE). Cases could be matched using a link between mother or baby for each case. Matches were made using combinations of two or more of the following fields: NHS number, date of birth, surname, or partial forename.

A linked case will not necessarily mean that a referral was made to clinical genetics for a stillbirth/infant death. It may indicate that the mother had been seen by clinical genetics before or after the death, i.e. in a previous or subsequent pregnancy. A non-linked case may have been referred to clinical genetics, but there was insufficient data to match the case routinely. Further attempts should be made to match deaths in some subgroups, e.g. unlinked deaths with metabolic disorders, on an individual basis.

Key findings

- Of the Birmingham stillbirth and infant deaths 2006-10, 51.2% of deaths from congenital anomaly were linked to clinical genetics records (Table 22). This was higher than the linkage rate for residents of the remainder of the West Midlands (42.7%).
- In deaths from other (non-anomaly) causes, 7.1% of cases were linked to clinical genetics records. This group of cases (n=65) will include cases classified to non-anomaly causes that have an underlying genetic disorder, probably diagnosed in subsequent pregnancies. These cases should be reviewed to see if retrospective genetic diagnoses can be made. 11.4% of non-anomaly deaths in the Pakistani population were linked to anomaly cases.
- Linkage rates were highest in deaths to Pakistani mothers (anomaly 66.7% and non-anomaly 11.4%) and Indian mothers (anomaly 66.7%). This may indicate a higher clinical suspicion of a genetic cause of mortality in cases from these ethnic groups.
- Linkage rates for deaths at Birmingham maternity units range from 37.5% (City Hospital) to 48.8% (Heartlands Hospital) for congenital anomaly and 2.5% (City Hospital) 6.5% (Heartlands Hospital) for other causes. Linkage rates were highest in those cases dying at Birmingham Children's Hospital (64.4% anomaly, 25.0% non-anomaly).
- Figure 9 and Figure 10 show ward level data on the rates of linked and unlinked stillbirths and deaths from congenital anomaly.

Table 22 - Linkage to clinical genetics stillbirth and infant deaths by ethnic group: Birmingham, 2006-10

Maternal Ethnic Group	Congenital anomaly			Other causes		
	link	no link	%link	link	no link	%link
White European	43	63	**40.6%**	25	306	**7.6%**
Black African	3	18	**14.3%**	4	77	**4.9%**
Black Caribbean	8	8	**50.0%**	S	97	
Indian	12	6	**66.7%**	S	48	
Pakistani	101	65	**60.8%**	30	234	**11.4%**
Bangladeshi	13	11	**54.2%**	S	26	
Other inc Chinese & Mixed	13	13	**50.0%**	S	57	
ALL ETHNIC GROUPS	**193**	**184**	**51.2%**	**65**	**845**	**7.1%**
WEST MIDS (EXC B'HAM)	**291**	**390**	**42.7%**	**181**	**2,069**	**8.0%**

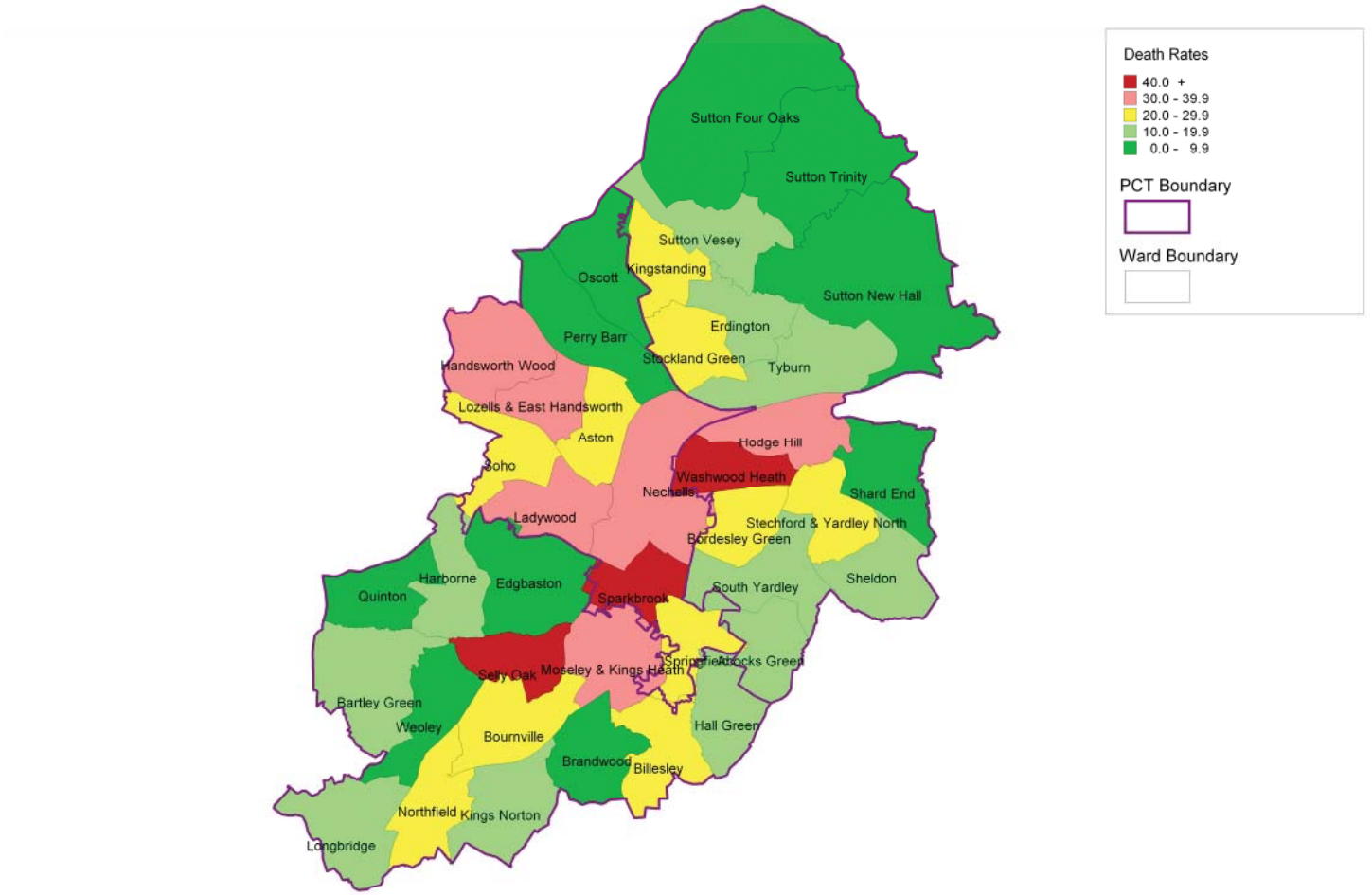
Source: PI & WMCAR notification
S = suppressed count or subtotal ≤3

Table 23 - Linkage to clinical genetics stillbirth and infant deaths by place of death (excluding deaths at home/elsewhere): Birmingham, 2006-10

Place of death	Congenital anomaly			Other causes		
	link	no link	%link	link	no link	%link
B'ham Women's	45	50	**47.4%**	19	287	**6.2%**
Heartlands	60	63	**48.8%**	19	273	**6.5%**
City	19	25	**43.2%**	3	118	**2.5%**
Good Hope	6	10	**37.5%**	4	63	**6.0%**
B'ham Children's	47	26	**64.4%**	14	42	**25.0%**
Other Hospital (outside B'ham)	9	8	**52.9%**	5	52	**8.8%**
Home/elsewhere						
ALL LOCATIONS	**186**	**182**	**50.5%**	**64**	**835**	**7.1%**

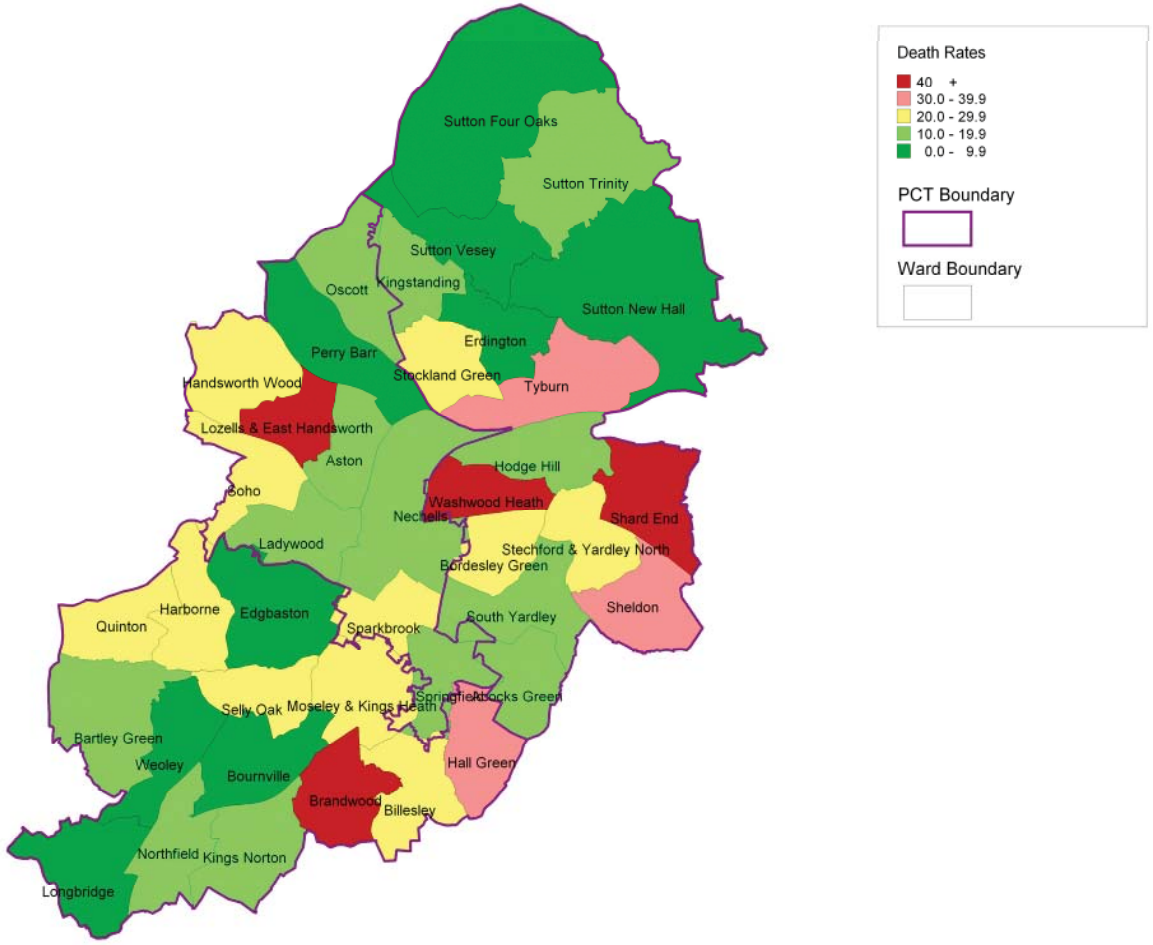
Source: PI & WMCAR notification
S = suppressed count or subtotal ≤3

