



Trinity College Dublin

Coláiste na Tríonóide, Baile Átha Cliath

The University of Dublin

**HOW ICT MIGHT SUPPORT ACCESS TO CLINICAL
EXPERTISE FOR TIMELY DIAGNOSIS OF GENETIC
DISORDERS IN IRISH TRAVELLERS AT POINT OF CARE**

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**A DISSERTATION SUBMITTED TO THE FACULTY OF COMPUTER
SCIENCE AND STATISTICS IN PARTIAL FULFILMENT OF THE
REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTERS OF
SCIENCE IN HEALTH INFORMATICS**

DUBLIN

JUNE 2018

DECLARATION

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ACKNOWLEDGEMENTS

I would like to thank all the people who helped to contribute to the completion of this dissertation.

I would like to thank my research supervisor, Prof Lucy Hederman, for all her time, dedication, help and hard work in guiding me through this process. Her experience and guidance have been invaluable to me through this journey. Thanks to all the course lecturers who made the course a memorable experience. Thanks to my classmates who have provided encouragement and support over the last two years; teamwork makes the dream work.

I would like to thank the clinicians and ICT professionals who have given their time and support to contribute to this study.

To my husband Andrew, my sons Naoise, Brendan and Daithi, and my mother, Toni, and my brother, Ian, thank you all for your support, encouragement and patience.

This dissertation is dedicated to my brother Shane. Pax et caritas.

HOW ICT MIGHT SUPPORT ACCESS TO CLINICAL EXPERTISE FOR TIMELY DIAGNOSIS OF GENETIC DISORDERS IN IRISH TRAVELLERS AT POINT OF CARE

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MSc Health Informatics 2018

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ABSTRACT

Irish Travellers have high levels of consanguinity, resulting in many rare genetic disorders. Most of these disorders are as a result of specific mutations unique to this population. Clinicians who are less familiar with this population have few resources to facilitate forming a differential diagnosis or in targeting genetic testing. For people with a rare disease, the mean average length of time from symptom onset to accurate diagnosis is approximately 4.8 years. 40% of rare disease patients are misdiagnosed at least once. The longer it takes to diagnose a rare disease, the more health care professionals the patient needs to see. This problematic journey to diagnosis and care can increase medical, economic and social burdens. An expert group of clinicians have recently collated the disorders to facilitate a targeted genetic approach to diagnostics in Irish Travellers.

The literature review demonstrates the availability of web-based ICT for the diagnosis of genetic disease in specific ethnic groups in other countries. A motive for this study is to support more timely diagnosis of these rare disorders in Irish Travellers by the introduction of a similar web-based initiative. Accordingly, the first aim of this study was to determine how a similar diagnostic support resource for genetic disease in Irish Travellers might look.

The barriers to timely diagnosis of rare genetic disease in Irish Traveller patients are explored. A gap in the literature established that there is scant material available relating to the means by which Traveller ethnicity is reliably captured in paper charts or electronic health records (EPR), thereby hindering implementation of a similar diagnostic support initiative for the Irish Travellers. The Beutler test was identified as an enhanced newborn screening process for all Traveller infants and was subsequently used as a starting point to explore the current process for capture of Traveller ethnicity in health records and EPR. The second project aim was to explore how Traveller ethnicity could be employed to trigger the use of the web resource at an appropriate point in the diagnostic workflow.

A qualitative method was devised to explore local expert knowledge to fill gaps identified in the literature. Thirteen domain experts were identified and chosen as participants for a semi-structured interview. Each question set was tailored to the participant, and interviews roughly fell into three categories: interviews to inform prototype, interviews to describe the Beutler process, and interviews to describe diagnostic workflows and order communications.

Literature review and qualitative analysis of interview findings facilitated construction of narrative descriptions of Traveller ethnicity capture in Irish health records, Traveller ethnicity as a trigger for the Beutler test and options for the creation of a Traveller flag in electronic health records. The means by which Traveller ethnicity is currently captured in Irish health records and EPR was defined. The enablers and obstacles to reliable identification of Travellers within national ICT projects are described. Ethical and legislative barriers are discussed.

Information gathered was used to inform prototype design of a web resource for the diagnosis of genetic disorders in Irish Travellers. A point of care for intervention, within the limitations of national ICT projects, is identified.

TABLE OF CONTENTS

DECLARATION	2
ACKNOWLEDGEMENTS.....	3
ABSTRACT.....	4
TABLE OF CONTENTS.....	5
LIST OF TABLES.....	8
LIST OF FIGURES.....	9
ABBREVIATIONS	10
CHAPTER 1: INTRODUCTION	11
1.1 Introduction	11
1.2 Background	11
1.2.1 Irish Travellers.....	11
1.2.2 Morbidity and mortality in Irish Travellers	11
1.2.3 Typical patient profile	13
1.2.4 Delayed diagnosis in rare disease	14
1.3 Diagnosis of genetic disorders in Irish Travellers.....	15
1.3.1 Expert knowledge	15
1.3.2 Disseminating expert knowledge.....	15
1.3.3 Additional barriers to timely diagnosis.....	16
1.4 Research question and study aims	17
1.4.1 Research question.....	17
1.4.2 Study aims.....	17
1.5 Overview of the research.....	17
1.6 Overview of the dissertation.....	18
CHAPTER 2: LITERATURE REVIEW	20
2.1 Introduction	20
2.2 Literature search strategy.....	20
2.3 Irish Travellers and health.....	21
2.3.1 Who are the Irish Travellers?	21
2.3.2 Irish Travellers, morbidity and mortality	22
2.3.3 What is consanguinity?	23
2.3.4 Consanguinity in Irish Travellers	23
2.3.5 Most common "rare" genetic diseases in Irish Travellers	24

2.3.6 Other genetic conditions.....	26
2.4 Consanguinity and health in other populations.....	27
2.4.1 Global genetic intervention in a consanguineous population	28
2.5 Practical application of expert clinical knowledge in other consanguineous populations.....	29
2.5.1 Omani Genetic Variations Database	30
2.5.2 Mediterranean Founder Mutation Database	31
2.5.3 Amish, Mennonite and Hutterite Genetic Disorder Database.....	32
2.6 Could similar ICT programs support a more timely diagnosis of genetic disorders in Irish Travellers?.....	33
2.6.2 Barriers to reliably targeting Irish Travellers for enhanced decision support	35
CHAPTER 3: METHODOLOGY	39
3.1 Introduction	39
3.2 Literature review.....	39
3.3 Research design	41
3.3.1 Access negotiation and ethics approval.....	42
3.3.2 Participant selection and recruitment	43
3.3.3 Data collection methods	50
3.3.4 Data analysis	50
3.4 Issues of validity and reliability	50
3.5 Ethical considerations	50
CHAPTER 4: RESULTS.....	51
4.1 Introduction	51
4.2 Overview of Interviews	51
4.3 Interview information collection method and analysis	52
4.4 Application of analysed information to the aims and objectives	53
4.4.1 Traveller ethnicity capture in Irish health records.....	54
4.4.2 Traveller ethnicity as a trigger for the Beutler Test	55
4.4.3 Creating a Traveller flag in EPR	57
CHAPTER 5: PROTOTYPE DESIGN	58
5.1 Introduction	58
5.2 Proposed web resource	60
5.2.1 Requirements to implement web resource	61
5.2.2 Proposed web resource prototype	65
5.3 Use of CDS in a non-EHR environment	67
5.4 Use of CDS in an EHR environment.....	67
5.5 Conclusion.....	67

CHAPTER 6: DISCUSSION.....	68
6.1 Introduction	68
6.2 Ethical and legislative barriers	69
6.2.1 Consent	69
6.2.2 Ethics of ethnicity collection in electronic health records.....	69
6.2.3 General Data Protection Regulation (GDPR).....	69
6.3 Future work.....	70
6.3.1 Petition HSE to include Traveller question as part of the basic data set.....	70
6.3.2 Develop phenotype entries for all disorders in database.....	70
6.3.3 Seek help and funding for coding	70
6.4 Conclusion - the case study revisited.....	71
REFERENCES.....	72
APPENDIX.....	85
Appendix A: Information Sheet for Participants.....	85
Appendix B: Informed consent form	86
Appendix C: Research Ethic Application	87
Appendix D: Research Ethics Approval.....	92
Appendix E: Expert Group Publication.....	93
Appendix F: Disease Table	94
Appendix G: Interview Summaries	96
Summary of Interviews to inform prototype.....	96
Summary of interviews to describe Beutler process	101
Summary of interviews to describe diagnostic processes and order communications	111

LIST OF TABLES

Table 1: Risk of recessive disorder to a pregnancy where consanguinity exists	23
Table 2: Osheroff's "Five Rights"	34
Table 3: Subjects selected to inform prototype design	43
Table 4: Subjects selected to inform the description of the Beutler process.....	43
Table 5: Subjects selected to inform the exploration of national ICT systems.....	44
Table 6: Interview questions to inform prototype design	46
Table 7: Interview questions to inform the description of the Beutler process.....	47
Table 8: Interview questions to describe diagnostic processes and ordering in national ICT systems	49
Table 9: Interviews informing prototype design.....	52
Table 10: Interviews exploring Beutler process.....	52
Table 11: Interviews exploring national ICT systems.....	52
Table 12: Proposed web resource features and corresponding source from research material	60
Table 13: Standard dictionaries behind data fields in data collection form in RedCAP database.....	62

LIST OF FIGURES

Figure 1: Profile 8 Irish Travellers	21
Figure 2: Global distribution of marriages between couples related as second cousins or closer	27
Figure 3: Screenshot of the homepage of the Jewish Genetic Disease Consortium	29
Figure 4: Screenshot of the homepage of the Omani National Genetic Database	30
Figure 5: Screenshot of the homepage of the Mediterranean Founder Mutation Database	31
Figure 6: Screenshot of the listed disorders within the Anabaptist Mutation Database	32
Figure 7: Newborn Screening Card data collection	37
Figure 8: Screenshot from MN-CMS -Is self/Partner a Member of the Travelling Community?.....	54
Figure 9: Screenshot from MN-CMS –Self and partner ethic background	54
Figure 10: Screenshot from MN-CMS –Pregnancy overview.....	54
Figure 11: Screenshot from MN-CMS –Please refer for Beutler Test.....	55
Figure 12: Newborn Screening Card – the card is used for Beutler and routine screening	55
Figure 13: MN-CMS Blood Spot section.....	56
Figure 14: MN-CMS Blood Spot Result section.....	56
Figure 15: MN-CMS screenshot - Patient risk flag displayed in the banner	57
Figure 16: MN-CMS screenshot – Specific risk factor displayed.....	57
Figure 17: Screenshot of data records holding knowledge base in RedCAP	61
Figure 18: Data collection form in RedCAP database	62
Figure 19: Hosting was originally proposed at NRDO website, later negotiated UCD	63
Figure 20: Prototype search window allowing entry of symptom/phenotype search terms.....	65
Figure 21: Prototype results window displays a list of differential diagnoses and presentation.....	65
Figure 22: Prototype disorder-specific window giving all relevant details and links.....	66

ABBREVIATIONS

BHIS	Beaumont Hospital Information System
CDS	Clinical Decision Support
EDD	Estimated Delivery Date
EUCERD	EU council recommendation on rare diseases
FBC	Full Blood Count
GDPR	General Data Protection Regulation
IHI	Individual Health Identifier
IPI	Individual Patient Identifier
iPIMS	Patient Administration System
KPI	Key Performance Indicator
LFT	Liver Function Test
LMP	Last Menstrual Period
MedLIS	Medical Laboratory Information System
NCCP	National Cancer Control Program
NNBSL	National Newborn Screening Laboratory
NRDO	National Rare Disease Office
NSC	Newborn Screening Card
OMIM	Online Mendelian Inheritance in Man
PDF	Portable Document Format
PSA	Prostate Specific Antigen
RedCAP	Research Electronic Data Capture
SNP	Single Nucleotide Polymorphism
UPI	Unique Patient Identifier

CHAPTER 1: INTRODUCTION

1.1 Introduction

This first chapter provides background information on Rare Genetic Disease in Irish Travellers, and a typical patient scenario is explained. The problems that occur in the diagnostic journey are explored, which provide a motive for this study. The research question is stated, followed by the smaller research questions that when answered will assist in answering the overall research question. An overview of the research plan is given, followed by an overview of the overall dissertation.

1.2 Background

1.2.1 Irish Travellers

The Irish Traveller population has been declared a distinct ethnic group. According to the Irish census 2016, there were 30,987 Irish Travellers in the Republic of Ireland, accounting for just over half of one per cent (0.66%) of the total population. A further ~ 1,800 (0.07% population) live in Northern Ireland. The 2010 All-Ireland study (All Ireland Traveller Health Study Team, 2010) estimated a higher figure of ~ 40,000 Irish Travellers living on the island of Ireland, arguing that the discrepancy in numbers was due to reluctance, in some, to self-identify as a Traveller.

Irish Travellers have a much younger population profile than the general population and are married younger. Irish Travellers spend fewer years in formal education and have higher levels of illiteracy than the general population. Half of families are reported to have five or more children.

The Irish Traveller population is consanguineous – i.e. first cousin marriage is common (cousin marriage rates approximating 71% of unions; first cousin 39%, first cousin once removed 11% and second cousin 21%).

1.2.2 Morbidity and mortality in Irish Travellers

Almost 1 in 5 Travellers are categorised as having a disability. High levels of consanguinity result in many rare autosomal recessive disorders. Due to founder effects and endogamy, most recessive disorders tend to be caused by specific homozygous mutations unique to this population.

The number of Traveller deaths in the 0-24 age group is six times higher than that of the general population. The excess infant mortality ratio is 10.5 per 1000 live births compared to the general population. Taking male and female together Irish Travellers in ROI have 3.5 times the mortality of the general population. Half of Irish Travellers die by the age of 39.

In addition to increased morbidity and mortality, there are additional and unnecessary costs associated with delayed diagnosis of rare genetic disorders. Clinicians who are less familiar with this population have no resource to facilitate forming a differential diagnosis or in targeting genetic testing.

The literature demonstrates that consanguineous populations have a higher incidence of rare disease due to recessive disorders. Diseases elsewhere classified as rare are not rare in consanguineous populations (Gura, 2012). Genetic disease and consanguinity is a sensitive subject in any population.

Presentation to health services can be inadequate as can the sharing of medical history, which can pose a challenge in the identification of genetic syndromes (Gilbert et al., 2017). There is a reluctance to share diagnoses amongst the wider family; privacy is a significant cultural concern (Mone, McAuliffe and Lynch, 2018). While many Irish Traveller disorders and their mutations are known to individual Irish-based clinicians, most remain unpublished or, if published, the ethnicity is not explicit (Lynch et al., 2018).

Irish Travellers have an overall health status which is more comparable to people living in underdeveloped countries than to those in developed Europe (Callanan, Evans and Syron, 2002). Although there is a growing body of knowledge about rare disease in the Irish Traveller population, this expertise is not available at the place where the patients present, leading to serious delays in diagnosis.

1.2.3 Typical patient profile

Case Study Shireen Connors, age 6.

Shireen was referred as a priority by her GP to the Midland Regional Hospital A&E. When her chart was recalled it was discovered that Shireen had multiple paper charts offsite and in the primary hospital storage, with variations of surname and address. The combined charts once confirmed to belong to the same patient, demonstrated a 6-year history of multiple presentations to A&E with a history of acute and chronic recurrent respiratory infections, bronchitis, pneumonia, sinusitis, and otitis media. Chest x-rays once collated, showed a finding of progressive bronchiectasis and an incidental finding of situs inversus.

After extensive investigations and assessments at the Midland Regional Hospital, The Children's University Hospital, Temple Street, and the National Children's Hospital, Tallaght, various disorders including Cystic Fibrosis were out ruled. Many tests were requested or repeated unnecessarily because laboratory and imaging reports did not make it into Shireen's chart(s). Multiple appointments were missed; Shireen's mother explained that they did not attend as they had not received appointment letters for some, that the family travelled to the UK during the summer months, and that she had changed her mobile phone number.

A diagnosis of the autosomal recessive genetic disorder, Primary Ciliary Dyskinesia (PCD) was eventually made after Shireen was seen at a clinical genetics outpatient appointment in Dublin (almost two years after her presentation at the Midland Regional Hospital).

Unfortunately, as Cystic Fibrosis was the focus, the PCD diagnosis was missed early in life so, despite displaying the characteristic signs and symptoms of PCD from infancy, Shireen at age 8, now requires a double lung transplant. It was noted in one of the versions of Shireen's chart, at her very first presentation, that her parents are first cousins, and are both members of the Irish Traveller community. This information was not provided with any of the orders for diagnostic tests.

The couple had a previous daughter, Margaery, who died aged three months, due to pneumonia, attributed, at the time, to their living conditions. Molecular genetic analysis was performed on archive pathology material from Margaery, and a diagnosis of PCD was confirmed. Shireen's youngest brother, age 2, and first cousin, age six months, were subsequently also diagnosed with PCD.

In the sadly, typical, case study provided, Paediatric A&E and OPD clinics would have potentially benefitted from access to clinical expertise for the diagnosis of and treatment planning for genetic disorders in the Irish Traveller population. Bias leads to a diagnostic mistake (Scott et al., 2009). For

example, a clinician may fail to diagnose an illness correctly because they have seen many patients with symptoms similar to those reported in their patient. The doctor then assumes that their current patient has the same condition (e.g. Cystic Fibrosis in Shireen) the other patients did.

1.2.4 Delayed diagnosis in rare disease

For people with a rare disease, the mean average length of time from symptom onset to accurate diagnosis is approximately 4.8 years. 40% of rare disease patients are misdiagnosed at least once (Engel et al., 2013). The longer it takes to diagnose a rare disease, the more health care professionals the patient needs to see. This problematic journey to diagnosis and care can increase medical, economic and social burdens (Rare Diseases UK, 2010).

1.3 Diagnosis of genetic disorders in Irish Travellers

1.3.1 Expert knowledge

Key clinicians and scientists have developed a wealth of knowledge from experience managing the rare disorders seen in the Irish Traveller population. Expertise in the diagnosis of these disorders resides within this small group of consultants across 12 ROI and NI Departments, spanning biochemical, neurology, haematology, metabolic, genetic, endocrine, and other specialities. These experts have recently come together to define these disorders and associated symptoms in the Irish Traveller population, developing a comprehensive catalogue of over 100 of the currently known disorders amongst the Traveller population, their causative mutations (where known), including several novel or previously unreported mutations, relevant publications and disease codes (Orphacodes, OMIM and ICD10 coding). A recent 2018 paper by this group, titled "Catalogue of inherited disorders found among the Irish Traveller population" (Lynch et al., 2018) collated the inherited disorders found in the Irish Traveller population to facilitate a targeted genetic approach to diagnostics in this ethnic group.

1.3.2 Disseminating expert knowledge

The EU council recommendation on rare diseases (EUCERD) came into force in October 2013. EUCERD identified key areas of interest for strategic development including centres of expertise, patient registries and databases, and indicators for national rare disease plans/strategies (Aymé and Rodwell, 2014). 70-80% of rare diseases are genetic, and rare disorders are prioritised within Clinical Genetics Services in Ireland as there is minimal to no support for many of the rare diseases elsewhere in Irish Healthcare. Development of a means of access to this expert group silo of knowledge of rare genetic disease in Irish Travellers for other clinicians is the next logical step as laid out by the EUCERD recommendations.

Searching existing literature and a number of international resources, it appears that some population-based genetic information sources are available. However many existing mutation databases support specific disorders or genes, rather than ethnic groups, and are very difficult to navigate and not very useful outside of expert genetic centres.

Any specific population databases tend to be focused on population frequency of specific single nucleotide polymorphisms (SNPs) at a broader level – i.e. Northern European, Sub-Saharan African, again not very useful outside of the genetic laboratory, and certainly not a useful tool for frontline clinicians. We have little knowledge of the frequencies and clinical significance of these

mutations/SNPs specifically within the Irish Traveller population; the data does not yet publically exist.

There are some lists, via websites, of disorders in specific ethnic populations, generally under individual body systems or medical speciality, but again, without expert consultation, it may be challenging to fit phenotype into specific categories when many Irish Traveller disorders are multisystemic. It is unlikely that such unfiltered resources have a point of care impact in the initial stages of the consanguineous patient's diagnostic journey.

1.3.3 Additional barriers to timely diagnosis

New disorders are frequently added to the catalogue of recessive genetic disease in Irish Travellers. There may not be any associated publication, and only the diagnosing and treating clinicians may know of the addition.

The Traveller population density varies across Ireland. Some clinicians may see Traveller patients frequently while it might be rare to ever have a Traveller patient in other facilities.

Another factor to consider is that although clinicians receive genetic training in undergraduate years, if they are not regularly practising in the area of rare disease or maintaining relevant continuing professional development they may lose their knowledge or it might be sufficiently out of date to render it useless.

Clinicians not native to Ireland may have difficulty recognising that the patient is from the Traveller population.

1.4 Research question and study aims

1.4.1 Research question

The primary research question of this study is:

How might ICT support access to clinical expertise for timely diagnosis of genetic disorders in Irish Travellers at point of care?

The overarching goal of this project is to investigate how ICT might support more timely diagnosis.

Based on literature review, support in other consanguineous populations takes the form of a web-based database of genetic conditions. The author seeks to design a web resource to support frontline clinicians once their patient has been identified as an Irish Traveller.

Early investigation of this topic identified that a key enabler for such support would be the reliable identification of Irish Travellers in healthcare processes. Therefore the author also seeks to examine how Irish Travellers are identified in national systems and how reliable identification might be achieved in an electronic health record (EHR).

1.4.2 Study aims

The aims of this study were to

- describe the causative factors for the high prevalence of rare genetic disease in Irish Travellers
- investigate population-specific genetic databases
- use information gathered to inform Irish Traveller genetic web resource prototype design
- determine optimal point of care for and means for intervention
- describe how Traveller Ethnicity is currently captured in Irish Health records
- describe processes by which Traveller ethnicity currently triggers the Beutler Test
- determine what the limitations are to identifying Travellers within national ICT projects
- explore how Travellers might be identified in EPR
- determine if any ethical and legislative barriers exist

1.5 Overview of the research

The first part of the research was to conduct an extensive literature review to provide background information on Irish Travellers and determine a number of genetic conditions seen more frequently in this group and associated diagnostic pathways.

The literature review was extended to ascertain if similar projects have been conducted in the area of support for genetic disease in specific ethnic groups. Interviews were conducted with lead Clinicians and developers of those existing genetic databases to ascertain the relevant population background, clinical application and technical specifications.

A number of Irish clinicians were consulted to help develop a prototype web resource that could support the Irish Traveller patient diagnostic process.

Interviews were conducted with several individuals involved in the laboratory, ICT and patient administration processes associated with the Beutler Test, an existing national standard, introduced in 1972, for enhanced diagnostics specifically in Irish Travellers.

Further investigation was performed to identify what national ICT applications already exist or are due to be introduced. Interviews were conducted with key personnel to identify how Traveller identity might be captured in each system and how it might be used to support access to the prototype web resource.

Further interviews were conducted with clinicians to gain information relating to ethics, consent, Traveller identity, and determine potential barriers.

1.6 Overview of the dissertation

This dissertation is split into six chapters.

