

# THE HIDDEN COSTS OF RARE DISEASES

A Feasibility Study



## GENETIC ALLIANCE UK

Genetic Alliance UK is the national charity working to improve the lives of patients and families affected by all types of genetic conditions. We are an alliance of over 180 patient organisations. Our aim is to ensure that high quality services, information and support are provided to all who need them. We actively support research and innovation across the field of genetic medicine.

Genetic Alliance UK undertakes various projects and programmes that add evidence and knowledge to improve health service provision, research and support for families. These initiatives include:



Rare Disease UK, a stakeholder coalition brought together to work with Government to develop the UK Strategy for Rare Diseases.  
[www.raredisease.org.uk](http://www.raredisease.org.uk)



SWAN UK (syndromes without a name), a UK-wide network providing information and support to families of children without a diagnosis.  
[www.undiagnosed.org.uk](http://www.undiagnosed.org.uk)

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# 1. CONCLUSIONS AND IMPLICATIONS FOR FUTURE RESEARCH

The Hidden Costs Feasibility Study supports the development of future research in this area in a number of ways. Findings revealed that:

- 1. Receiving coordinated care is important for rare disease patients, yet remains a challenge**

Care coordination is particularly important for those affected by rare conditions, which are often serious, chronic and complex in nature. Yet, research conducted by Rare Disease UK in the last six years indicates that poorly coordinated care is a major issue for patients and families affected by rare conditions (Rare Disease UK, 2010; 2013; 2015). In fact, the mapping exercise carried out for this study found that there is huge variation and inequity in the way that services are organised, and even though good examples do exist, there is no one agreed model being implemented across rare diseases. Patients and families involved in the feasibility study reported particular challenges associated with the way their

services were organised including excessive and uncoordinated appointment scheduling; lack of communication between providers; and a lack of resources and capacity within services.

- 2. The full costs and benefits associated with different models of care for rare disease patients are unknown**

The project has identified a major gap in the current literature. The true costs of rare conditions are unknown. Although evidence relating to the cost and burden of managing rare conditions is limited, some evidence suggests that they are a significant economic burden (Angelis et al, 2015). It is hoped that care coordination is key to improving patient experience and lowering the cost of health care (Solberg, 2011). However, it has been argued that there is a lack of evidence more generally about the benefits of better coordination and the association between coordination, improved patient experiences, care

outcomes and financial efficiencies (Øvretveit 2011, cited in King's Fund, 2013). The full costs associated with managing rare conditions, through coordinated and non-coordinated services, have not been investigated. Such information, when collected, should be valuable evidence for decision makers and commissioners as they plan service developments and support best practice.

### **3. Patients and families face significant ('hidden') costs (both financial and psychosocial) associated with the way that their care is managed**

The qualitative interviews carried out for this study demonstrated that costs are varied and incurred by not only health and social care providers, but also patients and families themselves. Patients and parents provided many examples of how their/their child's rare condition impacted on them. The financial impact on families related to both medical appointments and wider condition management costs. 'Time' was a frequently reported cost, particularly in the absence of efficiently coordinated services. The interviews also revealed the specific impact of uncoordinated care on patients, carers and their wider families, physically, psychologically and socially.

### **4. There are significant limitations associated with existing data sets for rare diseases**

Existing data sets are unlikely to be sufficient to collect the different types, and full range, of costs that were identified in this study and any future research project would need to consider the use of new tools

to collect the relevant data. We have developed and piloted a patient diary which could be considered for future research.

We conclude that future research could focus on the following:

- Measuring the burden/cost of illness (particularly for the undiagnosed community, where no evidence has been captured to date and where no specific service exists) to assess the true and full impact of rare conditions.
- Understanding the different ways that services for rare conditions are organised and what might represent best practice.
- Evaluating the cost-effectiveness of different service configuration models for rare disease patients.
- Capturing and evaluating a broader range of costs and benefits (including the financial and psychosocial costs to patients and families).

The feasibility study findings have already informed the development of a draft research proposal. See appendix 5.

# 2. INTRODUCTION

## 2.1 Background

Statistically, it is not unusual to be affected by a rare disease: there are between 5000 and 8000 different rare diseases and together they affect the lives of three million people in the UK (Department of Health, 2013). One in 17 people are likely to be affected by a rare disease at some point in their lives (Rare Disease UK). The impacts of rare diseases are felt not only by the patient but by family members, carers, the health service and wider society. According to the Department of Health, 'they represent a significant cause of illness, making considerable demands on the resources and capacity of the NHS and other care services' (Department of Health, 2013, pg 5).