Figure 9 - Rates of linked deaths to clinical genetics by ward, stillbirth and infant deaths from congenital anomaly: Birmingham, 2006-10



Source: numerator - PI & WMCAR notification
denominator - ONS Vital Statistics
Note: rate per 10,000 births

Figure 10 - Rates of non-linked deaths to clinical genetics by ward, stillbirth and infant deaths from congenital anomaly: Birmingham, 2006-10



Source: numerator - PI & WMCAR notification
denominator - ONS Vital Statistics
Note: rate per 10,000 births

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APPENDIX A – ASCERTAINMENT OF STILLBIRTH AND INFANT DEATHS FROM CONGENITAL ANOMALY

The Perinatal Institute EGSP report (May 2012) included analyses of stillbirths and infant deaths from congenital anomaly (n=377). These deaths, and others from non-anomaly causes, were linked to referrals to the West Midlands Clinical Genetics Service (Table 22). The linkage identified 65 deaths ascribed to non-anomaly causes that were linked to clinical genetics referrals using mother or baby records. This suggested that some anomaly deaths may have been wrongly ascribed to non-anomaly causes with the EGSP analysis.

Methods

The SHIRE (Clinical Genetics) records of 65 non-anomaly deaths linked to genetics referrals were reviewed by a Consultant Clinical Geneticist to determine if an anomaly was present that should have been ascertained by WMCAR and/or recorded as the cause of death.

Key findings

- Of the 65 cases reviewed, 25 had anomalies that were ascertained by WMCAR, but had died from other causes.
- There were 14 cases with significant structural/chromosomal anomalies that were not ascertained by WMCAR. In these deaths, the congenital anomaly was likely to have been the underlying cause of death.
- There were 13 cases with other congenital anomalies that were not ascertained by WMCAR. These cases had anomalies that are not routinely collected by WMCAR. The proportion of these cases where the congenital anomaly was the underlying cause of death is not known, however many of the anomalies were not lethal in infancy e.g. sickle cell disorders, retinitis pigmentosa.
- Between 14 and 27 (14+13) cases were likely to have been wrongly classified as deaths from non-anomaly causes Therefore ascertainment rates of stillbirths and infant deaths from congenital anomalies within the PI EGSP report were between 93.3% (377/391) and 96.4% (377/404).

Table I - Stillbirth and infant deaths from non-anomaly causes linked to Clinical Genetics Referrals: Birmingham, 2006-10 (n=65)

Clinical Genetics Referral Summary	WMCAR case Other cause of death	no WMCAR record
Affected case – congenital anomaly		
WMCAR anomaly – structural/chromosomal/metabolic	11	14
Other congenital anomaly – haemoglobinopathy, neuromuscular disorder, tumour, other	8	13
Minor anomaly	4	4
Unaffected case - other referral reason (e.g. family history, affected sibling)	1	6
Insufficient information/did not attend	1	3
ALL REFERRALS	**25**	**45**

APPENDIX B - STILLBIRTH AND INFANT MORTALITY FROM CONGENITAL ANOMALIES OF AUTOSOMAL RECESSIVE ORIGIN

Methods

During the five year period 2006-2010, there were 377 stillbirths and infant deaths from congenital anomaly (PI EGSP report - May 2012, Table 13). To determine the proportion of mortality that was autosomal recessive (AR) in origin, a sample of deaths was reviewed. The cases were selected by year of death, and reviewed by a Consultant Clinical Geneticist.

151 deaths from congenital anomalies occurred during the last 2 years of the study period (2009-10, n=151). Summary details from the WMCAR notification were reviewed in all cases, along with SHIRE (Clinical Genetics) records in those cases referred to the West Midlands Clinical Genetics Service.

The likely inheritance pattern for each congenital anomaly reviewed was categorised into 4 groups:

Autosomal Recessive (AR) Inheritance	Non-AR Inheritance
Definite AR confirmed diagnosis of known AR condition, which may be made clinically, pathologically or following biochemical or DNA testing	**Possible AR** some evidence e.g. parental consanguinity to suggest AR inheritance, but the pattern of anomalies does not fit with current knowledge of recognised AR conditions or not enough information available
Probably AR sufficient evidence to make diagnosis of an AR condition highly likely but no definitive diagnosis reached; likely to include more than one of the following: parental consanguinity, more than one affected child, including affected females, pedigree analysis supports AR inheritance, pattern of anomalies common in AR conditions even in absence of diagnosis	**Not AR in origin** sporadic in origin (e.g. trisomy 21 or isolated structural anomaly), or inherited in other ways (e.g. X-linked)

Mortality from AR congenital anomalies is reported as a proportion of mortality from congenital anomalies and mortality from all causes for 2009-10.

Previous analyses for EGSP were undertaken for stillbirth and infant mortality combined. Within this appendix there are additional analyses for infant deaths alone to inform the NHS and Public Health Outcome Frameworks that both include infant mortality as an indicator. In order to present data without the need for suppression of small cell counts, Black African, Black Caribbean, Indian, and Other (including Chinese & Mixed) ethnic groups were combined.

Key findings – all ethnic groups

- Of the 151 stillbirths and infant deaths from congenital anomalies during 2009-10, 53 cases were categorised as definitely or probably AR in origin.
- The stillbirth and infant mortality rate from definite/probably AR congenital anomalies for 2009-10 was 1.52 per 1,000 (95% CI 1.11-1.93, Table I).
- The corresponding infant mortality rate from AR congenital anomalies was 1.13 per 1,000 (95% CI 0.77-1.48, Table II).
- Deaths from AR congenital anomalies (n=53) comprised 35.1% of stillbirth and infant mortality (combined) from all congenital anomalies, and 10.4% of mortality from all causes (Table III).

- When the analysis was restricted to infant deaths alone, AR congenital anomalies (n=39) accounted for a larger proportion of infant mortality; 40.2% of infant mortality from all congenital anomalies, and 15.2% of infant mortality from all causes (Table IV).

Key findings – EGSP ethnic groups (Pakistani and Bangladeshi)

- Mortality from AR congenital anomalies was significantly higher in Pakistani (4.90 per 1,000 births, OR 37.7 9.1-156.1) and Bangladeshi (2.98 per 1,000 births, OR 22.9 4.4-118.2) ethnic groups, when compared to the White European group.
- Mortality rates in Pakistani or Bangladeshi mothers from congenital anomalies with other patterns of inheritance (non-AR anomalies) were not significantly different to the White European group.
- **Pakistani mothers**
    - 11 stillbirths and 29 infant deaths were categorised as definitely or probably AR in origin in the 2 year period 2009-10.
    - The stillbirth rate from AR anomalies in the Pakistani group was 1.36 per 1,000 births (95%CI 0.56-2.13) and the infant mortality for AR anomalies was 3.58 per 1,000 live births (95%CI 2.28-4.87).
    - AR anomalies contributed to 61.5% of stillbirths & infant deaths from congenital anomaly (65.9% of infant mortality alone – congenital anomalies) and 26.5% of stillbirths & infant deaths from congenital anomaly (37.2% of infant mortality alone – all causes).
- **Bangladeshi mothers**
    - 5 infant deaths were categorised as definitely or probably AR in origin in the 2 year period 2009-10, there were no stillbirths from AR congenital anomalies in Bangladeshi mothers.
    - The infant mortality rate from AR anomalies in the Bangladeshi group was 3.00 per 1,000 live births (95%CI 0.37-5.63).
    - AR anomalies contributed to 45.5% of stillbirths & infant deaths from congenital anomaly (50.0% of infant mortality alone – congenital anomalies) and 20.8% of stillbirths & infant deaths from congenital anomaly (29.4% of infant mortality alone – all causes).

