An Investigation of the Information Processes and Requirements in the Care of Patients with Hypermobility Type Ehlers-Danlos / Joint Hypermobility Syndrome.

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Author Declaration

I declare that the work described in this dissertation is, except where otherwise stated, entirely my own work, and has not been submitted as an exercise for a degree at this or any other university. I further declare that this research has been carried out in full compliance with the ethical research requirements of the School of Computer Science and Statistics.

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Abstract

Joint Hypermobility Syndrome (JHS) is considered virtually indistinguishable from Ehlers Danlos Syndrome Hypermobile Type (EDS-HT), although full consensus may not occur until the genetic marker is found. Although this rare, heritable connective tissue disorder (HCTD) has a variety of potentially disabling systemic effects, clinical scepticism of its impact on the patient still exists. The myriad of associated dysfunctions affect virtually every body system. The financial burden of the syndrome is likely to be considerable.

Recently, strategies for recognition and management of rare diseases have been developed at international and national level. Information technology can play a key role in the implementation of these strategies.

Education, communication and information gaps exist at almost every stage of the EDS-HT patient journey. Ideally, all clinicians involved in the care of EDS-HT patients would have timely access to valid, reliable and complete patient data at point of care.

Standardisation of the essential information or data that is relevant to the care of EDS-HT patients, can ensure that data is complete, relevant comparable and capable of aggregation for population studies, thus attracting interest and funding for further research. This research presents the methodology and the first iteration for development of an EDS-HT minimum dataset.

The design and development of appropriate informatics solutions may facilitate safe storage and timely retrieval of data and an opportunity to support and transform care for patients with EDS-HT.

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Abbreviations

CCM	Chronic Care Models
CDE	Common Data Element
CoE	Centre of Expertise
DE	Data Elements
DOH	Department of Health & Children
DSE	Disease Specific Elements
EDS	Ehlers Danlos Syndrome
EDS-HT	Ehlers Danlos Syndrome - Hypermobile Type
EHR	Electronic Health Record
EpiRare	European Platform for Rare Diseases Registries
GH	Generalised Joint Hypermobility
GRDO	Genetic and Rare Disorders Organisation
HCTD	Heritable connective tissue disorder
HGVS	Human Genome Variation Society
HIQA	Health Information and Quality Authority
HPO	Human Phenotype Ontology
HRQOL	Health Related Quality Of Life
HSE	Health Service Executive
HT	Hypermobile Type
ICCC	Innovative Care for Chronic Conditions
ICS	International Classification of Diseases
JHS	Joint Hypermobility Syndrome
LIMS	Laboratory Information Management System
LRG	Locus Reference Genomic
MDS	Minimum Data Set
NIMIS	National Integrated Medical Imaging System
OMIM	Online Mendelian Inheritance in Man
PAS	Patient Adminstration System
POTS	Postural Orthostatic Tachycardia Syndrome
RD	Rare Disease
TMJ	Temporomandibular joint
VPN	Virtual Private Network
WHO	World Heath Organisation

1 Introduction

1.1 Study Background

Joint Hypermobility Syndrome (JHS) is considered virtually indistinguishable from Ehlers Danlos Syndrome Hypermobile Type (EDS-HT), although full consensus may not occur until the genetic marker is found (Tinkle et al., 2009, Grahame and Kazkaz, 2014). Although this rare heritable connective tissue disorder (HCTD) has a variety of potentially disabling systemic effects, clinical scepticism of its impact on the patient exists (Graham and Bird 2001). The myriad of associated dysfunctions affect not only joint mobility but also skin elasticity and repair, mental health, sleep, vision, autonomic regulation, pain mechanisms, dental and bone health, genito-urinary and gastrointestinal systems (Adib, 2005, Grahame and Kazkaz, 2014, Engelbert, 2003, Mishra, 1996).

European criteria define rare disease as a chronic or debilitating disorder affecting no more than 5/10,000 of the population (Aymé, 2012). Long considered a heterogeneous group of rare genetic disorders, the Ehlers Danlos Syndromes affect from 1-5000 to 1-20000 individuals (Steinmann, 2002, Beighton et al., 1998). EDS-HT, the most common type, is thought to represent up to half of all EDS presentations although there are no epidemiological studies confirming its true incidence (Castori, 2012a). By contrast, the incidence of asymptomatic generalised hypermobility is estimated to be 10-30% (Hakim, 2006). According to Castori (2012a) differentiating between generalised hypermobility and HCTDs is of utmost importance for preventing potentially life threatening complications and/or early detection and management of long-term disabilities.

The financial burden of the syndrome has not been estimated but is likely to be considerable.

1.2 Rationale for the Study

The term ‘hypermobility’ is often interpreted clinically in its purest definition, and mistakenly considered synonymous with ‘hypermobile syndrome’. Clinicians who are unfamiliar with the syndrome, but who provide ongoing or episodic care for persons

diagnosed with JHS, may assume that hypermobility is merely a benign, non- systemic peculiarity, particularly if the referral received or the patient themselves does not explicitly mention a 'syndrome'. This lack of knowledge, both of the equivalence of JHS with EDS-HT, and the systemic non-joint related symptoms, may lead to dismissal of symptoms, delays or errors in treatment, patient frustration , and lack of faith in the clinician.

Since self-management is critical to successful management of this lifelong condition, patient education and access to validated information is vital. The development of expert patient programmes acknowledges the role of the informed patient in the management of chronic diseases (NHS, 2014, Lorig, 2001, Wagner et al., 1996, Holman and Lorig, 2004). Ideally, all clinicians involved in the care of EDS-HT patients would have timely access to such information and could direct the patient to this information as needs arise.

Communication of information about the syndrome, its presentation and management, is paramount to delivering knowledge based care. Although there has been an exponential increase of both clinical literature and online information about the syndrome, clinicians must firstly become aware of their own knowledge gaps in order that they seek out or 'pull' the information to support and care for patients with EDS-HT. In the absence of this knowledge, particularly in ongoing primary care, EDS-HT patients must rely on the transfer or 'push' of information from experts to non-experts. This may be achieved by standardizing the essential information or data that is included on an EDS-HT patient record, and ensuring that the record is available at the appropriate time. Informatics solutions may ensure timely delivery of information during episodic or ongoing care.

1.3 Relevance of the Research

The overall aim of this research is to provide an essential information template for use by all clinicians involved in the care of patients with EDS-HT / JHS and by its use to promote awareness and knowledge of EDS-HT / JHS amongst clinicians who provide primary or episodic care for this patient group so that they are directed to both clinical and patient information sources as needs require.

The research will contribute to the development of a model of care for EDS-HT / JHS patients. The research is timely, as the feasibility of a national specialist hypermobility service for Ireland is being investigated. The design and development of appropriate informatics solutions may facilitate safe storage and timely retrieval of data and an opportunity to support and transform care.

1.4 Objectives of the research

The research focused on identifying what information is essential to care for individuals with EDS-HT. The development of a minimum dataset for inclusion in any potential technology solutions was a key priority. The objectives of the study are identified in Table 1.

Table 1 Objectives of the Study

To identify the likely clinical information break points in the care of patients with EDS-HT / JHS,
To identify essential data collection which should be included in referral / transfer of care in ongoing primary care or episodic specialist care of this patient group,
To investigate information technology solutions for the safe storage and timely access to this data,

1.5 Research Question

The aim of this dissertation was to investigate the information processes and requirements in the care of patients with EDS-HT /JHS and to establish the essential data required for that care. The research was designed to answer the following question;

What information and knowledge, as identified by expert EDS-HT clinicians, do clinicians who are non-expert in EDS-HT need, to care for and support patients with EDS-HT?

1.6 What Is The Purpose Of The Research?

The purpose of this study is to propose and evaluate a standard description of essential data in the care of patients with EDS-HT / JHS and to identify potential technological solutions and any challenges that may exist.

1.7 Overview of the dissertation

Chapter 1 This chapter provides the background to the research, rationale for the research, the research questions, and an outline of the dissertation.

Chapter 2 Presents the literature review to provide background information on rare diseases, and the evaluation and diagnosis of EDS-HT. The challenges to provision of care to this group are outlined. The potential role that information technology can play is discussed.

Chapter 3 Identifies successful methodologies for the development of minimum data sets.

Chapter 4 Presents the research design and methodology used for the research.

Chapter 5 Presents the literature review for identification of the data elements relevant to EDS-HT.

Chapter 6 Presents the results, analysis and discussion

Chapter 7 Presents the recommendations for future work and conclusion of the dissertation.

2 Literature review

2.1 Introduction

The following chapter will define rare disease and identify the challenges to provision of care for patients with rare diseases. Generalised Joint Hypermobility (GH), Joint Hypermobility Syndrome (JHS) and EDS-HT will be defined and discussed in the context of both a rare and chronic disease.

The literature review will then identify information and communication gaps in the care of patients with EDS-HT. The role that information technology can play in bridging these gaps or providing solutions will be discussed.

2.2 Rare Disease

2.2.1 Overview

Rare Disease is defined within the European Regulation on Orphan Medicinal Products as a life-threatening or chronically debilitating disease affecting no more than 5 people per 10,000 (Ayme and Rodwell, 2014). Although the low prevalence of a particular disease renders it rare, collectively 5000-8000 rare diseases exist, affecting 6-8% of the European population or 27-36 million Europeans (Council of the European Union, 2009). Rare disease thus represents a serious international health burden.

Nationally, the Department of Health Ireland have adopted the EUCERD definition and state that up to 300,000 Irish citizens may be affected by rare disease during their lives (Dept. of Health and Children, 2014). This national rare disease plan acknowledges that the prevalence of various rare diseases in Ireland may differ from the international or European experience. Notably, the report states that the six rare diseases screened for at birth, namely cystic fibrosis, phenylketonuria, homocystinuria, classical galactosaemia, maple syrup urine disease and congenital hypothyroidism, all have a significantly higher prevalence in Ireland than worldwide.

2.2.2 Challenges to provision of care identified by RD stakeholders

The WHO considers the highest attainable standard of health to be a fundamental right of every human being, including access to timely, acceptable, and affordable health care of appropriate quality (WHO 2013). Particular challenges in meeting the healthcare needs of patients with rare diseases and their families have been identified by the European Commission (2008) and Eurordis (2013). Common challenges identified include;

- Lack of specific health policies for rare diseases,
- Lack of expertise, leading to delays in diagnosis or misdiagnosis,
- Difficult access to appropriate multidisciplinary healthcare,
- Lack of quality information and support for patients, families and clinicians.

Accordingly, these factors result in additional physical, psychological and intellectual impairments, inadequate or even harmful treatments and loss of confidence in the health care system. Social consequences of erroneous or delayed diagnoses may include altered relationships or isolation due to familial / social disbelief in the presence or impact of any illness, perhaps mirroring clinical scepticism. Furthermore, misdiagnosis often ends the quest for the correct diagnosis resulting in further delay and erroneous treatments. Such delays in correct diagnosis were reportedly 2.5-14 times longer for patients who received an initial psychological or psychiatric misdiagnosis (Eurordis, 2013).

Dept. of Health and Children (2014) recognises that the challenges faced by rare disease patients, their families and health professionals may be amplified in a country with a small population such as Ireland, where patients with a particular rare disease may be few in number.

Although timely diagnosis remains a key challenge amongst diseases of low prevalence, post-diagnosis management poses further challenges. While, some rare diseases are compatible with normal life, most rare diseases are complex, all are chronic or debilitating and all require appropriate management. Lack of clear, accessible, effective and integrated care pathways may further delay treatment or management of a disease. The development of these care pathways spanning primary care, local hospitals, regional centres and specialist clinical centres is integral to the care of rare disease patients (Dept. of Health (UK), 2009). A multi-disciplinary

approach to care is most frequently required, although the number of clinical disciplines and the frequency of clinical input may vary widely between diseases and from patient to patient within a particular disease.

In the last two decades, the global burden of chronic disease has attracted interest in developing strategies and models of care to enhance the continuum of chronic care in a cost effective manner. Whilst a number of fundamental differences exist between relatively common chronic diseases and rare diseases, an understanding of the models of care for chronic disease could provide a basis for the development of models of care for rare diseases which require a prolonged, shared care approach.

2.2.3 Chronic Care Models (CCM)

The Wagner CCM is an evidence based, conceptual framework designed to improve outcomes among patients with chronic illness (Wagner et al., 1996, Wagner et al., 2001) (Figure1). It consists of four essential components namely, efficient healthcare delivery systems, clinical and administrative decision support, supportive clinical information systems and self-management support, all nested within an appropriately organised health care system with links to community resources and supportive policies.

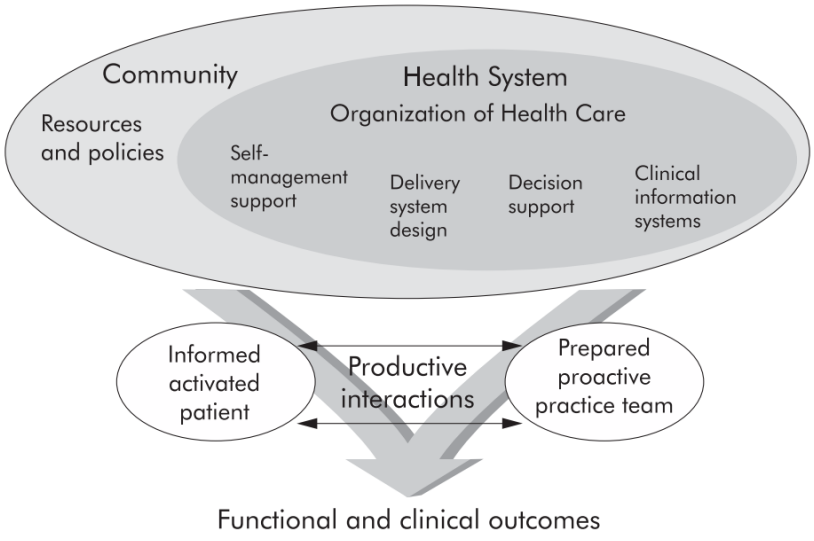


Figure 1 Chronic Care Model source Epping-Jordan et al., (2004)

This CCM was further developed by the WHO (2002,) (Figure 2) to address chronic care on three levels; micro (individual and local), Meso (broader community and healthcare organisations) and macro (population strategy and policy).

Wagners' original CCM stipulated that evidence based guidelines or protocols should form the bedrock of care for chronic conditions, but the subsequently amended model states that protocols are only useful if they are embedded within clinical and administrative workflow and practices such as reminders and alert notifications.

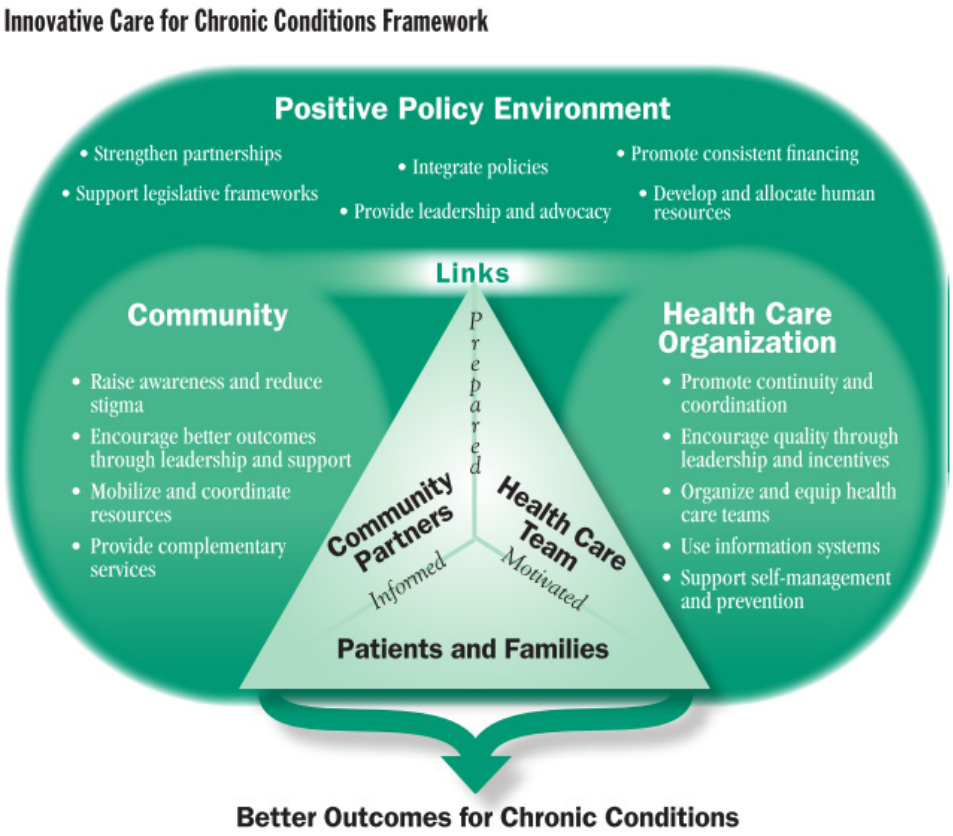


Figure 2 ICCC Framework source WHO 2002

Both models stipulate that traditional health care systems, designed to address acute illness are unlikely to be successfully adaptable to chronic care needs or expectations, thus new patient centred delivery systems are required which engage appropriate multidisciplinary team members at appropriate times. Furthermore, all healthcare providers must have timely access to professionals with clinical experience and expertise in the care of patients with any particular condition. Information technology has the potential to connect geographically distant clinicians to experts globally in a timely manner.

Self-management programmes help to develop informed and active patients who collaborate with prepared, proactive healthcare teams to maximise quality of life and

minimise the disease burden. Patients and their families must be empowered to better care for their illness through self-management support, including provision of information, skills, physical and psychological supports. A number of self-management programmes have significantly improved health outcomes and reduced disease burden at relatively low financial cost. The Stanford self-management programme has delivered significant improvements in self-efficacy, health status, and health behaviours, across a range of chronic conditions, delivered as a generalised or disease specific programme or delivered online (Lorig et al., 2001, Lorig et al., 2005, Lorig et al., 2008).

Robust information systems are essential at both individual and population level, to ensure timely access to information and data, and thus to appropriate treatment and management strategies. Currently, clinical and administrative information about an individual is gathered and stored in numerous locations on numerous isolated systems or paper charts. Moreover, information which is unavailable at point of care takes time to gather, resulting in frustration both for the individual and the health care worker and may even result in medical errors (I.O.M., 1999). Accordingly, the use of information technology has the potential to transform chronic care, allowing timely electronic sharing of information at point of care. Secondary use of data has the potential to facilitate population based decisions and strategies as well as provide opportunities for research and new treatments (Dept. of Health and Children, 2013).