Chapter 1 of the dissertation provides background information on morbidity and mortality in Irish Travellers, and diagnosis of Genetic Disorders in Irish Travellers, and introduces the problems posed in timely diagnosis of Genetic Disease in this patient cohort. This chapter identifies the research question and the study aims. A case study of a typical patient journey demonstrates the impact of a delayed diagnosis of genetic disease in an Irish Traveller.

Chapter 2 is a literature review of how consanguinity impacts health in Irish Travellers, what interventions exist in other consanguineous populations and potential barriers to employing similar interventions in the Traveller population. Areas requiring further research are identified from gaps in the literature.

Chapter 3 explains the research methods used in the study undertaken as part of this thesis. The selection and recruitment of participants are described. Interview questions designed to inform prototype, to describe the Beutler process, and to describe diagnostic processes and order communications are presented.

Chapter 4 documents the analysis of the results found from the research interviews and how these findings along with the literature answer the research questions of how Traveller ethnicity can be captured and how might it trigger use of the resource for diagnostic support.

Chapter 5 explains how a prototype web resource was designed based on information obtained from the literature review and the analysis of the research study. How Traveller identity in EPR might support the diagnostic process is discussed.

Chapter 6 concludes by reviewing the study findings, discussing emergent themes of consent and ethics of ethnicity capture and GDPR regulation. Future work is outlined, and the case study is revisited demonstrating use of prototype to support a more timely diagnosis of genetic disease.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

This chapter opens with the search strategies used to find information in the literature relating to Irish Travellers, consanguinity, the resultant risk for recessive genetic disease, and the common genetic disorders in Irish Travellers. The search was expanded to include an overview on the current state of the art in the area of ICT support for recessive genetic disease in specific ethnic populations elsewhere. The literature demonstrates how the absence of an explicit description of Traveller ethnicity hinders diagnosis. A broader search defined recommendations for implementation of ICT support for clinical decisions, highlighting the importance of filtering patients so that support is only available when relevant, pointing to the identification of Traveller ethnicity in medical records as a critical enabler for implementation of diagnostic support. The literature identified an expedited test for newborn screening in Irish Travellers; the literature search was then focussed on material relating to this process as a means to ascertain how Travellers are identified in medical records to prompt this Beutler test.

2.2 Literature search strategy

In January 2018, searches of the following electronic databases were conducted PubMed, Stella, MEDLINE, EMBASE, Cochrane Library, Rian, Tara, Lenus, Web of Science, IEEE, TCD dissertation abstracts, and OpenGrey. These searches were complemented by a focused Google search for combinations of the relevant terms and by use of Google Scholar.

Studies were included if they had sufficient focus on Irish Traveller populations or recessive genetic disease in other specified populations; and if reported data was pertinent to healthcare. Only reports in the English language were included. Search Terms included Irish Traveller, ethnicity, consanguinity, genetic, database, disease, computerised clinical decision support, genetic screening, newborn screening. Excluded phrases were mental health, suicide, drug abuse, alcohol abuse, and immunisation. Study findings were analysed thematically, and a narrative synthesis reported.

The Ireland 2016 Census Data available online from the Central Statistics Office and the All Ireland Traveller Health Study (AITHS), published via University College Dublin, and derived technical reports, published via the Department of Health, are significant sources for relevant statistics for this literature review.

2.3 Irish Travellers and health

2.3.1 Who are the Irish Travellers?

Taoiseach Enda Kenny announced formal recognition for Irish Travellers as a distinct ethnic group within the State of Ireland on 1st March 2017 (The Irish Times, 2017). Irish Travellers are an ethnically Irish endogamous nomadic population, whose origins date back many centuries. Gilbert et al. suggest that low-resolution genetic analysis shows a common Irish origin between the settled and the Traveller populations, with an estimated time of divergence from the general Irish population before the Great Famine of 1845-1852 (Gilbert et al., 2017).

According to the Irish census 2016 (Cso.ie, 2018), there were 30,987 Irish Travellers in the Republic of Ireland accounting for just over half of one per cent (0.66%) of the total population. Census 2016 Profile 8, seen in figure 1 below, provides a comparative overview of Traveller demographics compared to the general Irish population. A further ~ 1,800 (0.07% population) live in Northern Ireland (Nisra.gov.uk, 2012). A 2010 All-Ireland study estimated a higher figure of ~ 40,000 Irish Travellers living on the island of Ireland (Health.gov.ie, 2014)

Irish Travellers have the highest fertility rate in Europe (Abdalla, Quirke and Fitzpatrick, 2011). Nearly half of Irish Traveller women aged 40-49 had given birth to 5 or more children, in stark contrast to just under 1 in 20 (4.2%) of women in Ireland overall in this age group (Cso.ie, 2018).

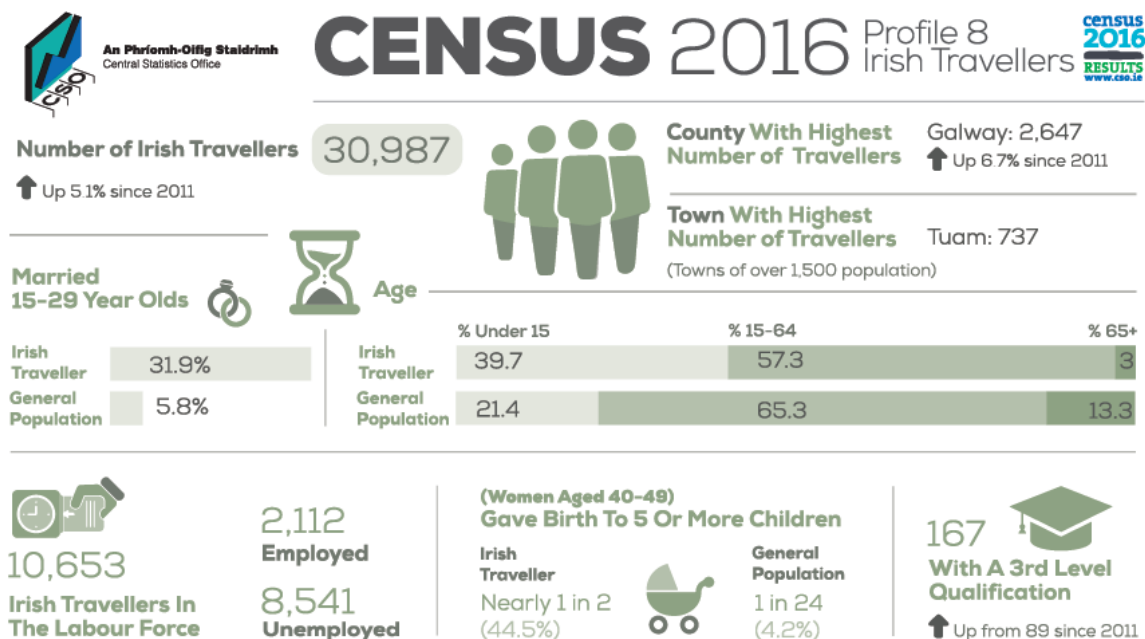


Figure 1: Profile 8 Irish Travellers

2.3.2 Irish Travellers, morbidity and mortality

Routine national data do not capture ethnic or cultural group status, but two major national studies in 1987 (Barry, Herity and Solan, 1987) and again in 2010 (All Ireland Traveller Health Study Team, 2010) showed that, despite absolute improvements in their survivorship over two decades, Irish Travellers continue to fare poorly in terms of infant mortality and life expectancy, when compared to the general population.

According to the Vital Statistics and Mortality Study (All Ireland Traveller Health Study Team, 2014), there were 12 Traveller infant deaths reported in ROI for 2008. In that period there were 849 Irish Traveller births. This gives a Traveller infant mortality rate of 12/849 or 14.1 per 1,000 live births. This means that Infant mortality is 3.6 times higher among the Irish Traveller population than in the general public (Hamid, Kelleher and Fitzpatrick, 2011). Alarming, the occurrence of sudden infant death (SIDS) is 12 times that of the general public (McDonnell et al., 1999).

Commitment to reduce these inequalities is reflected in the national policy target of narrowing the life expectancy gap between Travellers and the general population (Publichealth.ie, 2001).

However, using only life expectancy to track health inequalities overlooks inequalities in non-fatal health outcomes. In the 2013 paper titled "Social inequalities in health expectancy and the contribution of mortality and morbidity: the case of Irish Travellers" (Abdalla et al., 2013), the authors calculated the absolute and relative life expectancy, healthy life expectancy and disability-free life expectancy gaps between Irish Travellers and the general population, seeking to answer questions relating to health expectancy, morbidity and mortality. They demonstrated that Irish Travellers had lower health expectancy than the general population and are expected to spend a higher proportion of their life in poor health and with a disability. The authors conclude that the results confirm the need for tailored policies for Irish Travellers and that action to interrupt disadvantage is necessary to reduce the burden of both fatal and non-fatal conditions and improve Travellers' quality of life.

2.3.3 What is consanguinity?

Consanguinity refers to the genetic relationship between two or more people who are blood relatives. In other words, consanguinity describes the relationship among people who descend from a common ancestor (Lasky, 2017). We all carry two copies of every gene (except for some genes found on the sex chromosomes), each inherited from one parent. Autosomal recessive disorders occur when both copies of a particular gene are defective. Both parents are healthy carriers, but if each parent passes on their defective copy of the gene to a child, the child will be affected by the disorder. Autosomal recessive disorders are more common in consanguineous communities than nonconsanguineous communities (Bundey, 1992). Table 1 outlines the increased risk due to consanguineous unions.

The degree of relationship to the pregnant woman	Increased risk to baby above population
Father/brother	30%
Uncle	10%
First cousin	3%
Second cousin	1%
First cousin once removed	1%
Double first cousins	5-10%

Table 1: Risk of recessive disorder to a pregnancy where consanguinity exists

2.3.4 Consanguinity in Irish Travellers

It is common for Irish Travellers to marry members of their extended family. The Irish Traveller Population is consanguineous, i.e. first cousin marriage is common. Cousin marriage rates approximating 71% of unions; first cousin 39%, first cousin once removed 11% and second cousin 21% (Flynn, 1997). As a result, they share a higher proportion of their genes and are at greater risk of having children with autosomal recessive genetic conditions. Some of these conditions are so rare that they are seen exclusively in the Irish Traveller community.

2.3.5 Most common "rare" genetic diseases in Irish Travellers

The literature describes the three most common Rare Genetic Diseases in Irish Travellers.

2.3.5.1 Hurler Syndrome

Ireland has the highest recorded incidence of Hurler syndrome - a genetic disorder potentially fatal among children. (Murphy et al., 2009) Also known as Mucopolysaccharidosis type 1 (MPS1), this recessive genetic condition presents with a range of phenotypes, from mildly affected to severely affected, fatal disease.

Affected children usually stop developing between ages 2 and 4. Children are short, have eyesight degeneration and hearing loss, speech difficulties due to a large tongue, progressive mental decline and loss of physical skills. By age two, coarse facial features, including a flat face and depressed nasal bridge, become distinctive. Life expectancy is often less than ten years.

Early treatment for MPS1 involves enzymes, but late diagnosis results in the need for bone marrow transplants and searches for suitable donors. Early diagnosis of the condition, preferably in the neonatal stage, means the earliest treatment and possible prevention of some of the many complications that this condition can cause.

Murphy et al. (Murphy et al., 2009) estimated the incidence of Hurler Syndrome for Travellers and non-Travellers in the Irish Republic using chart review of all live MPS1 patients attending two specialised centres. Of note, 73% of the Hurler patients were Irish Travellers. The authors calculated a carrier frequency of 1 in 81 for non-Traveller Irish; for Irish Travellers, the carrier frequency is 1 in 10. The birth incidence was 1 in 26,206 births for non-Travellers, in Irish Travellers the incidence was 1 in 371; the highest recorded incidence of Hurler Syndrome in any population worldwide. Age at presentation ranged from antenatal detection through to a late diagnosis at aged seven years. Children identified during the neonatal period all had an affected family member, and all were Irish Travellers. The typical diagnostic journey starts with laboratory analysis of white cell enzyme, a test sent via local paediatric/neonatal laboratory services to the specialist Willink Laboratory in Manchester. 25 of the 26 patients mentioned received bone marrow transplant as treatment.

Murphy et al. recommend targeted newborn screening for this population as delayed treatment results in increased morbidity and mortality, but to date, it has not been added. There is a successful targeted neonatal screening programme for MPS1 in the Ojibway-Cree aboriginal consanguineous population in Canada (Greenberg et al., 2002).

2.3.5.2 I-Cell Disease

Mucopolidosis II (ML II, I-cell disease) is a slowly progressive inborn error of metabolism with clinical onset at birth. Most affected children die in early childhood. Growth is limited with contractures in the large joints. Other orthopaedic abnormalities at birth may include thoracic deformity, a kyphotic curvature of the spine, clubfeet, long bone deformities, and hip dislocation, the child's facial features are coarse, and the skin is thickened. There is mitral and aortic valve insufficiency. Progressive mucosal thickening narrowing the airways exacerbated by skeletal deformities leads to respiratory insufficiency, the most common cause of death for those with I-Cell Disease

McElligott et al., 2011 estimated the incidence of ML II for non-Travellers was 1.56 per 100,000 live births. The carrier rate amongst Irish non-Travellers remains rare at 1 in 512. The incidence amongst Irish Travellers was 114 per 100,000 live births, suggesting a carrier frequency of 1 in 15. The median age of death in patients of the Traveller community was 232 days. Newborn screening for ML II is not yet performed in Ireland but is available in the US (Matern et al., 2015).

Diagnosis is confirmed by analysis of UDP-N-acetylglucosamine: lysosomal hydrolase N-acetylglucosamine-1-phosphotransferase (GNPTAB) enzyme activity. Demonstration of nearly complete inactivity (<<1%) of the enzyme, UDP-N-acetylglucosamine: GNPTAB (EC 2.7.8.17) encoded by GNPTAB, confirms the diagnosis of ML II. This analysis requires specific substrates, laboratory techniques, and experience. As for Hurler syndrome, the white cell enzymes test is sent via local paediatric/neonatal laboratory services to the Specialist Willink Laboratory in Manchester.

2.3.5.3 Galactosaemia

Galactosaemia is an autosomal recessive condition caused by a deficiency of an enzyme galactose-1-phosphate uridylyltransferase. This enzyme is essential for the breakdown of galactose, one of the sugars in lactose, the primary sugar in all animal milk (including breast milk, most infant formulas, cow's milk, goat's and sheep's milk). Coss et al., 2012 state that galactosaemia is particularly prevalent among infants born to Traveller parents, in whom the incidence is approximately 1 in 450 births. In the non-Traveller Irish community, the incidence occurs in about one in every 36,000 births. Murphy et al. , 1999 calculate the classical galactosaemia carrier frequency to be 1 in 11 among Travellers, compared with 1 in 107 among non-Travellers.

Deficiency of the enzyme causes galactose and galactose-1-phosphate to accumulate in the infant's blood; galactose-1-phosphate is toxic. The infant may be jaundiced and, if not detected and treated

during infancy, the disorder may cause fatal damage to the liver. Affected infants tend to bleed spontaneously, potentially resulting in a brain haemorrhage. *E. coli* septicaemia and cataract development are other complications. Early detection and treatment with a galactose-free diet prevent the early clinical symptoms of the disorder.

As the incidence of galactosaemia is so high in Ireland, the test has been added as one of the six tests included in the national newborn screening. However, as the condition is so prevalent in infants born to Traveller parents, a special expedited screening test, the Beutler test, is offered to all infants born to Traveller parents and siblings of known cases at birth. Infants are held on a galactose-free feed (soy-based) until the result of the test is available. The test is available via the Newborn Screening laboratory at the Children's University Hospital Temple Street, Dublin.

2.3.6 Other genetic conditions

The literature has provided much information about the three most prevalent genetic disorders in Irish Travellers. Many other genetic disorders typically considered to be rare occur in this population more commonly than the 5 in 10,000 European threshold for rare diseases and should, therefore, be considered common for this population. However, beyond the three conditions described above and a handful of other disorders, literature directly relating to these disorders in Travellers is scarce. While many Irish Traveller disorders and their mutations are known to individual Irish-based clinicians, most are not published or, if published, the Traveller ethnicity is not explicit within the publications. The author is aware of a number of publications where the subjects are Travellers, but the papers were not identified by the literature search strategy as there is no mention within of Irish Traveller identity (Rocha et al., 2017); (Hand et al., 1999); (Hand et al., 2017); (Kurian et al., 2004);(Bargal et al., 2006); (Gomez-Herreros et al., 2014); (Brett et al., 1998); (Geranmayeh et al., 2010);(Alston et al., 2015); (Bae et al., 2014); (Tarkar et al., 2013); (Scully et al., 2014); (Camellieri et al., 2012); (Mansour et al., 2012); (Cappelo et al., 2013).

Irish experts have recently come together to define all genetic disorders and associated symptoms in the Irish Traveller population, developing a comprehensive catalogue of over 100 of the currently known disorders amongst the Traveller population, (Lynch et al., 2018). The full list of disorders is available in Appendix F. The expert group strongly recommend explicit description of subjects as members of the Irish Traveller population in any relevant future publications.

It is important to note that the literature has identified that galactosaemia screening is performed for Irish Traveller infants as part of newborn screening, further investigation of this process may inform the author of how Traveller identity is currently collected in healthcare records.

The author next looked to the literature to determine how similar local expert clinical and genetic knowledge is published and utilised in other consanguineous populations.

2.4 Consanguinity and health in other populations

There are many countries with high levels of consanguinity in North Africa, the Middle East and Western Asia (Benar et al., 2017); with intra-familial unions collectively accounting for 20 to 50% of all marriages. Arab countries display some of the highest rates of consanguineous marriages, with a rate of 58% in Jordan (Hamamy et al., 2005) and Saudi Arabia (El Mouzan et al., 2008), and as high as 68% in Alexandria, Egypt (Mokhtar, 2001). Figure 2 below displays the global frequency of consanguineous marriage (Bittles et al, 2010).

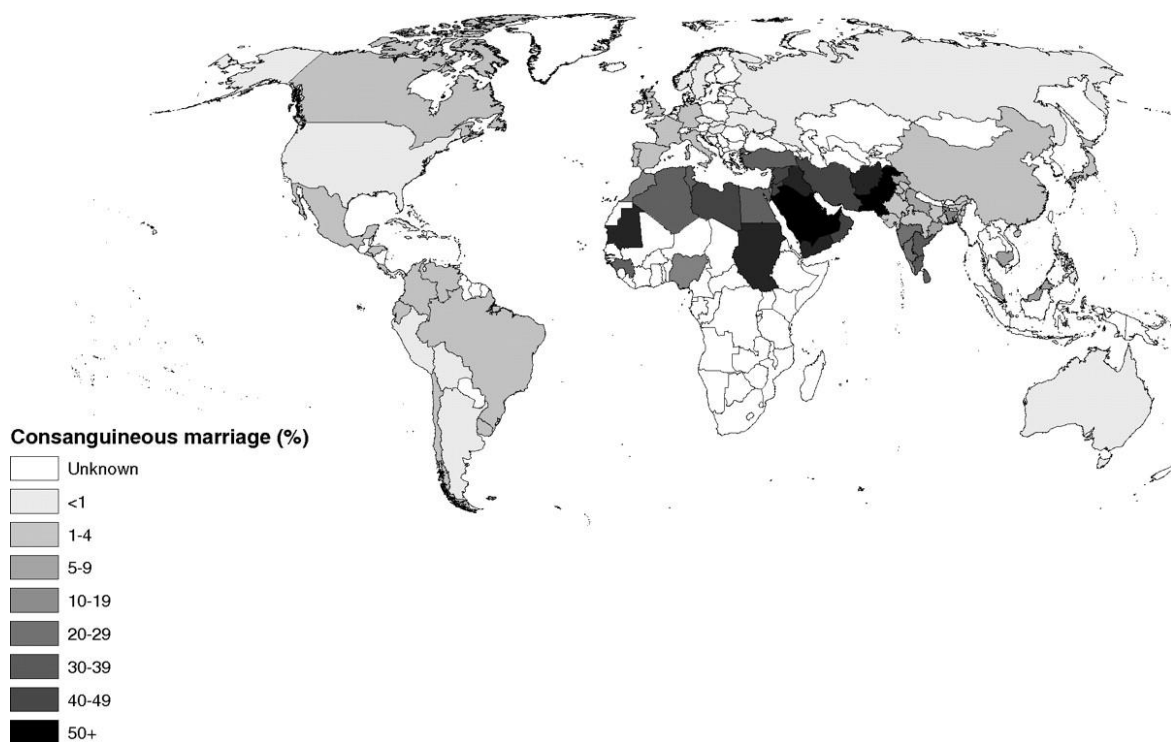


Figure 2: Global distribution of marriages between couples related as second cousins or closer

Several authors reported the common effect on health of inbreeding in these other consanguineous populations, focusing mainly on its impact on reproduction, childhood mortality and rare genetic disease (Bener and Hussain, 2006); (Bener, Hussain and Teebi, 2007); (Bittles and Black, 2009); (Bittles et al., 2002); (Bener, Denic and Al-Mazrouei, 2001); (Ben Arab et al., 2004); (Wright and Hastie, 2001); (Bittles, 2003); (Abdulrazzaq et al., 2008); (Penderson, 2002).

Also, within these journal articles, there exists some limited information on the possible role of consanguinity and recessive genes in polygenic common adult diseases such as diabetes and heart disease.

A number of articles describe cases where consanguineous couple have a prenatal diagnosis of a genetic disease, and choose to continue the pregnancy, the early diagnosis enables their healthcare provider to set a strategy for the child's treatment and follow-up (Bener, Hussain and Teebi, 2007); (Modell and Darr, 2002); (Tadmouri et al ., 2009); (Anwar, Khyatti and Hemminki, 2014).

2.4.1 Global genetic intervention in a consanguineous population

The DorYeshorim program began with screening for Tay-Sachs disease in 1983 (Ekstein and Katzenstein, 2001). It is surprising that, despite the program being so successful and running for such an extended period, the phrase "DorYeshorim" only results in 14 articles in PubMed.

The DorYeshorim program involved voluntary testing of large portions of the religious Jewish population, initially in New York City. Heavily funded by private donors, (the cost to participants is \$200 -\$270 per person), the program is now available wherever concentrations of Orthodox Jews live. The DorYeshorim has developed anonymous testing to achieve early premarital screening, thus preventing genetic disease and avoiding carrier stigma.

25,000 individuals are screened every year. As marriage is typically by age 20, the DorYeshorim program primarily offers to test high-school girls and boys (90% of tests obtained through DorYeshorim). Each individual is assigned an ID number. The samples are tested on a panel of recessive genetic conditions. The standard Ashkenazi panel consists of 9 disorders; an optional testing panel of 7 less common additional Ashkenazi disorders is available for another \$75. The alternative Sephardic Jewish panel includes testing for 16 disorders.



Figure 3: Screenshot of the homepage of the Jewish Genetic Disease Consortium

Results are stringently entered into a highly sophisticated database. When a couple is considering marriage, both parties exchange ID numbers and day and month of birth. They can each ring DorYeshorim's automated hotline to request a compatibility check. DorYeshorim staff compares the test results and the couple are only told whether they are compatible or not; they are only incompatible if they both carry the same recessive genetic disease, they are not told the specifics of their genetic analysis.