Table I - Stillbirth and infant death rates from congenital anomaly by inheritance and ethnic group: Birmingham, 2009-10

Maternal Ethnic Group	Anomaly AR Inheritance			Anomaly Other Inheritance			Total births
	n	rate	(95%CI)	n	rate	(95%CI)	
White European REFERENCE	**2**	**0.13**	**(0.00-0.31)**	**40**	**2.61**	**(1.80-3.42)**	**15,332**
Pakistani	40	†4.90	(3.38-6.41)	25	3.06	(1.86-4.26)	8,167
Bangladeshi	5	†2.98	(0.37-5.59)	6	3.58	(0.72-6.43)	1,678
Other ethnic groups	6	0.62	(0.12-1.12)	27	2.80	(1.75-3.86)	9,631
ALL ETHNIC GROUPS	**53**	**1.52**	**(1.11-1.93)**	**98**	**2.82**	**(2.26-3.37)**	**34,808**

Source: numerator - PI & WMCAR notification
denominator - ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: AR = definite/probable autosomal recessive
rate per 1,000 births
† significantly different to reference population (i.e. 95% confidence limits for odds ratio exclude 1)

Table II - Infant death rates from congenital anomaly by inheritance and ethnic group: Birmingham, 2009-10

Maternal Ethnic Group	Anomaly AR Inheritance			Live births
	n	rate	(95%CI)	
White European REFERENCE	**2**	**0.13**	**(0.00-0.31)**	**15,227**
Pakistani	29	†3.58	(2.28-4.87)	8,111
Bangladeshi	5	†3.00	(0.37-5.63)	1,666
Other ethnic groups	3	0.31	(0.00-0.67)	9,565
ALL ETHNIC GROUPS	**39**	**1.13**	**(0.77-1.48)**	**34,569**

Source: numerator - PI & WMCAR notification
denominator - ONS Vital Statistics & PEER adjusted maternal ethnic distribution
Note: AR = definite/probable autosomal recessive
rate per 1,000 births
† significantly different to reference population (i.e. 95% confidence limits for odds ratio exclude 1)

Table III - Stillbirth and infant deaths, proportion of mortality from autosomal recessive congenital anomaly by ethnic group: Birmingham, 2009-10

Maternal Ethnic Group	SB+IDs FROM AR CONGENITAL ANOMALIES			SB+IDs CONGENITAL ANOMALY	SB+IDs ALL CAUSES
	n	% of mortality from CONGENITAL ANOMALY	% of mortality from ALL CAUSES		
White European REFERENCE	2	4.8%	1.1%	42	188
Pakistani	40	61.5%	26.5%	65	151
Bangladeshi	5	45.5%	20.8%	11	24
Other ethnic groups	6	18.2%	4.1%	33	148
ALL ETHNIC GROUPS	**53**	**35.1%**	**10.4%**	**151**	**511**

Source: numerator - PI & WMCAR notification
Note: AR = definite/probable autosomal recessive

Table IV - Infant deaths, proportion of mortality from autosomal recessive congenital anomaly by ethnic group: Birmingham, 2009-10

Maternal Ethnic Group	INFANT DEATHS FROM AR CONGENITAL ANOMALIES			DEATHS CONGENITAL ANOMALY	DEATHS ALL CAUSES
	n	% of mortality from CONGENITAL ANOMALY	% of mortality from ALL CAUSES		
White European REFERENCE	**2**	**7.1%**	**2.1%**	**28**	**97**
Pakistani	29	65.9%	37.2%	44	78
Bangladeshi	5	50.0%	29.4%	10	17
Other ethnic groups	3	20.0%	4.7%	15	64
ALL ETHNIC GROUPS	**39**	**40.2%**	**15.2%**	**97**	**256**

Source: numerator - PI & WMCAR notification
Note: AR = definite/probable autosomal recessive

Appendix 5 Activity data requirements for primary care, clinical and education strands

Primary Care Monitoring Information

Practice Demographics	
Number of patients on practice register at end of period	
Number of patients aged over 16 on practice register at end of period	
Number of male patients aged over 16 on practice register at end of period	
Number of female patients aged over 16 on practice register at end of period	
Ethnic origin category of patients*	
British/mixed	
Irish	
Other white	
W&B Caribbean	
W &B African	
White and Asian	
Other mixed	
Indian/British	
Pakistani/British	
Bangladeshi/British	
other asian	
Caribbean	
African	
Other black	
Chinese	
other not stated ethnicity	
PERIOD	

Haemoglobinopathy and Autosomal Recessive Conditions in that period INCIDENCE	
Number of patients diagnosed with haemoglobinpathy on practice register (ie. Affected) DURING PERIOD	
Number of patients on practice register diagnosed as a carrier of a haemoglobinpathy DURING PERIOD	
Number of patients diagnosed with other AR conditions on practice register (ie. Affected) DURING PERIOD	
Number of patients tested and found to be carriers of other AR conditions on practice register DURING PERIOD	
Number of patients who are carriers of or affected by haemoglobinopathies on practice register with information on consanguineous partnership on notes DURING PERIOD	
Number of patients who are carriers or affected by other AR conditions on practice register with information on consanguineous partnership on notes DURING PERIOD	
Genetic Testing event during the period	
Number of patients approached for testing DURING PERIOD	
Number of patients who declined testing DURING PERIOD	
Number of patients who consented to testing as documented in medical notes DURING PERIOD	
Number of patients who consented to testing who received a positive result (carriers and affected individuals) DURING PERIOD	
Number of patients who received a positive result during the period for being affected by thalassaemia DURING PERIOD	
Number of patients who received a positive result for being carriers of thalassaemia DURING PERIOD	
Number of patients who received a positive result for being affected by sickle cell anaemia DURING PERIOD	
Number of patients who received a positive result for being carriers of sickle cell anaemia DURING PERIOD	
Number of patients with at least 1 of the following on notes consent given to testing/consent not given/test offered /positive result/negative result	
Number of patients who received a positive test result for haemoglobinopathy with a pedigree attached to notes DURING PERIOD	

Clinical strand monitoring information

Table 1 Patient Review

Start and end date of period		Period 2	Period 2
Item		Number	Percentage where relevant
a	Number of affected individuals on CGU system at start of project	n/a	n/a
b	Number of affected individuals on CGU system at start of period (for the conditions reviewed in that period)	n/a	n/a
c	Number of affected individuals on CGU system at end of period (for the conditions reviewed in that period)	n/a	n/a
d	Number of individuals reviewed in period		n/a
e	Number of individuals who have not been reviewed in period (i.e. those who will carry over to next review period)		n/a
f	Number of individuals reviewed where it is not possible to reach a molecular diagnosis		n/a
g	Number of reviewed individuals not eligible for EGSP		n/a
h	Number of reviewed individuals found to be eligible for EGSP		n/a
i	Number of letters regarding eligible individuals sent to CGU consultant		n/a
j	Number of instances where CGU consultant has indicated that the individual is not suitable to contact		n/a
k	Number of letters regarding eligible individuals sent to GP		n/a
l	Number of instances where GP has indicated that the individual is not suitable to contact		n/a
m	Number of eligible individuals/their parents re-contacted by EGSP		n/a
n	Cumulative number of individuals/ their parents recontacted by EGSP letter		n/a
o	Cumulative number of recontacted individuals who have been offered genetic counselling (total number and percentage)		
p	Cumulative number of those offered genetic counselling who accepted (total number and percentage)		
q	Cumulative number of those offered genetic counselling who declined (total number and percentage)		

r	Cumulative number of those who accepted genetic counselling who have been offered genetic testing (total number and percentage)		
s	Cumulative number of those offered genetic testing who accepted (total number and percentage)		
t	Cumulative number of those offered genetic testing who declined (total number and percentage)		
u	Cumulative number and percentage of individuals/parents where full clinical pathway as specified by protocol was followed (to the end point as relevant for each patient)		
v	Number of eligible individuals with a genetic test result recorded (on CGU system or in file)		n/a
w	Number of reviewed individuals with ethnicity recorded in period (total and percentage)		
x	Cumulative number of reviewed individuals with ethnicity recorded (total and percentage)		
y	Ethnic breakdown of reviewed individuals-please list in rows below providing the number and percentage		
	Pakistani		
	Bangladeshi		
	Unknown		
	Other Asian		
	White British		
	Yemeni		
	Indian		
	not recorded		
	Yugoslavien/ Slovenian		
	Iranian		
	Turkish		
	Afghani		
	Iraqi		
	not stated		

Table 2 Genetic Test Development and Monitoring of Testing Undertaken

Item		Number/Cost			
a	Number of tests developed in period				
	Diseases				
	Genes				
	individual tests				
b	Number of patients **fulfilling EGSP criteria** offered EGSP developed genetic tests in period				
		Clinical genetics	BCH	Other	Total
	Total number of referrals				
	Referrals for full gene screens				
	Referrals for carrier tests/prenatals				
c	Number of diagnoses achieved in period for patients **fulfilling EGSP criteria** as a result of the testing using EGSP tests				
		Clinical genetics	BCH	Other	Total
	Diagnosis				
	Carrier Positive				
	Carrier Negative				
	Prenatal positive				
	Prenatal Negative				
d	Number of patients living in West Midlands who **do not fulfill EGSP criteria** offered EGSP developed genetic tests in period				
		Clinical genetics	BCH	Other	Total
	Total number of referrals				
	Referrals for full gene screens				
	Referrals for carrier tests/prenatals				
e	Number of diagnoses achieved in period for patients living in West Midlands who **do not fulfill EGSP criteria** and were offered EGSP developed genetic tests				
		Clinical genetics	BCH	Other	Total
	Diagnosis				
	Carrier Positive				
	Carrier Negative				
	Prenatal positive				

	Prenatal Negative				
f	Number of patients living **outside the West Midlands** offered EGSP developed genetic tests in period				
		Clinical genetics	BCH	Other	Total
	Total number of referrals				
	Referrals for full gene screens				
	Referrals for carrier tests/prenatals				
g	Number of diagnosis achieved in period of patients living **outside the West Midlands** offered EGSP developed genetic tests				
		Clinical genetics	BCH	Other	Total
	Diagnosis				
	Carrier Positive				
	Carrier Negative				
	Prenatal positive				
	Prenatal Negative				
h	Number of patients **fulfilling EGSP criteria** offered **non-EGSP developed genetic tests** in period				
		Clinical genetics	BCH	Other	Total
	Total number of referrals				
	Referrals for full gene screens				
	Referrals for carrier tests/prenatals				
i	Number of diagnosis achieved in period for patients **fulfilling EGSP criteria** and offered **non-EGSP developed genetic tests** in period				
		Clinical genetics	BCH	Other	Total
	Diagnosis				
	Carrier Positive				
	Carrier Negative				
	Prenatal positive				
	Prenatal Negative				
j	Cost of testing for EGSP patients in period using **non ESGP developed tests**				
k	Cost of testing for EGSP patients in period using **newly developed EGSP tests**				
l	Number of newly developed EGSP tests ordered by services outside of West Midlands in period				

m	Cost of testing of **newly developed EGSP tests** ordered by services outside of West Midlands in period				