Boult et al. (2008) developed a Guided Care Model, for care delivery to patients with complex, multi-morbid chronic disease by using the principles of the CCMs, combined with multiple technological innovations and driven by a highly skilled nurse. Following assessment and data entry into a specifically designed 'Guided Care EHR' the patient's individualized care guide is generated electronically using decision support algorithms, reviewed and modified collaboratively by the nurse, physician and patient/carer who receives a durable, hard-copy, summary action plan. The nurse monitors the patient and adapts the plan proactively in person or by telephone. The nurse is the key care co-ordinator particularly during care transitions and organising social care and receives electronic reminders if appointments are missed. The patient attends a disease self-management course, and this is enhanced with motivational interviewing technique by the nurse. Whilst this model is reserved for highly complex cases, guided care offers patients assistance in accessing and navigating complex multidisciplinary care needs. This model of care has the potential to be adapted to rare disease care. Figure 3 is a graphical representation developed to illustrate guided care.

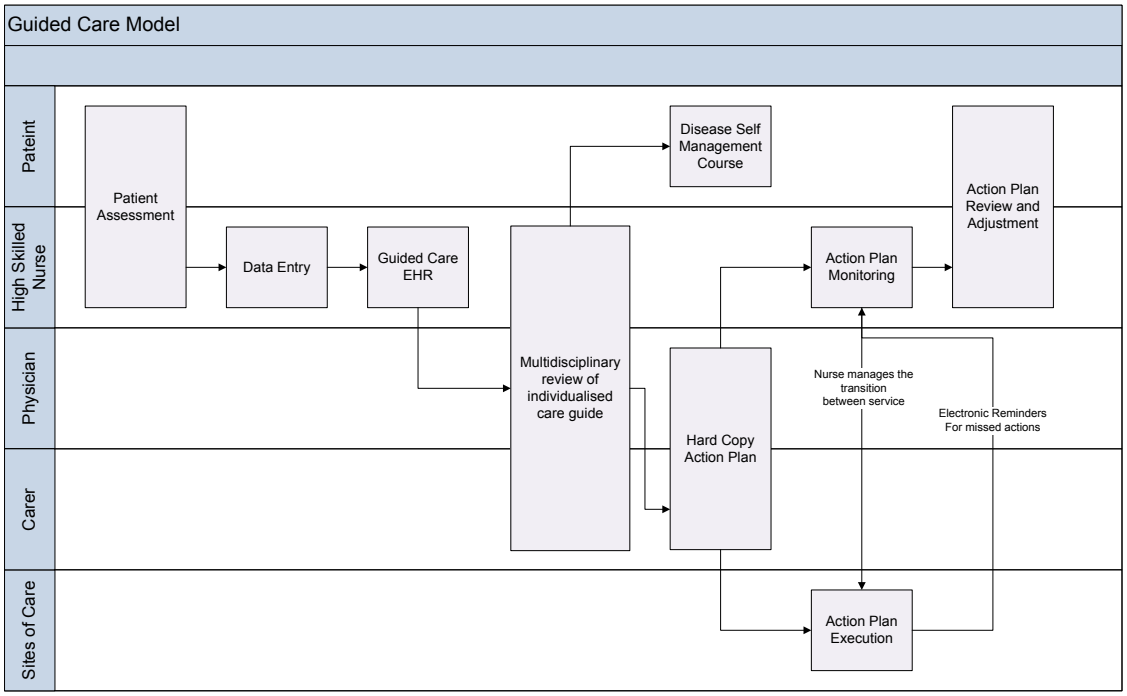


Figure 3 Guided Care Model adapted from Boult 2008

2.2.4 CCMs and Rare Diseases

In developing care models for rare disease a number of parallels can be drawn between rare disease and chronic disease.

Firstly, rare diseases by definition are either chronic and debilitating or life-threatening or both, therefore those that are chronic often require multiple healthcare interactions by a variety of healthcare and social care providers, at multiple locations over a prolonged time period. Clinical, commercial and governmental interest in developing systems designed for the delivery of health care in chronic diseases has increased in the last decade (WHO, 2002,, Young et al., 2007). These delivery systems may be adaptable to rare disease care.

Secondly, rare diseases are often incurable, thus learning to cope with the effects of the disease and preventing secondary complications or worsening disease state are potentially amenable to education and self-management programmes. When knowledge of a particular rare condition is lacking, either in clinical or social encounters, the skills to advocate for care and services could be developed through similar programmes. Furthermore, acknowledging and developing the role of the

patient as an expert in their particular rare disease often results in mutually beneficial healthcare interactions (Dept. of Health (UK), 2009).

Thirdly, developing clinical and administrative decision supports is essential to improving outcomes for rare diseases, since clinical knowledge and particularly experience with rare diseases is naturally limited due to the low number of cases. Protocol driven decision support is likely to improve care and outcomes in these cases.

Fourthly, clinical information systems can provide timely access to individual information and data, and also connect geographically remote population cohorts, enhancing disease information, expertise and elusive treatment and management strategies. Rare disease registries are fundamental to enhancing research and knowledge about the diseases.

Finally, all of the aforementioned must be nested within healthcare organisations, healthcare communities and wider society which is appropriately organised to support and enhance rare disease outcomes by provision of policies, strategies and resources.

2.3 The case of JHS / EDS-HT

2.3.1 Generalised Hypermobility (GH)

A hypermobile joint is one whose range of movement exceeds the norm for that individual, taking into consideration age, sex, and ethnic background (Grahame, 1999). GH which involves laxity of multiple joints is common in the general population, it affects more females than males (3:1) more Asians and Africans than Caucasians and decreases with age (Remvig et al., 2007). GH is confirmed using the 9 point Beighton scale (Table 2) when a score greater than 4 is achieved (Beighton, 1989). Traditionally considered to represent the upper end of normal, generalised pauciarticular or polyarticular hypermobility is estimated to affect between 10-30% of the population, the majority of whom remain symptom free throughout life (Hakim and Grahame, 2003a). Hypermobility can be acquired through training and is considered advantageous to some activities (Simmonds and Keer, 2007). However, hypermobility is also an unifying feature of many rare genetic connective tissue disorders (OMIM, 2015).

Table 2 Beighton Hypermobility Score source Beighton (1989)

The nine point Beighton hypermobility score

The ability to	Right	Left
(1) Passively dorsiflex the fifth metacarpophalangeal joint to > 90^0	1	1
(2) Oppose the thumb to the volar aspect of the ipsilateral forearm	1	1
(3) Hyperextend the elbow to > 10^0	1	1
(4) Hyperextend the knee to > 10^0	1	1
(5) Place hands flat on the floor without bending the knees	1	
Total	9	

Score: One point may be gained for each side for manoeuvers 1-4, so that the hypermobility score will have a maximum of nine points of all are positive

Source Beighton (1989)

2.3.2 Joint Hypermobility Syndrome (JHS)

The term hypermobility syndrome was first defined by Kirk et al. (1967) as "the occurrence of musculoskeletal symptoms in the presence of joint hypermobility in healthy individuals", whilst Grahame et al. (2000) agreed that JHS is diagnosed in the absence of other rheumatological conditions, when GH becomes symptomatic according to the revised Brighton Criteria. Formerly termed the Benign Joint Hypermobility Syndrome (BJHS), the increasingly recognisable multi-systemic nature of the condition and the potential for marked disability and reduced quality of life has led to widespread removal of 'benign' from the name (Adib, 2005, Baeza-Velasco et al., 2011). Whether or not JHS is a symptomatic continuum of GH is debatable (Engelbert et al., 2003, Castori, 2012a).

The diagnostic Brighton Criteria for JHS takes account of the clinical symptoms that occur as a result of the disorder, and also allows for historical hypermobility, thus taking account of the reduction in joint laxity that occurs with age (Table 3). Hakim and Grahame (2003b) developed a 5 point questionnaire to reliably diagnosis historical hypermobility, an important diagnostic adjunct, which if not recognised may result in delayed or incorrect diagnosis.

Table 3 Brighton Criteria and Hypermobility Questionnaire

Brighton Criteria (JHS)	**Hypermobility** **Historical 5-point questionnaire**
Major criteria Beighton score ≥4/9 Arthralgia for >3 months in >4 joints **Minor criteria** Beighton score of 1–3 Arthralgia in 1–3 joints History of joint dislocations Soft tissue lesions >3 Marfan-like habitus Skin striae, hyperextensibility, Or papyraceous scarring Down slanting palpebral fissures, Lid laxity, Myopia, History of varicose veins, hernias, visceral prolapses JHS confirmed by presence of Both major, or One major and two minor, or Four minor, or Two minor & first-degree affected relative(s). *Source* (Grahame et al., 2000)	• Could you ever place your hands flat on the floor without bending your knees? • Could you ever bend your thumb to touch your forearm? • As a child did you amuse your friends by contorting your body into strange shapes *or* could you do the splits? • As a child or teenager did your shoulder or kneecap dislocate on more than one occasion? • As a child or teenager did you consider yourself double-jointed? Hypermobility confirmed if positive for two or more questions. *Source* (Hakim and Grahame 2003)

JHS is considered to be the most common but least diagnosed Heritable Connective Tissue Disorder (HCTD) and is also considered to be clinically indistinguishable from the Hypermobility Type of Ehlers Danlos Syndrome (Fikree et al., 2013).

2.3.3 Ehlers Danlos Syndromes (EDSs)

The earliest known cases of EDS were identified by their dermatological manifestations, described by Ehlers and Cutis (1901) as a tendency to skin haemorrhage and loose joints, and subsequently by Danlos (1908) as skin laxity with chronic bruising of the elbows and knees. Throughout the 20th century the clinical picture of EDS evolved to encompass a diverse group of heritable connective tissue disorders all of which have variably expressed joint hypermobility, and cutaneous and visceral fragility and hyperelasticity. The Berlin nosology containing 11 EDS phenotypes was revised by a group of experts in Villefranche in 1997 to comprise 6 EDS subtypes with distinct genotypes and phenotypical diagnostic criteria (Beighton et al., 1988, Beighton et al., 1998). Table 4 shows the Villefranche Criteria shown beside Brighton Criteria for comparison. The Villefranche criteria for other EDS types is included in Appendix H.

Table 4 Brighton Criteria and Villefranche Criteria

Brighton Criteria (JHS)	**Villefranche Criteria (EDS-HT)**
Major criteria Beighton score ≥4/9 Arthralgia for >3 months in >4 joints **Minor criteria** Beighton score of 1–3 Arthralgia in 1–3 joints History of joint dislocations Soft tissue lesions >3 Marfan-like habitus Skin striae, hyperextensibility, Or papyraceous scarring Down slanting palpebral fissures, Lid laxity, Myopia, History of varicose veins, hernias, visceral prolapses JHS confirmed by presence of Both major, or One major and two minor, or Four minor, or Two minor & first-degree affected relative(s). *Source* (Grahame et al., 2000)	**Major criteria** Beighton score ≥5/9 Skin - hyperextensibe and/or smooth, velvety **Minor criteria** Beighton score of 1–3 Recurring joint dislocations Arthralgia in 1–3 joints Chronic joint/limb pain History of joint dislocations Positive family history EDS-HT confirmed by presence of Both major criteria minor criteria are supportive *Source* (Beighton et al., 1998)

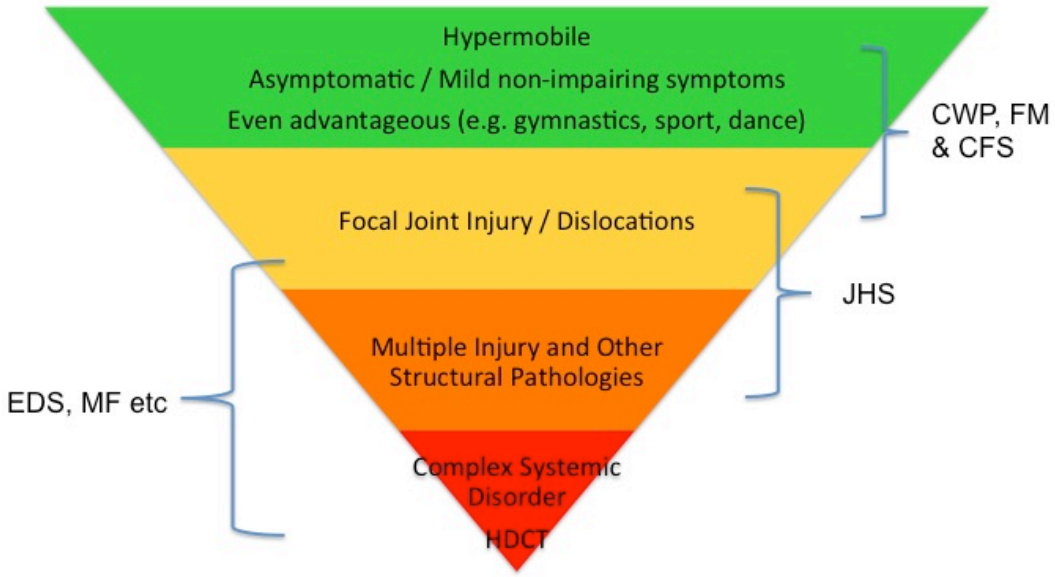
While genetic markers had been found for 5 subtypes (classic, vascular, kyphoscoliotic, arthrochalasis, and dermatosparaxis), molecular diagnosis of the Hypermobility Type (EDS-HT) remains a challenge Appendix H. Furthermore, the comparative subtlety of clinical signs and the range and variability of symptoms in this type, often results in long delays in diagnosis. (Castori, 2012a, Tinkle et al., 2009).

Revision of the Villefranche nosology is warranted as; numerous molecularly distinct EDS-related phenotypes have been recognised but not yet incorporated into a classification scheme (Byers and Murray, 2014, Mayer et al., 2012, De Paepe and Malfait, 2012). This task will be undertaken by major international stakeholders and medical professionals at the EDS International Symposium in 2016, the primary goal of which is to reclassify diagnostic criteria for all types of EDS (EDNF, 2015, EDS UK, 2015).

The correlation of EDS-HT with JHS was not defined in the Villefranche nosology, however, the revised Brighton criteria for diagnosis of JHS reflects the Villefranche

major and minor criteria for diagnosis of EDS-HT (Grahame et al., 2000). EDS-HT and JHS are considered by many experts to be clinically indistinguishable, possibly identical syndromes, although homo/heterogeneity will only be confirmed when the causative genetic mutation is found (Fikree et al., 2013, Tinkle et al., 2009, Castori, 2013). Until such time, EDS-HT and JHS should be managed clinically as a single entity and for the purpose of this research EDS-HT is considered synonymous and interchangeable with JHS.

The Villefranche and Brighton Criteria should in theory, render the diagnosis of EDS-HT simple. The clinical reality is that the overlapping nature of signs and symptoms of many of the heritable connective tissue disorders complicates the diagnosis, especially in complex cases or when clinicians are not familiar with these disorders. Figure 4 illustrates the complexity of categorically diagnosing these conditions.



CWP – Chronic Widespread Pain; FM – Fibromyalgia; CFS – Chronic Fatigue Syndrome;
JHS – Joint Hypermobility Syndrome; EDS – Ehlers Danlos Syndrome; MFS – Marfan Syndrome

Figure 4 Complexity of Diagnosis of Overlapping Syndromes *source* Hakim (2010)

2.3.4 Prevalence

As with many rare diseases, there is little epidemiological evidence of the true prevalence of EDS-HT. Overall prevalence of all types of EDS is estimated at between 1/5,000 - 1/20,000 worldwide, whilst some EDS subtypes may be as rare as 1:100,000 particularly those inherited recessively (Beighton et al., 1998, Steinmann, 2002, Mayer et al., 2012). EDS-HT is considered to be the most prevalent subtype accounting for 50-80% of all cases with a suggested frequency of 0.2-0.6% in Europe and USA (Castori, 2012a, Levy, 2012).

2.3.5 Impact of EDS –HT

Long considered a primarily rheumatological disorder, there is a burgeoning body of literature identifying JHS/EDS-HT as a multisystem disorder affecting many of the systems of the body which, whilst not life-threatening, have the potential to result in marked disability and poor quality of life (Voermans and Knoop, 2011, Fikree et al., 2013, Hakim and Grahame, 2004, Castori et al., 2013). Awareness of the systemic multi-morbid effects of the condition remains poor, even amongst rheumatologists and physiotherapists who are often the diagnostician and prime clinician involved in care (Grahame and Bird, 2001, Lyell et al., 2015, Palmer et al., 2015). Patients continue to experience long delays and errors in diagnosis, often being treated for a myriad of seemingly unconnected injuries or disorders, enduring psychosomatic and hypochondriasis labels and unable to access appropriate care and support (Eurordis, 2013). Improving clinical awareness of the condition is crucial for early diagnosis and management of potentially disabling complications (Castori, 2012a).

Three clinical phases have been described by Castori et al. (2010) namely the hypermobility phase present in the first years of life, followed in the second decade by the pain phase and finally the stiffness phase as joint mobility progressively declines. Spanning these phases, a variety of systemic effects may contribute to reduced physical and mental health, time lost at work/school and poor health related quality of life. Defects in connective tissue, the underlying matrix inherent in and supporting all of the bodies' tissues and organs have the potential to affect virtually every bodily system.

2.4 Challenges to provision of care in EDS-HT

The challenges identified to provision and access to appropriate care for rare diseases as discussed in section 2.2.2 are naturally experienced by people with EDS-HT and these will be discussed in context in the coming paragraphs. Patients with all types of EDS expressed their opinion in the European wide survey 'The voice of 12,000 Patients' (Eurordis, 2013).

Whilst no breakdown by subtype of EDS is reported, it can be inferred from prevalence estimates, that EDS-HT represents at least half of all respondents. It is noteworthy that of all 16 rare disease patient groups surveyed, poorest results were reported by the EDS group. The alarming results highlight the challenges which must be addressed to reduce the disease burden for the individual, and for healthcare providers at local, community and national level.

2.4.1 Lack of Specific Health Policies

The recent development of rare disease strategies nationally and internationally provides the foundation for development of disease specific strategies. However, tangible improvements in rare disease management and outcomes will depend on political, economic and clinical drive to implement the strategic recommendations.

Regarding EDS and particularly EDS-HT, the current absence of any clinical guidelines or protocols for disease management present a significant barrier to provision of appropriate care. Castori et al. (2012a) have proposed a process map for treating pain and fatigue in EDS-HT which will enhance this part of the patient journey. The development of universal guidelines for management of the condition post-diagnosis is the second goal of the EDS symposium to be held in 2016. This will provide the framework to significantly improve the entire patient journey.