DorYeshorim is a worldwide program available to all who request to participate; however, prospective participants must not have engaged in private testing or already be in a committed relationship. The database of participants is thus used as clinical decision support allowing preconception screening for genetic disease, avoiding the ethical and religious controversies surrounding prenatal analysis of genetic disease and termination of pregnancy.

2.5 Practical application of expert clinical knowledge in other consanguineous populations

The literature was further reviewed to identify existing population-specific genetic databases and to determine how the information is accessed and used.

Scouring the literature for population/ethnicity-specific databases of genetic disease produced a number of results. However many of the existing databases are used for single nuclear

polymorphism frequency in various populations or are single disease or single gene data repositories. Like the Omani and Mediterranean databases described below, they are primarily used by expert laboratories and research institutes for the development of diagnostic tests and validation of genetic variant results and do not have a direct role in point of care diagnosis of Rare Genetic Disease. A further article identified the specific clinical use of a database for the Plain People – the Amish, Hutterite and Mennonite populations of Canada.

2.5.1 Omani Genetic Variations Database

The Sultanate of Oman is a rapidly developing country in the Persian Gulf, with mature government-funded health care services, and rapidly expanding medical genetic facilities. The preservation of tribal structures within the Omani population, coupled with geographical isolation, has produced unique patterns of rare mutations and genetic islands.

Rajab et al. (2015) collated and analysed all of the disease-associated mutations identified in the Omani population. The dataset contains 300 mutations, within 150 different genes. Over half of the genetic variations have not previously been described and are specific to the Omani population. Many novel Mendelian disease genes have been discovered in Omani nationals. The study provided information useful for genetic care in Oman and was the starting point for the Omani genetic variation database, as seen in figure 4 below.

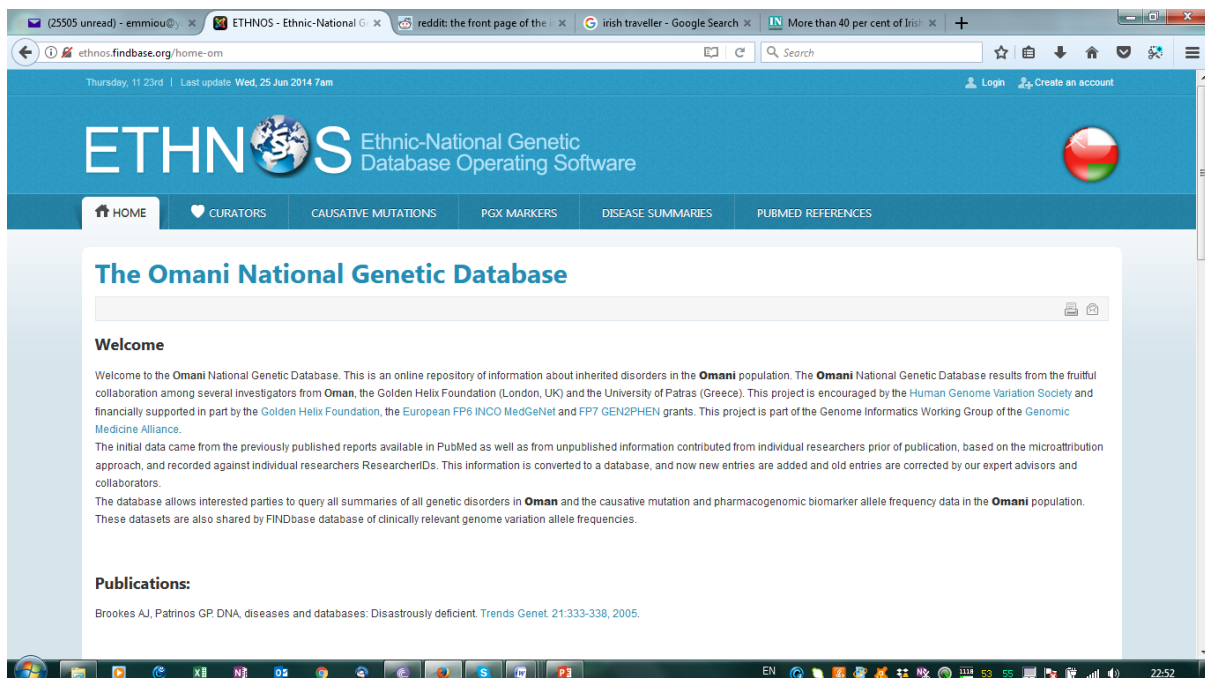


Figure 4: Screenshot of the homepage of the Omani National Genetic Database

2.5.2 Mediterranean Founder Mutation Database

Throughout prehistoric and historical times the Mediterranean basin has been the centre of migration crossroads followed by the settlement of several waves of different populations and ethnicities. This has significant consequences for genetic and genomic variation within the region. Charoute et al. (2015) describe the publically accessible web-based Mediterranean Founder Mutation Database (MFMD), homepage displayed in figure 5, below. The authors collected mutation data from the literature and other resources and systematically reviewed and assembled it within a database. At the time of publication, the database contained 383 founder mutations in 210 genes, related to 219 Mendelian diseases. The authors conclude that their database will facilitate more rapid and less expensive design of genetic diagnostic tests for this population.

Home Statistics Data Submission Contact

Mediterranean Founder Mutation Database (MFMD)

Search

Disease Name
Gene Symbol
Population Name
Disease OMIM
Gene OMIM

By Disease
A B C D E F G H I J K L M
N O P Q R S T U V W X Y
Z [0-9]

By Gene
A B C D E F G H I J K L M
N O P Q R S T U V W X Y
Z

Last update

21/6/2017

Welcome

The **Mediterranean Founder Mutation Database (MFMD)**, a comprehensive database established to offer a web-based access to founder mutation data in Mediterranean population. The database provides an overview about the spectrum of founder mutations for Mediterranean population to the scientific community. Furthermore, MFMD will help scientists to design more efficient diagnostic tests provides beneficial information to understand the history and the migration events of the Mediterranean population. This database maintained by the **Laboratory of Human Molecular Genetics at Pasteur Institute of Morocco**.

Database curation team:

- Hicham Charoute, PhD Student
- Amina Bakhchane, PhD Student
- Houda Benrahma, PhD
- Abdelhamid Barakat, PhD

Home | Statistics | Data Submission | Contact

Pasteur Institute of Morocco | Laboratory of Human Molecular Genetics © 2014 All rights reserved

Figure 5: Screenshot of the homepage of the Mediterranean Founder Mutation Database

2.5.3 Amish, Mennonite and Hutterite Genetic Disorder Database

The Amish, Mennonite, and Hutterite (Anabaptist) Genetic Disorder Database was created in Ontario, Canada, to serve as a resource for research and the diagnosis of genetic conditions in these ethnic groups. It was initially compiled by performing a literature search within PubMed and Online Mendelian Inheritance in Man (OMIM) using the keywords “Amish”, “Mennonite” or “Hutterite”. In addition, some of the disorders and mutations have been entered based on personal observation by specialist genetic clinicians familiar with the population (Payne et al., 2011).

New disorders are added through periodic review of the literature or can be submitted for inclusion after expert review. Hosted on a website at the Biochemical Genetics Laboratory, London, Ontario, users can search by disorder, mutation, or clinical signs and symptoms, and are directed to the corresponding page.

The clinical search feature, whereby the user can search the database by clinical symptoms is particularly useful when the diagnosis is unknown. The resulting list of differential diagnosis and associated symptoms is a useful tool for Clinical Decision Support for those working with these Anabaptist populations.

The screenshot shows a web browser window displaying the 'Amish, Mennonite, and Hutterite Genetic Disorder Database'. The page title is 'Amish, Mennonite, and Hutterite Genetic Disorder Database'. Below the title, there is a search bar and a list of disorders. The disorders are listed in a table with columns for 'OMIM #', 'Disorder', and 'Seen In [?]'. The 'Seen In' column contains letters A, M, H, OCM, and OOM, indicating the source or status of the disorder. The table is sorted by OMIM number.

OMIM #	Disorder	Seen In [?]
#210210	3-Methylcrotonyl-CoA carboxylase 2 deficiency	A M
#610198	3-Methylglutaconic Aciduria, Type V	H
%201550	Adducted Thumbs Syndrome	A
#202110	Adrenal hyperplasia, congenital, due to 17-alpha-hydroxylase deficiency	M
#201910	Adrenal hyperplasia, congenital, due to 21-hydroxylase deficiency	A OCM
#201810	Adrenal hyperplasia, congenital, due to 3-beta-hydroxysteroid dehydrogenase 2 deficiency	A
#202010	Adrenal hyperplasia, congenital, due to steroid 11-beta-hydroxylase deficiency	A
#612952	Aicardi-Goutieres syndrome 5	A
#300600	Aland Island Eye Disease	A
#606952	Albinism, oculocutaneous, type 1B	A
+107400	Alpha-1 antitrypsin deficiency	OOM
#203800	Alström Syndrome	M
#609056	Amish infantile epilepsy syndrome	A
#300068	Androgen Insensitivity Syndrome	H
#208900	Ataxia Telangiectasia	A M
#607585	Ataxia-telangiectasia - Variant	M

Figure 6: Screenshot of the listed disorders within the Anabaptist Mutation Database

2.6 Could similar ICT programs support a more timely diagnosis of genetic disorders in Irish Travellers?

As a catalogue of genetic disorders identified in the Traveller Community now exists, and taking into consideration the relatively small size of the population of Travellers in Ireland and the UK, an approach similar to DorYeshorim could work if acceptable to the Traveller Community. However, factors such as poor health literacy, high mobility and a reluctance to seek medical advice would likely influence the development of a carrier testing program in this population (Watson, Kenny, McGinnity, 2017).

While pre-conception screening for recessive genetic conditions would be an optimal approach from a clinical genetics perspective, any pre-conceptual programme for Irish Travellers would interfere with the choice of marriage partners. This is likely to be met with hostility. Pre-conceptual screening in any population is a very sensitive subject and is more likely to succeed if the population in question initiates a screening program themselves (Mone et al., 2018). The Irish Traveller population have not requested a pre-conception screening service at this time. Currently, despite knowledge of consanguinity and the risk of having a child with an autosomal recessive syndrome, Irish Travellers will proceed with conception (Wiggins, 2013).

An interface and database similar to the Amish, Mennonite and Hutterite Genetic Disorder Database for Irish Traveller genetic disease could allow non-expert clinicians to access differential diagnoses for their patients quickly. There is adequate information provided in the expert group publication (Lynch et al., 2018) to begin development of an online web resource with data fields similar to those in the Amish, Mennonite and Hutterite Genetic Disorder Database. A similar clinical search feature (Payne et al., 2011) would allow for phenotype/symptom driven determination of differential diagnoses.

2.6.1 Bringing diagnostic support to the point of care

The literature identified the four databases previously discussed. The Amish, Mennonite and Hutterite Genetic Database and the DorYeshorim program both demonstrate aspects of clinical decision support; however, the literature does not describe whether these knowledge bases are incorporated into workflow processes at the front line. Clinical decision support systems (CDSS) are healthcare information technology applications that relate individual patient health data to established knowledge bases and thereby assist in clinical decision making and health management (Yu, 2015).

Osheroff (Osheroff et al., 2012) describes the five rights for successful clinical decision support interventions, as listed in Table 2 below.

The five rights concept states that in order to provide benefits, CDS must include:	
The right information	e.g. evidence-based guidance, response to clinical need
To the right people	e.g. entire care team, GP in primary care
Through the right channels	e.g. EHR, mobile device, patient portal
In the right intervention formats	e.g. laboratory or imaging order sets, flow sheets
At the right points in the workflow	e.g. point of care, for decision making or action

Table 2: Osheroff's "Five Rights"

The five rights must take place at the "relevant point of care." The relevant point of care is defined as, "when the intervention can influence clinical decision making before diagnostic or treatment action is taken in response to the intervention."

Musen has described three categories of CDSS (Musen et al., 2014). First, CDSS can provide access to medical literature related to a clinical question, and by displaying contextually relevant disease information, augments the knowledge of the healthcare provider. Use of an Info button within an electronic health record is an example. The second type of CDSS helps to focus the clinician on specific health data, an example of which are drug-drug interactions alerts. This type of CDSS is critical for improving situational awareness and reducing the risk of errors. The third type of CDSS uses artificial intelligence to provide guidance on diagnostic interventions based on patient-specific data, integrating a medical knowledge base with an individual patient's data through a CDSS engine that applies a prespecified logic.

The catalogue of genetic diseases in Irish Travellers by Lynch et al., 2018 is populated with peer-reviewed phenotype/genotype information and likely contains the right information, an established knowledge base. Further research is required to ascertain what the right format of this information is and how any resource might best meet Osheroff's other recommendations, or if the resource fitting into one of the three categories of CDSS can be designed in the context of existing and proposed Irish healthcare resources. There is a gap in the literature about the use of Clinical Decision Support Systems across hospital sites in Ireland.

Considering the common claim that ‘Laboratory medicine data influences 70% of clinical decisions’, or minor variations around this figure (60–80%) (Hallworth, 2011), and as all of the diagnostic processes demonstrated heavy use of hospital laboratory and imaging services in the numerous papers underpinning the Irish Traveller genetic disease catalogue by Lynch et al., Order Communications as a potential launching point for any specific diagnostic support resource requires further exploration.

While there is much literature espousing the benefits of ethnicity-specific disease databases, there is very little literature on how ethnicity or race is reliably captured in paper charts or electronic health records, and more specifically, literature relating to the capturing of Traveller ethnicity in Ireland outside of the National Census is scant.

2.6.2 Barriers to reliably targeting Irish Travellers for enhanced decision support

2.6.2.1 Ethnicity in health records

Of the 104 disorders listed within the expert group paper (Lynch et al., 2018), 51 have previously been published in Irish Traveller families, but ethnicity is only explicit in a small minority.

Family name, address, and accents are frequently used in clinic to identify patients as Travellers. Traveller surnames are well documented (Traveller Heritage, 2018); however, all of these surnames are also shared with non-Travellers. Merely using the surname to identify Travellers, while sensitive, would not reach adequate specificity levels to employ within health systems as a flag that the patient could be a member of the Travelling Community.

Address in conjunction with surname is more useful, but only 50% of Travellers live within traditional halting sites, and only 12% of Travellers now live in a caravan or mobile home (Mone et al., 2018), so sensitivity is an issue.

Many IT systems have the option to assign ethnicity to a patient – however, some have only Irish white/British white as options. Even when Irish Traveller is an available option, Travellers may be unwilling to self-identify; this is reflected in the difference in counts of Travellers in Ireland between the All Ireland Traveller Health Study 2010 (AITHS, 2010) and the official census figures (CSO, 2010).

Ethnicity outside of the Irish Traveller population may need more than one field to be sufficiently descriptive; an individual may be half Irish, one-quarter Polish, one-quarter Slovakian – a study in

New Zealand recommends a minimum of six fields to collect ethnicity. Ethnicity data from the NHS is difficult to process as the "Other" field is frequently used.

Many data fields for ethnicity assume that individuals can have only one ethnic identity (Fearon, 2003): the only way to capture individuals who self-identify as a combination of different ethnicities is to list them for each type of combination (e.g., "of Nigerian and Irish heritage"; "of Irish, Polish, and Slovakian heritage"), or to create an "Other race or two or more races" group (Alesina et al. 2003).

Ethnic identities can also be nested: a Traveller of Irish descent may consider herself primarily British/Irish Caucasian. However, if she identifies with her Traveller heritage as well as the overall category of British/Irish Caucasian, a data set that categorises her as solely British/Irish Caucasian would miss this point (Wimmer, 2013)

Concerning capturing Traveller Identity, a field denominating Irish Traveller or not would be more useful as there is little intermarriage between Travellers and non-Travellers, and once marriage is outside of the Traveller Community, the risk associated with consanguineous recessive disease is eliminated.

2.6.2.2 Existing capture of Traveller ethnicity in health records

The literature and other sources were interrogated to investigate whether there might exist a process to capture Irish Traveller identity within health records. As described previously, newborn screening for galactosaemia is expedited in Irish Traveller Infants.

A Practical Guide to Newborn Screening in Ireland (2001) recommends that the Beutler test, biochemical analysis of red cell GALT enzyme activity on newborn blood spot, should be routinely offered to all Traveller infants and siblings of known cases of Galactosaemia, owing to the high incidence of the condition amongst these groups. This test should be carried out on an urgent basis before ingestion of breast milk or cow's milk, on the first day of life and before any blood transfusion.

Documented in "Review of the national born screening programme for inherited metabolic disorders"(HeBE Programme of Action for Children, 2004) the working group recommended that ethnic group identifiers should be developed and included on the Newborn Screening Card (NSC) to

facilitate timely screening of high-risk infants. The working group stated that "The introduction of an ethnic group identifier would alert medical and nursing personnel to the need for additional screening for Travellers and appropriate advice regarding infant feeding pending newborn screening test results". Despite these recommendations, to date, in 2018, there is no field for ethnic group identifiers on the newborn screening card (see Figure 7).

Figure 7: Newborn Screening Card data collection

The National Newborn Screening Laboratory (NNBSL) received 1745 Day 1 Beutler cards in 2016, out of a total of 72,745 screening cards. Some of these will be for non-Travellers, non-Irish with a family history of galactosaemia but these are usually very obvious from non-Irish surnames. It is very rare for Irish Travellers to opt out of the screening (personal communication, Loretta O’Grady, Chief Medical Scientist, National Newborn Screening Laboratory, December 2017).

These 1745 requests were initiated and completed within maternity units throughout Ireland, with the Director of Nursing for each unit ultimately being responsible for the collection of samples for newborn screening (HeBE Programme of Action for Children, 2004). While the general process for newborn screening cards is very formal, the actual process of how high-risk group infants are

identified for Day 1 Beutler tests is not, and the literature did not provide further clarification of how infants are identified as Travellers in their health records.

Part D of Technical Report 2 is the AITHS Birth Cohort Study Follow Up (Hamid et al., 2011) and was published in September 2011. Virtually all Travellers in both ROI and NI are born in a hospital, and no domiciliary/home deliveries were recorded. In part B of the same technical report, we see that 30.6% of total Traveller births occur in the three Dublin maternity hospitals, with 69.4% of Traveller births at maternity units outside Dublin. Four major maternity units, namely the Coombe Women & Infants University Hospital; Mid-Western Regional Maternity Hospital Limerick; Galway University Hospitals and The Rotunda Hospital, Dublin account for almost 50% of all Traveller births in the cohort.

As the literature demonstrates that all Irish Traveller babies born in Ireland are born in hospital and communication with the NNBSL suggests that all Traveller parents opt in for screening, the Beutler test represents a process during which Traveller ethnicity is identified by some means for all Traveller infants born in Ireland, therefore representing a relevant starting point for further exploration of the current methods of capture of Traveller identity in health records.

As the Rotunda Hospital is identified as one of the centres where Traveller woman attend to have their children, and has recently gone live with the national maternity and newborn electronic health record (MN-CMS) further research may describe how Traveller identity is captured specifically in an electronic health record and whether that capture is used to prompt any action, such as the Beutler test.

CHAPTER 3: METHODOLOGY

3.1 Introduction

This chapter outlines the methodology adopted by the author. It describes the research aims and objectives, the research design, the participants, ethical approval, data collection, and the data analysis process.

3.2 Literature review

According to Creswell (2009), a prerequisite in the research process is to review the literature thoroughly to reduce and refine the scope of a proposed study. Several themes were identified and used as a basis for the literature review, as discussed in detail in the literature review section. The primary purpose of the literature review was to gather information on the following areas:

- What are the causative factors for the high prevalence of rare genetic disease in Irish Travellers?
- What are the ICT supports for rare genetic disease in specific ethnic groups in other countries?
- What are the barriers to successful implementation of similar initiatives for the Irish Travellers?

The literature review identified a gap in the research literature as there is insufficient material available on how ethnicity or race is reliably captured in paper charts or electronic health records, and more specifically, despite the Beutler test being available since 1972, there is no literature relating to the necessary capture of Traveller ethnicity for that purpose.

There is also a gap in the literature about the use of Clinical Decision Support across hospital sites in Ireland.

After the thorough literature review, the following questions remain unanswered:

- What might a similar diagnostic support resource for genetic disease in Irish Travellers look like?
- How can Traveller ethnicity be captured?
- How might Traveller ethnicity be employed to trigger use of the resource?

As the literature is lacking, alternative methods must be employed to answer these questions.

Creswell states that qualitative research is typically based on descriptive data (Creswell, 2009). Qualitative analysis of interviews where the subject is asked to provide their opinion and advice on the author's research matter within their area of expertise may provide answers to those research questions where literature is lacking. Gill describes how using the qualitative method to define areas to be explored, but also allowing the interviewer or subject to deviate to pursue an idea or response in more detail. This approach is commonly used in healthcare and was deemed a suitable interview format to identify the key factors, as it provides participants with some guidance on what to talk about, which many find helpful (Gill et al., 2008).

The flexibility of this approach, particularly compared to structured interviews, also allows for the discovery or elaboration of information that is important to participants but may not have previously been thought of as pertinent by the author. Participants are asked to give an opinion on factors identified during the literature review and by other participants.

Therefore, based on the literature by Gill and Creswell, semi-structured interview employing tailored person-specific questions with identified domain experts is the methodology most suitable for the author to fill the gaps in literature to fully explore the clinical background, Traveller ethnicity capture, barriers, facilitators and critical success factors in the development and resource design of ICT support for rare genetic disease in Irish Travellers.

As the first two research aims, describing the causative factors for the high prevalence of genetic disease in Irish Travellers and investigating population-specific genetic databases, have been met by literature review.

The remaining research aims and objectives are:

- use information gathered to inform Irish Traveller genetic web resource prototype design
- determine optimal point of care for and means for intervention
- describe how Traveller ethnicity is currently captured in Irish health records
- describe processes by which Traveller ethnicity currently triggers the Beutler Test
- determine what the limitations are to identifying Travellers within national ICT projects
- explore how Travellers might be identified in EPR
- determine if any ethical and legislative barriers exist

Therefore, in addition to informing prototype design, the purpose of the interviews is to meet the remaining research aims above by clearly identifying a combined narrative answer to the specific research questions.

- How are Travellers currently identified within maternity services using the Beutler test as a model?
- How are Beutler test and Traveller ethnicity captured within the newly introduced MN-CMS?
- How might Traveller Identity be fed into EPR beyond the newborn record to act as a trigger for Traveller-specific clinical decision support for genetic disease?
- What is the optimal point of intervention for the resource as a CDS within diagnostic workflow?

From her background in clinical genetics, from teaching material provided by TCD Health Informatics lecturers, attendance at HIMSS events, and from literature review providing examples of ethnicity driven diagnostic supports in other regions, the author is aware of a number of individual domain experts likely to have relevant experience to advise design for a diagnostic support for genetic disease in Irish Travellers.

From her background in laboratory medicine and from teaching material provided by TCD Health Informatics lecturers, and attendance at eHealth Ireland events, the author is aware of a number of national health informatics projects, including MedLIS and MN-CMS, where domain experts are likely well informed of any existing clinical support and also likely to be better placed to provide answers relevant to capture of Traveller ethnicity and use of ethnicity to launch a diagnostic resource in an Irish context.