Table 3 Monitoring of Clinical Pathways for Cascade Testing

	Submission date		
	Table 3 Monitoring of clinical pathways for cascade testing		
		Period	**Period**
Start and end date of period			
Item		**Number**	**Percentage where relevant**
a	Total number of EGSP eligible families (reviewed & referred families) in period		
b	Total number of eligible families with a pedigree at start of period		
c	Number of **reviewed & referred** families who have been recontacted (i.e. by telephone/home visit/clinic appointment)		
d	Number of recontacted families where pedigree has been updated		
e	Number families where at risk relatives have been identified		
f	Number of families who are 'at risk' with **1-10 family members on pedigree**, where most family members live in the West Midlands PCTs and so are eligible to be included in the EGSP		
g	Number of families who are 'at risk' with **11-20 family members on pedigree,** where most family members live in the West Midlands PCTs and so are eligible to be included in the EGSP		
h	Number of families who are 'at risk' with **21-30 family members on pedigree** where most family members live in the West Midlands PCTs and so are eligible to be included in the EGSP		
i	Number of families who are 'at risk' with **31+ family members on pedigree** where most family members live in the West Midlands PCTs and so are eligible to be included in the EGSP		
j	Total number of 'at risk ' family members identified who are eligible to be included in EGSP and could be contacted by the proband (using an information letter or through verbal communication) in period		
k	Number of 'at risk' family members identified who are eligible to be included in the EGSP and have been discussed with proband or parents with a view to the proband contacting them		

l	Cumulative number of 'at risk' family members identified since March 2012 who are eligible to be included in the EGSP and have been discussed with proband or parents with a view to the proband contacting them		
m	Cumulative number of l where it is agreed to contact relative (and percentage of l)		
n	Cumulative number of those relatives in l. who have been contacted by relative		
o	Cumulative number who are eligible for follow up who have been offered genetic counselling (total number and percentage)		
p	Cumulative number of those offered genetic counselling who accepted (total number and percentage)		
q	Cumulative number of those offered genetic counselling who declined (total number and percentage)		
r	Cumulative number of those who accepted genetic counselling who have been offered genetic testing (total number and percentage)		
s	Cumulative number of those offered genetic testing who accepted (total number and percentage)		
t	Cumulative number of those offered genetic testing who declined (total number and percentage		
u	Cumulative number and percentage of patients who are eligible for follow up where full clinical pathway as specified by protocol was followed (to the end point as relevant for each patient)		
v	Number of 'at-risk' children identified who may be interested in carrier testing once they reach the appropriate age at which they can decide on testing		
w	Number of 'at-risk' family members identified who have decided not to marry within the family		
x	Number of families with eligible conditions identified in period		
y	Cumulative number of families with eligible conditions identified throughout project		
z	Number of families with consanguineous partnerships recorded in period (total number and percentage)		
z1	Cumulative number of families with consanguineous partnerships recorded (total number and percentage)		
z2	Number of families with consanguineous partnerships by ethnic group (total and percentage of for each ethnic group) Please list on separate sheet		
z3	Diagnoses in consanguineous families by ethnic group (total number per diagnosis and percentage) Please list on separate sheet		

Table 4 Monitoring of Self- Referrals

Submission date:			
	This may be for any conditions not just eligible conditions for EGSP		
Start and end date of period			
Item		**Number**	**Percentage**
a	Number of self referrals in the past 6 months at start of project from target ethnic groups		n/a
b	Number of self referrals for 3 month period from target ethnic groups		n/a
c	Number of self referrals for 3 month period from non target ethnic groups		n/a
d	Number of self referrals from patients registered with participating GPs		n/a
e	Number of self referrals from contact with EGSP education strand (if known)		n/a
f	Number of self referrals to EGSP from contact with the 'Talking genetics' website		n/a
g	Cumulative number of self referrals who have been offered genetic counselling (total number and percentage)		
h	Cumulative number of those offered genetic counselling who accepted (total number and percentage of g.)		
i	Cumulative number of those offered genetic counselling who declined (total number and percentage of g.)		
j	Cumulative number of those who accepted genetic counselling who have been offered genetic testing (total number and percentage)		
k	Cumulative number of those offered genetic testing who accepted(total number and percentage)		
l	Cumulative number of those offered genetic testing who declined (total number and percentage)		
m	Cumulative number and percentage of referred patients where full clinical pathway as specified by protocol was followed (to the end point as relevant for each patient) (total number and percentage)		
n	Number of 'at-risk' children identified who may be interested in carrier testing once they reach the appropriate age at which they can decide on testing		

Table 5 Referrals from other specialisms

	Table 5: Referrals from other specialisms		
			Period
Start and end date of period			
Item		**Number**	**Percentage**
a	Number of referrals from all 'different specialties' at start of project for past 6 month period (baseline information so only to be submitted at start of Project)		n/a
b	Number of referrals from GPs in 3 practices within EGSP at start of project for past 6 month period (baseline information so only to be submitted once		n/a
c	Number of referrals from GPs in 3 EGSP practices in period		n/a
d	Number of new diagnoses as a result of referrals by GPs in EGSP in period		n/a
e	Number of referrals from GPs not in EGSP at start of project (baseline information so only to be submitted once **)**		n/a
f	Number of referrals from GPs not in EGSP in period		n/a
g	Number of new diagnoses as a result of referrals by GPs not in EGSP in period		n/a
h	**(Please add specialisms as appropriate)** Number of referrals by each specialty in period	***Renal***	
		Genetics	
		Obs & Gynae	
i	Number of new diagnoses as a result of referrals by specialty for period		n/a
j	Cumulative number of referrals who have been offered genetic counselling (total number and percentage)		
k	Cumulative number of those offered genetic counselling who accepted (total number and percentage of j)		
l	Cumulative number of those offered genetic counselling who declined (total number and percentage of j)		
m	Cumulative number of those who accepted genetic counselling who have been offered genetic testing		
n	Cumulative number of those offered genetic testing who accepted (total number and percentage)		
o	Cumulative number of those offered genetic testing who declined (total number and percentage)		
p	Cumulative number and percentage of referred patients where full clinical pathway as specified by protocol was followed (to the end point as relevant for each patient) (total number and percentage)		

q	Number of 'at-risk' children identified who may be interested in carrier testing once they reach the appropriate age at which they can decide on testing		

Table 6 New cases in known families

		Period
Start and end date of period		
Item		**Number**
a	Number of new patients diagnosed whose parents are couples known to clinical genetics service **before the patient was born**	
b	Number of these couples in a. offered genetic testing prenatally	
c	Number of these couples in b. who took up testing prenatally	
d	Number of couples in b. who declined prenatal testing	
e	Number of couples in c. who took up testing and had a negative result	
f	Number of couples in c. who took up testing offer and had a positive result	
g	Number of couples in f. who decided to continue with pregnancy after a positive result	
h	If possible to identify - number of couples in f. who terminated pregnancy	

Education Strand Monitoring

Information for capturing activity in the education strand:

Education needs Assessment process monitoring

Monitoring of contacts for professional/community education on genetics

Name of organization	
Name of contact	
Best means of contact (telephone number, email)	
Role in education of professionals/ in community	
Rating of importance of contact (1= low, 4 =high)	
Date of initial contact	
Dates of recontact	
Initial reaction to contact	
Priorities for education identified	
Support required from EGSP	
Other organizations to contact arising from this contact	
Other issues to follow up	
Actions to undertake	
Actions undertaken arising from contact with dates	

In addition evaluation forms to be completed and submitted to the evaluation for each educational session with health professionals and where possible educational sessions in the community

Appendix 6 Service Level Agreeement between HoBtPCT and Participating Practices

The service level agreement (dated 1 March 2009) between HoBtPCT and the two participating GP practices provided details of what each practice was expected to accomplish.

The key points are set out below:

'An initiative in pilot GP practices…. to undertake opportunistic screening for thalassemia carrier status within the practice as a vehicle to raise the genetic literacy of the population. This will be done through identifying families most likely to benefit from such screening (utilising local GP knowledge) or through opportunistic screening of patients attending the practice. As part of this process a detailed family history will also be taken to identify affected and extended families that could benefit from input from specialised genetic services (i.e. those where there is evidence of the presence of a rare autosomal recessive disorder) who will be referred to the relevant other parts of the initiative (i.e. West Midlands Regional Genetics Service). Local and national surveys suggest a key issue is lack of genetic literacy with high perceived need for more information.

Practices will receive extra resources in the form of funding for GP sessions. This is to be used to increase capacity allowing the issue of Thalassemia screening to be raised in current consultations and to run specific 'genetic' GP sessions. Dependent in a pro rata manner on the number of GP sessions extra resources will also be provided for management and facility costs of undertaking the initiative and for the provision of extra healthcare professionals to take blood samples and provide education/outreach. Funding will also include costs for any training required and it is expected that both GPs and healthcare professionals in the project attend the relevant training and undertake to provide education/outreach inline (sic) with current best practice.

'The exact configuration of provision of services will be decided by each practice as appropriate to there (sic) individuals circumstances. However it is expected that for each GP session funded an average of 7 individuals are seen (plus/minus 15%).

Appendix 7 Patient and Staff Experience of Primary Care Strand

Qualitative Review of the Haemoglobinopathies Screening Programme

Introduction

This paper reports the findings of a qualitative review that was carried out following a haemoglobinopathies screening program at a GP practice in Birmingham. This screening program is part of the primary care strand of the Enhanced Genetics Services Project (EGSP).

Birmingham has significantly higher infant mortality and morbidity rates than England and Wales.

Genetic disorders are known to contribute significantly towards the high perinatal and infant mortality rates in Birmingham and autosomal recessive conditions are particularly common in the children of couples who have married within the family. Raising awareness of genetics and the genetics service within the community is necessary in order to enable families to take full advantage of new developments in diagnostic tests including genetic tests for carrier status and potential treatments.

The Primary Care strand

Three GP Practices in HoBtPCT participated in this project and offered a screening programme for inherited blood disorders. They raised awareness of other genetic disorders and identified families appropriate for specialist referral.

Aims

The aims of the screening programme were:

- To screen all patients for haemoglobinopathies carrier status and counsel them accordingly
- To identify the prevalence of consanguineous marriages in the ethnically diverse practice population.
- To increase genetic literacy amongst the practice population
- To identify families at risk of autosomal recessive conditions and refer them to clinical genetics.

This review has been undertaken to learn from the experiences of the patients and practice staff involved in the screening programme in order to capture:

- The experiences of some of the patients involved their understanding of the screening programme, their understanding of the results and implications for themselves and their families.
- The experiences of the staff involved in the screening programme.