2.4.2 Lack of Expertise, Leading To Delays in Diagnosis or Misdiagnosis

During the search for EDS diagnosis, half of all patients experienced a 14 year delay from onset of symptoms to correct diagnosis, whilst quarter of all patients waited 28 years, 20% of patients consulted more than 20 physicians, 56% were misdiagnosed (20% psychiatric misdiagnosis) resulting in inappropriate treatment (70%) and harmful consequences (86%) (Eurordis, 2013). Despite the volume of extensively published

literature by knowledgeable and highly experienced clinicians, knowledge of the syndrome and its multi-systemic effects remains poor (Grahame and Bird, 2001, Billings et al., 2013, Rombaut et al., 2015, Russek et al., 2014).

2.4.3 Difficulty Accessing Appropriate Multidisciplinary Healthcare

Eurordis (2013) also report that access to diagnosis required 37% of EDS patients to travel outside of their region or country and a financial contribution was needed from 58% of patients resulting in delayed access to diagnosis in 25% of patients. Each EDS patient needed an average of 12 health disciplines, but many found this difficult or impossible (Figure 5).

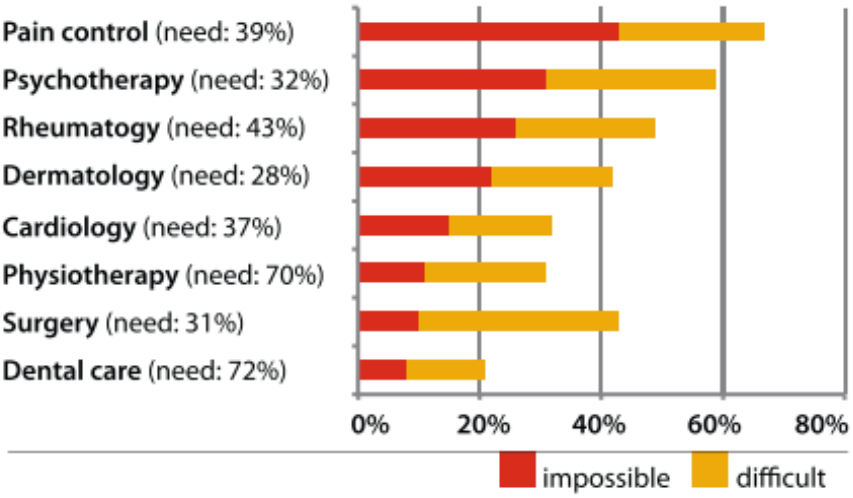


Figure 5 Need for and access to medical services for EDS *source* Eurordis (2013)

Furthermore, the number and wide variety of clinicians who provide care for individuals with EDS-HT are often in disparate disconnected locations. Where health information systems exist, patient information is predominantly accessed only at that location and is not shared among healthcare providers. This is particularly challenging in emergency situations when access to information can prevent medical errors and reduce length of stay (White et al., 2004, Stiell et al., 2003).

2.4.4 Lack of Quality Information and Support for Patients, Families and Clinicians

EDS patients reported that following diagnosis many (34%) received no disease information, no psychological support (81%), and no genetic counselling (74%) (Eurordis, 2013). Furthermore, this EDS population believe that training non-specialist local healthcare professionals in EDS specific needs is essential. These views are reiterated by Gurley-Green (2001) who states that people with EDS-HT feel that medical practitioners do not understand the impact of the disease nor can the medical community provide effective treatment.

The result is clinical frustration and difficult interactions between clinicians and patients. In the absence of easily accessible validated information, social media groups and websites containing unregulated information and publications have proliferated, substituting the traditional scientific knowledge (Knight, 2015). This is the particularly the case in Ireland where there is a complete lack of validated information available to patients or interested clinicians. By contrast, two UK patient charities, HMSA and Ehlers-Danlos UK, have world renowned clinical expert panels, websites which have achieved an information quality standard, and a wealth of information available for clinicians, patients and families.

2.5 Information Requirements and Gaps in EDS-HT Patient Journey

2.5.1 Introduction

The amount and quality of information available to health care professionals in patient care has an impact both on the outcomes of patient care and the continuity of care (Häyrinen et al., 2008). It is imperative therefore, that healthcare information is accessible, reliable, relevant, accurate, valid, timely, legible and complete. In the absence of this information medical errors in the form of delays in diagnosis or treatment or costly duplication of tests are likely.

Healthcare is information-intensive, and the process of gathering, searching for and storing information is time consuming for clinical administrative and social care staff (HIQA, 2014). Moreover, patients spend time repeating the same information time and again or awaiting services in waiting rooms, hospital beds, treatment rooms or at home,

while information in the form of referrals, results, opinions and imaging are transferred between clinicians.

The Department of Health and Children (2013), in its' eHealth strategy, states that digital technology will catalyse change in the existing model of healthcare by providing an increased level of information flow, transparency, customisation, patient choice and empowerment for self-care, thus supplementing the current models of care and developing new services including quantitative, predictive and preventive care.

Figure 6 illustrates the multiple silos of information that exist across different organisations with only limited connectivity. In many cases, there is no connectivity between the tier 3 systems across the fragmented system

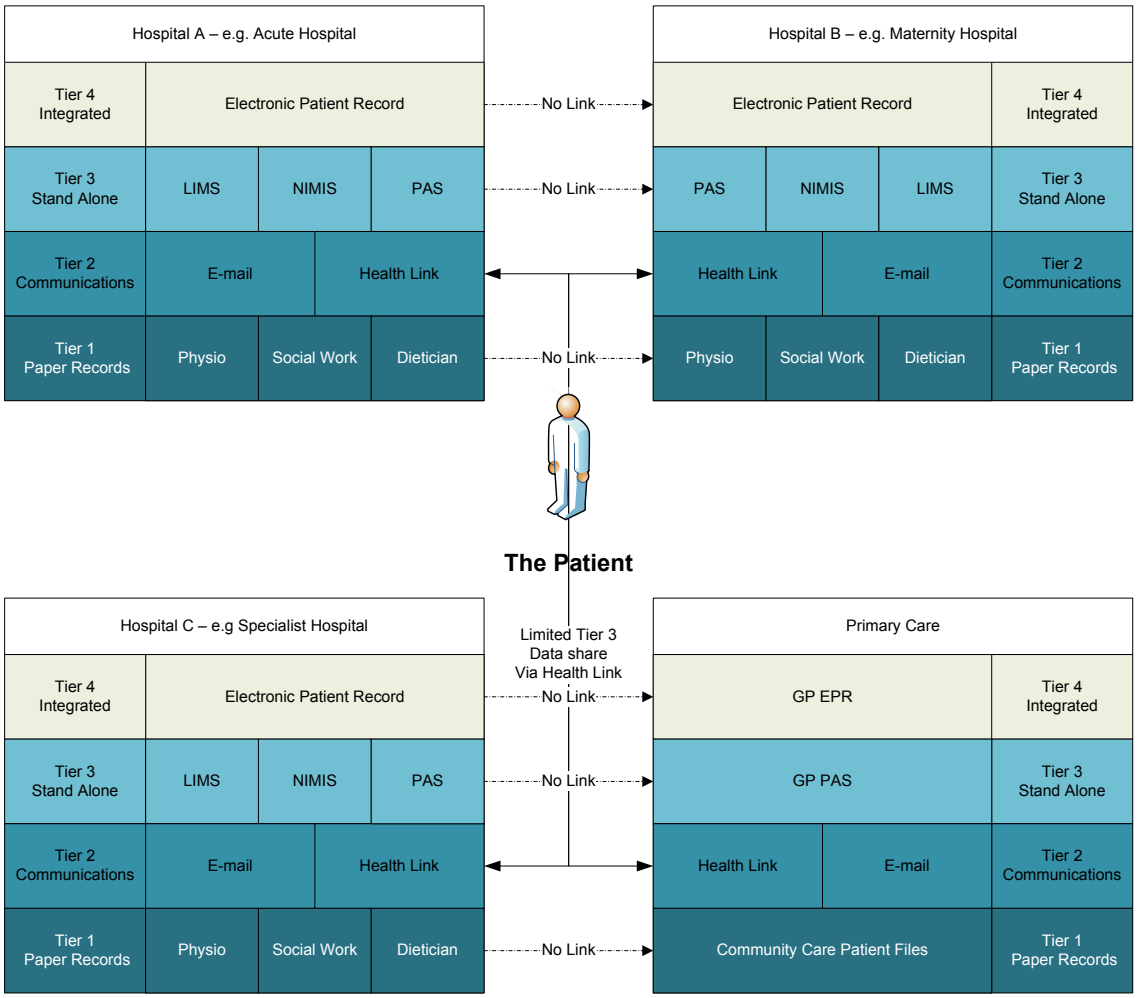


Figure 6: Patient Interaction across multiple data sources

2.5.2 Information Gaps and Requirements

The EDS-HT patient journey is currently disjointed and fragmented with no model of care to guide clinicians or patients. Moreover, the education and information gaps from onset of symptoms of EDS, result in unacceptably prolonged delays in diagnosis, misdiagnosis, and fragmented inappropriate treatments (Eurordis, 2013).

The impact of these gaps in knowledge translates into patient perceived reluctance (95%) and rejection (35%) by health professionals, due to the complexity of the condition. Many clinicians continue to believe that EDS-HT equates with a functional generalised hypermobility and that other symptoms if present, represent hypochondriasis or psychosomatic disorders, possibly due to the lack of definitive genetic tests (Challal et al.). Updating the diagnostic criteria and the development of universal management guidelines is essential to the recognition and management of the syndrome. However, translating these guidelines into clinical practice represents a fundamental educational challenge which will require innovative informatics solutions (WHO, 2013). Education and information gaps co-exist and both must be addressed in tandem.

Information gaps occur when relevant, previously collected data or information is unavailable to a clinician at point of care. Currently information gaps exist at almost every clinical encounter in an EDS-HT patient journey. This is particularly the case in Ireland where no Centre of Expertise (CoE) exists to assist in diagnosis, or guide the clinical journey. EDS patients identified sharing of medical information, collaborating and communicating with researchers, other CoEs and professional networks, and training local professionals on EDS specific needs as the key functions of a CoE (Figure 7) (Eurordis, 2013).

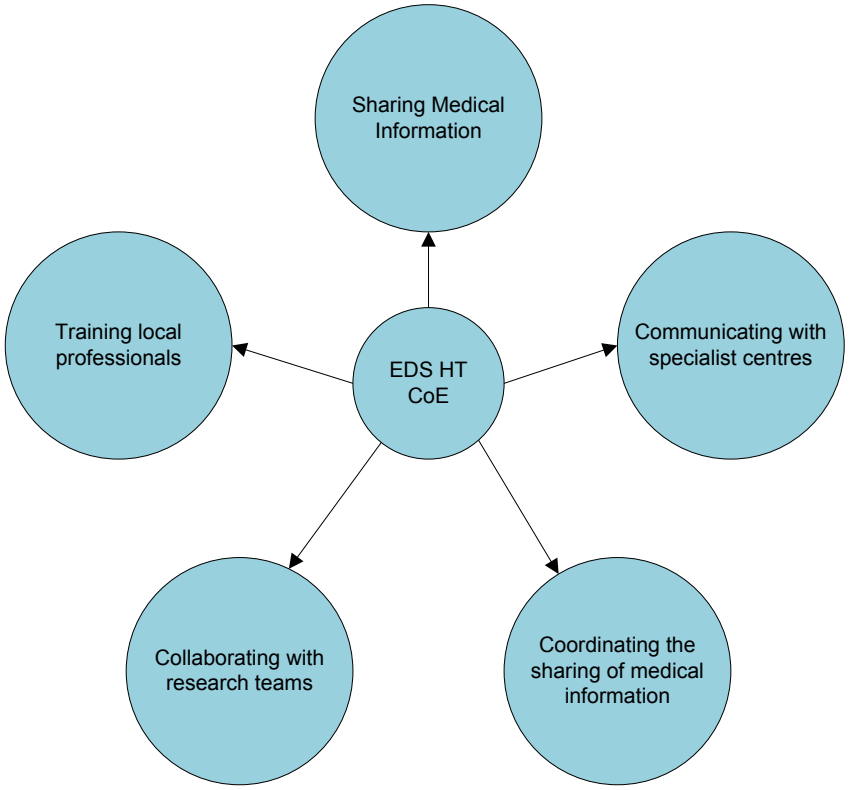


Figure 7 Role of CoE Identified by EDS Patient Groups

Improving care for EDS-HT patients requires timely access to current and relevant data by appropriate stakeholders at the appropriate stage of the journey. Furthermore, aggregated data is essential in order to secure funding for population strategies and research. The number of disciplines involved in the care of EDS-HT patients along with the spectrum of locations where care may be sought requires that an interoperable, integrated information solution.

2.6 Potential Technology Solutions

Shared EHRs have the potential to transform the EDS-HT patient journey by improving the many communication processes inherent in a rare and lifelong disorder. Transfer of information between multiple hospital systems and across the many interfaces of hospital and primary care is possible by use of message oriented middleware and open distributed systems. Fundamental to this information transfer is the standardisation of terminology and messaging which will ensure interoperability and data quality. The following paragraphs will look at some potential informatics solutions applicable to many patient groups but particularly when multidisciplinary care spanning primary, secondary, tertiary and social care is required.

2.6.1 Electronic Health Record

The US' Institute of Standards and Technology defines an EHR as ''a longitudinal collection of patient-centric health care information available across providers, care settings, and time''. While, the ISO define an EHR as "a repository of retrospective, concurrent and prospective information regarding the health status of a subject of care, in computer process-able form, stored and transmitted securely and accessible by multiple authorized users, having a standardized or commonly agreed logical information model that is independent of EHR systems and whose primary purpose is the support of continuing, efficient and quality integrated health care"(ISO, 2005). Undoubtedly an EHR will bridge the many information gaps inherent in the EDS-HT patient journey. However, the development and deployment of national EHRs will require major investment and political and clinical commitment. In the absence of national EHRs the development of modular interoperable systems can facilitate exchange of information in a standardised format to ensure data quality and security.

2.6.2 Summary Care Record (SCR)

SCRs are designed to be available at point of care across multiple sites, both in emergency / unexpected healthcare encounters or in shared care situations. SCRs do not contain detailed or exhaustive health information but instead a smaller subset of essential information necessary for episodic events or continuity of care. The development of patient summary care records has been identified as a priority project in eHealth strategies both nationally and internationally and is seen as integral to the sharing of information between care providers and across multiple locations (Dept. of Health and Children, 2013, European Commission, 2006).

The minimum essential data contained within a SCR is likely to include patient demographics, medical history, allergies and alerts, active problems, test results, and medication lists. However, by design a SCR may include further information considered necessary to provide seamless transitions across the care continuum and to enable appropriate and timely clinical decision making to optimise care. Disease specific SCRs and continuity of care records (CCRs) have been successfully deployed for the management of chronic diseases and multi-morbid disorders requiring multidisciplinary, multi-sector, planning and provision of care (Schnall et al., 2012, Silvester and Carr, 2009).

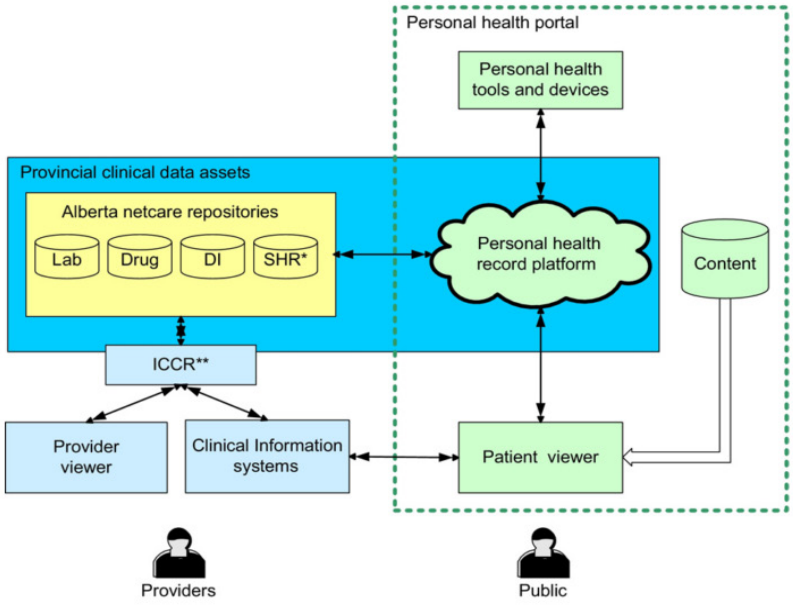
The successful deployment of the Scottish Emergency Care Record prompted the equally successful implementation of the same technology in Northern Ireland, although less success and uptake is reported in SCR's in England (Greenhalgh et al., 2013).

Successful implementation of SCRs requires connectivity for point of care access, interoperability, privacy and data governance and clinical and managerial leadership.

2.6.3 Portal

A number of successful portals have been developed for access to shared healthcare records. In Northern Ireland a single portal accessed via a single logon, is used to access the Northern Ireland Electronic Care Record (NIECR) contains multiple sources of clinical information (Purvis, 2015). Solutions were found to allow interoperability with legacy systems, privacy and data protection.

In Alberta Canada, clinical and personal portals allow viewing of clinical information via patient records from a network of data repositories and information systems. The data is collected at point of care including hospitals, primary care and pharmacies and uploaded to the record via secure messaging (Brisson, 2011). Figure BELOW illustrates the architecture used.



*SHR, shared health record data repositories; **ICCR, interactive continuity of care record

Alberta's Personal Health Portal *source* Brisson (2011)

Figure 8 Alberta's Personal Health Portal

2.6.4 Healthlink and Health mail

Healthlink is a web-based messaging service operational in Ireland since 1995, which allows secure transmission of clinical patient information between hospitals, healthcare agencies and GPs in real time. All Messages are formatted in HL7 standard format and transmitted via VPN and V-LAN between various stakeholders using unique, secure ID. Healthlink is currently used for referral requests, radiology and laboratory orders and results, and admissions and discharge notifications (Healthlink, 2015). This technology has scalability to include appropriate summary care records and to be available to all members of the multidisciplinary team.

The recent addition of Healthmail, a secure e-mail system to allow electronic communication of patient identifiable data between primary and secondary care providers, has facilitated information transfer on an individual basis. Although Chen et al. (2010) found email to be an effective method for communication of discharge summaries, data from email is generally not standardised or interoperable, nor is the information available within a shared record.