3.3 Research design

The study design is evaluative. Qualitative methods were used to address the main research questions. The flexibility of this approach, particularly compared to structured interviews, also allows for the discovery or elaboration of information that is important to participants but may not have previously been thought of as pertinent by the author. Participants were asked to give an opinion on factors identified during the literature review and by other participants.

3.3.1 Access negotiation and ethics approval

Access to the Interview participants was negotiated by email on a one-to-one basis by the author. Interview participants signed a declaration that each was answering interview questions in their capacity and not on behalf of any organisation; therefore ethics approval was not sought from individual institutions.

Ethics approval for the research was an absolute requirement and was sought from the SCSS Research Ethics Committee via the TCD Research Ethics WebApp, on the 12 March 2018, and was approved, on 22 March 2018 (Appendix D).

3.3.2 Participant selection and recruitment

Thirteen domain experts were sent an email invitation to participate in the study by the author. These individuals are chosen MedLIS, laboratory, MN-CMS, clinical and nursing team members. All participants were over 18 years of age. These individuals have been identified as key personnel within the ICT teams implementing and using the national maternity EPR, or national MedLIS; or are identified as clinical or nurse experts in the area. The process of identifying participants for an interview was led by a cascade of names provided from initial approach to project managers via contact details on the national eHealth website; discovered employing literature search; or previously known to the author via their professional role. Participants were all approached initially via email from the author's TCD account.

Five subjects were approached by email and agreed to be interviewed about the topics to inform prototype design.

Subject ID	Domain Description
Subject 1	Clinical expert Ireland
Subject 2	Clinical expert Canada
Subject 3	Technical expert Canada
Subject 4	Clinical expert Ireland
Subject 5	Traveller genetics expert Ireland

Table 3: Subjects selected to inform prototype design

Five subjects were approached by email and agreed to be interviewed around the topics relating to the Beutler process and capture of ethnicity in EPR.

Subject ID	Domain Description
Subject 6	Midwife maternity hospital
Subject 7	MN-CMS team member maternity hospital
Subject 8	MN-CMS team member maternity hospital
Subject 9	Laboratory newborn screening specialist
Subject 10	Laboratory point of care specialist maternity hospital

Table 4: Subjects selected to inform the description of the Beutler process

Three subjects were approached by email and agreed to be interviewed around the topics relating to diagnostic processes, order communications and capture of ethnicity in national laboratory systems.

Subject ID	Domain Description
Subject 11	MedLIS clinical lead
Subject 12	MedLIS order communications project manager
Subject 13	MedLIS team member national office

Table 5: Subjects selected to inform the exploration of national ICT systems

The participants were given a copy of the participant information leaflet (Appendix A), the informed consent form (Appendix B) and the author's contact details.

The participants were given an opportunity to direct any questions that they may have had to the author to explain the research before agreeing to be interviewed. A date was arranged for an interview with each of the seven face-to-face interview participants in a private meeting room at their institution.

The author took consent from participants at the meeting, and again, before the interview, they were given the opportunity to ask any questions they may have about the project. While every effort was taken to anonymise identifiable data, given the small number of participants from distinct disciplines each participant was informed that even after anonymising the data, participants might be unintentionally identifiable by their discipline. This was stated verbally by the author to the participants before the signing of the informed consent form and the start of the interview. Participants were also informed that they could withdraw from the interview at any time at their request, without giving a reason,

Following this, the participants were asked to sign the informed consent form. All participants were capable of giving their informed consent. Participants were given a second copy of the participant information leaflet and the informed consent form for their records. When the participants were satisfied that they have been fully informed about the project and the interview, they were asked to sign the consent form in the presence of the author.

Each interview took approximately 30 minutes. It was recorded by audio-tape and transcribed for analysis. All answers from the interviews were kept strictly confidential. Participant identities and

identifiable data were anonymised to protect participants. Participants were advised that data would not be disseminated for any other purpose or be further processed in any other way.

Participants were made aware of the steps taken to ensure confidentiality. These included the following:

- the removal of self-identifying information from transcripts
- field codes identified participants
- no data published would be associated with named individuals
- password protection was used for all computer data files

3.3.2.1 Interview questions to inform prototype

Five subjects were approached by email and agreed to be interviewed about the topics to inform prototype design.

Subject 1 Clinical expert Ireland
<ul style="list-style-type: none"> • Why is rare genetic disease in Irish Travellers are of particular interest? • What are the problems with existing publications? • Have you had many people contacting you from outside Ireland? • Is it difficult to keep track of specific disorders in the families when there is that travelling aspect, and not having the same address continuously? • What is the process of referral? • How does knowing someone is a Traveller aid diagnosis? • If the MN-CMS Traveller data point could be continued into the paediatric record - would that be useful for enhancing diagnosis in this group? • Are these not conditions that, generally, clinicians should be familiar with? • Can you give your opinion on the ethics of identifying somebody as a Traveller in health records? • By whom and how do you see the database being used?
Subject 2 Clinical expert Canada
<ul style="list-style-type: none"> • Who created the Amish database? • How are clinicians made aware of the database? • Is it used it at the point of care? • How is the database updated? • Are there any issues with liability? • Has it been integrated into any electronic patient records as clinical decision support? • How are the Plain People identified as plain people by your clinicians? • Is it captured within an electronic patient record? • How does a non-expert know to identify a patient as Amish and refer them on for expert clinical geneticist consultation?

Subject 3	Technical expert Canada
	<ul style="list-style-type: none"> • When did you build the Amish database? • How was it designed? • Who can edit the database? • What are the technical requirements needed to build and host a similar resource?
Subject 4	Clinical expert Ireland
	<ul style="list-style-type: none"> • Why is rare genetic disease in Irish Travellers are of particular interest? • What are the problems with existing publications? • Have you had many people contacting you from outside Ireland? • Is it difficult to keep track of specific disorders in the families when there is that travelling aspect, and not having the same address continuously? • What is the process of referral? • How does knowing someone is a Traveller aid diagnosis? • If the MN-CMS Traveller data point could be continued into the paediatric record - would that be useful for enhancing diagnosis in this group? • Are these not conditions that, generally, clinicians should be familiar with? • And the ethics of identifying somebody as a Traveller in health records? • By whom and how do you see the database being used?
Subject 5	Traveller genetics expert Ireland
	<ul style="list-style-type: none"> • What are important resources for Traveller Health? • What impact do recessive genetic conditions have on this population? • Other than consanguinity, what else leads to increased morbidity and mortality in this population? • How can clans or surname be used to identify Travellers in health records? • What are the essential factors to consider when designing diagnostic support for genetic disease in Irish Travellers?

Table 6: Interview questions to inform prototype design

3.3.2.2 Interview questions to describe Beutler process

Five subjects were approached by email and agreed to be interviewed around the topics relating to the Beutler process and capture of ethnicity in EPR.

Subject 6	Midwife maternity hospital
	<ul style="list-style-type: none"> • How are Traveller patients recognised as such? • How do they get the Beutler test? • What is the process for the Beutler test and how are results acted upon? • Is there any decision support or flagging in MN-CMS to trigger the midwives to take blood for the Beutler test on day 1? • Do non-Irish Clinicians find it challenging to identify who belongs to the Traveller community?

<ul style="list-style-type: none"> • Is there decision support for other processes such as haemoglobinopathy screening for Asian or African women? • What is the process for haemoglobinopathy screening?
Subject 7 MN-CMS team member maternity hospital
<ul style="list-style-type: none"> • How long has MN-CMS been live? • Can you describe the booking-in process within MN-CMS? • Does everybody get asked if he or she are a Traveller? • Are there any other decision supports within the system say if mum and dad are Asian; is there support for haemoglobinopathy screening? • Have you had any reluctance from people about having all this information caught electronically; has there been a difference in attitude when compared to paper charts? • Do samples for blood spot go to the Laboratory here? • Do you know if those Day One tests particularly for the Travellers, that they get that Beutler test - is that the same process? • The screening process is entirely separate in MN-CMS for the Beutler Test? • Is there a way to create a flag that the patient/infant is a Traveller? • In the absence of paediatric EPR is there a discharge summary to the GP and is their risk Factor included in the discharge communication? • MN-CMS has its Order communications system, is this separate from MedLIS development?
Subject 8 MN-CMS team member maternity hospital
<ul style="list-style-type: none"> • Can you explain how the Beutler test order request is made? • How is the information that Mum is a Traveller collected into MN-CMS? • Can use that data point to create a flag/alert linking out of MN-CMS Order communications to an online resource? • Does the booking-in ticked box indicating that Mum is a Traveller in any way prompt the team to take the Beutler card? • What prompts the midwife to take the card?
Subject 9 Laboratory newborn screening specialist
<ul style="list-style-type: none"> • Traveller newborns get enhanced screening - can you explain that process? • The Census and the All Ireland Traveller Health Study differ between the two of them. Do you have an accurate number of how many Travellers are born in Ireland? • If we did not have the Traveller population, our level of Galactosaemia would be equal to that in the UK? • Are there any other conditions in specific targeted ethnic groups that could be added to newborn screening in Ireland? • In CN-MNS there is a specific tick box for the question "Are you a member of the Irish Traveller Community?" do you see it being useful perpetuating that data point into paediatric EPR and on into adult records? Do you think it could enhance diagnosis? • Are Day One cards for the Travellers all done in a hospital? • Is the consent process for the Beutler specific, or is it the same as the newborn screen?
Subject 10 Laboratory point of care specialist maternity hospital
<ul style="list-style-type: none"> • How is the Beutler Test request recorded on the laboratory system in this maternity hospital with MN-CMS?

Table 7: Interview questions to inform the description of the Beutler process

3.3.2.3 Interview questions to describe diagnostic processes and order communications

Three subjects were approached by email and agreed to be interviewed around the topics relating to diagnostic processes, order communications and capture of ethnicity in national laboratory systems.

Subject 11	MedLIS clinical lead
<ul style="list-style-type: none">• In MN-CMS there is a specific tick box for asking is the patient or partner a Traveller. In Order Communications biographic/demographic window would you have that this person is recognised as a Traveller?• Is there going to be functionality within the Order communications to use demographic data to inform test selection?• Is there any function in MedLIS to have the likes of a link out to something else is there any support outside or is it all just pop-ups in MedLIS itself?• In current exiting protocols Travellers and non-Caucasians already have different screening algorithms in everyday practice at a national level. Within maternity services, it is self-identified by both parents – would it be possible to continue this Traveller ID into EHR?• Is Traveller ethnicity collected in MedLIS?• You have suggested using AI and natural language processing in EHR to support diagnosis in Travellers – is this quite ambitious when Order communications cannot reject a PSA request on a female patient?• We hope to include a search feature using SNOMED and ICD-10 terms - would using structured language have any benefit?• At which stage of the diagnostic process do you see an intervention for diagnostic support in Travellers having the most impact?• The proposed search feature offers a list of potential conditions – allowing you to refine the search or entirely excluding the listed differential. Would that be useful clinically and if so, how might it be incorporated into the clinical diagnostic process?• You have described an EPR function – can you please elaborate on how that might support diagnosis in Irish Travellers?• What are the ethical barriers to implementing diagnostic support for targeted ethnicities?	
Subject 12	MedLIS team member national office
<ul style="list-style-type: none">• Does MedLIS use the demographic information in any way, for example, to prevent an order of PSA for a female patient? Are there demographic based rules?• Although ethnicity is a filed in iPIMS, it is seldom used – can you explain why?• Some Traveller support is built into MN-CMS around the Beutler test, is there anything similar being built into Order communications?• Is applying rules a challenge?• Subject 11 stated that there might be a button linking from Order communications to the National Laboratory Handbook. Why is difficult to get something so simple in the system?• Would Order communications be a suitable location to trigger and launch a CDS if you could pull the demographic data point, in the absence of EPR?• Travellers represent only 1% of the population – is it, therefore, difficult to build a case for specific support in national systems?	

<ul style="list-style-type: none"> • Are there any Traveller-specific care sets being designed in order communications? • How is the collection of ethnicity data affected by GDPR? • Travellers self-identify in maternity services because the Beutler process is accepted. Do we need to maintain that robust Traveller Identity into all EPR to close the Health gap? • Is there anyone else requesting that ethnicity be part of the minimum data set for MedLIS? • Some studies recommended a minimum of 6 fields to record ethnicity. How is it best recorded for Travellers? • Subject 11 advises that collection of Traveller ethnicity in national systems would need to be agreed with the Traveller groups or there could be a backlash. Should there be an external consultation process? Was there for MN-CMS? • How far off having IHI are we? • Is there any other clinical decision support in the laboratory system?
<p>Subject 13 MedLIS team member national office</p>
<ul style="list-style-type: none"> • Can you please provide demonstration and screen capture of relevant windows and functions in MedLIS order communications?

Table 8: Interview questions to describe diagnostic processes and ordering in national ICT systems

3.3.3 Data collection methods

Data collection for 7 participants took the form of one-to-one semi-structured interviews. Interviews were recorded by audio-tape, transferred to password protected encrypted USB device, transcribed and collated into a Word document stored electronically on the password protected encrypted USB device. Due to time constraints and geographical location, data collection for 6 participants took the form of one-to-one email interviews. Interviews were collated into the previously mentioned Word document. Data collection, storage and analysis were in line with the Data Protection (& Amendment) Acts and best practice in scientific research. No patient data was collected for this study.

3.3.4 Data analysis

Qualitative data was gathered in a sequential order during the research project and used to answer the four research questions described above. Information garnered during each interview was used to outline relevant questions for subsequent participants. Following all the interviews, the author performed the analysis based on the interview transcripts and screenshots provided by the participants. Key points discussed in the interviews were summarised. There was a thematic analysis of qualitative data from the interviews. The objective of this research is exploratory; it is designed to explore the questions and is not looking for an immediate solution.

3.4 Issues of validity and reliability

Concerning the interviews, the author is aware that her current and prior organisational roles and research role may influence the subject's responses. However, no subjects are currently immediate colleagues of the author or have a dependent relationship with the author, which limited the possibility of coercion. The interviews were conducted in a neutral manner with the risks associated with being an insider mitigated as the author and subjects in most cases are not employed by a common institute, allowing the role of being a researcher to be prioritised over the author's role as an organisational member.

3.5 Ethical considerations

Participants felt comfortable enough to suggest additional members of the organisation who would be worth interviewing as part of the research. The interview questions were designed in a neutral manner. They were not expected to cause distress or potential harm to participants. The interviews were not expected to discuss any topics or issues that might be sensitive, embarrassing or upsetting. There was no direct benefit to any participant for taking part in this study. The author conducted the interviews in a neutral manner.

CHAPTER 4: RESULTS

4.1 Introduction

This chapter provides an overview of the methodology used to gather information from each interview subject. Interview summaries are available in Appendix G. The analysed information is applied to the research questions, and the research aims and objectives.

4.2 Overview of Interviews

Seven face to face interviews were conducted and recorded. They were analysed in relation to the research questions and summaries were composed for five of the interviews.

One face to face interview was not summarised as upon analysis no new themes were discussed and information garnered was previously discussed and summarised (Appendix G). One face to face interview was an overview of MedLIS order communications and therefore was not transcribed or summarised.

Six interviews were conducted via email exchange and the relevant information from each summarised (Appendix G).

Subjects 4, 9 and 11 provided screenshots for key processes in MedLIS and MN-CMS (Appendix G).

4.3 Interview information collection method and analysis

Subject ID	Domain Description	Information collection method and analysis
Subject 1	Clinical expert Ireland	Full interview, summarised
Subject 2	Clinical expert Canada	Email interview, summarised
Subject 3	Technical expert Canada	Email interview, summarised
Subject 4	Clinical expert Ireland	Themes discussed by Subject 4 were previously discussed by subject 1, so the interview has not been summarised
Subject 5	Traveller genetic expert Ireland	Email interview, summarised

Table 9: Interviews informing prototype design

Subject ID	Domain Description	Information collection method and analysis
Subject 6	Midwife Rotunda	Email interview, summarised
Subject 7	MN-CMS team member Rotunda	Full interview summarised. Provided MN-CMS screenshots
Subject 8	MN-CMS team member Rotunda	Email interview, summarised
Subject 9	Laboratory specialist NNBSL	Full interview, summarised
Subject 10	Laboratory POCT specialist Rotunda	Email interview, summarised

Table 10: Interviews exploring Beutler process

Subject ID	Domain Description	Information collection method and analysis
Subject 11	MedLIS Clinical lead	Full interview, summarised
Subject 12	MedLIS order communications project manager	Overview of MedLIS order communications workflow; not summarised. Provided order communications screenshots
Subject 13	MedLIS team member national office	Full interview, summarised

Table 11: Interviews exploring national ICT systems

4.4 Application of analysed information to the aims and objectives

The research aims and objectives outlined in chapter two are:

- to describe how Traveller ethnicity is captured in Irish health records
- to describe processes by which Traveller ethnicity currently triggers the Beutler Test
- to explore how creating a Traveller flag might be achieved in EPR
- to define the facilitators and barriers in the implementation of Traveller-specific clinical decision support for genetic disease
- to use the analysed data to inform prototype design

The first two research aims are comprehensively addressed by compiled information provided during the interview with subjects 6, 7, 8, 9 and 10. Analysis of information gathered during the interview with subject 7 informs us that although a Traveller flag could easily be created within EPR, subject 11 advises that it might be a sensitive and incendiary issue. Subject 12 suggests that inclusion of Traveller identity as a data point within the HSE basic patient data set might be more useful, appropriate and acceptable to the Traveller community. A narrative of the processes is provided in sections 4.4.1 to 4.4.3.

Subjects 11 and 12 provided information relating to facilitators and barriers and this will be discussed in greater detail in the final chapter (Chapter 6).

Subjects 1, 2,3, 4, 5 provided information used to outline the CDS prototype discussed in the next chapter (Chapter 5).

4.4.1 Traveller ethnicity capture in Irish health records

At the booking in process for a pregnant patient, a midwife sits down with the patient and goes through a set list of questions. One of these questions, in the family history, is whether the patient or partner is a member of the Travelling community. All women are asked the question at booking in. The question of whether the patient's partner is a blood relative is also asked of all patients, so consanguinity is recorded here in addition to Traveller status. In paper records, the information is recorded as part of the patient demographics. In MN-CMS the information is recorded as a tick box underneath the question (Figure 8).

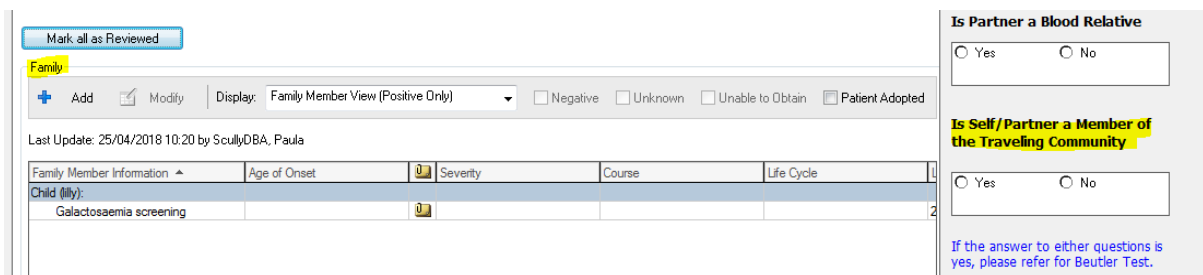


Figure 8: Screenshot from MN-CMS -Is self/Partner a Member of the Travelling Community?

The patient and partner are recorded as Irish Travellers if they self-identify in the genetic history section (Figure 9). Ethnicity information is then displayed in the pregnancy overview (Figure 10).

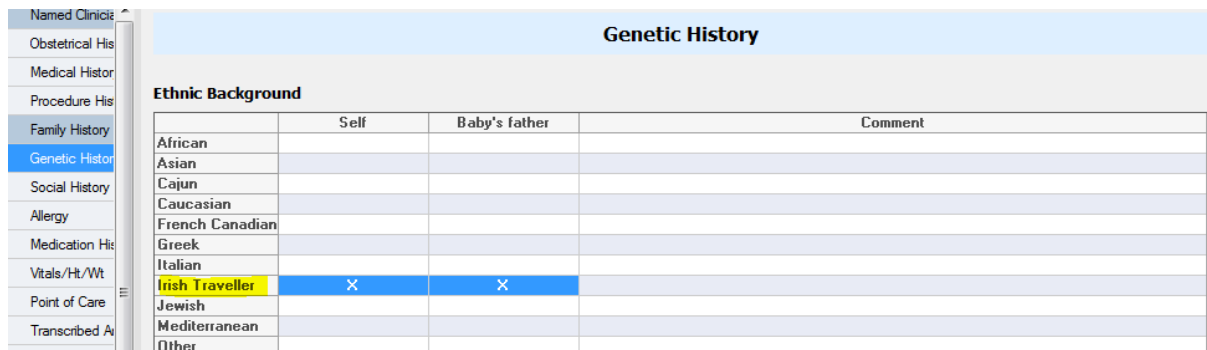


Figure 9: Screenshot from MN-CMS –Self and partner ethnic background



Figure 10: Screenshot from MN-CMS –Pregnancy overview

4.4.2 Traveller ethnicity as a trigger for the Beutler Test

As described in the previous section, in MN-CMS, if the patient is a member of the Travelling community, there is actually a line underneath it to state please refer for the Beutler test, so it acts as a reminder for the booking-in midwife to advise the parents that the baby will need to have the Beutler blood test done within 24 hours and to consider Wysoy feeding, see Figure 11 below.

Figure 11: Screenshot from MN-CMS –Please refer for Beutler Test

There is no decision support or flagging in MN-CMS to trigger the midwives to take blood for Beutler test once the baby is born. It stills depends on clinicians to check if the baby belongs to the Traveller community or not. For Traveller infants the sample is taken on the ward within 24hours of birth. The data collected on the newborn screening card is seen in Figure 12 below.

Figure 12: Newborn Screening Card – the card is used for Beutler and routine screening

The Beutler Test is not recorded on the MN-CMS laboratory system as it is a point of care test. Blood cards are taken on the ward, brought to the paediatric outpatient department, and dispatched to the National Newborn Screening Laboratory (NNBSL) at the Children's University Hospital, Temple Street.

The NNBSL received 1745 Beutler test requests in 2016 and a total of 72,745 screening cards. 99% of Beutler tests are from the Traveller population. The card says Irish Traveller, soy feeds, Beutler, or family history of galactosaemia. The consent for the Beutler is specific in that it is taken for that card and again for the routine card on day 3 when consent for the routine screen would be retaken. Both use the same consent on the blood spot card and parent information leaflet.

The card is scanned into MN-CMS, and it would also be recorded the date, and the time it was taken. Figure 13 shows the blood spot screen window.

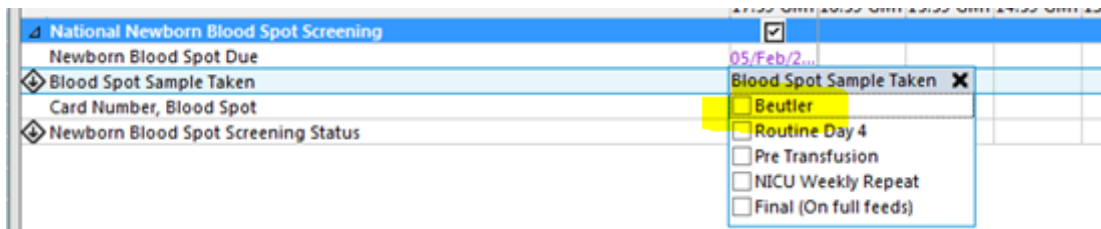


Figure 13: MN-CMS Blood Spot section

The Beutler test has its own section within the infant's record. Once you open up that it is a Beutler performed, whether it was a sufficient sample and whether the test result was normal or abnormal is displayed. NNBSL phones if the result is abnormal. Figure 14 shows the test marked as complete.