This research has been carried out by the Community Educator for the EGSP. The feedback obtained will be used as a guide and information tool for implementing similar schemes in primary care settings and more specifically will be used by EGSP to inform the educational strand of the project to help determine the educational needs of the community.

EGSP Methodology

The screening programme was implemented by the practice over a two year period between April 2009 and April 2011. All eligible Patients over the age of 16 were initially contacted by letter and then by telephone to present for a blood test. Opportunistic testing was also carried out by surgery staff with the patient's agreement. All patients taking part in the program should have been informed about the screening and its purpose before consenting to the blood test.

Qualitative Review Methodology

To help capture the experiences of the patients and staff, questionnaires were designed and the responses obtained by conducting semi structured interviews.

The participants were chosen from the patients that took part in the screening programme. They were contacted by telephone and asked if they would be willing to take part in the qualitative review. In total 14 participants were interviewed 7 men and 7 women. The practice manager explained that the patients who they thought would attend for interview were contacted. All staff involved in the programme were interviewed.

The interviews took place at the GP practice. The interviews were recorded using a Dictaphone and then transcribed. Patients and staff were asked to sign a consent form before the start of the interview.

All but one of the participants spoke English. This one participant spoke Urdu, as the investigator can also speak Urdu this interview was conducted in Urdu and then transcribed into English.

Findings on Patient Views

Demographics

Age range	Under 20	20-30	31-40	41-50	Over 50
	0	3	2	4	5

Ethnicity									
Number	British white	British Black	Asian British	African Indian origin	Bangladeshi	Caribbean	Irish	Indian	Pakistani
	1		1 (Pakistani/ British mixed)	2 (Tanzanian)	1	1	1	4	3 (1 Kashmiri)

Results

Understanding of the screening process

Questions 1 and 2 explored the understanding of the process.

Question 1: ***Did you understand why you were being invited for testing? (from the letter and other information from the practice eg. posters, information from staff)***

11 of the 14 participants said they did understand why they were being invited for the test.

The remaining 3 responses were:

Participant 1	Not really I had a random blood test and I find out I have the trait, no I think it was just a general blood test.
Participant 6	Yes doctor said it was regarding Thalassaemia.
Participant 9	I was told it was for the research for this Thalassaemia thing

Question 2: ***Did you understand what would be involved?***

11 of the 14 participants said that they did know what would be involved.

The 11 participants that said that they understood the process and what would be involved explained that they were going to have a blood test. None of the participants mentioned that the blood test was for a screening programme. These responses raise questions around the extent to which the programme's aims were explained to patients. Only one participant explained that the blood test was for sickle cell screening.

3 participants said they were not aware of the reason for the blood test

Participant 1	No
Participant 6	No not to sure
Participant 9	Told me I was ok – to do with blood related illness

These responses suggest that there was no clear understanding amongst the participants interviewed about the screening programme at this stage of the process.

Understanding the Information given and Results

Question 3: ***Did you understand what information the blood test would provide?***

12 of the 14 participants said they did understand the information. The remaining 2 participants gave the following responses:

Participant 1	Not really, Not that I can remember as it was a long while ago now.
Participant 9	No

Question 4: ***Did you understand the results of the test when you received them?***

7 participants that said they understood the information and results responded by just saying 'yes', and none offered to explain any further. It is difficult to determine from these responses if the participants have understood the information and results and more importantly that they have understood the risk to other family members or passing on carrier status to their children.

4 participants gave responses which suggested that the information given to them was not really understood, examples given below. Participant 1 went on to say that it made no difference to his health further suggesting that the genetics information had not been understood.

Participant 1	Yeah I was told I have got the trait, not the full blown version, that's it really.

Participant 3	All I was told I was fine
Participant 6	I wasn't exactly told, I was just told that test was taken when you rang up to say, wasn't exactly sure.
Participant 9	I don't think so, I understood them. (Was it some time ago or?)I think it was more than 6 months.

One participant was an elderly gentleman who was confused about the whole process but said it was not relevant for him because of his age. One female attended the interview because she needed information about genetics but not about this particular screening programme.

The information and explanation of the results is the key part of the screening process and at this stage it is difficult to determine if the participants understood the information given to them.

It is important to consider that unless information is made very clear, some of those tested will not retain the information that is provided. Positive results can affect others, so again the information needs to be retained. This may be a significant drawback of opportunistic testing.

What it means to be a carrier and implications for family members

Question 5: ***Can you explain what being a carrier of Thalassemia or sickle cell means in terms of your health?***

The responses to this question by most of the participants (see appendix 3) suggest that there is confusion and misunderstanding about the word carrier and that the participants have not understood what it means to be a carrier in terms of their own health. This lack of understanding will impact on any further genetic risk information that is discussed.

The 2 participants that said yes they could explain were participants 6 and 9. However both of these responses suggest that the participants may not understand what being a carrier means in terms of their own health.

Participant 6	Yes if you are a carrier you have got a risk of getting child with same thing and if you both the parents are then it's a higher risk of the child, and have to do a transfusion or something. Yes my sister is a carrier, and she has found out that my nephew is as, well he is a carrier but I don't think my niece is
Participant 9	All I know is that I am just a carrier at the moment, and I need to get married to somebody who's got no Thalassaemia.

Question 6: ***Do you understand the implications for other members of the family from the results of your test?***

All 14 of the participants said that they understood that a genetic disorder can be passed onto children.
The message that there are genetic risks associated with couples who are both carriers seems to have been understood. However the responses to question 5 suggest that maybe the information has not been understood completely and may cause confusion and misunderstanding.

Attitude towards the Screening Programme

Question 7: ***Do you think it is a good idea or a bad idea for GPs to offer this type of testing? Please explain your answer.***

All 14 participants said that the screening was a vital service and they were happy to take part. They linked this with information that is vital for people who wish to have a family. The following table provides some examples

of their responses

Participant 2	No think should get tested especially before your thinking of getting married because that's when it's most important.
Participant 3	I think it's very good. Very good indeed because if it saves a couple bringing their child into the world, it is better that they don't suffer
Participant 11	I think it's a good idea, because one would never know would they. (You didn't know before then?) did not have a clue, I have never had a days illness in my life, never……..

Information Needs

Questions 8: ***What was your overall experience of being offered testing for whether you are a carrier of Thalassaemia or sickle cell disease?***

All the participants said the overall experience of taking part in the screening programme was positive.

Participant 1	Good. I feel I know about it as it came up in the test, put it down as good.
Participant 3	I felt fine; it's good to be tested.
Participant 6	I was quite pleased to know, so that I know, my sister is and I am not.
Participant 9	It wasn't negative; it was just so you are just a carrier so it's not going to give me any problems.

Question 9*:* ***Is there any further information you want on genetic conditions such as Thalassaemia*?**

The responses to question 9 were 5 participants said yes further information would be useful, 7 said no and 2 said it wasn't relevant for them

The 5 participants that said yes all mentioned that would be beneficial for the future of their children

The participants that felt they did not need any more information (see table below) responded with various reasons for example participants 1 and 9 , these responses suggests that maybe they have not understood the genetic risks associated with being a carrier. The response from participant 5 suggests a lack of understanding .Participant 2 explains that she knows all the information, however this may be debatable if her response to question 5 is considered

Participant 1	*If it's beneficial, yes but I am not really too concerned.*
Participant 2	*No I think I know most of it now, and seen as they have told me that when I want to get pregnant again, I have ……..*
Participant 5	*No at this stage I don't think so. I don't feel like any other symptoms as a carrier.*
Participant 9	*I think I didn't ask for any more information.*
Participant 8	*I have always had a interest to find out why it's happening so I haven't gone in to it that far yet. So yes I really like to, would like to yes.*

At this stage, it seems that there is a need for a more structured genetics information process so that patients are able to make informed decisions.

Question 10: ***A part of this project will be offering genetics education to the Birmingham community, do you think prior understanding of genetics and carrier testing would have made this screening process easier for you and the community?***

In response to this question, 10 participants said yes it would be beneficial 3 thought there was no need.

The responses from participants 1 and 9 suggest that they do not think that genetic education is relevant for them as they feel they have all the information they need. Participant 2 felt she knew enough and did not need any further knowledge

Participant 1	*No not really.*
Participant 2	*I knew everything about it, before we got married we got tested. I knew what I had to do ……*
Participant 5	*Yes it would in one sense yes, it would give me some information but it would be better for my children to have it rather than me*
Participant 6	*Sometimes a person doesn't exactly understand, they know the word but they don't know the in-depth of what Thalassaemia is. Ok you know certain parts of it, not all of it.*
Participant 9	*I think it would have been easier well because I am just a carrier. Doesn't make much difference.*

The participants that were older all agreed that education was more applicable to the younger generation rather than the older generation.

Talking about genetic risk to family members and views on Cousin Marriages

Question 11: ***Do you now feel that you understand genetics and inheritance enough to be able to talk about risks and carrier testing with you families?***

8 participants said that they knew how to pass on the genetic risks information to their families, 1 participant felt that more information was needed and 3 participants gave non relevant responses.

8 participants said they knew enough to discuss genetic risk with their families; however in response to previous questions it seems that they haven't really understood the genetics information that is needed to be able to discuss genetics and inheritance. These responses suggest that the participants may feel they know enough about genetic risk to talk to their families, but it is doubtful if it is the right information. Participant 1's response implies a lack of understanding that you are born with the trait and so a lack of understanding of the message of the screening. Participant 12 seems confused and probably would not be able to inform relatives.

Participant 1	*Yes a lot of people are unaware of different types of conditions, things that can happen, I was unaware of all of this until I got the trait.*
Participant 4	*I say I need more information really at the moment. I know enough but not enough to pass it on really, fully.*
Participant 6	*I think so, because if you know what you're having the test for you would want to know more. More confidence and you know what happens, you know what you are.*
Participant 12	*It's a difficult one that because in practice marrying relatives has come up as a children born with elements and all that, but as you well know within our societies its been going on for generations and its never been, when you look at the over side of it, it doesn't have to be a relative to, you can still get it, I don't think its personally, to me that's my view ……*

Question 12: ***What is your understanding of marriage with a relative in relation to genetic risk?***

The question on cousin marriages received various responses and it has proved difficult to assess whether the participants understood the risks associated with consanguinity or not. As is quoted below, participant 2 who feels well informed about genetic risks doubts that it is related to cousin marriages.