2.7 Interoperability and Standards

“In healthcare, interoperability is the ability of different information technology systems and software applications to communicate, exchange data, and use the information that has been exchanged” (HIMSS, 2013)

Technical, structural and semantic interoperability is required for exchange of healthcare information. Structural interoperability ensures that an agreed syntax is used for exchanging data. Semantic interoperability ensures that data exchanged between systems is used and interpreted in the same way by use of a common language. Standardisation of both syntax and semantics is essential to health information to ensure meaningful use of data exchanged. Accordingly, the use of these standards in the development of minimum data sets is essential for seamless integration within electronic medical records to serve the purpose of care, epidemiology and public health, and research (Choquet et al., 2015).

Interoperability of healthcare technology systems facilitates smooth individual patient journeys and also secondary use of data for research, public health and epidemiology. The adage “collect once use many times” is as pertinent to the individual patient and

their clinicians during single or multiple care encounters, as it is to the bigger picture of understanding and developing population based strategies and solutions to healthcare.

However, the fragmented reality of information systems persists, often even within a single location where administrators and clinicians collect the same data repeatedly from a single patient (HIQA, 2014). Moreover, where IT systems have been implemented within a particular care setting, information remains within a silo, contributing neither to the care of a single patient across multiple locales, nor to care across a population level In most cases, data collected within the clinical setting still does not easily lend itself to re-use.

In Ireland, under the Health Act 2007, HIQA has responsibility for setting health information standards and monitoring their compliance. The development of national and international standards for collection, transfer and storage of health data, promises interoperability and quality data for reuse both at individual and population level (HIQA, 2013b). The standards applicable to health information include the Health Level Seven International (HL7) messaging standard, OpenEHR, and ISO EN 13606.

While no national health care data dictionaries exist a number of clinical ontologies continue to evolve (LOINC, SNOMED CT (clinical terms) Orphanet (orphan drugs, rare disease diagnosis), Human Phenotype Ontology (HPO) (signs), Online Mendelian Inheritance in Man (OMIM) (genes), Human Genome Variation Society (HGVS) Mutnomen, and GenATLAS (genes and mutations).

2.8 Summary

This chapter began by looking rare diseases and the challenges that are faced in provision of care for this population. Parallels were drawn between rare disease and chronic disease in order to learn from the experience of providing care across many healthcare sectors and many healthcare providers over a prolonged timeframe. JHS and EDS-HT was discussed along with the challenges to diagnosis and management of the disorder, in order to outline the education and information gaps that exist in this patient journey. Potential information technology solutions were identified and the importance of interoperability and standards was highlighted. The essential message from this chapter is that timely information is fundamental to providing care for long term conditions. Moreover, any information solution must ensure that the quality of the

data gathered is sufficient to fulfil its purpose. To this end this research will develop a minimum dataset (MDS) for EDS-HT. The next chapter will look further at data quality and particularly at the development of a Minimum dataset.

"The gaps and uncertainties in health-care professionals' medical knowledge concerning EDS symptoms cause these patients to struggle for their credibility and dignity." (Berglund et al., 2010)

3 Developing a Minimum Data Set

3.1 Introduction

The previous chapter identified the need for standardised interoperable data. This chapter will investigate successful methodologies for developing a minimum data set (MDS) so that a suitable method can be chosen to develop an EDS-HT MDS.

3.2 Defining a Minimum Dataset

A minimum dataset (MDS) consists of a defined set of data elements (DEs) which are considered the minimum essential components required to meet a particular purpose. Many disease specific or function specific MDSs have been developed for clinical or epidemiological use and various MDSs have been developed for national level data collection (Ghaneie et al., 2013). Kelly et al. (2012) demonstrated that transfer of essential clinical data was significantly improved post implementation of a MDS. There has also been growing interest in development of MDSs for rare disease internationally. The French MDS–RD was developed to allow mandatory collection and reporting of rare disease data at a national level (Choquet et al., 2015).

Healthcare delivery is information intensive and data is routinely collected at point of care. This data is processed according to need at episode level (during an episode of care), case level (an aggregate of all episodes for an individual) and system level (an aggregate of all data elements in a particular region) (HIQA, 2010). MDSs thus provide a structure for electronic data to support and compare care across care settings. Further, analysis of aggregated MDSs can illuminate and project trends thus providing information to assist in clinical, administrative and policy decisions. Patient outcomes and effectiveness of interventions can be assessed by comparison of aggregated data using MDSs.

Goossen (2002) stated with regard to nursing MDSs that all pertinent DEs must be identified, defined accurately, have all possible values for each DE identified and must be capable of documenting patient data. Therefore, the data development process should specify the representation, format and definition of common data elements to ensure data quality and enable comparison of data across systems. Furthermore, it is

essential that data from individual records can be aggregated and coded so that it may be used for intended purpose.

3.3 Models for developing a MDS

Development of MDSs must follow a robust methodology to ensure widespread engagement by stakeholders and ultimately high quality data. In the development of clinical MDSs, Svensson-Ranallo et al. (2011) propose that DEs identified from the literature and patient charts “are critically evaluated by domain experts through a formal and iterative process”. This approach ensures consideration of a comprehensive set of clinically relevant DEs. The proposed methodology for developing clinical MDS is illustrated in Figure 9.

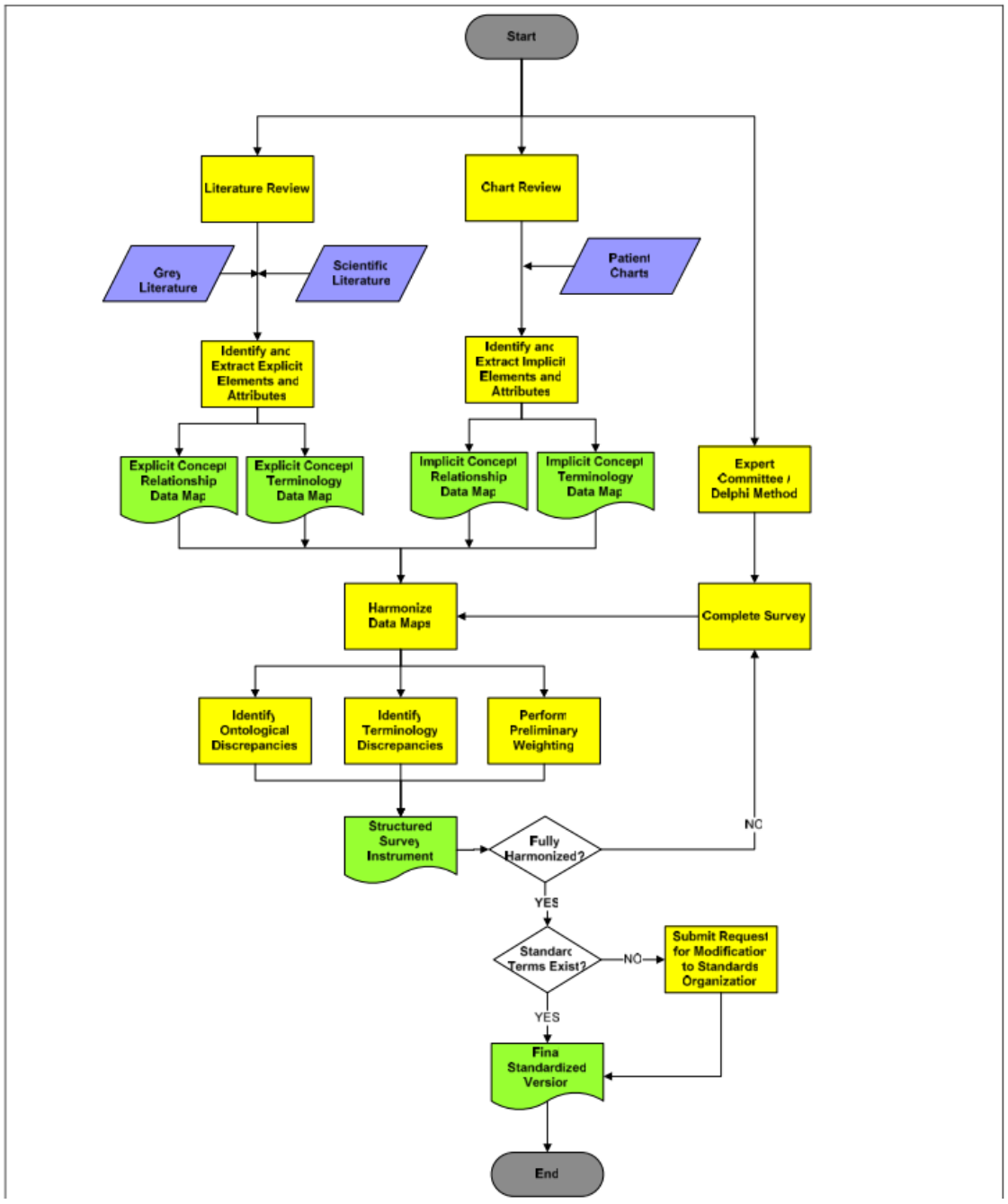


Figure 9 Methodology for developing MDSs source Svensson-Ranallo (et al 2011)

A similar approach was successfully used to develop the French minimum data set for rare diseases (Choquet et al., 2015) (Figure 10).

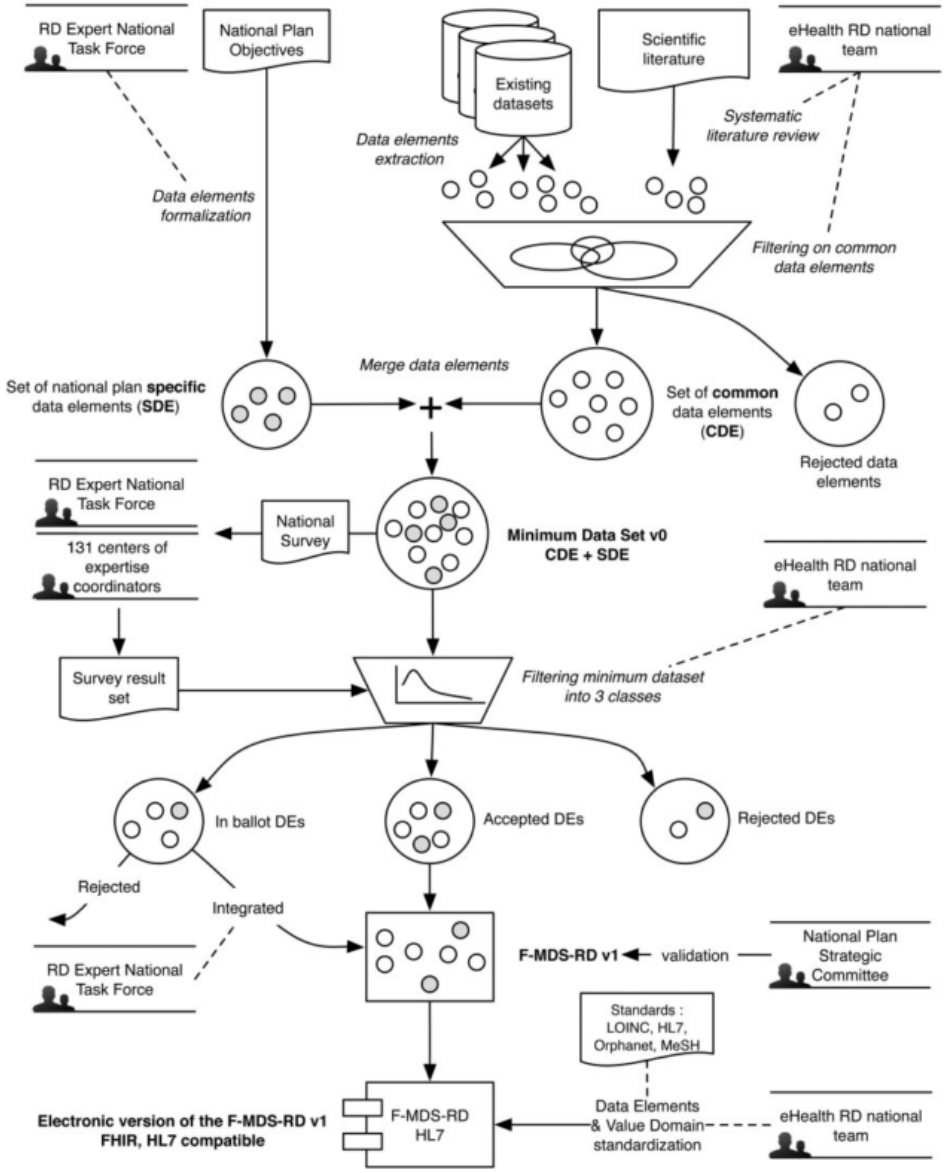


Figure 10 Methodology used for development of French rare disease MDS *source* Choquet et al (2015).

3.4 Methodology for developing a MDS

Based on the models in the previous sections a six stage methodology can be summarised

3.4.1 Establish and Expert Group

A minimum data set is developed with the assistance of an expert group, which brings together health and social care professionals, Government Health policy leads, University representatives other partner organisations and advocates. Input from the reference group forms the first stage of the development of the data set. This group has oversight of the complete end of end process and supports and guides the team during the process

3.4.2 Literature Review

Following the establishment of the expert group, the next step in the process is to conduct a thorough literature review. In this approach, the researcher conducts a review based on keyword searches from scientific databases and journal content over a defined period of time. Other key documents for this review are local, national and international policies and guidelines, and clinical charts or electronic health records. This ensures that the dataset is not limited to local or current DE's.

A formal and iterative process is then used to analysed and categorise the data. The aim of this step to identify a comprehensive and relevant set of data elements while ensuring that the scope is manageable. The output of this phase is a set of common data elements (CDE's) and a set of disease specific elements (SDE's)

3.4.3 First Draft Minimum Data Set

Once the Literature review has been completed, the CDE's and SDE's are tabulated into a structured document for expert review. In this document, the data elements are structured into groups and the purpose of each data element is explained.

3.4.4 Expert Panel review

Once the first draft minimum data set is prepared, the team meets back with the expert group. This will normally take place in a two phase process.

Phase 1 will be a series of 1:1 meetings with the individual experts. In these reviews, the merits of inclusion of each data element are reviewed and data elements to be removed are highlighted by the team.
Phase 2 will be a joint review with all the experts. During this review, only the data elements that were considered for removal of data elements proposed by the expert group are discussed. The output of the phase 2 review is a first draft minimum data set

3.4.5 Validation with Broad Stakeholder group

Once the expert review board has agreed the minimum data set, the document is distributed to a broader set of stakeholders for review and consideration. These stakeholders would include those that are part of the service provision including primary care, social care and community services. This review is best managed via an online survey where the MDS is provided electronically and a series of questions are posed to the stakeholder for consideration. Care needs to be taken in formulating the questions to ensure that outcomes are not biased.

3.4.6 Standardised Minimum Data Set

Once all feedback has been received, the proposed amendments are shared with the expert group for consideration. Based on the output of this final review, a minimum data set document can be approved. Once this has been received, the requirements document can be converted into a standardised HL7 compatible technical specification. This technical specification will allow the development of an EHR, shared or summary care record and can be included in a patient registry.

3.5 Summary

This chapter defined a MDS and identified methodologies for the development of MDSs. A suitable methodology was identified for development of the EDS-HT MDS. The research methodology and the chosen MDS methodology for the research will be discussed in the next chapter.

4 Research Methodology

4.1 Introduction

This chapter describes in detail the research design and methodology for this thesis. The research was broken into two key phases based on the objectives of the research and in order to answer the research question.

Phase 1 Primary Literature Review

To identify the likely clinical information break points in the care of patients with EDS-HT / JHS,
To investigate information technology solutions for the safe storage and timely access to this data,

Phase 2 Minimum Data Set Development

To identify essential data collection which should be included in the EDS-HT patient record to assist in ongoing primary care or episodic specialist care of this patient group.

The following sections will review how the minimum data set development was approached.

4.2 Research Design

The methodology from Choquet et al. (2015) and Svensson-Ranallo et al. (2011) for developing a MDS was adapted for this research to develop a MDS for use in care of patients with EDS-HT.

A six stage process was developed and adopted as illustrated in Figure 11 and research deliverables were identified for each stage (Table 5).