There is much anecdotal, and some systematic, evidence of the costs to patients and their families, and to the NHS, of managing undiagnosed and diagnosed rare conditions. The journey to diagnosis can be long and seemingly inefficient, and patient care can suffer in the absence of a diagnosis. Even with a diagnosis, the complexity of many rare conditions is challenging to manage, especially where no coordinated approach to health services exists. Although an increasing number of rare diseases are

managed through 'coordinated' services (for example via multidisciplinary clinics within specialised and highly specialised services), most are not managed in this way.

Services for rare and very rare conditions are planned and monitored across the whole of England. The current budget for these specialised services (including highly specialised services) is £15 billion, which accounts for 10% of NHS spending. The commissioning process is competitive, and services/new treatments must show that they save costs, or are at least cost neutral. Currently, such decision making focuses on NHS costs including inpatient and outpatient attendances. It excludes other costs such as primary care costs, social care costs and costs to patients and families.

The cost, both economic and psychosocial, of managing rare disease patients (including those without a diagnosis) through coordinated and non-coordinated services has not been investigated. Such information should be valuable evidence for decision makers and commissioners as they plan service developments and support best practice. Genetic Alliance UK's Hidden Costs Feasibility Study sought to prepare the

ground for a full-scale research project in this area.

### **What do we mean by ‘care coordination’?**

There is no universally accepted definition of what ‘care coordination’ means and it is a term often used interchangeably with other phrases such as ‘integrated care’, ‘disease management’ and ‘multidisciplinary team working’ (McDonald et al, 2007 cited in King’s Fund, 2013). In 2011, the National Coalition on Care Coordination defined the following features of care coordination:

‘Care coordination’ is a person-centred, assessment-based, interdisciplinary approach to integrating health care and social support services in a cost-effective manner in which an individual’s needs and preferences are assessed, a comprehensive care plan is developed, and services are managed and monitored by an evidence-based process which typically involves a designated lead care coordinator. (National Coalition on Care Coordination 2011, cited in King’s Fund, 2013)

The NHS identified a number of events where care coordination is appropriate including scenarios where there are a lot of different staff groups and agencies involved in supporting an individual and their family; where intervention and care will be required over a long period of time; when the level of need increases and multiple services are required; and for those who may be likely to experience a number of unplanned emergency admissions (2011). Therefore, care coordination is particularly important for those affected by rare conditions, which are often serious, chronic and complex in nature.

### **Political context**

In the UK, care coordination has been high on the policy agenda, particularly in response to the rising demands placed on the National Health Service (Kings Fund, 2013). The Health and Social Care Act (2012) sought to encourage and enable more integration between services through a range of provisions aimed to provide a basis for better collaboration, partnership working and integration across local government and the NHS at all levels.

A number of initiatives taking place at a European level have focused specifically on improving the care and treatment that patients affected by rare diseases can access. In 2009, The Council of the European Union called for each Member State to adopt a rare disease plan or strategy before the end of 2013. Following this, the departments of health in each of the four UK nations worked together to develop the UK Rare Disease Strategy. The Strategy, published in November 2013, makes commitments in a number of areas including ‘diagnosis and early intervention’ and ‘care coordination’. The strategy states:

- Well coordinated care is essential when several specialists and hospital departments are involved in a person’s care - it is not the best use of time and resources if patients have to visit different departments at the same hospital on different days.
- Following a diagnosis, a patient should have an evidence based care plan (setting out responsibilities of specialist, general and primary care services).

- It is essential to coordinate across the boundaries of services including: between healthcare, social care and voluntary sectors and between primary, secondary, tertiary and quaternary health services.
- Improving coordinated care requires a joined up approach to find a balanced and innovative way forward.

More recently, the need for such integration has been highlighted by the European Commission, who set up an expert group focusing on the incorporation of rare diseases into social services and policies (April, 2016). They recommended the following:

- Centres of Excellence should play a key role in facilitating integrated health care provision by bringing together or coordinating a multi-disciplinary team.
- European Reference Networks (ERNs) also have a key role in collaborating with patient groups, health providers and social care providers.
- Member states should promote multi-disciplinary team working, holistic approaches, continuous, person centred and participatory care in both health and social care.

Importantly, the expert group recognised that socio-economic research in the field of rare diseases is needed, particularly cost effectiveness studies, burden of illness studies and research addressing the appropriateness of services.

## Patient and family experiences

As stated previously, rare diseases are often chronic and life-limiting. They are likely to be ‘multisystem’ meaning that they affect several systems in the body. Consequently, those affected require complex care and support from a range of health and social care professionals. However, research conducted by Rare Disease UK in the last six years indicates that poorly coordinated care is a major issue for patients and families affected by rare conditions (Rare Disease UK, 2013). For example, as few as 13% of patients with rare diseases have access to someone to fulfil a care coordinator role. In comparison, almost 90% of people with cancer are given the name of a clinical nurse specialist, whose role includes coordination (Rare Disease UK, 2013).