Participant 1	*I know it is a risk, that you take, I was just told that I had this trait, and that's it, life has carried on as normal and made no difference to me what so ever*
Participant 2	*To be honest I do not think it has anything to do with being related, I mean because he could have been just a random person, and he could have had it as well, it really doesn't matter about being related or not related, its just we are related, everyone thinks its more common, and there are people who I know who are not related and both got the same thing anyway.*
Participant 7	*I understand. If it's both carriers then your child is 1 in 4 chance of getting a major.*

The responses received suggest that there may be some lack of understanding of genetic information, however all the participants accepted that there is a link between genetic risk and consanguinity, participants also understood these concepts in the context of their own experiences rather than the scientific facts.

Findings

This qualitative review has highlighted some important factors about education and screening programmes which should be taken into consideration when programs of this nature are run for the community.

Points to consider:

- the type of information given to patients
- how the information is given, confirmation that the information has been understood
- the introduction to the screening programme and an understanding of the disorders being screened for.

Understanding of the screening process

The results suggest that the participants were not clear about being involved in a screening programme at the start of the process. An explanation for this may be that the haemoglobinopathy screening was carried out as part of other routine blood tests. The practice did confirm that the screening was carried out in conjunction with a well person clinic and a cardiovascular risk program.

Understanding the Information given and Results

Most of the participants did not seem to have an adequate understanding of haemoglobinopathies that were relevant to them. This suggests that more time needs to be allocated to those patients that are carriers of a trait to help them understand the condition and what it means in terms of their own health and their families. Unless the information is made very clear some of those tested will not retain the information. The results if positive can affect others and so again the information needs to be retained. This may be a particular issue for opportunistic screening.

What it means to be a carrier and implications for family members

A theme that was evident throughout the interviews suggests that the participants did not understand what the status of being a carrier really meant. Some had an idea but were not sure and because of this the rest of the genetic information may not have been understood.

The participants did link genetic conditions with inheritance and risks for children.

Attitude towards the Screening Programme

All the participants were happy to take part in the screening and thought it was a valuable programme for the community.

Information Needs

Participants felt they knew enough to talk about genetic risk to their families. But their responses to some questions suggested that they maybe had not understood all the information and hence there is a risk of them passing on incorrect and confusing information to family members.

Talking about genetic risk to family members and views on Cousin Marriages

The participant felt genetics education was important for the community. All the participants were aware of the risks of genetic disorders and consanguinity although many did not understand the genetics.

Staff Results

The two GPs, practice manager and receptionist involved in the screening program were interviewed.

What is the purpose of the screening program and how the program was run

Question 1: ***What do you think is the purpose of the project?***

Question 2: ***Can you explain how the scheme operates (eg. who is invited, how they are invited, what happens if they do not attend, how they get the results, how other family members registered and not registered with the practice are contacted where there has been a positive result).***

All four staff members explained that the screening program was to raise awareness of genetic risk and improve genetic literacy amongst the community. One GP said it was to educate people and help them make informed reproductive choices.

The process used to run the program was described similarly by all four staff members. There was an emphasis on having a blood test for haemoglobinopathies. This may be the reason why the participants interviewed were confused about the screening program as it seems there was no information given prior to the blood test.

Understanding of carrier status for Thalassaemia or Sickle Cell disease in terms of the patient's health and implications for other family members

Question 3: ***Can you explain what being a carrier of Thalassaemia or Sickle Cell disease means in terms of the patient's health and implications for other family members?***

This was really well explained by the GPs.

The responses from the non-clinical staff suggested that there was confusion in their understanding for example - 'Blood disorders, a lot of stress, they can pass it on to the children', and 'If two carriers married and had children the risk was very high of them having a positive Thalassaemia, Sickle Cell disease or a Cystic Fibrosis baby'. These two staff members do not mention what a carrier status means in terms of the patients health. This lack of explanation of carrier status is reflected in the confusion that some of the participants had about what being a carrier means.

The GPs also explain what it means in terms of starting a family and risk to offspring rather than offering an

explanation of carrier status and basic genetics information.

Additional workload generated by the project and particular problems encountered

Question 4: ***Did the project generate additional workload? – if yes, please can you describe what extra work was required and how much extra time was taken up (per day, per week)***

Question 5: ***Did you encounter any particular problems linked to the project?***

All staff members said that the work load was greater than the time allocated to the project. This was due to: the administration and the task of re-contacting patients that did not attend appointments, counselling patients and the extended family when carriers were identified. There were also the project plans and protocols for the screening and generating the reports.

There were a few problems encountered as one GP explained 'Yes, obviously the media did play a big part in terms of what the impact was going to be, there were different points of views, with all our partners in other strands, that in itself was quite stressful at the time' The screening program was featured on the Dispatches documentary on cousin marriages.

Also another point raised was the amount of work generated for the laboratories as this can be an issue with a large practice and the turn-around time for result.

Training needed for Staff and benefits from the screening programme for the patients and the practice

Question 6: ***What training do you think is needed for practice staff to be involved in this type of screening and for someone in your particular role?***

Question 7: ***What do you think was the overall value of the project for patients and the practice?***

The responses to the training that staff need were confused and didn't seem to answer the question asked, it may be that the question was not asked in the right way.

A staff member said 'Just awareness and we should know what we are basically, if we are trying to explain to someone you have got a blood disorder we have to know what we are trying to tell them, because I have rung up people and have said you have got Thalassaemia and they say nobody has told us and afterwards, then have to go back to the GP and say have you explained it to them so what are ringing about, talking about'. This response doesn't explain what training this member of staff needed or had.

Another response was 'I think training is needed because first of all yes it is needed but you see the doctors and nurses and GP practice staff they need to be educated. Do you know there are some doctors, some Pakistani/ Indian doctors who actually deny that this is a problem? Now they need to be educated first, because if you are going to deny something so obvious then how are you going to pass the message. So the GPs need to be educated, then the nurses and the practice staff because if you don't consider this as a problem you are not going to do anything about it'.

These responses suggest that the staff place a great importance on the risk of consanguinity and it is this information that they have passed onto the patient. There seems to be a lack of endorsement on information to patients about the actual conditions, what this means for them and basic genetics education.

All the staff said that many patients informed them that they were really grateful for the screening and for information they received on consanguinity and genetic risk.

A GP responded 'In terms of patients it has obviously generated a lot of awareness we have had some members of our patient population actually asking for the test. There has been a lot of discussions mainly following the

Dispatches regarding genetics and consanguinity, and it seems that we have underestimated some of our patients, they are actually quite aware of the issues and the interplay between cultural values and genetics, and I think attitudes are changing, particularly the younger patients, where they are more receptive, so no I think that has enabled them more informed choices I think and hopefully that's an advantage in terms of genetic literacy' This statement is verified by the responses from the patients interviewed they did all have an awareness of the risks of passing on genetic conditions to offspring.

All the staff agreed that the programme was a benefit for the practice in terms of increasing the awareness and knowledge of the staff and helping to bring the discipline of genetics into the primary care domain 'In terms of the practice I think genetics is the next frontier in medicine, and I think that's the forthcoming in holistic practice and I think it has taken away the myth of the complexity of genetics , in terms of being involved more often, I think we find that clinicians are now more comfortable dealing with genetic risks were as before you were more likely to run away. I think the general GP practice has - there is certainly more awareness, may be not to the extent of being fully competent with counselling, but there is still more awareness of genetic issues and particularly where identifying patients are concerned. In the future the main role of the GP is really going to be identification and patient selection, there will be a few in the general subset who will be happy to do counselling with previous experience, skills and training but in general the way I foresee this is probably become a more related discipline and it may not be uncommon to have genetic counsellors who take on the next stage, and GPs have consulted the patients about the risks.'

Recommending this project to others and improvements that could be made to the project

Question 8: ***Would you recommend the project to other practices?***

Question 9*:* ***Is there anything you would change about the project?***

All the staff agreed that they would recommend the project to other GP practices 'Yes, it is a good exercise in research skills, organisational skills and obviously genetics as well and it is obviously a great benefit for the patient' a non-clinical staff member said 'I would definitely recommend to practices that have a high ethnic population - definitely.'

All the staff agreed that the project did run well. As it was a pilot project, processes had to be changed as problems were identified. It was suggested that there were some challenges in working with the PCTs with regards to consent processes, and particularly with regards to the media and the Dispatches programme for Channel 4.

Findings

The staff qualitative review has proved to be an important aspect of this study, as the responses received from the staff link directly to the understandings and perceptions of the participants.

- The staff members all placed a great importance on consanguinity and genetic risk, this is reflected in the participants' understanding. All the participants had an awareness of inheritance, genetic risk and how this can be passed on in families.
- All the staff and participants agreed that screening was important and were grateful that the practice offered this service.
- It appears that genetics education and haemoglobinopathies information may not have been provided to the patients in a structured way. This suggests that there is a need for further training for staff and or specialist genetics input for patients who need to understand genetics information and pass it onto to their families.
- The staff identified that more time needs to be allocated to run projects of this type efficiently.
- The staff suggested that it is important for the discipline of genetics to be understood in primary care. Structured and tailored genetics education needs to be available for staff involved in this type of screening.

Recommendations

This review has been an important part of the screening programme as it has helped identify important aspects of the processes used to screen and educate patients that could be improved and also highlighted best practice that can be shared.