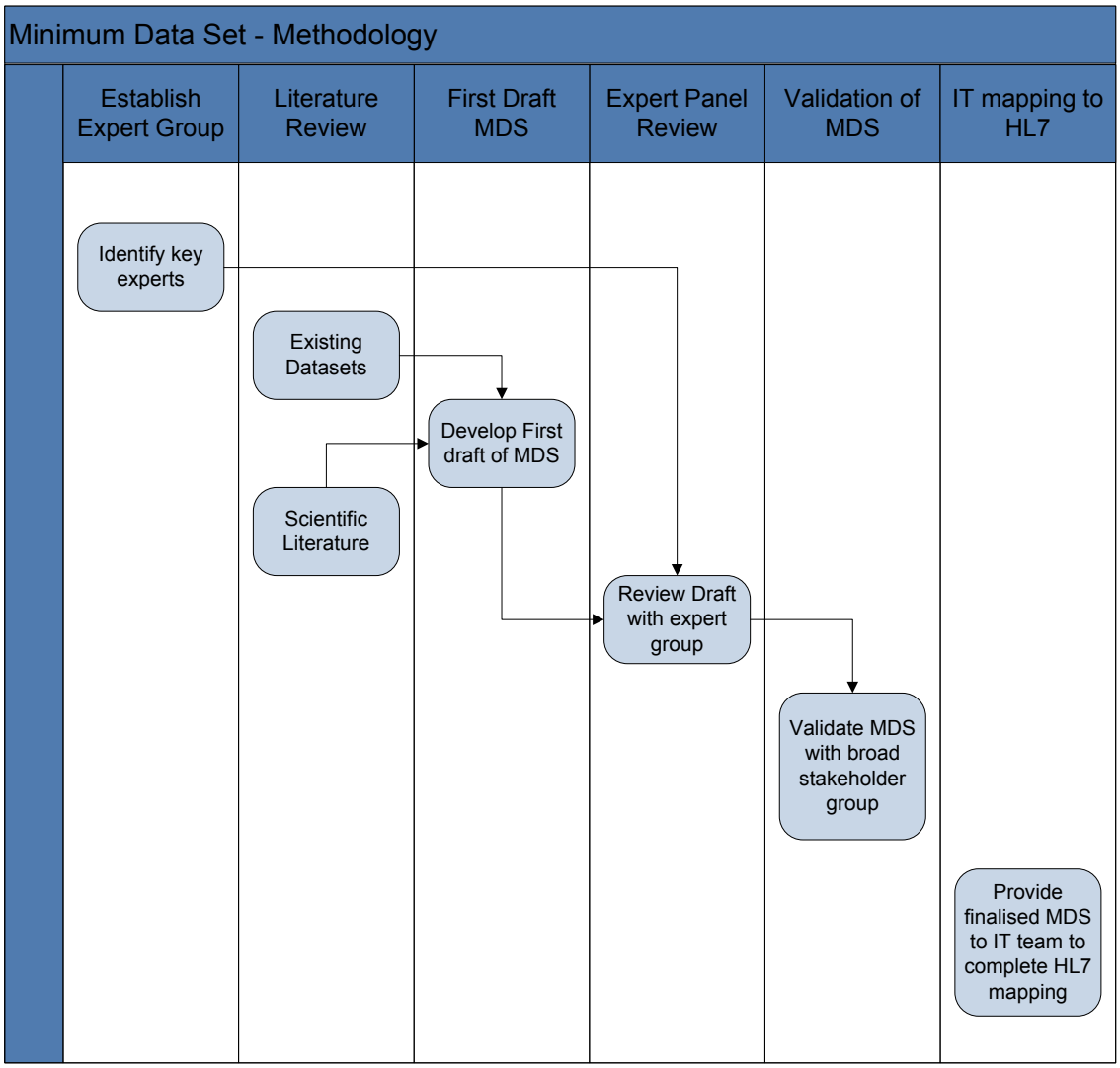


Figure 11 MDS Methodology

Table 5 MDS Methodology and Deliverables

	Step	Deliverable
1	Establishment of Expert Groups	Expert Group formed
2	Literature review for common data elements	Conduct Literature Review and identify common data elements
3	Development of the MDS V.0;	Develop first draft MDS
4	Expert survey to review MDS V.0;	Review MDS with Expert Panel
5	Validation of the MDS.	Develop survey for MDS Review Post expert panel review. It was beyond scope of the research to send survey to stakeholders
6	Development of standardised interoperable electronic format of the MDS.	Not is scope - show in methodology for completeness

4.2.1 Establishment of Expert Groups

While no Centre of Expertise (CoE) for EDS-HT /JHS exists in Ireland, ORPHANET (2015) currently lists 56 CoEs globally for medical management of the condition and a further 4 for medical management and genetic counselling. The primary specialisation of 36 of these centres is rare skin disease, while 10 centres list Ehlers Danlos Syndrome as their primary speciality and a further 8 as specialist in a various heritable connective tissue disorders. Notably, while dermatologists are likely to identify the cutaneous manifestations of the disorder and may indeed make the initial diagnosis, long term management of the condition is more likely to require input from other specialists. Furthermore, many of the specialist centres listed only accept referrals of complex presentation of suspected EDS in order to provide genomic clarity to an elusive diagnosis.

Since no CoE exists in Ireland, identification of EDS-HT clinical experts is challenging and often is based on 'word of mouth' both by patients and by clinicians who may only see a small number of patients. Diagnosis and management of the syndrome in Ireland, primarily falls within the realm of rheumatology, but as a non-inflammatory condition with no clearly defined management pathway, waiting times for first referral can be extremely prolonged and subsequent holistic management, encompassing the systemic manifestations is challenging. Furthermore, it is likely that many undiagnosed patients are receiving care for isolated manifestations of the disorder such as anxiety, or gastrointestinal symptoms. There is currently no means to identify specialists or allied health professionals who have knowledge or interest in EDS–HT and although individuals may require a multidisciplinary team approach, there is no inclusive professional support network. Although most rheumatologists recognise the syndrome, few have expressed specialist interest in EDS-HT and those who have face the challenge of finding specialists across the disciplines who have interest and knowledge of EDS-HT and who can engage with the multi-systemic nature of the disorder. Gastrointestinal, cardiovascular, neurological, urogynaecological or chronic pain specialists, who have knowledge and experience of EDS–HT have not been identified and may not yet exist in Ireland.

4.2.2 Rheumatic and Musculoskeletal Disease Unit (RMDU)

The RMDU is a tertiary referral unit based at Our Lady's Hospice and Care Services (OLH&CS) in Harold's Cross, for individuals who require specialist, multidisciplinary medical management and intensive individually tailored rehabilitation due to chronic rheumatologic or musculoskeletal conditions. As part of the rare disease strategy to develop national CoEs, the HSE requested a small specialist clinical group from the RMDU to investigate the possibility of establishing a Hypermobility CoE at the RMDU. The group consisted of a rheumatologist, physiotherapist, nurse specialist, occupational therapist and social worker. The HSE (through patient requests for funding to travel to the United Kingdom) and the RMDU specialist group identified 'The Hypermobility Unit at the Hospital of St John & St Elizabeth' in London as a centre providing excellence in research, diagnosis and care of hypermobility syndromes. The specialist group travelled to London to review the care model at 'The Hypermobility Unit', to establish the suitability of that care model in the Irish context and to identify the requirements of a CoE at the RMDU. Within the time constraints, the RMDU specialist group was chosen to peer review the first draft of the MDS.

4.2.3 Literature Review for Common and Disease Specific Data Elements

A comprehensive literature review and appraisal was conducted to extract the common clinical data elements in EDS-HT. The researcher conducted a series of systematic searches on available online databases including Science Direct, PubMed, Cochrane database of systematic reviews, and Google Scholar. These databases were searched using a combination of the following key words;

> Hypermobility Syndrome / Joint Hypermobility Syndrome / Benign Joint Hypermobility Syndrome / Ehlers Danlos Syndrome Ehlers Danlos Type 3 / Ehlers Danlos Type iii / Ehlers Danlos Hypermobility Type

Further searches for common data elements was conducted by searching google for relevant government strategies and policies.

4.2.4 Development of the MDS V.0;

Based on the results for the literature review, all the data elements identified were categorised into relevant data sets. These data sets were them tabulated into a

working document – see Appendix A. This document provided the structure for review of DE's by the expert group.

4.2.5 Expert survey to review MDS V.0;

The first draft MDS along with a comprehensive information sheet was made available to all potential participants prior to face to face meetings. The expectation set out was that the expert would review the MDS prior to the meeting and identify what data elements should remain, what should be removed and what was missing

Semi – structured interviews with individual experts in EDS-HT / JHS were conducted to further develop the data set, process requirements, and technological solutions and to identify challenges.

4.2.6 Validation of the MDS

It was agreed in consultation with the expert group that validation of the MDS by a wider stakeholder group could be best achieved via online survey of members of the Irish College of General Practitioners (ICGP) and via shared care practices.

A questionnaire was developed and ethics approval received for post expert review of the MDS. However, the MDS was not sufficiently developed after the expert review to complete this part of the research. The questionnaire is in Appendix B.

4.3 Qualitative Data Analysis

A qualitative data analysis of the DE's reviewed by the experts was undertaken. This review took the form of review of the inclusions, exclusions and omissions as identified by the experts and also any additional feedback provided by the experts. The output of the semi-structured interviews was analysed by themes. These outputs are discussed in the results section, (chapter 6)

4.4 Ethical Considerations

Ethical approval was sought and received from Trinity College Dublin. All potential participants received a comprehensive information form and had the opportunity to

have any concerns clarified. Participation in the research was voluntary and participants were free to withdraw at any time, without penalty and without providing a reason. There was no risk involved in participation. There are no conflicts of interest.

Data was gathered and stored during the research according to the Data Protection Acts (1988 and 2003) until the completion of the research and the Master of Healthcare Informatics Degree. Audio data was stored by the researcher until transcripts were prepared and verified, after which it was destroyed. A summary of the findings of the research is available upon request to all participants.

4.5 Summary

This chapter detailed the design and methodology for the overall research and further developed the methodology chosen for development of the MDS for EDS-HT, in order that the research question can be answered. Methods for data analysis, and ethical issues were also outlined.

5 Literature Review for EDS-HT Data Elements

5.1 Introduction

This section includes the results of the literature review to identify EDS-HT disease specific data elements (SDE's) and the common data elements included in patient records.

5.2 Disease Specific Data Elements (SDE's)

The diagnosis of EDS-HT is based on Beighton and Brighton Criteria as discussed in sections 2.3.2 and 2.3.3. However, hypermobility is a common clinical sign in across the spectrum of EDS and many other heritable connective tissue disorders (HCTD), these disorders must be considered as part of the differential diagnosis (Castori, 2012a).

Diagnosis SDE's
Localised Hypermobility / Generalised Hypermobility
Beighton score / Brighton Score / Hypermobility 5 part questionnaire
Other Heritable Connective Tissue Disorder

5.2.1 Musculoskeletal SDE's

A partial or complete Marfanoid habitus is commonly expressed in EDS-HT and can act as a confounding feature or clue to diagnosis (Grahame et al., 2000).

Features Of The Marfanoid Habitus SDE's
Arachnodactly (Steinberg +ve wrist signs)
Scoliosis / Pectus excavatum / Pectus carinatum
Span: height /ratio >=1.03
Crown / pubis : pubis / floor ratio <0.89
Hand : height ratio >11% Foot : height ratio >15%

Musculoskeletal symptoms must be present according to the Brighton criteria in order that JHS be diagnosed. Non-inflammatory, frequent joint pain is present in 100% of

subjects, predominantly during and after activity and improves with rest (Pacey et al., 2014, Voermans et al., 2010a).

Arthralgia's of more than three months duration most frequently affect the knees, ankles and feet (Adib, 2005). Whilst the most common joints to sublux or dislocate are the patella and shoulder, many other joints can be affected including the hands, elbows, feet, hips, cervical spine and temporomandibular joint (Wainwright et al., 1993, Buckingham et al., 1991, Dabbas et al., 2008, Janssen and Kopta, 1985, Rames and Strecker, 1991, Kirk et al., 1967). Soft tissue injuries occur more frequently in EDS-HT and recovery time is usually prolonged (Pacey et al., 2014, Castori et al., 2010).

Musculoskeletal SDE's
Subluxation / Dislocation / Arthralgia / Myalgia
Pain Local / Regional / Widespread
Peripheral Joints / Spine /TMJ/ Headache

5.2.2 Dermatological SDE's

Skin is described as fragile, velvety soft, doughy and hyper-elastic in EDS-HT (Castori, 2012a, Remvig et al., 2009). Striae atrophicae may develop during periods of growth and scars may be thin and papyraceous (Hakim, 2006). In the absence of haematological disorders, excessive bruising and haematomas may be present, may occur spontaneously or with minimal trauma and have frequently raised suspicion of non-accidental injury in children particularly, in the absence of a diagnosis (Steinmann, 2002, Parapia and Jackson, 2008). Once a mistaken diagnosis of physical child abuse has been made, it may be difficult to repair the parental distress (Wardinsky, 1995).

Dermatological SDE's
Skin – Hyperelastic / Velvety Soft / Doughy
Striae Atrophicae / Thin Papyraceous Scars / Easy Bruising

5.2.3 Gastrointestinal SDE's

Functional gastrointestinal disorders are commonly associated with EDS-HT, although the pathogenic mechanism is not yet understood. (Zarate et al., 2010). Early satiety,

gastro-oesophageal reflux, constipation, delayed gastric emptying, dysmotility and diarrhoea occur more frequently in the EDS-HT population than the general population (Fikree et al., 2014). Symptoms of abdominal pain, bloating, nausea and vomiting have also been reported in this cohort. Abdominal visceroptosis may occur rarely in EDS-HT (Reinstein et al., 2012). Dysphagia may intensify the gastrointestinal disorders which in extreme cases require total parenteral nutrition (Fikree et al., 2011). In a recent small study, celiac disease was found to be 10–20 times more common in EDS-HT compared to the Italian general population (Danese et al., 2011). Furthermore, an association between joint hypermobility and inflammatory bowel / Crohn's disease was found by Vounotrypidis et al. (2009)

Whilst early literature describes an increased association of diverticular disease with EDS, the subtype is often not specified (Levard et al., 1989). Handa et al. (2001) describe bladder diverticula in a patient with unspecified EDS and Marfanoid hypermobility syndrome.

Gastrointestinal SDE's
Abdominal Pain / Bloating / Nausea / Vomiting /Dyspepsia
GERD/ Hiatus Hernia / Dysphagia / Delayed Gastric Emptying
Dysmotility / Constipation / Diarrhoea / Diverticulae Inflammatory Bowel Disorders / Faecal Incontinence

5.2.4 Cardiovascular SDE's

While the Brighton Criteria recognise that varicosities occur more frequently in the JHS population, there is no significant correlation with catastrophic cardiovascular events in EDS-HT unlike some of the rarer forms of EDS. However, vascular fragility may result in varicosities. Aortic root dilation and widened Valsalva sinus has been reported with greater frequency in EDS-HT, although this appears to be non-progressive and thus of minor clinical consequence (Wenstrup et al., 2002, McDonnell et al., 2006, Atzinger et al., 2011, Balli et al., 2014). Atzinger et al also found a 6% incidence of mitral valve prolapse, a six fold increase than that of the general population and Balli et al demonstrated diastolic dysfunction in children with JHS. These finding are in agreement with Camerota et al. (2014) whose study suggest the cardiac phenotype for EDS-HT to consist of moderately prolonged PR interval and P wave, heart rate and

conduction abnormalities and mitral and tricuspid valve insufficiency with possible mitral valve prolapse.

Cardiovascular SDE's
Echocardiogram / ECG / Varicosities
Aortic Root Dilation / Aortic/Mitral Valve Prolapse

5.2.5 Dysautonomia SDE's

The relatively recent and emerging phenomenon of Postural Orthostatic Tachycardia Syndrome (POTS) is increasingly associated with EDS-HT. POTS is defined as the presence of symptoms of orthostatic intolerance for at least 6 months accompanied by a heart rate increase of at least 30 beats/min within 5-30 minutes on assuming an upright posture, but not associated with a fall in blood pressure (Raj, 2006). Patients with POTS complain of palpitations, light-headedness, headache, visual disturbances, 'brain fog', exercise intolerance and extreme fatigue. Symptoms are due, at least in part to an orthostatic increase in pelvic and lower limb blood volume concurrent with reduction in thoracic and cerebral blood volume (Stewart and Montgomery, 2004, Low et al., 2009). Other pathomechanisms suggested include peripheral neuropathy, connective tissue abnormalities, and deconditioning (Gazit et al., 2003, De Wandele et al., 2014b). Although syncope rarely occurs, orthostatic intolerance is extremely debilitating, and for some people it is the most disabling symptom of EDS.

De Wandele et al. (2014a) found that dysautonomic symptoms of orthostatic intolerance and gastrointestinal symptoms occurred more frequently and were more severe in EDS-HT than in classical or vascular EDS, causing a marked reduction in quality of life, and greater pain and fatigue. De Wandele also speculated that, the lack of association with affective distress and deconditioning indicates that these factors are unlikely to be primary causative factors in the development of autonomic symptoms.

Other reported symptoms of dysautonomia include secreto-motor, (altered perspiration, dry eyes/mouth) vasomotor symptoms, (Raynaud symptoms, dependent limb discolouration), pupillo-motor symptoms and urinary tract disorders (urinary retention, residual retention, urgency/ frequency) (De Wandele et al., 2014a, Gazit et al., 2003, Farmer et al., 2014).

Dysautonomia SDE's
Orthostatic intolerance / POTS / Gastrointestinal symptoms
Urological Symptoms / Dependent Pooling / Raynauds

5.2.6 Neurological SDE's

Reduced proprioception, and balance associated with hypermobility have been reported widely in the literature (Falkerslev et al., 2013, Fatoye et al., 2009, Iatridou et al., 2014, Mebes et al., 2008). Mild-to-moderate muscle weakness and atrophy, reduction of vibration sense, peripheral and compression neuropathies occur in EDS-HT less frequently than the other EDS subtypes but in greater proportion than in the general population (Voermans et al., 2009). Abnormal stretching of or pressure on peripheral nerves due to subluxation or dislocation as a result of capsular ligamentous laxity or due to underlying connective tissue abnormality within the perineurium and endoneurium of the nerves may be responsible for peripheral or plexus neuropathy (Castori and Voermans, 2014).

Furthermore, pain sensitisation is likely to increase disability and decrease function. Dysfunction of the autonomic nervous system is thought to play a role in many of the symptoms of EDS.

Neurological SDE's
Altered Balance / Proprioception / Vibration
Neuropathies / Myopathies
Pain - Sensitisation / Chronic Regional / Chronic Widespread

5.2.7 Uro-gynaecological SDE's

A number of urological problems have been noted to occur more frequently in EDS-HT, namely urovesicular reflux, bladder diverticulae, recurrent urinary tract infections and increased frequency and urgency (Mastoroudes et al., 2013). It is likely that both neurogenic and underlying connective tissue abnormalities are involved in the development of symptoms. The incidence of stress incontinence in children with JHS was recently and surprisingly reported to be 26% (Pacey et al., 2015). Urovesicular

reflux was present in 60% of children with JHS and 70% with neurogenic bladder and JHS had “failure to thrive” in a recent study (Beiraghdar et al., 2013).

A hormonal effect on incidence and severity of symptoms is highly likely given the preponderance of females presenting with the syndrome, although the mechanism is not yet understood. Castori et al. (2012b) found symptomatic deterioration of the condition during pregnancy in 40% of 83 patients, including not only pelvic and musculoskeletal pain but also fatigue, GI symptoms, anxiety, depression and sleep disturbances. However, 13% of patients reported amelioration of symptoms suggesting a complex hormonal / homeostatic / musculoskeletal interaction during pregnancy. Furthermore, Castori et al. (2012b) postulate that a combination of dysautonomia, tissue and vascular fragility may increase the risk of haemorrhage, poor wound healing and abnormal scar formation for both caesarean and vaginal delivery. Incidence of pelvic organ prolapse is also increased in this population, possibly due to the underlying connective tissue disorders (Norton et al., 1995). Although a recent study by Knoepp et al. (2013) found generalised joint hypermobility was not associated with postpartum pelvic floor dysfunction, a population survey found the prevalence of both urinary and faecal incontinence to be significantly higher in females with confirmed JHS when compared with females without JHS (Arunkalaivanan et al., 2009).

Uro-gynaecological SDE’s
Urovesicular Reflux / Bladder Diverticulae / Incontinence
Recurrent Urinary Tract Infections / Increased Frequency Urgency / Hormonal / Pregnancy

5.2.8 Pulmonary and Ear, Nose, and Throat (ENT) SDE’s

Morgan et al. (2007) reported an increased frequency of respiratory symptoms including asthmatic symptoms and atopy, reduced exercise tolerance, increased distensibility and airway collapse in EDS-HT. Soyucen and Esen (2010) postulate that recent increases in childhood asthma may be due to the underlying connective tissue defect present in JHS, which may affect the structure of the airways and lead to airway collapse and persistent wheezing.