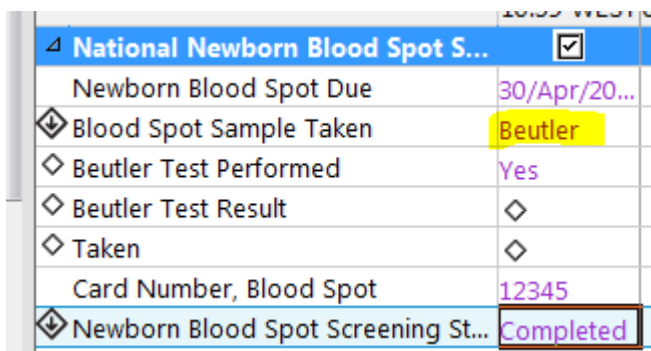


Figure 14: MN-CMS Blood Spot Result section

After delivery, Beutler status also needs to be recorded as part of the discharge checklist for the baby which goes across to the discharge summary for the GP and public health nurse. The MN-CMS

project team have discussed integration with the NNBSL IT system, but it is not in scope at the moment.

If the HSE advised that the identification of Traveller status is something that should be supported in national health IT systems, then it would be adopted. iPIMS, the patient information management system within Cerner Millennium EPR, would have to include it, and the HSE would have to advise its inclusion in the basic data set for any National System including MedLIS.

4.4.3 Creating a Traveller flag in EPR

In MN-CMS it is possible to create a patient flag. It will appear in the banner. When this patient's pregnancy overview is opened, we see that there is a risk flag (Figure 15).

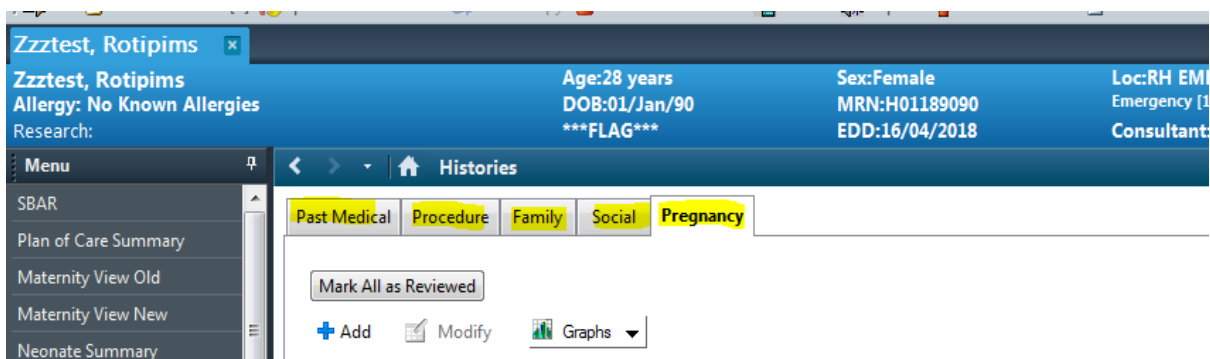


Figure 15: MN-CMS screenshot - Patient risk flag displayed in the banner

It will not display what the flag is; the user must click into it to see what the specific risk is, figure 16 below shows how the window appears once the risk factor window is opened.

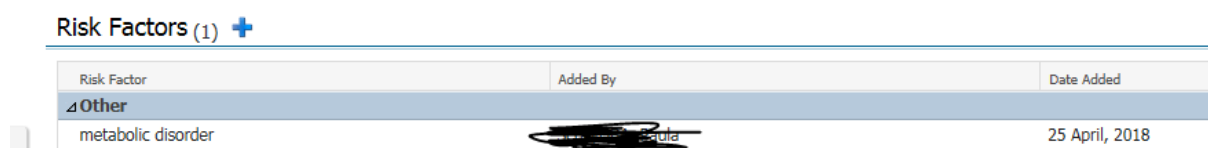


Figure 16: MN-CMS screenshot – Specific risk factor displayed

This can be used to flag clinical risk, social risk or infection risk depending on needs, but it is not used currently to flag Traveller status. There is the option to use a consanguineous flag. Alternatively, if a specific risk is not named within the list provided, there is a field called "other", where a free text description of the risk may be entered.

In the absence of paediatric EPR, risk factor included is communicated via patient discharge summaries. Diagnoses and problems are included when a patient is discharged. A summary including risk factors is produced for the patient and the infant and is sent to the patient's GP.

CHAPTER 5: PROTOTYPE DESIGN

5.1 Introduction

The primary research question posed by the author is whether we can employ ICT to bring expert knowledge to the point of care in Ireland.

The catalogue of genetic diseases in Irish Travellers by Lynch et al., 2018 is populated with peer-reviewed phenotype/genotype information, and although it likely contains the right information clinically, further research was required to ascertain what the right format of this information is.

Based on examples of population genetic databases found in the literature search, a prototype web resource similar to the Amish database was designed, taking into consideration information and advice provided by subjects 1, 2, 3, 4, 5 and 13.

The author used advice from subjects 5, 11, 12 and 13 and the literature to explore how a web resource might be used in both an EHR and non-EHR environments to create clinical decision support (CDS) for more timely diagnosis of genetic disease in Irish Travellers.

Within MN-CMS we have demonstrated Traveller ethnicity captured as a single, distinct, binary data point. This could be used to create an alternative diagnostic pathway once non-standard tests are requested in the order communications module, i.e. not merely when an FBS or LFT is requested. Subject 12 explained that the current order communications module is MN-CMS is due to be replaced by the more extensive MedLIS Order communications module once available, and that Traveller care sets are already in development in conjunction with the national metabolic laboratory.

If the data point is fed from MN-CMS into future paediatric EHR, again, the Traveller data point could be used as a trigger for a Traveller diagnostic pathway linking out of order communications to the web resource. If such a link from Order communications would not be possible, due to constraints discussed by subjects 11 and 12, a link could be included in the National Laboratory Handbook, which is currently in development with the MedLIS order communications project Team and proposed to be linked via a button in the order communications module.

Subject 1 stated that 5% of the rare genetic disorders cause foetal death, and about 30% of the disorders cause congenital malformations and are present in the neonatal period (Subject 7 stated

that infants age out of MN-CMS at 28 days old). A high percentage of the rare genetic disorders will have onset in childhood, but won't necessarily be picked up in that first month of life. Subject 1 further explained that 15% of the rare genetic disorders are adult-onset only. EPR is to be introduced in the new national paediatric hospital. Without venturing anywhere as far as adult EPR, the interventions described above could cover 85% of presentations of rare disease in Irish Travellers.

Osherhoff's five CDS interventions must take place at the "relevant point of care." The relevant point of care is defined as, "when the intervention can influence clinical decision making before diagnostic or treatment action is taken in response to the intervention".

Subject 5 had advised that identification of the front line users would be critical to the success of any intervention for diagnostic support in Irish Travellers. The proposed web resource would facilitate open access to clinicians from primary to tertiary care or anywhere; the enhanced use of the Traveller data point as a trigger to link to the resource overcomes any lack of awareness on behalf of the clinician of the potential relevance of rare genetic disease to the diagnostic process in their Traveller patient.

All of the intervention stages described above could be available to anyone ordering diagnostic tests within EPR, those using order communications in the absence of an EPR, those referring to the national laboratory handbook for guidance or as a standalone web resource.

5.2 Proposed web resource

Based on literature review and analysis of interview findings and advice from domain experts (Subjects 1, 2, 3, 4, 5 and 13) the following design and functionality were proposed for a web resource to support the diagnosis of rare genetic disease Irish Travellers:

Feature/functionality	Source
the database containing data from expert group publication by Lynch et al., 2018	all identified web resources for genetic disorders had expert knowledge database compiled and curated locally
the website has a layered search feature allowing phenotype search to be built	identified in Amish and Mediterranean genetic databases websites via the literature search
the user enters patient phenotype from lists using structured language	observation of Snomed CT for medical history and family in MN-CMS demonstrated by subject 7; subject 2 described the process of adding phenotype data as taking over one year, using the correct dictionary should reduce the workload, standardise entries and facilitate future interoperability
shortlist of potential diagnoses and their associated phenotype is displayed	identified in Amish and Mediterranean genetic database websites via the literature search
the user can click on any entry and see further details of each condition and information on how to order a confirmatory test or links to clinician experts for further assessment	identified in Amish and Mediterranean genetic database websites via the literature search

Table 12: Proposed web resource features and corresponding source from research material

5.2.1 Requirements to implement web resource

Subject 3 provided the following list of requirements to implement web resource. Available resources negotiated with various institutes are described for each.

5.2.1.1 Database

Subject 3 stated that the Plain People website was written in PHP on a MySQL database

Available resource: The prototype database uses RedCAP, a browser-based, metadata-driven EDC software solution and workflow methodology for designing clinical and translational research databases. Developed by an informatics team at Vanderbilt University, with on-going support from NCCR and NIH grants, RedCAP is available at no charge to institutional partners. Access to RedCAP was negotiated with University College Dublin and facilitated by Dr David Joyce, Postdoctoral Research Fellow at the School of Medicine and Medical Sciences, University College Dublin.

The key publication "Catalogue of inherited disorders found among the Irish Traveller population" has online supplementary data describing the identified conditions, the mutation isolated and relevant links and references (Appendix F). The table was copied to CSV format and mass imported into the author's RedCAP account.

Traveller Database

Data Exports, Reports, and Stats [VIDEO: How to use Data Exports, Reports, and Stats](#)

[Create New Report](#)
[My Reports & Exports](#)
[Other Export Options](#)
[View Report: All data \(all records and fields\)](#)

Number of results returned: **104**
Total number of records queried: 104

[Stats & Charts](#)
[Export Report](#)
[Print Page](#)

All data (all records and fields)

Record ID	transcript	cDNA	protein	reference	orpha_code	icd_10	observed_occurrence	publication_link	presentation
1					20	E71.1	P		
2	NM_030813.5	c.1424G>A	p.(Arg475Gln)		289902	E71.1	P		
3	NM_000197.1	c.325A>T	p.(Lys109*)		752	E29.1	F		
4	-	-	-		90787	E29.1	F		
5	NM_001127660	c.2119C>T		6,46	2398	E88.8	C		
6	NM_001127660	c.2119C>T		6,46	99947	G60.0	C		
7	NM_002693.2	c.2542G>A; c.1399G>A	p.(Gly848Ser); p.(Ala467Thr)		726	G31.8	P		
8	NM_005144	IVS12+2insT	no prediction	47-48	86819	L65.8	F		

Figure 17: Screenshot of data records holding knowledge base in RedCAP

Subject 2 advised that it took her team over one year to complete the clinical features field for all

the disorders in their database. The presentation field is in development for the table of disorders. It will be time-consuming and require input from clinical colleagues; therefore an instrument was designed for future data entry by database curators. Appropriate dictionaries were applied to the relevant fields to maximise use of structured language for future interoperability, and these are readily available as a feature in RedCAP, those chosen for the data collection form include

Data field	Data dictionary
diagnosis_or_phenotype	SNOMED-CT is the underlying data dictionary
OMIM_NO	Data dictionary linked to Online Mendelian Inheritance in Man
ORPHA_CODE	Each disease in Orphanet is attributed a unique and stable identifier, the nomenclature of rare diseases
ICD_10	International statistical classification of diseases and Related Health Problems, 10 th edition
presentation	Human Phenotype Ontology, HPO, a standardised vocabulary of phenotypic abnormalities encountered in human, dictionary applied to the presentation field

Table 13: Standard dictionaries behind data fields in data collection form in RedCAP database

Current instrument: **Data Collection Form** [Return to edit view](#)

NOTE: Please be aware that branching logic and calculated fields will not function on this page. They only work on the survey pages and data entry forms.

Record ID	<input type="text"/>
publication_id	<input type="text"/>
diagnosis_or_phenotype	<input type="text"/>
inheritance	<input type="text"/>
omim_no	<input type="text"/>
gene	<input type="text"/>
transcript	<input type="text"/>
cdna	<input type="text"/>
protein	<input type="text"/>
reference	<input type="text"/>
orpha_code	<input type="text"/>
icd_10	<input type="text"/>
observed_occurrence	<input type="text"/>
publication_link	<input type="text"/>
presentation	<input type="text"/>

Figure 18: Data collection form in RedCAP database

5.2.1.2 Web host

Subject 3 advised that a place to store and serve the website and database is necessary. He further advised that possibly there would be free web hosting available through the university. This could be beneficial (cost savings) or limiting (the university might have restrictions on what technologies can be used – in particular, they might support a website but not a database).

Available resource: The database and web pages will reside on the website of the School of Medicine, UCD. The National Rare Disease Office (NRDO) was an alternative location (figure 19) – but as subject 3 advised, having free web hosting at UCD and their support and experience with RedCAP meant they were a more suitable option, and although the hospital governing the NRDO were supportive of a website, the same did not hold not true for a database.



The screenshot shows a webpage titled "Healthcare Professionals" with a navigation menu on the left. The menu includes links for "Apply & Register", "Everyday Care", "Care when you need it", "Community and Social Care", "Specialist Care", "Addiction Services", "Sexual Health Services", "Public Health", "National Rare Diseases Office", "Cancer Services", and "Kerry Health Services". The "National Rare Diseases Office" link is highlighted with a red arrow. The main content area features a section titled "RD Information Databases" with a sub-section "Orphanet" and several links to external resources like "National Organization for Rare Disorders (NORD)", "Online Mendelian Inheritance in Man (OMIM)", "PubMed", "Genetic and Rare Disease Information Centre", "Gene reviews", and "GeneTests". A "Share:" button with social media icons is visible in the top right corner.

Figure 19: Hosting was originally proposed at NRDO website, later negotiated UCD

5.2.1.3 Domain name or URL

Subject 3 advised that the web resource needs a name and an address.

Available resource: based on the likely location of the web resource within the academic centre on rare disease and the working title of GDiT (working name Genetic Disease in Travellers, the URL will potentially be <http://www.ucd.ie/medicine/researchcentres/academiccentreonrarediseases/GDiT>

5.2.1.4 Code

Subject 3 advised that there are plenty of different technologies available; the Plain People website was written in PHP on a MySQL database, and more recently he had created websites with ASP.NET on a Microsoft SQL Server database. He advised that probably an off-the-shelf solution would probably not be suitable, and therefore some code would be required to get the desired functionality.

Available resource: UCD Research IT department provides limited support for hosting web pages and RedCAP technical support; however, some code will be required to complete the search feature and landing page for the web resource. This is an area for future work.

5.2.2 Proposed web resource prototype

5.2.2.1 Search feature

Search window to be developed allowing search by phenotype, disease name, or OMIM code. Subject 3 described his use of PHP for this function. Subjects 1, 5, 9, 11, and 12 describe it as a clinically useful feature.

Search Database

Clinical

You may also use the drop-down menus to select a phenotype. Click "Add" to automatically add it to the list. Disorders that include all given features will be listed.

Select Body System

Add

Search

- Abnormality of the cardiovascular system
- Abnormality of blood and blood-forming tissues
- Abnormal test result
- Abnormality of the endocrine system
- Abnormality of the musculature
- Abnormality of the digestive system
- Abnormality of the skeletal system
- Abnormality of limbs
- Abnormality of prenatal development or birth
- Growth abnormality
- Abnormality of the genitourinary system
- Abnormality of connective tissue
- Abnormality of the ear
- Abnormality of metabolism/homeostasis
- Abnormality of the eye
- Abnormality of the nervous system
- Neoplasm
- Constitutional symptom
- Abnormality of the immune system
- Abnormality of the voice
- Abnormality of the respiratory system
- Abnormality of head or neck
- Abnormality of the breast
- Abnormality of the integument

Figure 20: Prototype search window allowing entry of symptom/phenotype search terms

5.2.2.2 List of differential diagnoses

Search results window listing different diagnoses and associated presentation for all relevant filtered disorders within the Traveller database.

Search Results

OMIM #	Disorder
#602471	Short stature, auditory canal atresia, mandibular hypoplasia, skeletal abnormalities (SAMS) short stature, atresia of the external auditory canal, mandibular hypoplasia, skeletal abnormalities, , respiratory tract infections,
#102700	Severe Combined Immunodeficiency, due to adenosine deaminase deficiency sepsis, pneumonia, respiratory tract infections, failure to thrive
#608644	Primary Ciliary Dyskinesia, Type 3 situs inversus, chronic sinusitis, bronchiectasis, infertility, chronic bronchitis, respiratory tract infections

New Search

Back to Home

Figure 21: Prototype results window displays a list of differential diagnoses and presentation

5.2.2.3 Disease-specific information

This screen describes the chosen disorder in greater detail and has relevant links. Advice on testing, links to Laboratory ordering, care sets and portal to expert advice could all be developed to be accessed from this window.

Primary Ciliary Dyskinesia, Type 3

Disorder	
OMIM #:	#608644 (Click to access OMIM database)
Disorder:	Primary Ciliary Dyskinesia, Type 3
Also known as:	CILIARY DYSKINESIA, PRIMARY, 3, WITH OR WITHOUT SITUS INVERSUS, KARTAGENER SYNDROME
Clinical	
Phenotype:	situs inversus, chronic sinusitis, bronchiectasis, infertility, chronic bronchitis, respiratory tract infections
Remarks:	
Mutations	
1	
Gene:	DNAH5
Base Change:	C>T, at nucleotide 4348
Amino Acid Change:	Gln1450Ter
2	
Gene:	DNAH5
Base Change:	c.10815delT
Amino Acid Change:	p.P3606HfsX23
Last updated:	2017-03-16

Figure 22: Prototype disorder-specific window giving all relevant details and links

5.3 Use of CDS in a non-EHR environment

The database is to be hosted on UCD School of Medicine website. Subject 11 and 12 described how an HTML link from national laboratory handbook within MedLIS Order communications is possible once the handbook has been finalised, or from their proposed national laboratory App. There would be no trigger provided by patient demographic information within PAS to indicate to the clinician that their patient is a Traveller and that the additional support web resource is available. Clinical employment of the CDS would require on-going education of clinicians and represents a lost opportunity for intervention at the appropriate time in the diagnostic workflow.

5.4 Use of CDS in an EHR environment

We have identified that MN-CMS holds Traveller identity as a data point separate from the ethnicity field. In EPR, at a stage in workflow between patient history taking and order communication execution, perhaps the ordering of non-standard blood tests for patient cohorts filtered by that Traveller identity point could prompt a link out to Traveller CDS.

The clinician uses the described search phenotype function to obtain a Traveller specific potential diagnosis list with all phenotypic features listed. If any disorder fits the patient's clinical presentation, then the clinician can click into the disease entry to obtain more specific information including care sets with recommended tests.

5.5 Conclusion

Subjects 1, 2, 3, 4, and 5 provided information used to outline the web resource and CDS prototype. Using features seen in genetic web resources along with advice given by all of the study subjects relating to how such a resource might interact with national ICT programs, the author has conceived a design for a web resource to demonstrate how ICT might support a more timely diagnosis of genetic disease in Irish Travellers.

CHAPTER 6: DISCUSSION

6.1 Introduction

The aims of this study were to

- describe the causative factors for the high prevalence of rare genetic disease in Irish Travellers
- investigate population-specific genetic databases
- use information gathered to inform Irish Traveller genetic web resource prototype design
- determine optimal point of care for and means for intervention
- describe how Traveller ethnicity is currently captured in Irish Health records
- describe processes by which Traveller ethnicity currently triggers the Beutler Test
- determine what the limitations are to identifying Travellers within national ICT projects
- explore how Travellers might be identified in EPR
- determine if any ethical and legislative barriers exist

Literature review described consanguinity and its impact on health in Irish Travellers and other endogamous populations, and also identified a number of web-based resources to support diagnosis and patient care in other countries where these consanguineous populations exist.

Analysis of interview findings informed a narrative description of how Traveller ethnicity is captured in electronic healthcare records (MN-CMS) and how the Beutler test process is initiated and recorded for Traveller infants.

Literature review and analysis of interview findings informed prototype design of web resource for diagnostic support of genetic disease in Irish Travellers, a critical area of interest for strategic development according to EU Council recommendation on rare diseases (EUCERD).

Literature review established the potential of order communications as the potential point of care for the web resource as a clinical decision support system; however as interview findings determined limitations of the basic data set and functionality within MedLIS, alternative solutions including the national laboratory handbook were described.

The remaining topic to be addressed is whether any ethical and legislative barriers exist.

6.2 Ethical and legislative barriers

6.2.1 Consent

Subject 9 described how consent for Beutler test is specific, and how data relating to Traveller status should only be used for that specific test, as that is all that the parents have consented for. Subject 11 voiced concerns that Travellers might be identified in their records without having given specific consent. Subject 7 demonstrated how Traveller identity is captured in MN-CMS outside of the blood spot process as part of booking-in appointment for women in maternity services; the data point is not collected solely for the Beutler test.

6.2.2 Ethics of ethnicity collection in electronic health records

Subject 7 demonstrated that other ethnicities are also captured in MN-CMS, and how this supports tailored ethnicity-specific care plans, targeted haemoglobinopathy screening in the antenatal period for women of different African and Asian ancestries, for example. Ethnicity-specific care algorithms are very much established; indeed, the Beutler test process for Traveller newborns in Ireland was introduced over 40 years ago.

Many of the interview subjects are wary of adopting any new population targeted processes and recommended consultation with representative Traveller groups before any Traveller specific supports are launched, citing GDPR as a concern.

6.2.3 General Data Protection Regulation (GDPR)

Article 9 (Regulation (EU) 2016/679 of the European Parliament) concerns the processing of special categories of personal data. Article 9 paragraph 1 states that "Processing of personal data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, or trade union membership, and the processing of genetic data, biometric data for the purpose of uniquely identifying a natural person, data concerning health or data concerning a natural person's sex life or sexual orientation shall be prohibited".

However, paragraph 2 goes on to state that Paragraph 1 shall not apply if the data subject has given explicit consent to the processing of those personal data or if the conditions of one of the subsequent subparagraphs are met. Relevant sections of subparagraph (H) and (I) outline conditions when processing of special categories of data is permitted in the absence of explicit consent. These include when processing is necessary for the purposes of preventive medicine, medical diagnosis, the provision of health care or treatment or the management of healthcare systems and services, or for reasons of public interest in the area of public health, such as ensuring high standards of quality and safety of healthcare.

This suggests that collection of ethnicity data, to be used to support diagnostic processes, is not prohibited by Article 9.

6.3 Future work

6.3.1 Petition HSE to include Traveller question as part of the basic data set

The literature review revealed that there is a national policy target of narrowing the life expectancy gap between Travellers and the general population (Publichealth.ie, 2001). Would the standardised collection of Traveller identity in health records have an impact on closing the health gap? Meaningful quality improvement must be data-driven. This is particularly true for quality control in healthcare.