- Information needs to be given to patients at each stage of the screening process and questions asked to determine that the patient has understood and retained the information. Genetic results often identify conditions that have an impact on children and the wider family and so it is important that the information is retained. This important fact needs to be addressed when opportunistic screening is offered.
- All the information given to patients is important for them and their understanding and not just what the health professionals feel is most important. In order for a patient to understand risks associated with consanguinity they need an understanding of basic genetics and its relevance for them and the wider community.
- More education/counselling time is needed if patients are to understand and retain information and share it with their families. This would also ensure that the screening programme benefits the community and makes an impact on genetic disorders and infant mortality.
- Qualitative reviews should to be carried out throughout the screening programme to ensure that patients have understood the information that test results may give.
- These findings also suggest that there is a need to provide genetics education for communities and in particular those that practice consanguinity, so that they are in a better position to understand genetics test results and are more able to make informed choices for themselves and their families.
- The results would have been more meaningful if more participants were involved and were randomly selected.

The findings of this review are important and need to be taken into consideration when implementing projects of this type.

EGSP will use this data to develop and adapt the Community Education it delivers, especially when:

- Delivering genetics education, a scoping exercise will be carried out to determine what the community already know about genetic risk and consanguinity, what their perceptions are of the risk with respect to their own health and adapt the teaching accordingly.
- Evaluating what the understanding is at the end of teaching sessions to determine if the right information and messages have been delivered.
- Adapting teaching and information according to the needs identified.
- Working jointly with health professionals to provide genetics information to families that they may understand.
- The teaching needs to be structured and progressive, ensuring that all the information has been understood at each stage.
- Liaising with key leaders within the community to help raise awareness of genetic risk and get the community involved.
- The families with genetic disorders, identified through the teaching sessions, are able to receive the appropriate help and information.

Acknowledgement

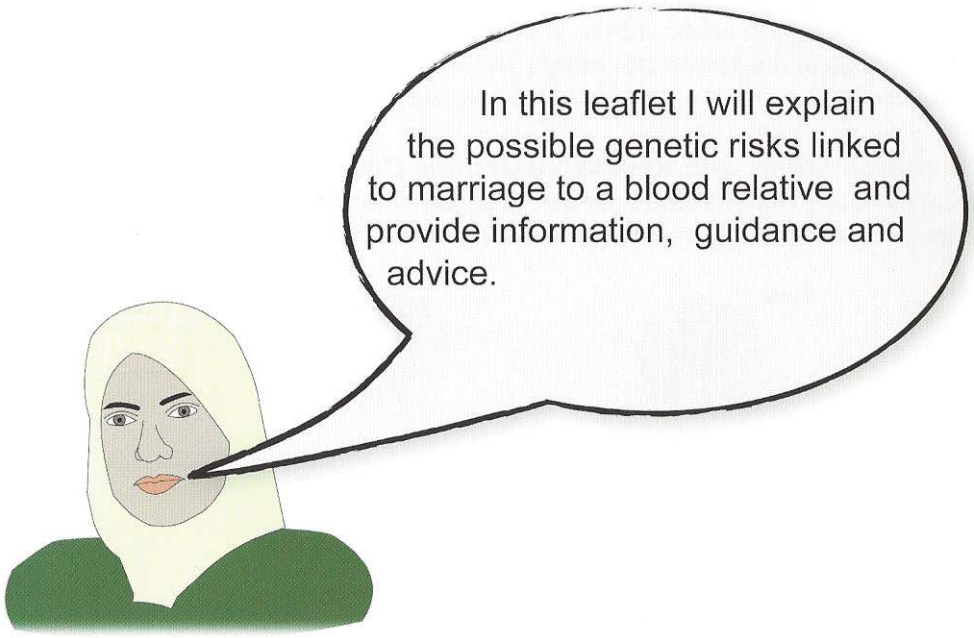
The research was undertaken by Zahira Maqsood, Community Educator for EGSP who also wrote the report that comprises Appendix 7.

Appendix 8 Leaflets

Birmingham Women's NHS
NHS Foundation Trust

Genetic Risk Explained for Parents who are blood relatives (Consanguineous)

Information for patients and families



Other leaflets in this series about genetics

Understanding Genetics and Inheritance

Sharing Genetics Information with Relatives

Genes

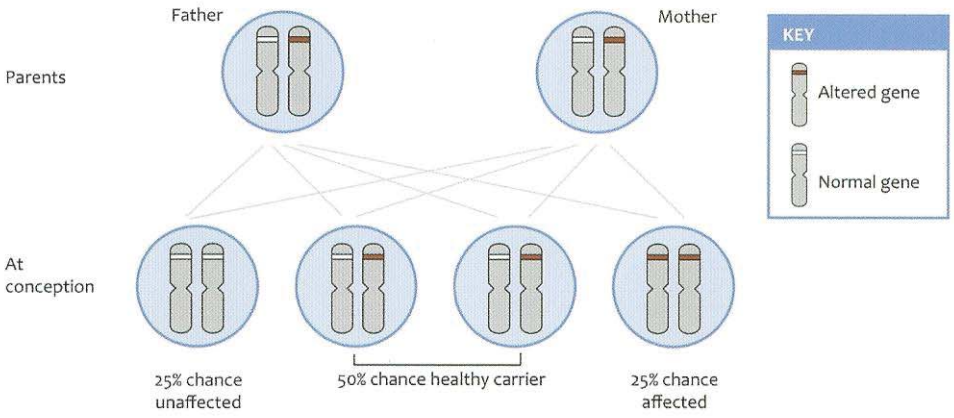
We inherit the 'instructions' which determine how our bodies work and develop from our parents, these instructions are called genes. We have about 30,000 human genes. Each cell in our body contains two copies of most of our genes , one inherited from the father and one from the mother.

Recessive Disorders

Sometimes inheritance of genes that do not work properly can lead to a genetic disorder.Throughout the rest of this information leaflet we refer to these genes as the 'altered gene'. One type of genetic condition is one inherited in a pattern which we call recessive inheritance. In recessive genetic disorders both copies of the gene are altered. Reassuringly although we often have one altered copy of a gene, the second copy is nearly always normal, this normal copy of the gene can compensate for the altered gene and there is no affect on our health. This is why this type of altered gene is called a recessive gene, as it can be passed on for generations with no ill effect. Individuals with just one altered recessive gene are known as carriers. In fact it is estimated that we are all carriers of a handful of recessive genetic conditions.

Having Children with Recessive Genetic Disorders

Healthy carrier parents who both carry the same copy of an altered recessive gene have a risk of having a child with a recessive genetic disorder.



There are four possible outcomes for each pregnancy regardless of the baby's sex

There is a 1 in 4 (25%) chance that the child will have two normal copies of the gene

There is a 2 in 4 (50%) chance that the child will be a healthy carrier of the condition

There is a 1 in 4 (25%) chance that the child will have inherited the altered gene from the mother and father and therefore have the condition

Consanguinity and Recessive Inheritance

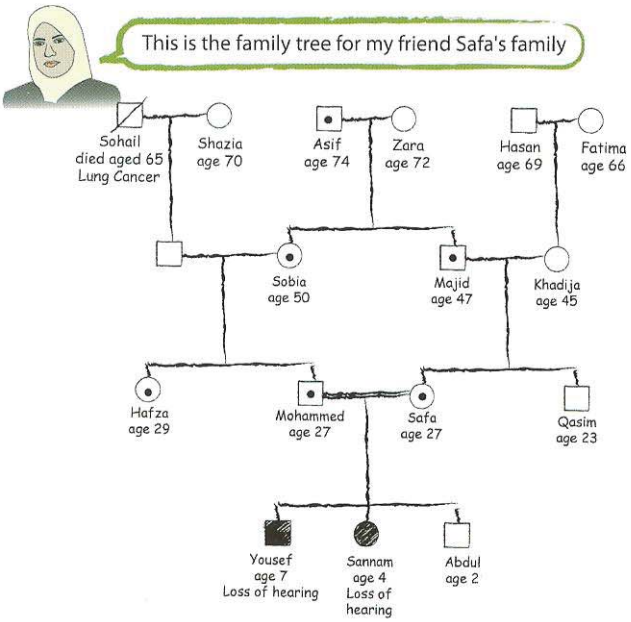
Marriage between close blood relatives (e.g. first cousins) is known as a consanguineous marriage. Consanguineous marriages are common in many parts of the world and are an integral part of many cultures often with many benefits.

People from the same family will share some of their genes as they have inherited them from common ancestors. This is why if two people from the same family get married there is an increased chance that they may both carry the same altered recessive gene.

Children of unrelated parents have on average a 2-3% chance of being born with a genetic disorder, this risk is doubled to 4-6% for children of consanguineous parents. This small additional risk is because these recessive genetic disorders are more common in consanguineous marriage. But it is important to remember that 90% of children will be born healthy and free from genetic disease.

Carrier testing

Healthy carriers of a recessive disorder may or may not be aware they carry an altered gene. In some families where the alteration in a specific gene has been identified , there may be a simple test that can be offered to possible carriers of the genetic condition. The genetics services will be able to help families and provide further guidance and advice.



In this family tree we have used 'squares' □ to represent male members of the family and 'circles' ○ to represent the female members.

If a family member is a carrier of a recessive condition this is represented by a dot in the circle or square. ⊙

A person affected by a recessive condition is represented by a shaded circle or square. ●

In this family there are two affected children, Yousef and Sannam.

Key information for families

- If you know of someone with a genetic disorder, then their parents and possibly other close relatives may be carriers of the disorder.
- Families may be able to seek advice and information and have carrier testing if the gene alteration is known.
- Those who wish to obtain genetics advice should contact their GP who can refer to the clinical genetics services.

Genetics Information

For further genetics information please see our other leaflets and DVD:

- Genetics and Inheritance
- Sharing Genetics information with Relatives
- Understanding Genetics DVD

Or if you wish to speak to someone you can contact the Birmingham Women's Hospital Clinical Genetics Unit either by telephone on 0121 6272630 or by e-mail at egsp@bwhct.nhs.uk

This information leaflet has been produced as part of a Health Initiative. This health initiative is the Enhanced Genetics Services project funded by the Heart of Birmingham PCT and the aims of the project are to raise awareness of genetics amongst the community so that they can make informed choices for themselves and their families.

Clinical Genetics Unit
Birmingham Women's NHS Foundation Trust
Mindelsohn Way
Edgbaston
Birmingham
B15 2TG

EGSP
Enhanced Genetics Services Project

Birmingham Women's NHS
NHS Foundation Trust

Sharing Genetics Information with the Family

Information for patients and families

Other leaflets in this series about genetics

Understanding Genetics and Inheritance

Genetic Risk Explained for Parents who are Consanguinous

Key information for families

Families with a child that has a recessive genetic condition should seek further information on ways to share this information with the wider family.