A slightly increased risk for spontaneous pneumothorax (0.9%) was found in with persons who present with both JHS and a Marfanoid Habitus, although this risk is much greater in vascular EDS (Bravo and Wolff, 2006).

ENT disorders associated with EDS-HT have begun to appear in the literature. Rimmer et al. (2008) report dysphonia from birth as the presenting sign in a case of EDS-HT, whilst an EDS population survey by Hunter et al. (1998) reported an occurrence of symptoms of dysphonia 28%, dysphagia 39%, and 48% speech and language difficulties, much greater than the expected prevalence of these symptoms in the general population.

Pulmonary and Ear, Nose, and Throat (ENT) SDE's
Asthma / Pneumothorax
Dysphonia / Dysphagia

5.2.9 Surgical and Anaesthetic SDE's

Few studies regarding surgical issues in EDS-HT have been published, although many catastrophic or high risk surgeries are described regarding vascular or unspecified EDS. It is unlikely that surgical risks are the same across the spectrum of subtypes particularly since the degree of fragility of skin, soft tissue and blood vessels varies between types. Accordingly prophylactic contraindication to surgery is not warranted in the case of EDS-HT (Grahame and Kazkaz, 2014). However, tissue fragility may result in delayed wound healing, separation of sutures, postsurgical hernias and minor bleeds, for which prophylactic recommendations exist (Castori, 2012b). Resistance to local anaesthetic is present in up to 60% of patients with EDS-HT and is widely reported in the literature (Adib, 2005, Hakim and Grahame, 2003a, Castori, 2012a). Temporomandibular joint dysfunction and occipito-atlanto-axial instability, dysautonomia and meningeal fragility require particular anaesthetic attention (Wiesmann et al., 2014).

Surgical and Anaesthetic SDE's
Local Anaesthetic Resistance / Poor Wound Healing
Wide Atrophic Scars / TMJ Dysfunction / Dysautonomia
Occipito-Atlanto-Axial Instability / Meningeal Fragility

5.2.10 Orthopaedic SDE's

Soft tissue injuries, impingement syndromes joint instability, subluxation and dislocation in EDS-HT often prompt orthopaedic attention, particularly in the early and late phase of the disorder. Prompt treatment and rehabilitation is necessary to prevent deconditioning. Surgical treatment is generally recommended only after conservative treatment has been exhausted since worsening of pain, deconditioning and recurrence of symptoms have been shown to occur in patients with EDS-HT (Shirley, 2012)
Gulbahar et al. (2006) found that hypermobility significantly increased risk for low bone mass in premenopausal women by 1.8%, and Roberto et al. (2002) reported significantly lower bone mineral density in children with hypermobility, both concluding that hypermobility is a risk for osteopenia. By contrast, two prior studies which reported no increased risk for bone loss in JHS, had used Beighton criteria, not taking account of age related reduction in hypermobility (Mishra et al., 1996, Dolan et al., 2003).

Orthopaedic SDE's
Osteopenia / Osteoporosis / Bone density / Soft Tissue Injuries
Impingement Syndromes / Dislocations / Subluxations

5.2.11 Orodental SDE's

Characteristic features of EDS-HT, include a narrow high arched palate with dental overcrowding, absence of labial and lingual frenulum, and a positive Gorlins' sign (Grahame and Kazkaz, 2014). Increased mucosal fragility can lead to gingival bleeding, recurrent gingival inflammations/infections, gingival retractions and rarely premature tooth loss (Castori, 2012a). Enamel hypoplasia, congenital dental deformities and rapid migration of teeth during orthodontic treatment have been reported, the latter possibly due to tearing of periodontal fibres coupled with poorly organised periodontal collagen (Abel and Carrasco, 2006).

Whist not part of the Beighton or Brighton criteria, the incidence of temporomandibular joint (TMJ) dysfunction is reportedly 70% in EDS-HT (De Coster et al., 2005). Chang et al. (2015) reported that patients with TMJ articular disc disorders are 6.7 times more likely to be diagnosed with JHS compared to patients without disc-related disorders, whist Buckingham et al. (1991) found a 54% incidence of JHS in patients with severe TMJ degeneration requiring surgery.

Orodental SDE's
Narrow High Arched Palate / Enamel Hypoplasia
Dental Overcrowding / Dental Deformities
Mucosal Fragility / TMJ Dysfunction

5.2.12 Psychological / Psychiatric SDE's

A range of psychological and psychiatric disorders have been associated with EDS-HT. Joint Hypermobility was associated with a 22 fold increase in risk for development of an anxiety disorder (particularly panic disorder and agoraphobia) but not to any major depressive disorder, compared to controls in a 15 year follow up study (Bulbena et al., 2011). Conversely, in a psychiatric population, 67.7% of patients presenting with anxiety disorders were found to have JHS compared to 10.1% of patients presenting with other psychiatric disorders and 12.5% of non-psychiatric patient (Bulbena et al., 1993). A number of systematic review have validated these findings (Baeza-Velasco et al., 2014, Bianchi Sanches et al., 2012). Celletti and Camerota (2013) suggest that the association of anxiety disorders with JHS/EDS-HT is due to the "high rate of medically unexplained symptoms and chronic pain" observed in these patients, whilst Bulbena (2011) suggests that "interactions between autonomic, physical and psychological disturbances are linked in a complex way in JHS, each 'fuelling' the other".

A confounding association with eating disorders might be expected in EDS-HT given the high incidence of gastrointestinal disorders, POTS and anxiety. Goh et al. (2013) found that joint hypermobility was significantly more common in patients with anorexia nervosa than in first degree relatives or and controls. Furthermore, they stipulate that many patients with anorexia nervosa also present with symptoms of POTS suggesting a common underlying pathomechanisms.

Psychological And Psychiatric SDE's
Anxiety / Eating Disorders

5.2.13 Ophthalmic SDE's

Blue sclera, antimongoloid palpebral slant, blepharochalasis (lid laxity), are commonly found in EDS-HT and are considered minor Brighton criteria (Grahame et al., 2000). Myopia, xeropthalmia, steeper corneas minor lens opacities and vitreal abnormalities are associated with EDS-HT, although treatment is usually only required for, xeropthalmia, and pathologic myopia (Castori, 2012a, Gharbiya et al., 2012).

Opthalmological SDE's
Myopia / Xeropthalmia / Mucosal Fragility
Blue Sclera / Antimongoloid Palpebral Slant
Blepharochalasis / Meiteniers sign / Steeper Corneas
Minor Lens Opacities / Vitreal Abnormalities

5.2.14 Health Related Quality Of Life (HRQOL) SDE's

Identification of the causative factors which reduce quality of life in in EDS-HT is essential in order that appropriate treatment strategies be developed.

Chronic pain, fatigue, gastrointestinal dysfunction, autonomic dysfunction and incontinence have been associated with significantly poorer HRQOL. Nonetheless, the study by Rombaut et al. (2010) reporting extremely poor HRQOL in EDS-HT across all eight sub-categories in the RAND-36 questionnaire and an associated reduction in physical activity is striking. Diminished HRQOL is replicated in adolescent and child EDS-HT populations. Zekry et al. (2013) found that in adolescents with EDS-HT, pain and fatigue are significant predictors of reduced HRQOL in the emotional, social and school function categories of the PedsQL and that the reduced HRQOL present in EDS-HT is comparable to that of patients with rheumatoid arthritis, cancer and inflammatory bowel disease. Cognitive fatigue associated with EDS-HT was a significant predictor of school function impairment, which if addressed early might prevent educational deterioration. Whilst these findings were recently replicated in a study by Pacey et al. (2015), stress incontinence and gastrointestinal dysfunction were also associated with reduced HRQOL children with pain, fatigue and stress incontinence accounting for 75% of the variance in child-reported HRQOL.

In a study by Voermans et al. (2010b) 77% of EDS patients reported severe fatigue, with the most severe fatigue associated with EDS-HT and with a greater reduction in HRQOL and increased psychological distress. Again, fatigue in EDS was greater than that reported in cancer or rheumatoid arthritis in the Dutch population. In this study severe fatigue in EDS was associated with sleep disturbances, concentration problems, social functioning, self-efficacy regarding fatigue, and pain.

De Wandele et al. (2014a) found that autonomic symptoms, particularly orthostatic intolerance and gastrointestinal symptoms, in EDS-HT were significantly associated with reductions in HRQOL and increased pain and fatigue but were not associated with deconditioning or affective distress suggesting that these are consequences of the condition rather than causes.

Quality of Life SDE's
Fatigue / Pain / Dysautonomia
Incontinence / Anxiety / Physical Activity

5.3 Common Data Elements CDE

5.3.1 Demographics

Patient demographics are essential to ensure identification and reconciliation of a particular individual with a particular dataset. It also provides essential contact information for the subject of care and next of kin. The demographic dataset has been standardised by HIQA (2013a). The inclusion of the national unique identifier allows for future national incentives and the inclusion of the rare disease identification is in line with rare disease strategy and allows for future inclusion in rare disease incentives (Taruscio et al., 2014, Dept. of Health and Children, 2014).

Demographics CDE's
National Unique Identifier / First Name / Last Name
Address / Street / City / Country
Date of Birth / City of Birth / Country of Birth
Date of Death / Gender
E-mail / Phone : Home / Phone : Mobile
Rare Disease ID
Next of Kin : Name / Next of Kin : Relationship
Next of Kin : Phone / Next of Kin : Address

5.3.2 Alerts and Allergies

Inclusion of essential allergies and alerts can prevent many medical errors, particularly medication allergies and is a common data element in patient records.

A number of SDE's identified in the previous sections may need to be included as alerts for EDS-HT due to the potential for adverse events. While these DE are disease specific, they fit under the common metadata item of alerts. Autonomic Dysfunction, Orthostatic Intolerance and POTS may rarely result in syncope and medical procedures may require adaptation of medication, patient positioning or time required (De Wandele et al., 2014a). Local anaesthesia resistance, will require adjusted dose or alternative methods (Wiesmann et al., 2014). Cervical instability may alter physiotherapy or anaesthetic procedures (Wiesmann et al., 2014, Milhorat et al., 2007, Keer, 2010).

Alerts and Allergies CDE's
Autonomic Dysfunction / Orthostatic Intolerance / Postural Orthostatic Tachycardia Syndrome
Local Anaesthesia Resistance / Cervical Instability

5.3.3 History

The following metadata items are commonly included in all patient records. They are included for review and to allow the opportunity for other important DEs to be identified by experts. The following metadata elements were considered as the minimum data for History (Walker, 1990)

History CDE's
Past Surgical History / Past Medical History / Familial History
Occupation / Hobbies

5.3.4 Medication

Current medication is an essential CDE in patient records. Recent medication may be relevant to prescribers. The following metadata elements were considered as the minimum data for Medication (Walker, 1990)

Medication CDE's
Current / Recent

5.3.5 Test Results

The following metadata elements were considered as the minimum data for Test Results (Walker, 1990).

Test Results CDE's
Imaging / Haematology / Lab

5.3.6 Genetics

EDS-HT is a genetic disorder although the genetic marker has not yet been found. Including genetic data fields in the EDS-HT MDS allows for future recording of genetic information. Furthermore, it allows for recording of negative test results in the event that genetic tests are performed as part of the differential diagnosis. In the case of genetic diseases, the following DEs are recommended (Taruscio et al., 2014).

Genetics CDE's
Chromosome number / Chromosomal reference sequence / accession and version number
RefSeqGene accession and version number / Locus Reference Genomic (LRG)
Variant description in HGVS format / Variant description in other format

5.3.7 Management – Plan of Care

The multi systemic nature of EDS-HT requires input from a wide variety of Healthcare professional (Castori et al., 2012a). Furthermore temporary or long term use of use of

aids and appliances may be necessary (Keer, 2010). The following metadata elements were considered as the minimum data for Management – Plan of Care

Management – Plan of Care CDE's
Medication / Physiotherapy / Occupational Therapy
Psychology / Podiatry / Speech and Language Therapy
Aids and Appliances

5.4 Summary

This chapter identified the disease specific and common data elements for inclusion in the first draft of the MDS. These DE's are summarised in Table 6.

Table 6 Summary of Data Elements from Literature Review

	Data Elements
Disease Specific DE's	**42**
Diagnosis SDE's	3
Features Of The Marfanoid Habitus SDE's	5
Musculoskeletal SDE's	3
Dermatological SDE'S	2
Gastrointestinal SDE's	3
Cardiovascular SDE's	2
Dysautonomia SDE's	1
Neurological SDE's	3
Urogynaecological SDE's	2
Pulmonary and Ear, Nose, and Throat (ENT) SDE's	2
Surgical and Anaesthetic SDE's	3
Orthopaedic SDE's	3
Orodental SDE's	3
Psychological And Psychiatric SDE'S	1
Opthalmological SDE'S	4
Quality of Life SDE'S	2
Common DE's	**49**
Demographics CDE	20
Allergies CDE	5
History CDE	5
Medication	2
Test Results CDE	3
Genetics CDE	7
Management – Plan of Care CDE's	7
Total number of DE's	**91**

6 Results, Analysis and Discussion

6.1 Establishment of Expert Group

The difficulty finding a panel of experts in Ireland was highlighted in section 4.2.1. This difficulty reflects the experience of many patients who seek care for rare disease. The panel of experts initially identified at the specialist RMDU consisted of a rheumatologist, physiotherapist, nurse specialist, occupational therapist and social worker. Neither the nurse specialist nor the social worker responded. The physiotherapist completed the initial review of the DE's but was unavailable for interview within the time frame due to personal circumstances. The rheumatologist and the occupational therapist completed the initial review and the semi-structured interview. A second physiotherapist with experience and knowledge of EDS-HT and employed at the RMDU was identified by snowballing. The second physiotherapist also completed the review of DE's.

As part of the review, three of the identified experts expressed concern over the use of the term 'Expert'. They stated that although they had some knowledge and experience of EDS-HT they would by no means call themselves experts. They acknowledged that they had visited a specialist hypermobility unit in the UK to establish if the model of care used there could be deployed in Ireland. This visit helped to identify their own gaps in experience by comparison with the UK site and one professional stated that

"*Both passion and knowledge are required to care for EDS-HT patients. Knowledge can be acquired but interest or passion cannot, and this must be present to develop an expert service. Passion is definitely present here.*"

6.2 Data Element Literature Review

The DE's identified in the literature review are contained in sections 5.2 and 5.3 and are summarised as follows in Table 7.

Table 7 Summary of Data Elements

	Data Elements
Disease Specific DE's	**42**
Common DE's	**49**
Total number of DE's	**91**

6.3 First draft MDS

The author is a physiotherapist with knowledge of musculoskeletal conditions and patient assessment. In addition to the data identified in the literature review, this medical knowledge was drawn upon in developing the first draft of the MDS.

Review of the DEs and dataset resulted in additions to the DEs to ensure completeness and to identify alternative terminology. Additions were made to "diagnosis" to allow for differential diagnosis of generalised or local hypermobility, other EDS types and of other HCTD's. Additions were made to "musculoskeletal" to allow for clinical CDE's including particular locations and types of symptoms. This level of detail may need to be further nested in the MDS.

Furthermore, the author reviewed a data set used at the specialist hypermobility centre in London. This data set was offered freely to the author, by Professor. R. Graham, who expressed an interest in the research during an appointment with the authors' adolescent son who has EDS-HT. This dataset was cross referenced with the MDS and a high level of correlation with the disease specific DE's was noted.

The first draft of the MDS included a total of 157 DEs categorised into 8 clinical constructs or metadata items. This MDS was tabulated for review by the expert group (Appendix G)

6.4 MDS expert panel review

The dataset was reviewed by four experts as discussed in section 6.1. Semi-structured interviews took place with two of the group. The following tables will identify the accepted DE's (green), the rejected DE's (red) and the DE's which require modification (yellow), according to each of the experts (P1-P4). Where there is a difference of opinion between the experts the DE's will be identified for further discussion. Figure 12 explains the colour coding throughout the datasets

Response	
Valid Data Object	
Expert Unsure	
Expert recommends removal	

Expert not qualified to comment	

Figure 12 Legend for the MDS Review

6.4.1 Demographic Data

Table 8 Demographic Data Set

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Identification	National Unique Identifier	National Unique Identifier				
Personal Information	Full Name	First Name:				
		Last Name:				
	Dates	Date of Birth:				
		Date of Death				
	Gender	Gender:				
	Birth Address	City of Birth				
		Country of Birth				
		Rare Disease ID				
	Next of Kin	Name				
		Relationship				
		Phone				
		Address				
Contact Information	Address	Address:				
		Street:				
		City:				
		Country:				
		E-mail				
		Phone : Home				
		Phone : Mobile				

Inclusions

No new data was identified as being required in this metadata set.

Further Development Needed

A number of respondents felt that city and country of birth were irrelevant to individual care. In interview this was clarified as possibly relevant to rare disease registries or population studies (Table 8).

6.4.2 Allergies and Alert Data

Table 9 Allergies and Alerts Data Set

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Allergies	Allergies	Allergies				
Alerts	Alert Types	Autonomic Dysfunction				
		Orthostatic Intolerance				
		Postural Orthostatic Tachycardia Syndrome				
		Local Anaesthesia Resistance				
		Cervical Instability				
	Other	Other : Please Specify				

Inclusions

No new data was identified as being required in this metadata set.

Further Development Needed

A number of respondents felt that autonomic dysfunction, orthostatic intolerance and POTS were too repetitive. POTS was identified as the most likely term to be used as an alert, with standardization of terminology necessary (Table 9).

6.4.3 Diagnosis

Table 10 Diagnosis Data Set

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Localised Hypermobility	Localised Hypermobility	Localised Hypermobility				
Generalised Hypermobility	Generalised Hypermobility	Generalised Hypermobility - Non Syndrome				
JHS	JHD	Joint Hypermobility Syndrome				
EDS	EDS	Hypermobility Type				
		Classic type				
		Vascular Type				
		Arthrochalasia Type				
		Kyphoscoliotic Type				
		Other: Please Specify				
Other Connective	Other Connective	Marfans' Syndrome				
Tissue Disorder	Tissue Disorder	Osteogenesis Imperfecta				
		Loetyz Dietz				
		Other: Please Specify				

Inclusions

Homocystinuria was identified for possible inclusion in the differential diagnosis under HCTDs.

Further Development Needed

While JHS was accepted by three experts, one felt that this should be considered as an alternative term for EDS-HT. The term “other connective tissue disorder” needs to be modified to state “Heritable” connective tissue disorder thus differentiating them from inflammatory connective tissue disorders. It was also suggested that this term was used as an umbrella term with a drop down list of all HCTD’s or the capability to add a disorder (Table 10).