Subject 12 informed the author that the HSE would have to advise the inclusion of the Traveller data point in the basic data set for a national system in order for it to be included in iPIMS and ubiquitous in national electronic health records. Collection of the data point in the national system MN-CMS is already well established. The author will present findings from this research study to encourage the expert group of clinicians involved in Traveller care to petition the HSE for the inclusion of the Traveller data point in the adopted basic data set.

6.3.2 Develop phenotype entries for all disorders in database

The full description of Traveller phenotypes for all disorders in the database is on-going. This feature underpins the clinical utility of the web resource so great care is necessary to optimise content. For many disorders, there is a requirement to contact original treating clinicians to fill gaps in clinical features described in existing publications. New disorders have been added at a rate approximating one new entry per month, so continuous curation will be required.

6.3.3 Seek help and funding for coding

To date, the database and hosting have been negotiated, however coding support to develop the website and search feature has not yet been arranged.

6.4 Conclusion - the case study revisited

In chapter one a case study describing a typical patient journey was presented. Applying what the author has learned, Shireen's story is revisited to demonstrate how the availability of the Traveller data point and described web resource could support a timely diagnosis of genetic disorders at the point of care.

Case Study Shireen Connors, age 12 weeks

Shireen was brought to the Midland Regional Hospital A&E at 11pm by her mother. She presented with symptoms of acute respiratory infection.

An on-call paediatric NCHD, Dr Ahmed, examined Shireen and ordered a chest x-ray, and noted that this was her second respiratory infection as the patient history in EPR demonstrated the family's GP had previously treated her. The x-ray illustrated hyperinflated lungs but also an unusual finding of situs inversus, a congenital condition in which the major visceral organs are reversed or mirrored from their regular positions. Dr Ahmed was aware that most people with situs inversus have no medical symptoms or complications resulting from the condition. However, as the region was experiencing a seasonal outbreak of respiratory syncytial virus (RSV), Dr Ahmed opened the order communications module of the paediatric EPR to execute a request for PCR test for RSV, his third RSV request of that shift.

As Shireen is identified as a Traveller by a distinct data point in her EPR, and RSV PCR was outside of the standard test catalogue, an additional window appeared in the order comms module asking if the requesting clinician would like to consider additional diagnostic support as his patient is a Traveller and rare disease should be considered.

Dr Ahmed chooses to accept the diagnostic support and is brought to a search entry box. He chooses repeat respiratory infections from the pull-down list and clicks search.

A shortlist of disorders is presented, with associated symptoms previously seen in Irish Travellers. Dr Ahmed discards two of the three options but notices situs inversus listed as a phenotypic feature of primary ciliary dyskinesia (PCD). He proceeds with the order for RSV PCR but also takes an EDTA blood sample as recommended in the disease-specific window. After discussing Shireen with the paediatric consultant the following morning, the sample is sent for targeted PCR for the PCD Traveller mutation, and the diagnosis is confirmed within one week.

An aggressive approach is taken to airway clearance and management of infections in Shireen; she is referred for comprehensive evaluation by the respiratory team at the National Paediatric Hospital. With a personalised management plan in place, Shireen maintains normal lung function and life expectancy.

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APPENDIX

Appendix A: Information Sheet for Participants

INFORMATION SHEET FOR PARTICIPANTS

DEAR PARTICIPANT, you are invited to take part in a research study entitled " How ICT might support access to Clinical expertise for timely diagnosis of Genetic Disorders in Irish Travellers at Point of Care". This research study is being undertaken in part fulfilment of an MSc in Health Informatics in conjunction with the University of Dublin, Trinity College, Ireland. Please read the following information carefully and please ask if you do not understand any part of it or would like more information.

VOLUNTARY PARTICIPATION Your participation in this study is voluntary and you are free to withdraw at any time without providing a reason. If you do not wish to answer any specific questions, these wishes will be respected by the author.

WHAT IS THE PURPOSE OF THE RESEARCH STUDY? The purpose of the study is to establish the challenges to the introduction of a Computerised Clinical Decision Support System (CDSS) for enhanced diagnosis of genetic disease in Irish Travellers. The study examines the recently implemented Maternal Newborn Electronic Patient Record (MN-CMS); outlining how Traveller identity is captured electronically; and how electronic transmission of this identity could to act as a trigger for CDSS at the appropriate stage of the diagnostic process.

WHY HAVE YOU BEEN CHOSEN? You have been chosen to participate in this study in your role as a domain expert.

WHO IS ORGANISING THE RESEARCH STUDY? This study is being organised by the lead researcher, Emma Ryan. There are no external collaborators involved in this study. The study is being supervised by a Trinity College supervisor, Prof Lucy Hederman. No funding is being provided for this study. The study will be completed between January 2018 and May 2018. The author has no conflict of interest to declare.

WHAT WILL HAPPEN TO ME IF I TAKE PART? If you choose to take part in this study I will contact you to arrange an interview. The time taken to complete the interview is anticipated to be approximately 15 minutes. The interview will be recorded. Informed consent will be requested for the study.

CONFIDENTIALITY - All information collected during the course of the research will be kept strictly confidential. The data collected will be aggregated for the purpose of the research and no participants or institutions will be individually named in my dissertation or any subsequent publications or presentations. Personal data will not be retained within the meaning of the Data Protection Act. This data will be held secure for the period of time required by the college. It will not be disseminated for any other purpose or be further processed in any other way.

HOW WILL DATA BE STORED AND PROTECTED? Data collection, storage and analysis will be in line with the Data Protection (& Amendment) Acts and best practice in scientific research. No patient data will be collected for the purpose of this study.

RESEARCH ETHICS APPROVAL The Research Ethics Committee of the School of Computer Science & Statistics, University of Dublin, Trinity College granted ethical approval for this study.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY? The results of the study will be presented in my dissertation for submission to the University of Dublin, Trinity College. In addition the research findings are likely to be presented at selected conferences, seminars and tutorials. The results will be made available, if requested, by email to all research participants on completion of the dissertation.

PROCEDURE TO BE USED IF ASSISTANCE OR ADVICE IS NEEDED In the event that you require further information, assistance or advice about this study please contact Emma Ryan by email: ryanel@tcd.ie or by phone: 0868727713.

THANK YOU for taking the time to read this correspondence and for considering taking part in the research study.

Yours sincerely, Ms. Emma Ryan

Appendix B: Informed consent form

TITLE OF RESEARCH: HOW ICT MIGHT SUPPORT ACCESS TO CLINICAL EXPERTISE FOR TIMELY DIAGNOSIS OF GENETIC DISORDERS IN IRISH TRAVELLERS AT POINT OF CARE

TIMEFRAME & DURATION OF RESEARCH: January – May 2018

DECLARATION:

- I am 18 years or older and am competent to provide consent.
- I have read, or had read to me, a document providing information about this research and this consent form. I have had the opportunity to ask questions and all my questions have been answered to my satisfaction and I understand the description of the research that is being provided to me.
- I am answering in my own capacity and not on behalf of my organization.
- I agree that my data will be used for scientific purposes and I have no objection that my data may be published in scientific publications.
- I understand that if I make illicit activities known, these will be reported to appropriate authorities.
- I understand that I may stop electronic recordings at any time, and that I may at any time, even subsequent to my participation, have such recordings destroyed (except in situations such as above).
- I understand that, subject to the constraints above, no recordings will be replayed in any public forum or made available to any audience other than the current researchers/research team.
- I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights.
- I understand that I may refuse to answer any question and that I may withdraw at any time without penalty.
- I have received a copy of this agreement.

PARTICIPANT NAME:	
PARTICIPANT SIGNATURE:	
DATE:	

STATEMENT OF INVESTIGATOR'S RESPONSIBILITY: I have explained the nature and purpose of this research study, the procedures to be undertaken and any risks that may be involved. I have offered to answer any questions and have fully answered such questions. I believe that the participant understands my explanation and has freely given informed consent.

RESEARCHER NAME:	Emma Ryan
EMAIL:	ryanel@tcd.ie
TELEPHONE:	0868727713
RESEARCHER SIGNATURE:	
DATE:	

Appendix C: Research Ethic Application

Research Proposal Submitted to the TCD Research Ethics Committee

PROJECT TITLE

HOW ICT MIGHT SUPPORT ACCESS TO CLINICAL EXPERTISE FOR TIMELY DIAGNOSIS OF GENETIC DISORDERS IN IRISH TRAVELLERS AT POINT OF CARE

PROJECT PURPOSE

The author is a part-time MSc in Health Informatics student, with a keen interest in patient safety and computerised clinical decision support. The motivation to conduct this research stems from fifteen years' experience as a clinical molecular geneticist within Our Lady's Children's Hospital, Crumlin, where inefficiencies in the diagnosis of complex genetic disorders in Irish Travellers, outside of expert centres, are recognised as having ongoing impact on morbidity and mortality rates.

The author plans to support dissemination of recently published expert knowledge from a range of clinical specialties outlining rare genetic disease in Irish Travellers, by examining existing clinical decision support systems in other countries, and investigating how such systems might be adopted in an Irish clinical workflow, with a specific focus on trigger and appropriate intervention stage.

The purpose of this project is to identify ICT requirements to support timely diagnosis of genetic diseases in Irish Travellers at point of care. This research will be used within a dissertation for submission to Trinity College Dublin, in partial fulfilment of the requirements for the degree of Master of Science in Health Informatics.

METHODOLOGY AND PLAN

This research requires the gathering, evaluation and analysis of qualitative data relating to ethnicity identifiers in Ireland and internationally, and of national systems in health and social care. The methodology used to collect the required data for the research is an evaluative and ethnographic case study. Each subject will be provided with a copy of the Participant's Information sheet (See Appendix 1) and will be asked to sign a copy of the informed consent (See Appendix 2) in the author's presence before the interview proceeds.

The collected data will be evaluated to find the most suitable model for adaptation to the Irish context. The purpose of the interviews is to clearly identify how Travellers are currently identified within maternity services using the Beutler test as a model. The author will use semi-structured interview to identify how Beutler test and Traveller ethnicity are captured

within the newly introduced MN-CMS. The author will interview relevant IT experts to determine how Traveller Identity may be fed into EPR beyond the newborn record to act as trigger for a Traveller-specific clinical decision support for genetic disease. The author will interview relevant national MedLis participants to determine optimal point of intervention for the CDS within diagnostic workflow. Interviews will be audio-recorded on a held-held device; please see section titled Legislation for proposed handling of these recordings.

PARTICIPANTS

Interviews will be conducted with approximately 15 specifically chosen MedLis, Laboratory, Cerner, MN-CMS, Clinical and Nursing team members (see Appendix 3). All participants will be over 18 years of age. These individuals have been identified as key personnel within the IT teams implementing and using the national maternity EPR, and/or national MedLIS; or are identified as clinical or nurse experts in the area. The process of identifying participants for interview was led by cascade of names provided from initial approach to project managers via contact details on the national eHealth website; discovered by means of literature search; or previously known to the author via their professional role. Participants were all approached initially via email from the author's TCD account.

DEBRIEFING ARRANGEMENTS

The author will inform all participants of the purpose of the research (see Appendix A). A transcript of the interview will be emailed to each participant for their approval. If participants request to view the final thesis the author will send on a PDF copy when the dissertation has been completed.

The results of this study will be presented to staff and participants as part of the weekly "Lunch and Learn" series within Beaumont Hospital; within National Rare Disease forum; and within Genetics and Metabolics Grand Rounds/Tutorials at The Mater Misericordiae Hospital, The Children's University Hospital, Temple Street, and Our Lady's Children's Hospital, Crumlin.

ETHICAL CONSIDERATIONS

This project is being undertaken in partial fulfilment of MSc Healthcare Informatics being completed by the author. There will be no identifiable patient data accessed as part of the study. Semi-structured interviews will be conducted with individual staff members from a number of national HCI projects and relevant institutions. The author does not work directly with any of the participants. There will be no discrimination, penalty or impact on career progression regardless of decision made by individuals to participate or not. Data obtained as part of this study will not be shared with management and will not be utilised as part of a performance review. No conflict of interest is anticipated.

LEGISLATION

As per the Data Protection Acts 1988 and 2003 the data will be anonymised and no disclosures of personal information will be provided, and no consent is required from the data controller. All research and analysis documents used for this dissertation are/will be stored on the author's external hard drive. Only the author has access to this hard drive, it is encrypted to AES-256 standard and password protected. All audio recordings will be saved to hard drive and at no point will cloud storage be employed.

The research and analysis documents include Dissertation, Literature review, and transcripts of the interviews, all produced in Microsoft Word. Due to the geographical location of some of the participants, interviews may be in the form of emailed two way discussion. When an email is received from such a participant, the author will copy the contents of the email into a Microsoft Word document. The contents of all subsequent emails will go into the same Microsoft Word document. Once the contents of the email have been copied successfully into the Word document, the original emails will be deleted.

Once the examination period is completed, all relating research documents and audio recordings will be deleted.


**School of Computer Science and Statistics
Research Ethical Application Form**

Details of the Research Project Proposal must be submitted as a separate document to include the following information:

1. Title of project
2. Purpose of project including academic rationale
3. Brief description of methods and measurements to be used
4. Participants - recruitment methods, number, age, gender, exclusion/inclusion criteria, including statistical justification for numbers of participants
5. Debriefing arrangements
6. A clear concise statement of the ethical considerations raised by the project and how you intend to deal with them
7. Cite any relevant legislation relevant to the project with the method of compliance e.g. Data Protection Act etc.

Part C

I confirm that the materials I have submitted provided a complete and accurate account of the research I propose to conduct in this context, including my assessment of the ethical ramifications.

Signed: 
Lead Researcher/student in case of project work

Date: 14/02/2018

There is an obligation on the lead researcher to bring to the attention of the SCSS Research Ethics Committee any issues with ethical implications not clearly covered above.

Part D

If external or other TCD Ethics Committee approval has been received, please complete below. N/A

External/TCD ethical approval has been received and no further ethical approval is required from the School's Research Ethical Committee. I have attached a copy of the external ethical approval for the School's Research Unit.

Signed: _____
Lead Researcher/student in case of project work

Date: _____

Part E

If the research is proposed by an undergraduate or postgraduate student, please have the below section completed.

I confirm, as an academic supervisor of this proposed research that the documents at hand are complete (i.e. each item on the submission checklist is accounted for) and are in a form that is suitable for review by the SCSS Research Ethics Committee.



Signed: _____
Supervisor

Date: 14th February 2018

Part B

<i>Please answer the following questions.</i>		Yes/No
Has this research application or any application of a similar nature connected to this research project been refused ethical approval by another review committee of the College (or at the institutions of any collaborators)?		No
Will your project involve photographing participants or electronic audio or video recordings?		Yes
Will your project deliberately involve misleading participants in any way?		No
Does this study contain commercially sensitive material?		No
Is there a risk of participants experiencing either physical or psychological distress or discomfort? If yes, give details on a separate sheet and state what you will tell them to do if they should experience any such problems (e.g. who they can contact for help).		No
Does your study involve any of the following?	Children (under 18 years of age)	No
	People with intellectual or communication difficulties	No
	Patients	No

CHECKLIST

Please ensure that you have submitted the following documents with your application:

1.	<ul style="list-style-type: none"> • SCSS Ethical Application Form 	✓
2.	<ul style="list-style-type: none"> • Participant's Information Sheet must include the following: <ul style="list-style-type: none"> a) Declarations from Part A of the application form; b) Details provided to participants about how they were selected to participate; c) Declaration of all conflicts of interest. 	✓
3.	<ul style="list-style-type: none"> • Participant's Consent Form must include the following: <ul style="list-style-type: none"> a) Declarations from Part A of the application form; b) Researchers contact details provided for counter-signature (your participant will keep one copy of the signed consent form and return a copy to you). 	✓
4.	<ul style="list-style-type: none"> • Research Project Proposal must include the following: <ul style="list-style-type: none"> a) You must inform the Ethics Committee who your intended participants are i.e. are they your work colleagues, class mates etc. b) How will you recruit the participants i.e. how do you intend asking people to take part in your research? For example, will you stand on Pearse Street asking passers-by? c) If your participants are under the age of 18, you must seek both parental/guardian AND child consent. 	✓
5.	<ul style="list-style-type: none"> • Intended questionnaire/survey/interview protocol/screen shots/representative materials (as appropriate) 	✓
6.	<ul style="list-style-type: none"> • URL to intended on-line survey (as appropriate) 	N/A

Notes on Conflict of Interest

1. If your intended participants are work colleagues, you must declare a potential conflict of interest: you are taking advantage of your existing relationships in order to make progress in your research. It is best to acknowledge this in your invitation to participants.
2. If your research is also intended to direct commercial or other exploitation, this must be declared. For example, *"Please be advised that this research is being conducted by an employee of the company that supplies the product or service which form an object of study within the research."*

Notes for questionnaires and interviews

1. If your questionnaire is **paper based**, you must have the following **opt-out** clause on the top of each page of the questionnaire: *"Each question is optional. Feel free to omit a response to any question: however the researcher would be grateful if all questions are responded to."*
2. If your questionnaire is **on-line**, the first page of your questionnaire must repeat the content of the information sheet. This must be followed by the consent form. If the participant does not agree to the consent, they must automatically be exited from the questionnaire.
3. Each question must be **optional**.
4. The participant must have the option to **'not submit, exit without submitting'** at the final submission point on your questionnaire.
5. If you have open-ended questions on your questionnaire you must warn the participant against naming **third parties**: *"Please do not name third parties in any open text field of the questionnaire. Any such replies will be anonymised."*
6. You must inform your participants regarding **illicit activity**: *"In the extremely unlikely event that illicit activity is reported I will be obliged to report it to appropriate authorities."*

Appendix D: Research Ethics Approval

Home > [HOW ICT MIGHT SUPPORT ACCESS TO CLINICAL EXPERTISE FOR TIMELY DIAGNOSIS OF GENETIC DISORDERS IN IRISH TRAVELLERS AT POINT OF CARE](#)

HOW ICT MIGHT SUPPORT ACCESS TO CLINICAL EXPERTISE FOR TIMELY DIAGNOSIS OF GENETIC DISORDERS IN IRISH TRAVELLERS AT POINT OF CARE

Status View Assign Supervisor

Current Status	Submission date	Last Status Update	Academic Supervisor / Lead Researcher	Application Number
Approved	Tuesday, January 30, 2018 - 18:46	Thursday, March 22, 2018 - 09:53	hederman	20180115

No workflow transitions are possible at this time.

Final Comments from the Research Ethics Committee

All issues have been addressed, we wish you the best with your study.

Status:
Approved

Timeline of state changes for this application

Thursday, March 22, 2018 - 09:53
State change:

ORIGINAL ARTICLE

Catalogue of inherited disorders found among the Irish Traveller population

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/jmedgenet-2017-104974>).

For numbered affiliations see end of article.

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Received 10 August 2017
Revised 21 December 2017
Accepted 22 December 2017
Published Online First
22 January 2018

ABSTRACT

Background Irish Travellers are an endogamous, nomadic, ethnic minority population mostly resident on the island of Ireland with smaller populations in Europe and the USA. High levels of consanguinity result in many rare autosomal recessive disorders. Due to founder effects and endogamy, most recessive disorders are caused by specific homozygous mutations unique to this population. Key clinicians and scientists with experience in managing rare disorders seen in this population have developed a de facto advisory service on differential diagnoses to consider when faced with specific clinical scenarios.

Objective(s) To catalogue all known inherited disorders found in the Irish Traveller population.

Methods We performed detailed literature and database searches to identify relevant publications and the disease mutations of known genetic disorders found in Irish Travellers.

Results We identified 104 genetic disorders: 90 inherited in an autosomal recessive manner; 13 autosomal dominant and one a recurring chromosomal duplication.

Conclusion We have collated our experience of inherited disorders found in the Irish Traveller population to make it publically available through this publication to facilitate a targeted genetic approach to diagnostics in this ethnic group.

Travellers vary as the nomadic Travellers frequently migrate across Europe even on a yearly basis. It is estimated that 58 000 Gypsies, including a proportion who are Irish Travellers, live in mainland UK⁴ and there are small populations of Irish Travellers in mainland Europe and in the USA.

Irish Travellers practise consanguinity with cousin marriage rates approximating 71% of unions; first cousin 39%, first cousin once removed 11% and second cousin 21%.² These high levels of consanguinity have resulted in many well-recognised autosomal recessive disorders among this population, the overwhelming majority being due to homozygous mutations. While many Irish Traveller disorders and their mutations are known to individual Irish-based clinicians, most are not published or, if published, the ethnicity is not explicit.^{4–10} Clinicians who are less familiar with this population have no resource to facilitate forming a differential diagnosis or in targeting genetic testing. We have therefore collated these data on known genetic disorders found among this population to facilitate rapid and affordable diagnostic testing. The majority of the data were collated from clinicians and scientists working on the island of Ireland, but some information was sought through clinicians and scientists managing Irish Traveller families living in the UK, New Zealand, Denmark and USA.

In this study, we present, for the first time, a comprehensive catalogue of the currently known disorders among the Traveller population, their causative mutations (where known) including several novel or previously unreported mutations, relevant publications and disease codes (Orphanodes, OMIM and ICD10 coding). We also present information on clustering of groups of disorders due to consanguinity within geographical regions or due to linkage disequilibrium. This information is presented to facilitate cost-saving, targeted and timely diagnosis in individuals from the Irish Traveller population.

METHODS**Molecular methods**

SNP data were used to perform a comparison of the homozygosity levels in the Irish Traveller population relative to the general Irish population and

INTRODUCTION

Irish Travellers are an ethnically Irish endogamous nomadic population, whose origins date back many centuries. The island of Ireland encompasses two countries with separate healthcare systems: the Republic of Ireland and Northern Ireland (a constituent unit of the United Kingdom). According to the Irish census 2016,¹ there were 30 987 Irish Travellers in the Republic of Ireland accounting for just over half of one per cent (0.66%) of the total population. A further ~1800 (0.07% population) live in Northern Ireland.² A 2010 All-Ireland study estimated a higher figure of ~40 000 Irish travellers living on the island of Ireland,³ arguing that the discrepancy in numbers was due to reluctance, in some, to self-identify as a Traveller. Numbers of

 Check for updates

To cite: Lynch SA, Crushell E, Lambert DM, et al. *J Med Genet* 2018;55:233–239.