Rare Disease UK’s Care Coordination report highlighted that those living with rare diseases should have access to a named care coordinator to ensure that they receive high quality care that is well coordinated, and they are not left to battle through fragmented care and treatment on their own. A care coordinator is a trained professional who makes sure that patients have a care plan in place, and that their care plan is implemented, as well as providing emotional and social support to patients and families along their journey. The report argues that introducing named care coordinators ‘makes practical and economic sense’, for patients, commissioners and healthcare providers. Similarly, findings of the 2013 Centres of Excellence for Rare Diseases report, which collected data from a range of stakeholders, argued that every centre of excellence should be characterised



by care coordination, engagement with people with rare conditions, and arrangements for the transition between paediatric and adult care.

Whilst some examples of good practice have emerged since the publication of the UK Rare Disease Strategy, overall, Rare Disease UK members have reported little improvement in the past five years. In 2010 and again in 2015, Rare Disease UK surveyed patients and families affected by rare diseases. With almost 600 responses, the survey in 2010 revealed the following:

- The majority of patients' care is poorly coordinated.
- Patients and families wait too long for a correct diagnosis, with a worrying number receiving incorrect diagnoses before their final diagnosis is made.
- Patients have to attend multiple clinics for different aspects of their condition, often at a long distance from where they live.
- The majority of patients do not have a specialist centre for their condition.
- Patients frequently experience problems with medical, psychological, financial, social and other issues at transition periods.

In the 2015 report (which captured the views of over 1400 patients and family members), little appears to have changed. For example, almost half of patients reported waiting over a year to receive a diagnosis and a quarter waited over five years. More than 1 in 3 patients received three or more incorrect diagnoses. The findings in relation to care coordination are telling:

- 1 in 3 patients have to attend three or more clinics for their condition.
- More than 8 out of 10 patients do not have a care coordinator or advisor.
- 4 out of 10 patients don't know if there is a specialist centre for their condition, and of those who are aware of a specialist centre, only 2 out of 3 patients accessed it.
- A high proportion of patients felt that coordination of care was an important role of specialist centres. However, only 1 in 10 patients reported that their centre did it. In addition, they felt that it was important for specialist centres to share expert knowledge with local care teams.

Similarly, Garinno et al (2015) highlighted the needs and difficulties faced by patients with different rare disease diagnoses in Italy, as well as the experiences of their health care professionals. The research demonstrated the value of a multidisciplinary approach to care. Patients reported the importance of a single place where they were recognised, felt welcome and could be followed up for medical advice, treatment, tests and check-ups. In fact, the subject of rarity was not considered the most problematic element if there were a diagnosis and an identified treatment centre. Such evidence is informative and useful for the improvement and development of quality health care services.

Many of the issues raised in the Rare Disease UK survey (2015) were especially pertinent to those living without a diagnosis; 4 in 5 of respondents felt that not having a diagnosis was a barrier to receiving appropriate

coordinated care. Before diagnosis, patients are likely to see several specialists and have a wide range of tests. For example, a quarter of undiagnosed respondents reported seeing more than ten doctors in their search for a diagnosis (Rare Disease UK, 2015). The journey to diagnosis can be prolonged. It has been argued that this, combined with sub-optimal care, can have serious and adverse implications for the health of patients and health service resources (PIRU, 2015).

### **Evaluating the cost of managing rare diseases and the impact of coordinated care**

Evidence related to the costs associated with managing rare diseases, from a service and patient perspective, is particularly limited.

Although numerous cost of illness studies have been conducted in the past 30 years across a range of conditions, few have addressed rare diseases (Angelis et al, 2015). Angelis et al (2015) reviewed the cost of illness evidence (including direct and indirect costs) relating to ten specific rare diseases: cystic fibrosis, Duchenne muscular dystrophy, fragile X syndrome, haemophilia, juvenile idiopathic arthritis, mucopolysaccharidosis (type I and VI), scleroderma, Prader-Willi syndrome, histiocytosis and epidermolysis bullosa. They identified a total of 77 studies during their search. Of these, 29 studies related to cystic fibrosis and 22 related to haemophilia. Therefore, the cost of illness information for the remaining rare diseases was extremely limited and for two of the rare diseases none was available. The reviewers noted that data availability

tended to correlate with the existence of a pharmaceutical treatment (rather than the rarity or severity of the condition). Indirect costs signify the burden of disease on the patients and families which in the case of scleroderma was found to be much higher than direct costs. However, evidence relating to indirect costs was limited across the ten conditions and in comparison to other more common conditions the true impact of rare disease is not well documented.