6.4.4 History

Table 11 History Data Set

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Patient History	Patient History	Past Surgical History				
		Past Medical History				
Family History	Family History	Familial History				
Social History	Social History	Occupation				
		Hobbies				
Other	Other	Other: Please Specify				

Inclusions

All experts felt that social history needed further development as this is often a measure of the impact of the disorder. Occupation should include part or full time, whether a person is a student, unemployed or if they have retired. DE’s need to be included which identify if a person has retired due to disability or illness. Hobbies also needed clarification to be able to regular physical activity levels, a measure both of the impact of the disease and the impact of treatments (Table 11).

6.4.5 Medication

Table 12 Medication Data Set

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Medication	Current	Current				
	Recent	Recent				

Further Development Needed

Recent medication needs to be relevant to the condition. Two experts identified that long lists of old irrelevant medication would interrupt workflow. One expert mentioned that over-reliance on medication should be discouraged in this group and therefore although it needs to be included, this should not be the focus of any EDS-HT record (Table 12).

6.4.6 Test Results

Table 13 Test Results Data Set

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Test Results	Test Results	Imaging				
		Haematology				
		Lab				
		Other : Please Specify				

All experts agreed that imaging and haematology results should be included but one felt that lab results were not necessary. Further more detailed result would need to be nested within result eg imaging would require x-ray, CT, MRI results. Access to both results and images according to profession was deemed important (Table 13). Other DE's identified for inclusion in test results were cardiac monitoring and tilt table testing.

6.4.7 Genetics

Table 14 Genetics Data Set

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Genetics	Genetics	Chromosome number				
		Chromosomal reference sequence accession and version number				
		RefSeqGene accession and version number				
		Locus Reference Genomic (LRG)				
		Variant description in HGVS format				
		Variant description in other format				
		Other : Please Specify				

All of the genetic information needs further development. One expert thought that this was irrelevant to clinical management and gave too much relevance to the biomedical side of the condition but that it may be relevant to clinical researchers. Others thought that it was important to be able to outrule other HCTD's. One expert thought that if this was present in an EDS-HT record it might prompt further testing in the case of an elusive diagnosis (Table 14).

6.5 EDS-HT Disease Specific Data

Table 15 Rheumatological SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Rheumatological/ Musculoskeletal	Rheumatological/ Musculoskeletal	Beighton Score				
		Brighton Criteria				
		Quality of Life Score				
		Functional Index				
	Joint Involvement	Right / Left / Bilateral				
		Hip				
		Knee				
		Ankle				
		Shoulder				
		Elbow				
		Wrist				
		Hands				
		Feet				
		TMJ				
		SternoClavicular				
		AcromioClavicular				
		CostoChondral				
	Spinal Involvement	Cervical				
		Thoracic				
		Lumbar				
		Sacral				
	Pain	Localised arthralgia's				
		Chronic Regional Pain				
		Chronic Widespread Pain				
		Fibromyalgia				
		Pain Scale				
		Other : Please Specify				

All of the experts agreed that the Beighton score be included although one was unfamiliar with the Brighton Criteria. At interview one expert stated that historical

hypermobility is essential due to loss of mobility with age but the other was not aware of the 5 point questionnaire for hypermobility. All experts agreed that a quality of life measure be included but that no particular measure was in use in the RMDU. They also stated that this needs the capability of breakdown into more functional elements. At interview, both experts mentioned the need to have links to what the various scores mean possibly adding decision support to aid diagnosis (Table 15).

Regarding joint involvement, all DE's were considered important but exhaustive. A better way to represent this is necessary. Furthermore, joint involvement may include laxity, subluxation, dislocation, pain, swelling etc. The possibility of including body charts or mannequins and an associated legend, as is the case in paper charts should be explored. Definition of dislocation / subluxation is necessary as patients often report dislocation in the absence of clinical evidence.

There was also disagreement about the DEs regarding pain and associated pain syndromes. Although pain is a significant factor in EDS-HT, this needs further development and some information may be included on the joint DE's review.

Table 16 Dermatological SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Dermatological / Cutaneous	Dermatological / Cutaneous	Fragility				
		Hyper-extensibility				
		Scarring -				
		Striae				
		Bruising / haematomas				
		Molluscoid Pseudotumors/ Spheroids/ Piezogenic Papules				
		Varicosities				
		Local Anaesthetic Response				
		Other : Please Specify				

Although all experts agreed, that some dermatological data can aid the diagnosis and needs to be included, they felt that the development of these SDE's required input from a dermatology expert experienced in recognition of EDS-HT (Table 16).

Table 17 Gastrointestinal SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Gastrointestinal	Gastrointestinal	Dyspepsia / Nausea / Vomiting				
		Abdominal Pain /Bloating				
		Gastro Oesophageal Reflux (GERD)				
		Hiatus Hernia				
		Delayed Gastric Emptying				
		Diverticular Disease				
		Dysmotility				
		Constipation				
		Diarrhoea				
		Faecal Incontinence				
		Other : Please Specify				

All the experts agreed that gastrointestinal issues can be extremely debilitating for patients with EDS-HT and often more problematic than the musculoskeletal symptoms. These SDE's which are important for inclusion require input from a gastroenterologist with specialist interest in EDS-HT. At interview one expert was unaware of any such gastrointestinal specialist, while the other expert knew of only one gastroenterologist with a special interest in EDS-HT who was recently appointed in the south west of Ireland (Table 17).

Table 18 Cardiovascular SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Cardiovascular	Cardiovascular	Cardiovascular				
		ECHO cardiogram				
		Mitral Valve				
		Aortic Valve				
		Aortic Root				
		Postural Orthostatic Tachycardia Syndrome (POTS)				
		Orthostatic Intolerance / Orthostatic Hypotension				
		Varicosities				
		Other : Please Specify				

All the experts agreed that while the cardiovascular SDE's are important for inclusion, these require input from a cardiologist with specialist interest in EDS-HT. No experts were aware of any such cardiology specialist. (Table 18)

Table 19 Urological SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Urological	Urological	Urological				
		Bladder Diverticulae				
		Increased Frequency				
		Urgency				
		Recurrent UTIs				
		Continence				
		Other : Please Specify				

All the experts agreed that while the urological SDE's are important for inclusion, their own knowledge was limited in this area and these SDE's require input from a urologist with specialist interest in EDS-HT. No experts were aware of any such specialist in Ireland. (Table 19)

Table 20 Gynaecological / Obstetrical SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Gynaecological / Obstetrical	Gynaecological / Obstetrical	Pregnancy				
		Hormonal				
		Other : Please Specify				

All the experts agreed that while the gynaecological and obstetric SDE's are important for inclusion, their own knowledge was limited in this area and these SDE's require input from an obstetric gynaecologist with specialist interest in EDS-HT. No experts were aware of any such specialist in Ireland. (Table 20)

Table 21 Pulmonary SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Pulmonary	Pulmonary	Asthma				
		Pneumothorax				
		Other : Please Specify				

The expert group was not aware of any links between EDS-HT and respiratory conditions but three of them felt that asthma and Shortness of breath would need to be included if present. The pulmonary SDE's need further iteration. (Table 21)

Table 22 Orodental SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Orodental	Orodental	Temporomandibular Joint Dysfunction				
		Mucosal Fragility				
		Other : Please Specify				

The experts agreed that orodental SDE's would require input from an orodental specialist because their own knowledge was limited in this area. No experts were aware of any such specialist in Ireland. One expert was unaware of any patients needing specialist treatment and thus queried including these SDE's. Further review of orodental SDE's is required. (Table 22)

Table 23 Opthalmological SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Ophthalmological	Ophthalmological	Myopia				
		Meitenier's Sign				
		Strabismus				
		Blue Sclera				
		Blurred Vision				
		Prescription				
		Other : Please Specify				

The experts agreed that opthalmological SDE's would require input from an ophthalmologist with a special interest in EDS-HT because their own knowledge was limited in this area. No experts were aware of any such specialist in Ireland. One expert was gave no input to these DE's. Further review of opthalmological SDE's is required (Table 23).

Table 24 Orthopaedic SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Orthopaedic	Orthopaedic	Osteopenia				
		Osteoporosis				
		Bone Density				
		Other : Please Specify				

The expert group agreed that the orthopaedic SDE's should be included. At interview both experts mentioned that this area required more specialist input, but that no orthopaedic consultants in Ireland have shown a special interest in EDS-HT despite the frequency that these patients attend orthopaedics with soft tissue injuries, subluxations and dislocations (Table 24).

Table 25 Psychological / Psychiatric SDE's

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Psychological / Psychiatric	Psychological / Psychiatric	Anxiety				
		Depression				
		Other : Please Specify				

All the experts agreed that psychological and psychiatric SDE's need to present in the MDS but needed further development. Greater definition of the terminology is required. Presence of cognitive impairment, personality disorder, eating disorders, previous psychiatric treatment, substance abuse and Munchausen's disorder should be considered for inclusion in the MDS. The lack of psychology services in Ireland is a major stumbling block to providing care to this cohort (Table 25).

Table 26 Management / Care Plan

Variable (Nesting Level 1)	Variable (Nesting Level 2)	Variables (Nesting Level 3)	P1	P2	P3	P4
Management – Plan of Care	Management – Plan of Care	Medication				
		Physiotherapy				
		Occupational Therapy				
		Psychology				
		Podiatry				
		Speech and Language Therapy				
		Aids and Appliances				
		Other : Please Specify				

All the experts agreed that management / plan of care DE's be included in the MDS although neither experts at interview were aware of any patients requiring speech and language therapy. Nursing care needs to be represented in the DE's particularly as nurses may play an essential role in education and be a contact person for the patient. Dietary plan / dieticians / feeding tubes also need to be included in the DE's due to the gastrointestinal symptoms. Aids and appliances need further development and categorisation (Table 26).

It was suggested that a DE of "specialists attended" by a patient be included on the MDS as this gives a quick insight into the burden or severity of the disorder.

6.6 Access to MDS data

It was agreed by all experts that administrators have access to demographic data only. Three experts felt all of the data should be available to patients but one did not. All experts agreed that doctors, allied health professional and nurses, in hospital or primary care should have access to data for a patient in their care. All experts agreed that de-identified data should be available to clinical researchers and patient registries, but that consent would be required. All experts agreed that insurance companies should not have access to the data. Two experts felt however that insurance companies should have access to diagnosis data for funding and reimbursement. Only one expert felt that government bodies should have access to de-identified data for the purpose of policy and strategy development.

6.7 Broader Validation of MDS

A questionnaire was developed using survey monkey and subsequently using Qualtrics with the intention of sending it electronically to ICGP members and shared care practices. Further re-development and expert review of the MDS is required before broader validation. This is in line with MDS dataset development where a number of iterations are required before broader validation.

6.8 Further results and analysis from the interviews

Semi structured interviews were conducted with two of the experts and this gave a richer analysis of the MDS data. The following three themes were also explored.

Clinical Process requirements
Technological Solutions
Benefits and Challenges

6.8.1 Clinical Process Requirements

The clinical process in caring for patients with EDS-HT needs to be improved. Both experts identified the lack of knowledge of the multi systemic nature of the condition by a majority of clinicians as a problem. This is particularly problematic with regard to accessing care for gastrointestinal, psychological, orthopaedic and autonomic issues. Access to tilt table testing, essential for diagnosis of POTS is also virtually impossible for this predominantly young population who have EDS-HT.

Developing a network of knowledgeable and interested clinicians is critical to improving the clinical process but this is very challenging in Ireland at the moment. Increasing awareness and knowledge of the condition is crucial. One expert felt that clinicians looking at this MDS data “might open their mind to the multisystemic nature of the disorder and assess EDS-HT patients from a broader more holistic viewpoint”.

For patients in Ireland, there is a level of anxiety observed due to the lack of information about this condition and also a level of anxiety inherent in the autonomic burden of the disorder. Therefore, it is essential that access to data for these patients, does not increase anxiety, rather decrease it. Suitable information links embedded

within an electronic solution that supports patient self-management would be invaluable.

6.8.2 Technological Solutions

Both experts felt that data must be available at point of care through a single user interface. The data must be valid and complete and privacy must be ensured. Data entry should take place at point of care and not need to be re-entered. Integration of systems is crucial particularly across multiple sites and in the community.

Embedded links to concise peer reviewed articles or best practice guidelines if included could support clinicians and enhance care and workflow. The experts were aware of a number of support groups in the UK who provide professional and patient literature. Establishing links with these groups would be useful.
Ideally, information should be mobile via tablets so that the information is available at point of care. Not all clinicians have access to computers while they are with a patient particularly allied health professionals.

6.8.3 Benefits and Challenges

The following benefits and challenges to implementing an EDS-HT record were identified by the experts;
Benefits
"Information is critical to understanding and managing the patients care".

"Patients would feel they are getting a holistic client centred approach".

"It would bring awareness of the co-morbidities that are associated with EDS for less experienced clinicians".

Challenges
"Improving information systems must be one of the highest priorities within the health service at the moment. While multiple strategies are being developed, lack of funding is a challenge to implement these strategies"

A lot of data is required to create the complete picture of the patient, but is not required by all clinicians or all of the time. How the relevant information can be presented to the different clinicians in an easy to use format is a challenge.

Crucially, systems must be fully integrated with a single sign on.

6.9 Summary

This chapter presented the results of the first iteration of the MDS and the expert feedback regarding the MDS. While many of the data elements have been agreed, many more data elements require input from a wider expert group. It was clear from the interviews that this expertise is not available in Ireland at present.

Furthermore, availability of complete information at point of care is essential to care for EDS-HT patients, but also challenging.

7 Conclusions and Future Work

7.1 Introduction

This aim of this research was to investigate the information processes and requirements in the care of patients with EDS-HT. The literature review identified education, communication and information gaps along the entire patient journey. Potential information technology solutions were explored. A methodology for developing an EDS-HT MDS was identified in order to answer the following research question;

What information and knowledge, as identified by expert EDS-HT clinicians, do clinicians who are non-expert in EDS-HT need, to care for and support patients with EDS-HT?

7.2 Research Summary

A methodology for developing an EDS-HT minimum data set was developed. A small expert group was identified. Common and disease specific data elements were identified by literature review. The dataset was reviewed and redeveloped in consultation with the small expert group. The dataset needs further review and development with a larger expert group in order to refine the data elements. Validation of the dataset across a broader stakeholder group should then take place.

7.3 Key Findings

Rare Diseases by their nature lack a depth of population data. This research found that clinical experts existed at an international rather than national level. Therefore, accessing knowledgeable and experienced clinicians is difficult for patients. Accessing specialists to advise on the systemic manifestations or complex cases is difficult for clinicians.

There is an urgent need for updated diagnostic criteria and for the development of international guidelines for the management of EDS-HT.

There are challenges in early diagnosis with some patients waiting up to 14 years to be diagnosed. Clinical decision support systems for early diagnosis of EDS-HT and other rare diseases should continue to be developed and utilised.

Once diagnosis has been established, there is a lack of knowledge of the condition by non-specialist “local” clinicians. Access to guidelines and protocols for management would improve clinical confidence and enhance patient outcomes. Awareness and education initiatives regarding EDS-HT should be implemented.

It is important that clinicians with knowledge and experience of EDS-HT challenge the misconceptions of their colleagues that JHS is clinically inconsequential. Early diagnosis and appropriate management is likely to reduce the burden of the syndrome and improve patient outcomes.

There is a requirement for a patient centric record that provides self-care guidelines, along with relevant information for the all the key clinicians who care for patients with EDS-HT throughout the patient journey.

7.4 Recommendations for Future Research

The EDS-HT MDS developed during the research should be reviewed by an international panel of experts, and further developed to standardised interoperable format.

An online continuous professional development module should be developed. This module could be deployed across a range of multidisciplinary professional bodies and thus enhance awareness and knowledge of the condition.

Decision support tools to aid in diagnosis could be developed for use within an electronic record. Essential phenotypical data could trigger an alert or prompt a clinician to consider EDS-HT.

Development of a guided care model for rare diseases could be considered. The model could allow for a care coordinator to guide both patients and clinicians along the care path and be a sign post for information when required

A registry for Ehlers Danlos Syndromes should be developed. A registry would allow for population studies finally addressing the lack of epidemiological data for this condition. The identification of patients for future research and management strategies and attraction of funding is a further benefit

7.5 Limitations of the Study

The expert group identified was extremely small and most of these experts stipulated that they would not in fact consider themselves expert by comparison with international experts that they have met. They do however represent some of the clinicians most knowledgeable about EDS-HT in Ireland.

The absence of a number of disciplines on the expert group resulted in poor development of some of the specialist data elements. These specialists could not be identified or do not yet exist in Ireland.

The author is the parent of an adolescent with EDS-HT and this may influence her selection of data elements.

7.6 Conclusions

Many challenges exist in provision of care for patients with rare diseases. This is particularly true in the case of EDS-HT, due to the lack of expertise in Ireland. This leads to long delays and errors in diagnosis. Furthermore, there is a common misconception that joint hypermobility syndrome equates with asymptomatic generalised hypermobility and is of little clinical consequence. This leads to dismissal of symptoms by clinicians who do not view the condition in its entirety, frustration for the patient and clinician and ineffective management of the patient.
Information and communication technology has the potential to transform care for people with EDS-HT.

"It is my experience that too little information
is the cause of anxiety among patients,
not too much" (Gurley-Green, 2001)

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Appendices

Appendix A: Ethics Committee Approval

Sara Gutierrez Llaneza <Sara.Gutierrez@scss.tcd.ie> **20 Apr**

to me, research-ethics

Dear Fiona,

Many thanks for these revisions. The Research Ethics Committee has approved your application. You may proceed with this study.

We wish you success in your research.

Kind regards,

Sara

From: Fiona Curran [mailto:fcurran@tcd.ie]
Sent: 19 April 2015 23:13
To: Sara.Gutierrez@scss.tcd.ie
Subject: Re: [Fiona Curran]: Ethics application EDS-HT Information Study

Appendix B: Information for Prospective Expert Participants

TRINITY COLLEGE DUBLIN
Information for Prospective Expert Participants

Dear Colleague,

I would like to invite you to take part in a research study entitled "An investigation of the information processes and requirements in the care of patients with Ehlers Danlos Syndrome Hypermobility Type (EDS-HT) / Joint Hypermobility Syndrome (JHS)". This research is being undertaken as part fulfilment of an MSc in Health Informatics in Trinity College Dublin (TCD). Please read the following information carefully and ask if you do not understand any part of it or would like more information.

WHO IS ORGANISING THE RESEARCH STUDY?