BMJ

Lynch SA, et al. *J Med Genet* 2018;55:233–239. doi:10.1136/jmedgenet-2017-104974

233

Appendix F: Disease Table

Diagnosis or Phenotype	OMIM no.	Orpha code	ICD-10
3-hydroxy-3-methylglutaryl-CoA lyase deficiency	246450	20	E71.1
3-methylglutaconic aciduria	250950	289902	E71.1
46,XY disorder of sex development due to 17-beta-hydroxysteroid 3 deficiency	264300	752	E29.1
46,XY sex reversal – STAR-like	400044	90787	E29.1
Adipose overgrowth - multiple symmetric lipomatosis	151860	2398	E88.8
Charcot-Marie-Tooth type A2A	609260	99947	G60.0
Alpers syndrome (MTDPS4A)	203700	726	G31.8
Atrichia with papular lesions	209500	86819	L65.8
Autosomal recessive congenital hydrocephalus	236600	2185	Q03.0
Autosomal recessive microcephaly (heterogeneous)	-	2512	Q02
Beaulieu-Boycott-Innes syndrome	613680	363444	Q87.0
Hereditary breast cancer	600185	227535	C50
Brugada syndrome	601144	130	I47.2
Byler disease (cholestasis, progressive familial intrahepatic type 1)	211600	79306	K83.1
Central hypotonia, neonatal respiratory failure, seizures	-	70587	P22.0
Cerebellar hypoplasia and mental retardation	224050	269523	G11.8
Chromosome 17q12 microduplication syndrome	614526	261272	Q92.3
Cohen syndrome	216550		
Colobomatous microanophthalmia (MCOPCB) and Matthew Woods syndrome	601186	2470	Q11.2
Congenital adrenal hyperplasia due to 21-hydroxylase deficiency	201910	90794	E25.0
Congenital hereditary endothelial dystrophy	217700	293603	H18.5
Congenital ichthyosis	612281	313	Q80.2
Congenital methaemoglobinaemia type I	250800	139373	D74.0
Cystic fibrosis	219700	586	E84.8
Dandy-Walker malformation (isolated)	220200	217	Q03.1
Deafness + scarring skin disease	-	--	--
Deafness, autosomal recessive type 18B	614945	96210	H90.3
Deafness, onychodystrophy, osteodystrophy, mental retardation	220500	79500	Q87.8
Dihydrolipoamide dehydrogenase deficiency	246900	765, 2394	D74.0
Dihydropteridine reductase deficiency	612676	226	E70.1
Dihydropyrimidine dehydrogenase deficiency	612779	1675	E79.8
Early-onset epileptic encephalopathy	308350	1934	G40.3
Epiphyseal dysplasia, multiple type 4	226900		
Factor X deficiency	613872	328	D68.2
Familial dilated cardiomyopathy	615396	217607	I42
Hypertrophic cardiomyopathy	115197	217569	--
Familial hyperinsulinaemic hypoglycaemia (HHF5)	147670	276525	E16.1
Familial hyperinsulinism	256450	276598	E16.1
Fanconi anemia, complementation group A	609054	84	D61.0
Fanconi anemia, complementation group A	609054	84	D61.0
Fanconi anemia, complementation group J	227650	84	D61.0
Fraser syndrome	219000	2052	Q87.0
Friedreich ataxia	229300		
Galactosaemia	230400	352	E74.2
Glutaric aciduria type I	231670	25	E72.3
Glycogen storage disease type IIIa	232400	79201	E74.0
Glycogen storage disease type V (McArdle disease)	232600	368	E74.0
Hemolytic uremic syndrome, atypical, susceptibility to, type 1	235400	2134	D58.8
Hemolytic uremic syndrome, atypical, susceptibility to, type 1	235400	2134	D58.8
Hereditary motor and sensory neuropathy type 1a	118220	101081	G60.0
Hereditary dehydrated stomatocytosis	194380	98365	D58.8
Hurler syndrome (mucopolysaccharidosis IH)	607014	93473	G71.0
Hurler-Scheie syndrome (mucopolysaccharidosis IH/S)	607014	93476	E76.0

Hyperprolinaemia type I	239500	419	E72.5
Hyperprolinaemia type I	239500	419	E72.5
Hyperprolinaemia type II	239510	79101	E72.5
I-cell disease (mucopolipidosis II)	252500	576	E77.0
Ichthyosis-prematurity syndrome	608649	88621	--
Infantile liver failure – multisystem involvement	615438	370088	K72.0
Intellectual disability, epilepsy & ataxia	616949	404493	G11.1
Leber congenital amaurosis type 4	604393	65	H35.5
Leber congenital amaurosis type 4	604393	65	H35.5
Leigh syndrome	256000	506	G31.8
Leigh syndrome	256000	506	G31.8
Leigh syndrome	256000	506	G31.8
Long QT1 syndrome	192500	768	145.8
Long QT1 syndrome	192500	768	145.8
Maple syrup urine disease	248600	511	E71.0
Meckel syndrome	249000	564	Q61.9
Medium chain acyl CoA dehydrogenase deficiency	201450	42	E71.311
Merosin-deficient congenital muscular dystrophy type 1A	607855	258	G71.2
Methylmalonic aciduria	251000	293355	E71.1
Mitochondrial complex II deficiency	252011	3208	G71.3
Familial pheochromocytoma-paraganglioma	168000	29072	C74.1
Natural killer cell and glucocorticoid deficiency, DNA repair defect (MCM4)	609981	75391	D84.8
NEK9-related lethal skeletal dysplasia	617022	464366	Q77.2
Neu-Laxova syndrome	256520	2671	Q87.8
Oculocutaneous albinism	203200	79432	E70.321
Osteogenesis imperfecta type VIII	610915	666	Q78.0
Osteopetrosis	259730	2781	Q78.2
Porencephaly	175780	99810	Q04.6
Phenylketonuria	261600	716	E70.1 E70.0
Phenylketonuria	261600	716	E70.1 E70.0
Polymicrogyria, bilateral perisylvian	615752	98889	Q04.3
Primary ciliary dyskinesia	615872	244	J98.0
Primary ciliary dyskinesia	615482	244	J98.0
Primary ciliary dyskinesia	612649	244	J98.0
Primary ciliary dyskinesia	612649	244	J98.0
Primary ciliary dyskinesia with heterotaxy	614679	244	J98.0
Sanfilippo syndrome (mucopolysaccharidosis III)	605270	581	E76.22
Severe combined immunodeficiency due to ADA deficiency	102700	277	D81.3
Sly syndrome (mucopolysaccharidosis VII)	253220	584	E76.2
Spinal muscular atrophy	271150	83420	G12.1
Stiff skin - like syndrome	184900	2833	L98.8
Sub-glottic stenosis	150360		
Thrombotic thrombocytopenic purpura	274150	93583	M31.3
Ureidopropionase deficiency	613161		
Van Maldergem syndrome type 1	601390	314679	--
Walker-Warburg syndrome	236670	899	Q04.3
Werner syndrome	277700	902	E34.8
Wilson disease	277900	905	E83.0
Wolcott-Rallison syndrome	226980	1667	E10

Appendix G: Interview Summaries

Summary of Interviews to inform prototype

Subject 1: CLINICAL EXPERT IRELAND

Summary of taped interview, transcript in full runs to 3648 words.

Why is Rare Genetic Disease in Irish Travellers are of special interest?

They are very rare, and so if you don't have the expertise is what they get, it will take you a long time to make a diagnosis. There are a number of disorders where the outcome is improved if you make a speedy diagnosis.

What are the problems with existing publications?

That the subjects are Irish Travellers is not explicit.

Have you had many people contacting you from outside Ireland?

Maybe six to ten cases a year from UK geneticists asking for advice about Irish Travellers based there.

Is it difficult to keep track of specific disorders in the families when there is that travelling aspect, and not having the same address continuously.

Yes, it is hard to keep track of families when the travel and address has changed. Phone numbers change every year. IPI patient identifier should help.

What is the process of referral??The practical thing that happens out there in the community most Traveller children with problems tend to go via Metabolics in Dublin because the Paediatricians have a high suspicion, and even though the child mightn't have a metabolic disorder it might have a different disorder. One of the Consultants does a clinic in Limerick. Malformations tend to be referred directly to Genetics.

How does knowing someone is a Traveller aid diagnosis?

There was a baby born in a particular part of Ireland with anophthalmia -you can tell by the surname, where they are from, what the diagnosis was - STRA6, and target the confirmatory test. In this case, surname and address is used to identify Traveller patients and make a differential diagnosis.

We would communicate back with the team ask them to confirm if the family are Travellers or not. It is vital important to pin that down. Traveller surnames are the same as "Irish" surnames, so some you will have a high suspicion but it is easy to miss.

MN-CMS records Traveller status. But that ages out now when the babies are 28 days. If that data point could be continued on into the Paediatric record - would that be useful for enhancing diagnosis in this group?

Quite a high percentage of childhood onset disorders, you won't necessarily pick up in the first month of life and about 15% that are adult only.

Are these not conditions that, generally, Clinicians should be familiar with?

Not when they are very rare. Some of them are ultra rare. NCHDs who are changing over every 3/6 months. The paediatrician wouldn't have had a clue where to start with the enormous differential for that child with anophthalmia. So it is the rarity of these conditions that makes this support so important. Else they will end up having to spend €5,000 on an exome instead of a targeted test at €300. Potentially most of these mutations could fit on one Traveller SNP chip.

And the ethics of identifying somebody as a Traveller in Health Records?

Traveller Health stats have not improved in 30 years. The average lifespan is still late 40s, one in 2 dead by the age of 39.

If we pussyfoot around the ethics, then are we just saying it's fine for the Travellers to die so young. When Travellers have a sick child, they want the best for their child. They don't want to be ignored and their children die....So I think the ethics get blown away by the fact that people want their best health for themselves, and their children. I have never had a Traveller at consultation having an issue with being identified as such.

By whom and how do you see the database being used?

When you have a paediatric NCHD On-Call or something, and you've got this new-born baby seizing. The baby is identified in the records and it offers a link to the database search – the NCHD types in epilepsy in a neonate, and the Traveller differential for newborn with seizures is presented. There are risks in not having/recognising that Traveller Identity in these children as well, other than the delayed diagnosis if you are going down a standard treatment route, for the likes of epilepsy, the traditional medications may be contraindicated in specific types of genetic epilepsy, and this could be missed all together.

Subject 2: CLINICAL EXPERT CANADA

Email interview, summary of information garnered from five correspondence exchanges.

Who created the database? My son actually created the database program when he was in high school, as a summer student project. The data input began the following year as a summer student project by a first year medical student who combed through OMIM and PubMed, searching for "Amish", "Mennonite", "Hutterite" and "genetic". We periodically update the database as we become aware of new disorders, either through our own centre, or other centres who work with the Amish and Mennonite population. We update the database ourselves, and anyone can notify us of a new disorder which they submit (there is a way to do this in the program) – and this is then entered.

How are clinicians made aware of the database? We published an article about the database. Also, I mention the database at every opportunity. We have the largest population of Old Order Amish and Mennonite families in Canada in our region. We attend meetings with others in the States who work with this population.

Is it used it at point of care? If I see a patient who is Amish/Mennonite and has specific features, I will go to the database to search on features and see what comes up as a possible diagnosis

Has it been integrated into any Electronic Patient Records as a Clinical Decision Support? No. I don't know how one would go about this.

How are the Plain people identified as plain people by your clinicians? By their dress, and recognition of common surnames. For those who have Plain background but have been assimilated into the general population, we know the 8 unique surnames in the OOA which we don't see in our general population. OOM who don't dress traditionally can be missed, because there is a very common surname of Martin. OCM are the most assimilated into the general population, and represent our largest group, but still have some unique surnames.

Is it captured within an electronic patient record? No

How does a non-expert know to identify a patient as Amish etc. and refer them on for expert Clinical Geneticist consultation? Most non-experts can't differentiate between Amish and Mennonite, but often classify them all as Mennonite if they dress differently.

Subject 3: TECHNICAL EXPERT CANADA

Email interview, summary of information garnered from four correspondence exchanges.

I built the Plain People Genetic Database website in 2006, in PHP on top of a MySQL database. There's a publicly accessible portion of the website where users can search it, and an administrative portion where disorders can be added or edited; it's entirely web-based. I still periodically support the website.

In a general sense, there are a few parts that you'll need in order to get your website running:

A web host. Specifically, you need a place to store and serve the website and database. Possibly you have free web hosting available through the university. This could be beneficial (cost savings) or limiting (the university might have restrictions on what technologies you can use – in particular, they might support a website but not a database).

A domain name or URL. Some code. There are plenty of different technologies available; the Plain People website was written in PHP on a MySQL database, and more recently I've created websites with ASP.NET on a Microsoft SQL Server database. You probably wouldn't be able to use an off-the-shelf solution, so you'd need some code (unless your website was just a Google Sheet, but I don't think that would have all the functionality you want).

Subject 4: CLINICAL EXPERT IRELAND

Themes discussed by Subject 11 were previously discussed by Subject 1 so the interview has not been summarised.

Subject 5: TRAVELLER GENETICS EXPERT RCSJ

Email interview, summary of information garnered from two correspondence exchanges.

The AITHS survey is really important, and also relevant to what you are trying to achieve, in improving health in the community and access to appropriate care.

Be careful about attributing a major part of Traveller health issues to consanguinity – I note the 100 rare/Mendelian conditions, but it's likely the vast majority of the health burden in the population is not due to consanguinity, or at least not due to recessive Mendelian genes (see the AITHS Birth Cohort study – very few cases detected, although still 10x rate in general population).

Regarding clans if you decide to use this– I'd suggest recording surnames of both parents, as the combination will be a better predictor of cluster/group membership in the community (we have some good data on this I can show you). Some surnames are across groups.

It would be good to clarify in your proposal exactly you see this tool working, and who uses it – i.e. is it GPs, specialists – primary, secondary, tertiary care? And how do you see it working – i.e. does one input phenotype terms that point towards a potential genetic condition? How does that in turn link to a genetic test – is it to channel potential genetic cases to clinical genetics?

Well done, it's a good concept, definitely worth exploring.

Summary of interviews to describe Beutler process

Subject 6: MIDWIFE ROTUNDA

Email interview, summary of information garnered from six correspondence exchanges.

I asked my midwifery colleagues and they told me that they usually ask at the time of booking admission if the patient belongs to Traveller community or not. We send the Beutler test ASAP to Temple street lab and start baby on Wysoy formula while waiting for the result. Normally, we ring or lab inform us about the result over the phone which sometimes delayed on the weekend. Beutler test is normal then we start the baby on normal formula.

But there is no decision support or flagging in MN-CMS to trigger the midwives to take bloods for Beutler test on day 1.

It stills depends on clinicians to check if the baby belongs to Traveller community or not. I suppose for Irish Clinicians, it is easy to identify Travellers but for non-Irish Clinicians it is difficult to identify who belongs to Traveller community or not. In that case decision support will surely help. Further, you could add the stats how many Medical graduates, NCHDS, midwives and neonatal nurses are non-Irish.

All the Asian or African mothers have their blood test for haemoglobinopathy with their booking bloods and if the result is positive only then they check baby's bloods at birth.

Subject 7: MN-CMS TEAM MEMBER ROTUNDA

Summary of taped interview, transcript in full runs to 7490 words

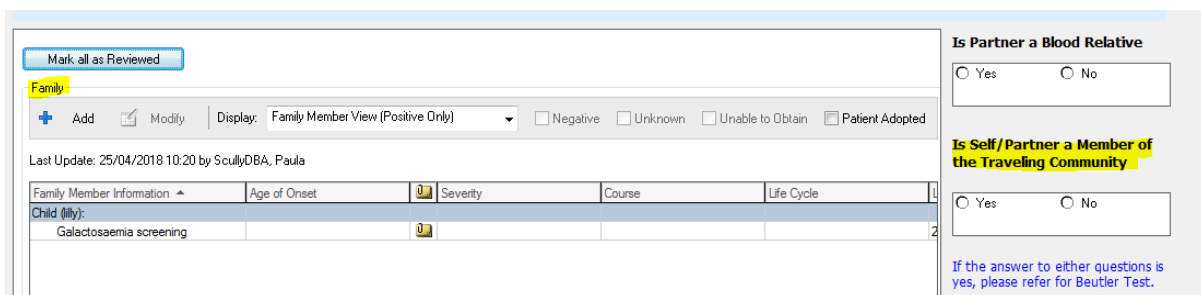
MN_CMS went Live 18th of November 2017.

Family history screen - a midwife sits down with the patient on front of them and they're going through these questions - on the right hand side here we have the self/partner member of the Travelling community.

You can see here where it asks is she a member of the Travelling community, there is actually a line underneath it to state please refer for the Beutler test, so that's like a little reminder to say to Mum, well your baby will need to have a blood test done within 24 hours and to consider the Wysoy feeding.

Does everybody get asked these questions?

Yes, because we don't know here today who is a Traveller or non-Traveller.



Family Member Information	Age of Onset	Severity	Course	Life Cycle
Child (M):				
Galactosaemia screening				

In the genetic history it's where you'll find more information. In relation to Travellers so going to Mum first you're going to say she **Irish Traveller** herself... and her partner also, and coming down into the genetic history

*Performed on: 30/04/2018 0757 WEST

Named Clinician

Obstetrical History

Medical History

Procedure History

Family History

Genetic History

Social History

Allergy

Medication History

Vitals/Ht/Wt

Point of Care

Transcribed At

Current Pregnancy

Abdominal Pain

Antenatal Education

Antenatal Risk

Anaesthesia

Blood Transfusion

Infectious Disease

Psychosocial/

DV

Mental Health

Physical Exam

Mental Status

HEENT

Thyroid

Genetic History

Ethnic Background

	Self	Baby's father	Comment
African			
Asian			
Cajun			
Caucasian			
French Canadian			
Greek			
Italian			
Irish Traveller	X	X	
Jewish			
Mediterranean			
Other			

Genetic Disorders History

	Self	Baby's father	Other relative	Comment
Birth Defect				
Congenital Heart Defect				
Cystic Fibrosis				
Down's Syndrome				
Haemophilia Genetic Screen				
Huntington's Chorea				
Maternal Metabolic Disorders				
Fragile X				
Muscular Dystrophy				
Neural Tube Defect				
Recurrent Pregnancy Loss or Stillbirth				
Sickle Cell Disease				
Tay Sachs				
Thalassemia				

Are there any other decision supports within the system say if mum and dad are Asian; is there support for haemoglobinopathy screening?

Yes, we have the adult haemoglobinopathy screen or the baby haemoglobinopathy screen. Looking after adults you have to fill out all the details, maternal family origin, drop down menu helps -which disorders you are checking for.

Search: Advanced Options Type:

Folder: National favourite folder Search within: All

Orders for Signature

Details for Haemoglobinopathy

Details Order Comments

*Collection date/time?:

Antenatal?:

Gestation (wks):

*Maternal family origin?:

Ireland, England, Scotland, N Ireland, Wales

Caribbean Islands

Africa (excluding North Africa)

Any other African or African-Caribbean

India or African-Indian

Pakistan

Bangladesh

China, Hong Kong, Taiwan, Singapore

Thailand, Indonesia, Burma

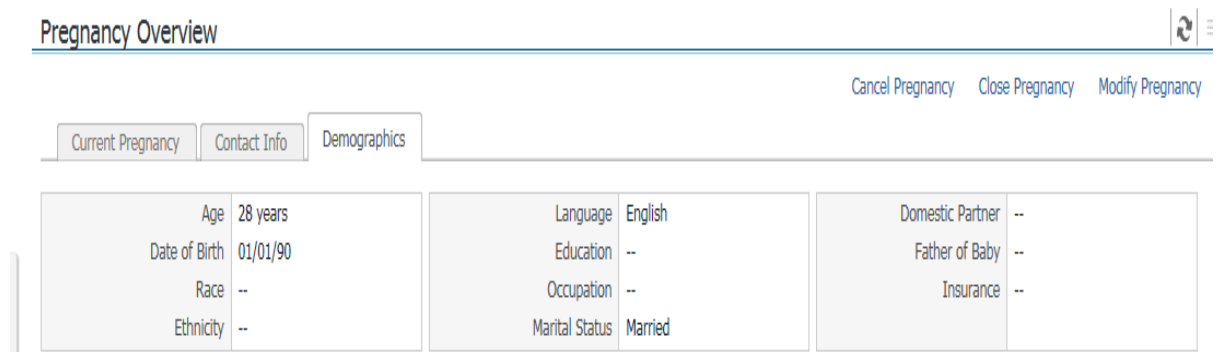
Malaysia, Vietn, Philipnes, Cambodia, Laos

Any other Asian family origins

North Africa, South America etc

Have you had any reluctance from people about having all this information caught electronically; has there been a difference in attitude when compared to paper charts?

No, people are quite willing to have their information and they know it's a health issue there is no difference now between the paper chart and the electronic system. We can see it displayed on the pregnancy overview.

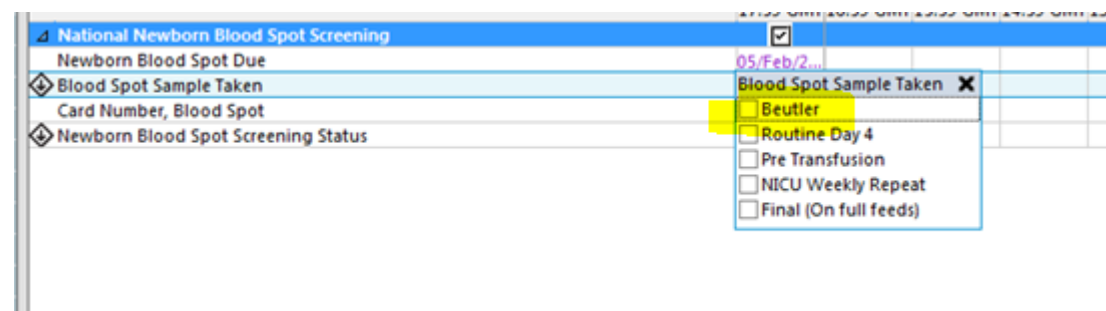


Do samples for blood spot go to the Laboratory here?.

No, it's point of care test.

Do you know if those Day One tests particularly for the Travellers, that they get that Beutler test - is that the same process?

Yes, it would be scanned in and it would also be recorded the date and the time it was actually taken. This is the Blood Spot Screen window.



So it's a completely separate here for the Beutler Test?

It has its own section within the record. There is specific support because once you open up that it is a Beutler performed, you have a section for whether it was a sufficient sample and whether the test


result was normal or abnormal. Temple Street ring if it's an abnormal results. And then that information will be added to whether it's abnormal or normal.

	10:00 -
	10:59 WEST 0
▾ National Newborn Blood Spot S...	<input checked="" type="checkbox"/>
Newborn Blood Spot Due	30/Apr/20...
▾ Blood Spot Sample Taken	Beutler
▾ Beutler Test Performed	Yes
▾ Beutler Test Result	◇
▾ Taken	◇
Card Number, Blood Spot	12345
▾ Newborn Blood Spot Screening St...	Completed

Is there a way to create a flag that the patient/infant is a Traveller?

Yes, It doesn't tell you what the flag is, you have to click into it to see what the risk is. You can flag clinical risk, or social risk or infection risk depending on needs, but I haven't seen any Travellers with that flag used that way.

Risk Factors (1) +

Risk Factor	Added By	Date Added
▾ Other		
metabolic disorder	 Paula	25 April, 2018

There is a consanguineous flag there. If the risk is not named on the list, there is a field called other, and you can just text in what the risk is so this is not a flag but it is a risk Factor...and will appear in the banner. When I opened this patient's pregnancy overview now I can see that there is a risk Factor and in there it shows the risk Factor and who added it. So you could have here that the patient is Irish and consanguineous.

The screenshot shows a medical software interface for a patient named Zzztest, Rotipims. The patient's details include Age: 28 years, Sex: Female, MRN: H01189090, and EDD: 16/04/2018. The interface has a 'Histories' section with tabs for Past Medical, Procedure, Family, Social, and Pregnancy. The Pregnancy tab is active, showing a table with columns for Delivery/Outcome Date/Time, Gestation Weeks, Pregnancy Outcome, Length of Labour, Gender, Weight, and Anaesth. Below the table is a 'Gravida/Para' section with input fields for Gravida (1), Para Fullterm (0), Para Preterm (0), Pregnancy Loss (0), and Living (0), along with a 'Child Living Comment' field.