Individuals and or families who wish to seek genetic information about carrier testing should contact their GP who will be able to arrange an appointment with a genetics specialist .

Genetics Information

For further genetics information please see our other leaflets and DVD:

- Genetics and inheritance
- Sharing genetics information with relatives
- Understanding genetics DVD

Or if you wish to speak to someone you can contact the Birmingham Women's Hospital Clinical Genetics Unit either by telephone on **0121 627 2630** or you can go to the website

www.talkinggenetics.co.uk

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Recessive Genetic Disorders

The diagnosis of an inherited genetic disorder in a family often means that brothers and sisters may also be at risk of the same condition or may be carriers of the condition, as well as other close family members such as aunts ,uncles ,cousins. This is something they will all need to think about when they come to have children of their own.

For some genetic disorders it may be possible to have a genetic test to confirm if you are a carrier for the disorder.

Sharing Information—what are the Issues

If there is a genetic test available for the genetic disorder in your family then it is possible to have a simple blood test that will tell you whether you are a carrier of the condition. You may choose to have a genetic test so that you can share this information with family members on whom it may have an impact.

It is often very difficult to discuss a genetic disorder that affects your child or yourself with other family members. But do remember that a genetic disorder in a family is no ones fault. Many people prefer to have a genetic test as it confirms their status , and they can use this information to make informed decisions about their own life.

Ideas for sharing genetic Information with the family

- Discuss sharing genetic information with your genetic counsellor and close family members.
- We can offer Information leaflets or write information letters for relatives
- Maybe take a family member along to the genetics session where you discuss the condition and its implications for you and your family. Then if you wish this family member can help you make contact with other family members to share the information.
- How you choose to discuss test results will depend on your relationship with individual family members

Consanguineous Marriages

It is particularly important for individuals and families who choose to marry a blood relative (consanguineous) to obtain information and guidance from a genetics specialist about genetic disorders and inheritance.

Relatives who are at a risk of being carriers for an inherited genetic condition are encouraged to talk to their doctor who can arrange for you to see a genetics consultant and/or a counsellor.

This is a quote form a recent study[1] ' patient groups commented that although no one wants to have a diagnosis of a genetic condition , that an accurate diagnosis can open doors to effective and appropriate support , disease management, and treatment ,equally the lack of diagnosis can mean that the families may not get the best care'

Information and Support for families

The issues that effect people with a genetic disorder do not exist in isolation and have an impact on all the members of a family, parents siblings and the wider family.

An understanding of the facts and issues related to a particular genetic condition can make living with the condition a little easier. Knowledge can empower you and help you access the right services. Talking about concerns and sharing them can make things easier to deal with.

Patient support groups can be a great source of information and can provide details of services that you may need as well as emotional support.

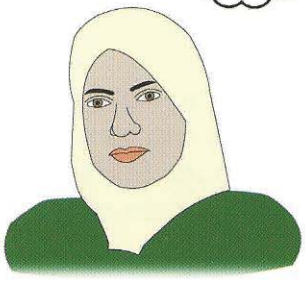
Support groups:
Genetics alliance UK
Talking genetics
CLIMB (children living with metabolic disease)
Contact –a-a Family
UNIQUE (rare chromosome disorder group)
UK Genetic Testing Group

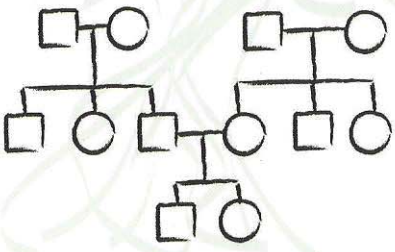
Birmingham Women's NHS
NHS Foundation Trust

Understanding Genetics and Inheritance

Information for patients and families

Have you ever wondered why members of the same family look alike or perhaps why you look like a brother or sister?



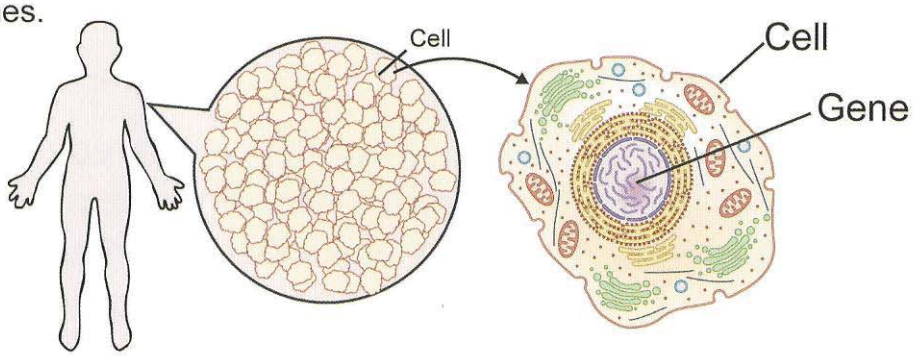


What is Genetics and Inheritance?

Genetics is the study of how characteristics such as features and appearance are inherited (passed on) from our parents to us. These traits are passed on from our parents in our genes. Genes contribute to the way we look and how our body is put together. We have two copies of most genes:

- One copy from our mother
- One copy from our father

Our body is made up of millions of cells and each cell contains our genes.



We have about 30,000 genes and they act as instructions for our cells, and help determine:

- Our appearance like our eye colour, hair colour, features, etc
- Our development
- Overall health of our body

Similarly, our parents' genes come from our grandparents – and our grandparents' genes come from our great grandparents and so on. A great long line of people have passed on their genes to us. Sometimes we can have changes in our genes that can have an effect on our health.

Why is Genetics important to you?

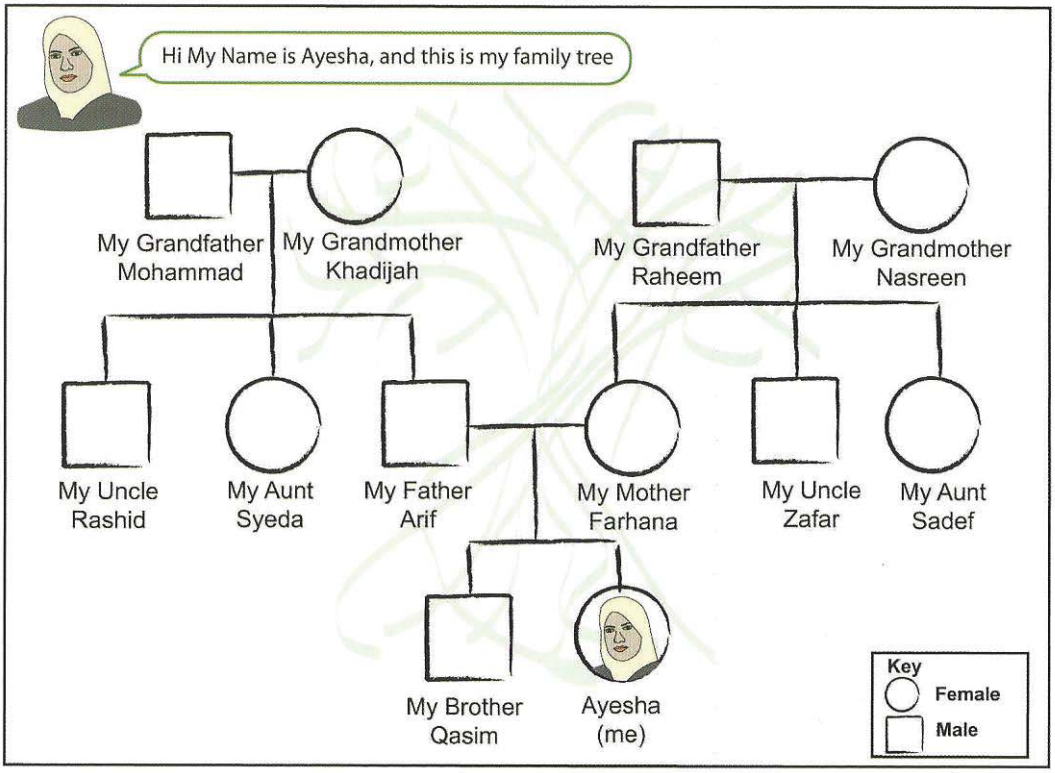
There are different types of illnesses, some of which are a result of our environment and some we experience as our body changes as we get older.

In addition some health concerns are genetic. There are many different types of genetic conditions and these are inherited in different ways. Some genetic conditions occur due to changes with certain genes. Some common examples include:

- Thalassemia
- Sickle cell disease

Inheritance can be complicated, and its effects vary depending on the genetic disorder involved

Family Tree



Families that are well informed about genetic conditions:

- Are in a stronger position to get services they need and are entitled to.
- Have knowledge to communicate their needs to with family members, friends and schools/colleges.
- Will hopefully deal better with the genetic condition and any associated disability.

Who can Help?

If you wish to speak to a specialist in genetics then please ask your GP to refer you to the West Midlands Clinical Genetics Service.

Genetics Information

If you wish to get more information on genetics and related resources or wish to speak to someone please contact the Clinical Genetics Unit at the Birmingham Women's NHS Foundation Trust either by telephone on **0121 627 2630** or by e-mail at egsp@bwhct.nhs.uk.

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phg foundation

making science work for health

About the PHG Foundation

The PHG Foundation is a pioneering independent think-tank with a special focus on genomics and other emerging health technologies that can provide more accurate and effective personalised medicine. Our mission is to make science work for health. Established in 1997 as the founding UK centre for public health genomics, we are now an acknowledged world leader in the effective and responsible translation and application of genomic technologies for health.

We create robust policy solutions to problems and barriers relating to implementation of science in health services, and provide knowledge, evidence and ideas to stimulate and direct well-informed discussion and debate on the potential and pitfalls of key biomedical developments, and to inform and educate stakeholders. We also provide expert research, analysis, health services planning and consultancy services for governments, health systems, and other non-profit organisations.

phg foundation
making science work for health

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