This research study is being undertaken by Ms. Fiona Curran as part of an MSc in Health Informatics in Trinity College, Dublin. The study will be completed between April and May 2015.

WHY HAVE I BEEN CHOSEN?

We are inviting you to participate in this study as you have been part of the expert group identified to investigate the establishment of a National Centre for Hypermobility in Ireland. This research study is concerned with the information requirements in the care of people with EDS-HT / JHS and the potential solutions which information technology can offer.

The overall aim of this research is to provide an essential information template for use by all clinicians involved in the care of patients with EDS-HT / JHS and by its use to promote awareness and knowledge of EDS-HT / JHS amongst clinicians who provide primary or episodic care for this patient group so that they are directed to both clinical and patient information sources as needs require.

Objectives

- To identify the likely clinical information break points in the care of patients with EDS-HT / JHS
- To identify essential data collection which should be included in referral / transfer of care in ongoing primary care or episodic specialist care of this patient group
- To propose information technology solutions for the safe storage and timely

access to this data

- To evaluate the proposed solutions
- To identify possible challenges

WHAT IS THE PURPOSE OF THE RESEARCH?

The purpose of this study is to propose and evaluate a standard description of essential data in the care of patients with EDS-HT / JHS and to identify potential technological solutions and any challenges that may exist.

WHAT WILL HAPPEN TO ME IF I TAKE PART?

You will be e-mailed a proposed data set and potential solutions for storage and retrieval of this data to review.

The researcher will then carry out a semi-structured interview with you where you will be asked questions to identify data which in your opinion should be excluded / included and the benefits and challenges of the proposed solutions.

The researcher will audio record and make written notes during the interview. These notes will be transcribed into a soft copy format and e-mailed to you. The audio recordings will be retained by the researcher until you confirm the accuracy of the transcribed interview. Audio recording will then be destroyed No audio recordings will be made available to anyone other than the researcher, nor will any such recordings be replayed in any public forum or presentation of the research.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

The results of the research will be analysed and included in a thesis to be submitted as part of the Health Informatics Masters degree in TCD. The work may be further developed with the intention of publication in a peer reviewed journal. The published results may be used by others for academic research. In addition the research outcomes are likely to be presented at selected conferences, seminars or workshops. The results can be made available to all research participants on completion of the research study.

CONFIDENTIALITY - WHO WILL KNOW I AM TAKING PART IN THE RESEARCH STUDY?

All personal information, which is collected during the course of the research, will be kept strictly confidential. I understand that if I make illicit activities known, these will be reported to appropriate authorities.

CONFLICT OF INTEREST:

There are no conflicts of interest.

EXPECTED DURATION:

It will take approximately 30 minutes to complete each interview.

PROCEDURE TO BE USED IF ASSISTANCE OR ADVICE IS NEEDED:

In the event that you require further information about this study please contact Fiona Curran who will be happy to answer your questions. Fiona can be contacted by email: fcurran@tcd.ie or by phone: 086-1994863.

VOLUNTARY PARTICIPATION

Your participation in this study is voluntary and you are free to withdraw at any time and without penalty without providing a reason. If you are happy to participate please complete the attached consent form and return to Ms. Fiona Curran before taking part.

Thank you for taking the time to read this correspondence and for considering taking part in this research.

Kind regards

Fiona Curran

Appendix C: Expert Participant Informed Consent for study entitled

Trinity College Dublin
Expert Participant Informed Consent for study entitled

An Investigation of the Information Processes and Requirements in the Care of Patients with Hypermobility Type Ehlers-Danlos Syndrome / Joint Hypermobility Syndrome

Lead Researcher: Fiona Curran

Background to the study:

The purpose of this study is to propose and evaluate a standard description of essential data in the care of patients with EDS-HT / JHS and to identify potential technological solutions and any challenges that may exist.

This research aims to contribute to the identification and dissemination of essential clinical information to non–EDS-HT-expert clinicians by identifying what information experts such as yourself consider to be the minimum data required for inclusion in the health record of a patient with EDS-HT / JHS

Procedures of this study:

The researcher will carry out a literature review. The research methodology will be to identify from the literature essential data to be included in health records of patients with EDS-HT / JHS and to propose possible technological solutions for the appropriate storage and retrieval of this data. A preliminary data set will be sent to all participants for review and development at interview. The lead researcher will carry out semi – structured interviews with experts in EDS-HT / JHS to further develop the data set, technological solutions and identify challenges.

A comprehensive information sheet will be made available to all potential participants.

This study will take place from late April to May 2015 and will form the basis of a thesis for submission as part of a Master in Healthcare Informatics in Trinity College Dublin.

There is no risk involved in participation.

Publication

The results of the research will be submitted in partial fulfilment of the Masters in Health Informatics at Trinity College, Dublin. The work may be further developed with the intention of publication in a peer reviewed journal. The published results may be

used by others for academic research. In addition the research outcomes are likely to be presented at selected conferences, seminars or workshops. The results will be made available to all research participants on completion of the research study.

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 understand the description of the research that is being provided to me.
- I understand that I may refuse to answer any question and that I may withdraw at any time without penalty.
- Notwithstanding that I have been identified as one of a small group of EDS-HT experts, I understand that no personal details about me will be recorded and that I will be identified only by my profession within the research.
- I agree that my data is used for scientific purposes as outlined in the information sheet and I have no objection that my data is published in scientific publications in a way that may reveal only my profession.
- 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 understand that if I or anyone in my family has a history of epilepsy then I am proceeding at my own risk.
- I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights.
- I have received a copy of this agreement.

Participants Name;_____

Signature;_____Date;_____

Statement of Researchers 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 fully answered such questions. I believe that the participant understands my explanation and has freely given informed consent.

Researchers contact details:
Fiona Curran can be contacted by email at fcurran@tcd.ie or by phone on 086 1994863

Researchers Signature;_____Date; _____

Appendix D: EDS-HT Ethics Permission from RMDU

Research Approval re Hypermobility Study

Inbox x

Fiona Curran <fcurran@tcd.ie> **16:47 (17 hours ago)**

to patpierce

Dear Patricia,

I am a chartered physiotherapist and I am also in my 2nd year of a Masters of Health Informatics in Trinity College Dublin.
Further to our phone call, I would be obliged if you could confirm that Our Ladys Hospice ethics committee approval is not required for the proposed study entitled
"An Investigation of the Information Processes and Requirements in the Care of Patients with Hypermobility Type Ehlers-Danlos Syndrome (EDS-HT) / Joint Hypermobility Syndrome (JHS)",

As I mentioned, this research will not involve patients or their data in anyway. It will involve a small number of Staff from Harolds Cross who have specialist knowledge about EDS-HT / JHS. They will be asked to review the type of information / data which could be of use to non-specialists caring for EDS-HT / JHS patients particularly in primary care. Semi structured interviews will then take place to further develop this information and to seek opinion how best to store and retrieve this information.

The research will be included in a thesis as part requirement for the Masters of Health Informatics in TCD and will be available to Our Ladys Harolds Cross.

If you require any further information please contact me by email fcurran@tcd.ie or by phone 086 1994863.

Kind Regards

Fiona Curran miscp

Pat Pierce **08:52 (1 hour ago)**

to me

Hi Fiona,

Yes, to confirm, for research involving staff (not patients), ethical approval is not required. However, if ethical approval was required the TCD process of ethical approval would be recognised by Our Lady's Hospice & Care Services.

Kind regards,

Pat Pierce

PA to CEO

Our Lady's Hospice and Care Services |Harold's Cross |Dublin 6W

Tel: (01) 406 87 25|Fax: (01) 406 88 07

www.olh.ie

Appendix E: Protocol for Semi-Structured Interviews With Experts

Protocol for Semi-Structured Interviews With Experts

Title of research study An Investigation of the Information Processes and Requirements in the Care of Patients with Hypermobility Type Ehlers-Danlos / Joint Hypermobility Syndrome.

Lead Researcher Fiona Curran Date: _____

Time start: _____ Time finish: _____

Thank you for accepting the invitation to participate.

I would just ask that you don't name third parties.

The purpose of this study is to propose and evaluate a standard description of essential data in the care of patients with EDS-HT / JHS and to identify potential technological solutions and any challenges that may exist.

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.
You received an e-mail of a preliminary minimum data set for use in an EDS-HT / JHS record, and some potential information technology solutions.
Was anything unclear? If yes, please outline
The following themes will be discussed during the interview

1 Data review and development of the preliminary dataset
2 Clinical process requirements
3 Technological solutions
4 Benefits and challenges

Please outline any key people that you are aware of that have expert knowledge in this area in Ireland.

Appendix F: Questionnaire for Primary Care Clinicians

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.

Please do not name third parties in any open text field of the questionnaire. Any such replies will be anonymised.

1. Does this Minimum Data Set (MDS) alter your knowledge of EDS-HT / JHS?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

2. In your opinion, would this MDS influence your clinical assessment of patients with EDS-HT /JHS?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

3. In your opinion, would this MDS influence your communication with patients with EDS-HT / JHS?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

4. In your opinion, would **self - management** by patients with EDS-HT / JHS be influenced by an EDS-HT / JHS record containing this MDS?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

5. In your opinion, would this MDS influence your pharmaceutical management of patients with EDS-HT / JHS?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

6. In your opinion, would this MDS influence your point of care clinical procedures for patients with EDS-HT / JHS (eg wound care, patient positioning during procedures, use of local anaesthesia, manual therapy etc)?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

7. In your opinion, would this MDS influence the appropriate referral of patients with EDS-HT / JHS to other clinical specialties / multidisciplinary team members?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

8. In your opinion, would this MDS influence your communication with multidisciplinary team members involved in the care of patients with EDS-HT / JHS?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

9. In your opinion, would this MDS influence continuity of care for patients with EDS-HT / JHS?

   Negatively
   Somewhat Negatively
   Not at all
   Somewhat Positively
   Positively

10. In your opinion, should links to care protocols be included in an EDS-HT /JHS care record?

    Yes
    No
    Not sure

11. In your opinion, should links to clinical information resources relevant to EDS-HT / JHS to be included in an EDS-HT / JHS care record?

    Yes
    No
    Not sure

12. In your opinion, should links to carefully selected patient information resources relevant to EDS-HT / JHS be included in an EDS-HT record?

    Yes
    No
    Not sure

13. In your opinion, with patient consent, who should have access to view this data? (tick all that apply)

    GPs
    Practice Nurses
    Allied Health Professionals in Primary Care
    Primary Care Administrators
    Accident and Emergency Staff
    Hospital based Doctors
    Hospital based Allied Health Professionals
    Government Bodies
    Insurance Companies
    Patient Registries
    Clinical Researchers
    Non-Clinical Researchers
    Other – please specify

14. In your opinion, which of the following solutions offers the best storage and retrieval of this data? Please see attached definitions

    Patient Care Record
    Summary Care Record
    Information Portal
    Electronic Delivery via Healthmail

A Patient Diary
Other – please specify

15. What modifications if any would you make to the data set?

16. What challenges can you identify to the successful adoption of an EDS-HT / JHS record?

17. Please record any other comments or feedback here.

18. Please state your
    Profession
    Specialties
    Type of practice Single / Shared
    Number of years in practice
    Age 20-30
    30-40
    40-50
    50-60
    60-70
    70+
    Gender

Thank you for your participation.

	Accept	Reject	Modify	Comments

Appendix G – EDS HT Dataset as input for Expert Review

Demographics					
	National Unique Identifier				
	First Name:				
	Last Name:				
	Address:				
	Street:				
	City:				
	Country:				
	Date of Birth:				
	City of Birth				
	Country of Birth				
	Date of Death				
	Gender:				
	E-mail				
	Phone : Home				
	: Mobile				
	Rare Disease ID				
	Next of Kin: Name				
	Relationship				
	Phone				
	Address				
	Other : Please Specify				

In your opinion who should have access to DEMOGRAPHIC DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.

In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.

Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments

Allergies and Alert				
Allergies				
Alerts				
Autonomic Dysfunction				
Orthostatic Intolerance				
Postural Orthostatic Tachycardia Syndrome				
Local Anaesthesia Resistance				
Cervical Instability				
Other : Please Specify				

In your opinion who should have access to this ALLERGIES AND ALERTS DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments
Diagnosis				
Localised Hypermobility				
Generalised Hypermobility - Non Syndrome				
Joint Hypermobility Syndrome				
Ehlers Danlos Syndrome				
Hypermobility Type				
Classic type				
Vascular Type				
Arthrochalasia Type				
Kyphoscoliotic Type				
Other EDS: Please Specify				
Other Connective Tissue Disorder				
Marfans' Syndrome				
Osteogenesis Imperfecta				
Loetyz Dietz				
Other : Please Specify				

In your opinion who should have access to DIAGNOSIS DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments

History				
Past Surgical History				
Past Medical History				
Familial History				
Social History				
Occupation				
Hobbies				
Other : Please Specify				

In your opinion who should have access to DIAGNOSIS DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments
Medication (Active Ingredient)				
Current				
Recent				

In your opinion who should have access to MEDICATION DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments
Test Results				
Imaging				
Haematology				
Lab				
Other : Please Specify				

In your opinion who should have access to this TEST RESULTS DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments
Genetics				
Chromosome number				
Chromosomal reference sequence accession and version number				
RefSeqGene accession and version number				
Locus Reference Genomic (LRG)				
Variant description in HGVS format				
Variant description in other format				
Other : Please Specify				

In your opinion who should have access to this GENETICS DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments
EDS Associated Dysfunctions				
Rheumatological / Musculoskeletal				
Beighton Score				
Brighton Criteria				
Quality of Life Score				
Functional Index				
Joint Involvement				
Right / Left / Bilateral				
Hip				
Knee				
Ankle				
Shoulder				
Elbow				
Wrist				
Hands				
Feet				
TMJ				
SternoClavicular				
AcromioClavicular				
CostoChondral				
Spinal Involvement				
Cervical				
Thoracic				
Lumbar				
Sacral				
Pain				
Localised arthralgia's				
Chronic Regional Pain				
Chronic Widespread Pain				
Fibromyalgia				
Pain Scale				

	Accept	Reject	Modify	Comments
Other : Please Specify				
Dermatological / Cutaneous				
Fragility				
Hyper-extensibility				
Scarring -				
Striae				
Bruising / haematomas				
Molluscoid Pseudotumors/ Spheroids/ Piezogenic Papules				
Varicosities				
Local Anaesthetic Response				
Other : Please Specify				
Gastrointestinal				
Dyspepsia / Nausea / Vomiting /				
Abdominal Pain /Bloating				
Gastro Oesophageal Reflux (GERD)				
Hiatus Hernia				
Delayed Gastric Emptying				
Diverticular Disease				
Dysmotility				
Constipation				
Diarrhoea				
Faecal Incontinence				
Other : Please Specify				

	Accept	Reject	Modify	Comments
Cardiovascular				
ECHO cardiogram				
Mitral Valve				
Aortic Valve				
Aortic Root				
Postural Orthostatic Tachycardia Syndrome (POTS)				
Orthostatic Intolerance / Orthostatic Hypotension				
Varicosities				
Other : Please Specify				
Urological				
Bladder Diverticulae				
Increased Frequency				
Urgency				
Recurrent UTIs				
Continence				
Other : Please Specify				
Gynaecological / Obstetrical				
Pregnancy				
Hormonal				
Other : Please Specify				
Pulmonary				
Asthma				
Pneumothorax				
Other : Please Specify				

	Accept	Reject	Modify	Comments
Orodental				
Temporomandibular Joint Dysfunction				
Mucosal Fragility				
Other : Please Specify				
Ophthalmological				
Myopia				
Meitenier's Sign				
Strabismus				
Blue Sclera				
Blurred Vision				
Prescription				
Other : Please Specify				
Orthopaedic				
Osteopenia				
Osteoporosis				
Bone Density				
Other : Please Specify				

In your opinion who should have access to EDS ASSOCIATED DYSFUNCTIONS DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments
Psychological/Psychiatric				
Anxiety				
Depression				
Other : Please Specify				

In your opinion who should have access to PSYCHOLOGICAL / PSYCHIATRIC DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

	Accept	Reject	Modify	Comments
Management – Plan of Care				
Medication				
Physiotherapy				
Occupational Therapy				
Psychology				
Podiatry				
Speech and Language Therapy				
Aids and Appliances				
Other : Please Specify				

In your opinion who should have access to MANAGEMENT – PLAN OF CARE DATA (Please Circle) -

In Hospitals: Doctors, Allied Health Professionals, Administrators, Nurses, Patients.
In Primary Care: GPs, Allied Health Professionals, Administrators, Nurses, Patients.
Other: Patient Registries, Government Bodies, Insurance Companies, Clinical Researchers, Non-Clinical Researchers.

Appendix H – Villefrance nosology for EDS adapted from Beighton (1998)

Type	Protein	Inheritance	Diagnostic criteria
Classic (type I/II)	Type V procollagen	AD	Major: Hyperextensible skin, widened atrophic scarring, and joint hypermobility. Minor: Easy bruising, smooth/velvety skin, molluscoid pseudotumors, subcutaneous spheroids, hypotonia, complications of joint hypermobility, surgical complications, and positive family history
Hypermobility (type III)	Unknown	AD	Major: Generalized joint hypermobility, and mild skin involvement Minor: Recurring joint dislocations, chronic joint pain, and positive family history
Vascular (type IV)	Type III procollagen	AD	Major: Excessive bruising, thin and translucent skin, arterial/intestinal/uterine fragility or rupture, and characteristic facial appearance. Minor: Acrogeria, early onset varicose veins, hypermobility of small joints, tendon and muscle rupture, arteriovenous or carotid cavernous sinus fistula, pneumo (hemo) thorax, positive family history, and sudden death in close relative
Kyphoscoliotic (type VI)	Lysyl hydroxylase 1	AR	Major: Severe muscular hypotonia at birth, generalized joint laxity, kyphoscoliosis at birth, sclera fragility, and rupture of the globe. Minor: Tissue fragility, easy bruising, arterial rupture, marfanoid habitus, microcornea, osteopenia, and family history
Arthrochalasis (type VIIA/VIIB)	Type 1 procollagen	AD	Major: Severe generalized joint hypermobility with recurrent subluxations, and congenital bilateral hip dislocation Minor: Skin hyperextensibility, tissue fragility, easy bruising, muscular hypotonia, kyphoscoliosis, mild osteopenia, and occasional fractures
Dermatosparaxis (type VIIC)	Procollagen-N-proteinase	AR	Major: Severe skin fragility, sagging, redundant skin, excessive bruising Minor: Soft, doughy skin texture and premature rupture of membranes

AD = Autosomal dominant, AR = Autosomal recessive