In the absence of paediatric EPR is there a discharge summary to the GP and is their risk Factor included in that communication?

Diagnoses and problems are included when you're discharging a patient, one letter goes to GP for mum and a second one for the baby .

You have your own Order communications system, is this separate to what's going on with MedLIS?

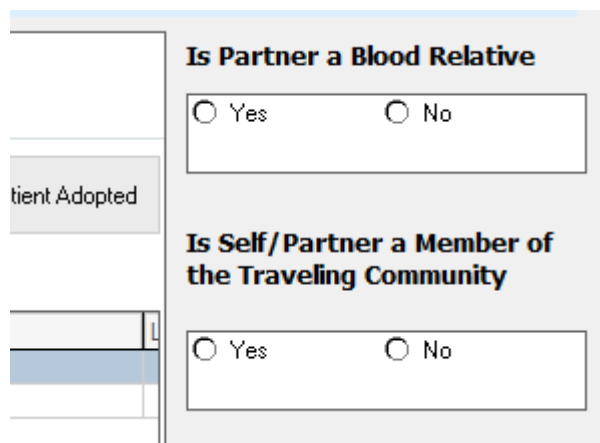
Whatever information is fed into iPIMS, as in the patient information, general basic information, will feed a cross into Millennium too. So all visits, all demographics information, next of kin, GP, will feed in here. We go to orders and in the search box we type in what we want, pick test, this will print out a label and then there is the specimen collection window. You're preparing the order here and then you have the collection step. Where you scan the patients wristband for positive identification. I print my label from that, it goes into a plastic bag, and down to the Laboratory.

Subject 8: MN-CMS TEAM MEMBER ROTUNDA

Email interview, summary of information garnered from three correspondence exchanges.

I was curious how this order request and the information that Mum is a Traveller is collected into MN-CMS. Can use that information to create flag linking a widget out of Order communications to our database?

Patients should be asked at booking if they are a member of the travelling community. This does not flag anything though and is only recorded.



The image shows a screenshot of a web form. On the left, there is a vertical sidebar with a button labeled 'Patient Adopted'. The main form area contains two questions, each with 'Yes' and 'No' radio button options. The first question is 'Is Partner a Blood Relative' and the second is 'Is Self/Partner a Member of the Traveling Community'. Both questions have their respective radio buttons unselected.

After delivery, Beutler status also needs to be recorded as part of the discharge checklist for the baby which goes across to the discharge summary for the GP & PHN. The Beutler is not ordered as a lab test and is sent to Temple Street as the POC test, as it always was before MN-CMS. The national team have discussed integration with Temple ST NBSS system but it's not in scope at the moment.

Does the booking-in ticked box indicating that Mum is a Traveller in any way prompt the team to take the Beutler card? I'm still not sure of how the midwife knows to take the card.

The tick box doesn't go anywhere. It's just documentation. There is no 'Flag' for the midwives at delivery.

Subject 9: LABORATORY SPECIALIST NNBSL

Summary of taped interview, transcript in full runs to 2562 words.

Irish Traveller newborns receive enhanced screening for Galactosaemia - can you please explain that process?

Bloodspot screening including Galactosaemia, at day 3-5, is offered to all babies born in the Republic of Ireland. For Travellers, a bloodspot sample is taken on Day One, before the child is on any kind of normal feeds, for us to rule out classical Galactosaemia, and we request that they keep the babies on soya - lactose or galactose free feeds until we have the results of that Beutler test.

You are one of the only sources of an accurate number of many Travellers are born in Ireland. The Census and the All Ireland Traveller Health Study differ between the two of them.

We know how many Beutlers we get in, - we got 1745 in 2016, and total of 72,745 screening cards. 99% of Beutlers are from the Traveller population. The card says Irish Traveller, Soy feeds, Beutler, or family history of galactosaemia.

If we didn't have the Traveller population, our level of Galactosaemia would be equal to that in the UK?

Yes. And it is worth noting that the UK don't screen for Galactosaemia. Scotland used to screen for Galactosaemia in their newborn screening up until 2012, and then they stopped screening.

Are there any other conditions in specific targeted ethnic groups that could be added to Newborn screening in Ireland?

ADH-SCID for Travellers, and maybe Sickle Cell in Afro-Caribbean.

In CN-MNS there is a specific tick box for the question "Are you a member of the Irish Traveller Community?" So it is a specific data point now collected, do you see it being useful perpetuating that data point into national Children's Hospital EPR and on into adult records - obviously, only if consented for? Do you think it could enhance diagnosis?

I suppose it sets off alerts if a child is unwell. If it cascades questions I can see as a being a very useful clinical diagnostic tool.

I know most non-Travellers get this card taken in the community as it is Day 3 and they have been discharged from hospital. Because these are Day One cards for the Travellers they would all be done in hospital?

Yes the majority are done in hospital. When the sample is taken, the parents are given a parental information leaflet before they consent.

Is the consent process for the Beutler specific, or is it the same as the all in one newborn screen?

The consent for the Beutler would be specific. The consent for the routine screen would follow again. Both use the same consent on the bloodspot card and parent information leaflet.

NATIONAL NEWBORN BLOODSPOT SCREENING LABORATORY				CPA Accredited Medical Laboratory Reference No: 2646		Laboratory number only	
Gest. Age webks	Time of Birth H H M M	Date of Birth D D M M Y Y	Baby's Unique Perinatal Identifier (UPI) - MANDATORY				
Birth Weight kgs	Rank	Gender <input type="checkbox"/> M <input type="checkbox"/> F	Date of First Feed D D M M Y Y	Baby's Surname			
RBC Transfusion Received? <input type="checkbox"/> Y <input type="checkbox"/> N If Yes	Date of First Transfusion D D M M Y Y	Time of First Transfusion H H M M	Baby's First Name				
Type of Feed <input type="checkbox"/> Breast <input type="checkbox"/> Artificial <input type="checkbox"/> TPN <input type="checkbox"/> IV fluids <input type="checkbox"/> Soya/Lactose free	Date of Last Transfusion D D M M Y Y	Time of Last Transfusion H H M M	Baby's Address				
Comments/Family Hx/Beutler			Hospital/Place of Birth				
Date of Collection D D M M Y Y	Time of Collection H H M M	Repeat Specimen <input type="checkbox"/> Y <input type="checkbox"/> N	Baby's Healthcare Record number (if transferred to another hospital)				
Sample taker's name (Print): _____			Mother's Surname				
Sample taker's Contact number: _____			Location Sample Taken <input type="checkbox"/> Community <input type="checkbox"/> Hospital / Ward				
Parent/Guardian preferred language: _____			Health Area				
I confirm that the details on this card are correct; I have read the information leaflet. I consent to my child being screened.			GP's Name and Address				
Parent/Guardian Signature: _____							

901201

Laboratory Copy

Subject 10: LABORATORY POCT SPECIALIST ROTUNDA

Email interview, summary of information garnered from five correspondence exchanges.

When asked how the Beutler Test is recorded on the laboratory system Subject 13 replied that they have no information on this as it does not come through the laboratory, and that samples are sent directly from the wards to NNBSL. Subjects 9 and 10 confirmed this and added clarification that the samples are collected on the wards, then brought to Paediatric Outpatients, from where they are collected and brought directly to NNBSL. Based on this information, interview was not conducted with Subject 13.

Summary of interviews to describe diagnostic processes and order communications

Subject 11: MEDLIS CLINICAL LEAD

Summary of taped interview, transcript in full runs to 7340 words

In MN-CMS there is a specific tick box for asking is the patient or partner a Traveller. In Order Communications biographic/demographic window would you have that this person is recognised as a Traveller?

I don't know that would be very sensitive. I'm not sure that it's in MedLIS now. If you look at there are 5 million liver function tests done annually... you can't really have a pop-up asking if the patient is a member of the Travelling community for all of those!

No, the demographic feed would filter Travellers. Is there going to be that functionality within the Order communications to use demographic data to inform test selection?

So you are asking first is there going to be anything that catches that data and then how does that interact? Whether the order comes in Cerner systems are clever enough to present different care sets to you when you're seeing somebody who's a member of the Travelling community? Certainly there are limitations. For example, when somebody tries to order a PSA on a woman it doesn't stop them. It seems terribly cumbersome to do anything that involves rules.

Is there any function in MedLIS to have the likes of a link out to something else is there any support outside or is it all just pop ups in MedLIS itself?

There is capability to have a small number of buttons at the top and were hoping that one of those we can claim for the National lab handbook which will be a suite of guidelines around all of the tests. Certainly we could have a link to the database in the handbook but, what you don't want to do is draw down any negative publicity, and you don't want there to be any concerns about identifying particular groups if it is sensitive. Has there been no exposure? – so unhappy going to Pavee Point?

They aren't the only Traveller group and they do not represent all Travellers. No one group does that.

Clinically, absolutely it's the right thing to do, but how acceptable it is depends a lot on how you handle it. If you have to identify Travellers, nobody is going to be happy to flag on a system something where the politics of it hasn't been dealt with.

In current exiting protocols Travellers and Non-Caucasians already have different screening algorithms in everyday practice at a national level. Within maternity services, it is self-identified by both parents.

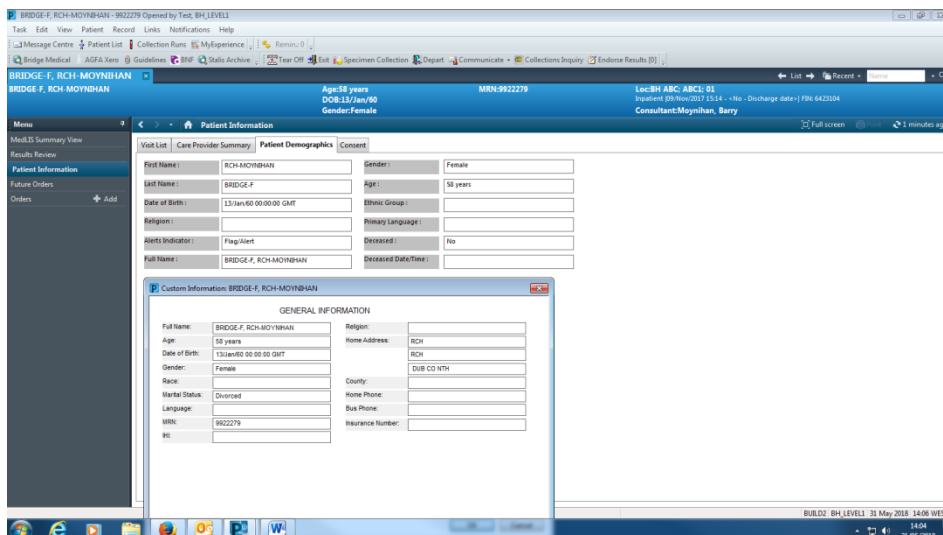
And those kids are now being captured as Traveller? MedLIS aren't going to put a button for a link to the Traveller database on something where there's going to be a huge amount of publicity when it goes live. To suddenly have the Travellers up in arms saying this is totally unacceptable, we knew nothing about this database, and here it is linked to the National Lab information systems...nobody will take that risk. And you can only process the data for the purpose it was collected, so the purpose the Traveller Identity was given here was for the day one heel prick test and the immediate management of that.

No, it is not explicit in the MN-CMS booking in what that data point is captured for. Consent for the Beutler is separate.

But it's probably not explained that it's envisaged that the label was stick with you?

Yes that is the issue of the data point being collected from Day One...that it only has to be collected once and it perpetrated throughout subsequent records with consent.

You see I don't think it's being collected on MedLIS



It is there as race/ethnicity... but it's not as a separate field as "Traveller or not" as in MN-CMS.

If it's not seen as necessary to collect it to do the test well then the information isn't there. I'm just trying to think even if ... it was recorded that somebody was a member of the Travelling community and say in the future if that was captured in an EPR and was imported to MedLIS, to me, then the

decision support of broadening your differential comes earlier in the process of seeing the patient. To me that belongs in the EPR Dash, family history ... if you had natural language processing in an EPR that you could analyze the history, that you've typed in, click on a process and it would give a prompt – have you considered these rare diseases?

It sounds quite ambitious when it can't reject a PSA request on a female patient.

Unfortunately Order communications doesn't pull the demographic information. Either I'm sufficiently well trained to know that this is a member of the Travelling community and I need to take a history while the patient is undressing for examination and you pop into the app and see and then you can always ask the extra few questions. The other thing is that you would have an EPR and you would fill in the history as you go and that ethnicity would be the question is there that's all been done at the registry... I'm not going to be asking people racial information when they're through the door with me unless they offer it. It should be captured when the patient registers and their electronic chart is made up. They come in to take a history - now there's a very strong argument to have natural language processing, to be able to capture things, and if there was some, it would almost have to be part of a larger decision support.

That is a whole different level of complexity but still taking keywords we're trying to include that in the linked-out search feature so that you're using your SNOMED and ICD-10 terms that the language is structured for when systems are eventually linked together.

It would be incredibly useful to know that there are these alternative disorders and these alternative signs that you should look for that you wouldn't look for in anyone else. If there are key words at the history that a message will feed two because this is a member of the Travelling community who has X and Y you should consider a and b and you have a link that you can press to see what are the other features that I should ask about because that comes back to your clinical assessment. If my patient, a Traveller, that has hypogammaglobulinemia, then I should look to see if there's an associated syndrome... and it tells me there are visual features, although I wouldn't normally examine the eyes - I want that information when I'm examining the patient, not afterwards. The patient is getting dressed; you're starting your blood form at that stage. Ideally, you take the history and based on the history and at that stage you're told what to think about.

That's what we're thinking... with all this support for symptoms and phenotype in the search... that it's telling you what to look for next to refine the search or totally exclude the listed differential.

But that's totally before I get to MedLIS. So what I'm trying to think about is you now have your patient - they've got dressed again. You've already spoken to them about what you've think it might be going on and said I'm going to test you for this that and the other and I then go into MedLIS to order tests and all of a sudden something else pops up... then you might have to say "Oh, can you take off your clothes again so I can look for this?" It doesn't flow, it doesn't fit into the workflow. You're going to have the history, the examination, then you're going to decide what test to do so it's not ideal to have a whole lot of new stuff thrown at you at the time when you're ordering the test. If that information is pushed at history stage to consider x y and z disorders and you can go back and look for additional clinical features then well and good, but what you don't want is Clinicians to just walk off and order a list of genetic tests for all these disorders because the patient is a Traveller and the consultation is already over. So it's really clinical decision making rather than test ordering - I don't think Order communications is the place to have it

You're dealing with something that's an EPR function and how do you do that for 1% of the population?

The Travellers always just got the Beutler test... and I don't know how that was discussed/agreed upon formally initially. Galactosaemia screening was introduced in Ireland in 1972. Antenatal and neonatal haemoglobinopathy screening programmes targeting high-risk ethnic groups were established in the early 2000's at individual Irish maternity facilities – I didn't find any documents relating to consultation with the relevant ethnic groups in my literature search.

That's fine as long as you're not going to make it part of a national system. If to do that in any way that is high profile you have to be careful. You need clarity around what the tool does and where it fits in the diagnostic process and you're talking about something that's relevant to kind of 1% of the population. MedLIS currently isn't capturing that 1% so I just can't see how you pulled that into Order communications.

I think what you're talking about is an EPR function. What we can do is put a link from the Lab handbook to the tool wherever it lives once people know it exists they know where to find us it. If you're saying there's this great tool for genetic diseases in the Travellers, well then the Travellers have to be aware of it. In the same way as...click on this button if they're black... nobody would say that unless it had been discussed with the relevant populations and patient representative groups. You can't ignore the sensitivity. In real life you can't so you can't risk a national laboratory information system failing because you link to a diagnostic resource for Travellers.

Subject 12: MEDLIS TEAM MEMBER NATIONAL OFFICE

Summary of taped interview, transcript in full runs to 7120 words

Subject 5 mentioned that MedLIS is quite limited in terms of what is available to link out to, that there are only a small number of buttons available for additional options such as link to National Lab handbook, as a PDF. She advised me to speak with you about the technical side of Order communications. She advised that MedLIS does not use the demographic information in any way, for example, not stopping an order of PSA for a female patient. No demographic based rules.

Yes, these are some, but interestingly we don't record ethnicity. All of our patient information will come from the local PAS system. We had to decide from a lab point of view which demographics we need. Actually ethnicity might be coming over.

I spoke with Subject 13 in Beaumont, she said ethnicity is there but whether it is used is a different story. Unfortunately with the national iPIMS system, there is very little standardisation, and 18 sites have it, it has been tweaked locally. So whatever you want to call an Irish Traveller, you can call it, but there wasn't any standard code applied.

Within ethnicity fields in MN-CMS- Irish Caucasian is higher up on list so you choose that before Irish Traveller is even revealed on the pull down list. The ethnicity field isn't an ideal field to hold the information. It is handled as a specific question/data point in MN-CMS outside of ethnicity, the direct question is asked - are you or your partner a member of the Travelling community. And there is prompt to tell Mum that a Beutler test should be done. So Traveller support is built into MN-CMS, much more than just an ethnicity field .It is very strong as a clear data point to be carried on out of the MN-CMS record.

Order communications wouldn't have any of that - the priority is electronic orders in and results out. That is the application the Cerner provides. If it is not about which test you are going to order, or looking at the result, then the support is not there.

I also saw some support for haemoglobinopathy screening in MN-CMS. There's probably a few bits and pieces when you order the test in the National Test Catalogue OEF - the test order form, will be different. We have tried to keep them as standardised as possible because 80% of what is being ordered are the same 50 tests. It is the other million lab tests that require the additional information.

Subject 5 said trying to apply all of the rules for immunology is challenging. We are trying to put in some rules, but they are more associate with the test itself - if you order an FBC there are no extra questions whereas depending on the test, even something as simple as coagulation screens you will

get questions asking whether the patient is on an anticoagulant. These are known as Order Entry Prompts. They are mandatory fields.

Subject 11 that she was hoping to get a button linking to the handbook, and that a lot of work has gone into that document. Why is difficult to get something so simple in the system?

This would be seen as the cherry on top. We are still working on basics around the common tests. 80% of diagnoses are made based on laboratory tests.

That is what prompted me to ask the question whether Order communications would be the correct location to trigger and launch the CDS, so it would be part of the diagnostic process - when the clinician is at the interface... in the absence of EPR this is where that opportunity exists - if you could pull the demographic data point.

The button that we are hoping to have link to the handbook, you could certainly have a link there.

Have you any experience in the Mater metabolics with disproportional workload from the Traveller population. Subject 11 said that as Travellers represent only 1% of the population it might be difficult to build a case for specific support in national systems.

We had to introduce many new tests. We set up care sets for our ED. If possible, come in here, if you feel unwell, for those patients to come to the Mater and the ED clinicians would know what to do to link in with experts. We will be building care sets into MedLIS. I've put forward the metabolic Traveller care sets to be included, they will be getting built into the system. Within Powerchart there is a metabolic medicine folder, you can see Traveller care sets in there. These spell out which tests to order depending on presentation, rather waiting for the Metabolic Consult and asking them if it is okay to order the tests. The results should start coming back even before the metabolic consultation.

Our disorders could even all nearly go onto a Panel chip - you could have just one test to cover everything, but that is really screening rather than a diagnostic test. It would be fast and sensitive though, and include carrier status. Could be applied in a similar manner to the DorYeshorim in the Jewish population in the US, where they have eradicated several common disorders by introducing this approach.

Subject 11 is linking in with all the specialties to develop care sets - if they design them, we can add them, but it isn't up to us in the National Office to make those decisions, it has to come from a national clinical program. That might be a route for getting metabolics care sets built into MedLIS, Traveller sets that would be different to non-Traveller sets.

Subject 11 was reluctant to have Traveller specific options. But it very clearly included in MN-CMS for optimal patient care, the data isn't just being collected for census reasons, it forms part of the risk assessment for the pregnancy.

And in GDPR that is perfectly okay. It makes sense; It is related to the patient's health care.

It's being given by the patient themselves as part of booking in, they are self-identifying as Travellers, the process around the Beutler is accepted. If we are trying to close the Health gap surely we need to maintain that robust Traveller Identity into all EPR. Subject 11 thinks it should be recorded as part of registration but it rarely is.

We would be looking for the HSE to approve a patient minimum data set. The only safe way to merge all patient data from a laboratory point of view is by having IHI in place. So if the record from St James and the Mater both have the same IHI their records will be merged in Millennium to create the Laboratory patient record, they are identified as the same patient. There are 3 and a half genuine duplicates in the country, which is name, date of birth, and gender. Of those only 82 if you include mother's birth surname, or eircode, or PPS number. We want to record one of those three additional pieces of information.

Is there anyone else requesting that ethnicity is part of the minimum data set for laboratory?

No we wouldn't ask for that, it is difficult to accurately record.

Yes, I looked at a New Zealand study that recommended a minimum of 6 fields to record ethnicity.

The more useful approach would be to have it as the single question, are you a member of the Traveller community, yes or no.

Yes that is the conclusion I have come to, and the approach taken by MN-CMS. Ethnicity just isn't the specific enough. This is mirrored in the publications forming the catalogue; Traveller ethnicity is not explicit, while Caucasian Irish or British is.

Yes agreed, a binary point. And everyone gets asked the question and that is it. I imagine that would be perfectly acceptable to ask and record.

Subject 11 advises it would need to be agreed with the Traveller groups or there could be a back lash.

That needs to go back to the PAS systems, where you are gathering the information. Either is displayed in the demographic information, or as a flag.

Subject 11 was reluctant for there to be any sort of Traveller flag anywhere in Order communications because it could be seen as discriminatory, without it being discussed with the representative groups, but I don't think the support built into MN-CMS had a consultation process with those groups.

Yes, and as a paper based process for many decades preceding MN-CMS. If the HSE advised that it would be something MedLIS should support than it would be adopted. iPIMS would have to include it, and the HSE would have to advise its inclusion in the basic data set for a National System. We want those three fields previously mention, mothers birth surname, PPS and eircode added to the basic data set. Eircode is due as a specific field in the next version of iPIMS rather than just part of address. Until we have IHI each person is going to have many different records in Millennium. The next time I go to OPD if they ask for that additional field - probably mother birth surname as nobody knows their PPS or Eircode.

Mums surname might not be so strong a fifth identifier in the Traveller population due to the endogamy. Eircode also might be difficult with multi-generational extended families living in close proximity in halting sites. How far off having IHI are we?

We are trailing loads of migrated data. CareXML by Stalis is subcontracted as a repository for all the laboratory records. All the previous results will be there, but you will only able to see your own organisation. What is going to feed into Millennium will be certain serology, blood transfusion and histology, the last ten years.

Any other clinical decision support in the laboratory system - Subject 11 says in belongs in the patient notes.

It should be in an EPR. The only information we need in the lab in the information to process the test and that is what will be on Order communications and MedLIS. For example, if the patient is on Warfarin for INR, where patient has travelled and did they take prophylaxis for Malaria requests, AKA algorithm for kidney damage, this data collection is all there for interpretation help/decision support in the laboratory.

Subject 13: MEDLIS ORDER COMMUNICATIONS PROJECT MANAGER

Interview with this participant was not recorded and involved demonstration and screen capture of relevant windows and functions in MedLIS Order communications.