Shire's Rare Disease Impact Report (2013) conducted in the UK and US found that the economic impact associated with lengthy journeys to diagnosis and ongoing disease management is significant. From the patient and caregiver perspective, it was shown that handling financial aspects such as travel costs and the inability to work, was a key challenge associated with the condition.

Although evidence is limited, where rare diseases have been examined there has been found to be a significant economic burden (Angelis et al, 2015). In a recent article, published in the European Journal of Health Economics, a number of challenges associated with health care systems and rare diseases were identified including:

1. The diagnosis of rare diseases is difficult; accelerated diagnostics could reduce health-related sufferings as well as the underuse and misuse of health care resources.
2. Because patient numbers are small, it is challenging to know how to organise care appropriately; health care and

treatment for people with rare diseases is costly.

3. There is a lack of evidence with regard to efficient and validated models of organisation and cross-border financing of complex networks such as European Reference Networks (ERNs).
4. It is expected that pharmaceutical companies will spend less on drug research for rare diseases, due to a highly specialised and limited market, and a longer payback period of research costs than other more common conditions.

In summary, the authors argue that collectively, rare diseases represent a huge financial and organisational challenge. They recommend the development of a network of high competence centres in Europe, a critical review of the reimbursement system and the installation of information systems for the diagnosis and treatment of rare diseases (von der Schulenburg and Frank, 2015).

It is hoped that care coordination is key to improving patient experience and lowering the cost of health care (Solberg, 2011). However, it has been argued that there is a lack of evidence more generally about the benefits of better coordination and the association between coordination, improved patient experiences, care outcomes and financial efficiencies (Øvretveit 2011, cited in King's Fund, 2013). In 2007, MacDonald et al suggested that whilst the strongest evidence shows a benefit for those affected by conditions such

as congestive heart failure, diabetes, severe mental illness, stroke and depression, the evidence is not clear for other patient populations who have obvious coordination needs. They identified over 20 different instruments and approaches to measuring coordination, yet there is some uncertainty around which might adequately capture the key components producing benefits (cited in Solberg, 2011).

Rare Disease UK's Care Coordination report (2013) sets out a number of examples where professionals in a care coordination role improve the quality of care and patient experience of care and offer value for money. In the case of rare neuromuscular conditions and sickle cell disorders, it has been argued that care coordinators can facilitate a more timely service, save consultants' and GPs' time, promote self-management, and help prevent unplanned hospital admissions (Muscular Dystrophy Campaign, 2011; Anionwu and Leary, 2012).

The Policy Research Innovation Unit (a unit funded by the Policy Research Programme of the Department of Health) identified a number of methodological challenges associated with measuring the diagnostic journey (and its impact) of rare disease patients. First, the small numbers of patients affected by each condition means that there is only weak statistical power to detect changes in the length of journeys. Second, the low incidence of each disease means that the collection of data on patients dispersed over a large number of providers is a logistical challenge and third, there is no universally agreed definition of the start and end points of diagnostic 'odysseys' (2015). These considerations

highlight some of the challenges in measuring the true costs of managing rare conditions.

# 3. ABOUT THE PROJECT

## 3.1 Aim and focus

The Hidden Costs project was a feasibility study to prepare the ground for a full scale research project. We anticipated that the research questions for a full scale project could be:

- What is the economic cost of coordinating versus not coordinating rare disease services within the NHS? The question includes costs to the NHS and to patients themselves.
- Is there a psychosocial benefit to patients and their families of coordinating rare disease services within the NHS, and if so how is this manifested?

The feasibility work was planned to refine the questions above and inform future research proposals and funding

applications. The feasibility study focused on a small, selected number of rare conditions (including those without a diagnosis) and addressed the following specific questions:

1. How are health services currently coordinated for these patients?
2. What is already known about the impact of coordinating/not coordinating health services for these conditions?
3. What outcomes would be meaningful and feasible to measure in a full scale research project?
4. What is the best data collection method to use in a full scale research project?

## 3.2 Methodology

The key stages of the feasibility study were:

### **Stage 1: Recruit steering group and refine feasibility study plan**

In 2014 a multi-stakeholder steering group was appointed to provide guidance and oversight throughout the feasibility study. The terms of reference and full membership list are shown in appendix 1. The group met at the outset of the project to help refine the project plan.

### **Stage 2: Identify conditions to study and apply for ethical approval**

A sampling frame was developed with the steering group to help identify a small number of conditions to focus on during the feasibility study. The sampling frame (shown in appendix 2) enabled the research team to select conditions which covered as many different variables as possible in order to maximise the learning potential from the study. The final conditions were: Niemann-Pick disease (Type C); spinal muscular atrophy (SMA) (types 1-3); Behçets disease; Alström syndrome; and mucopolysaccharidosis type II (MPS II). Undiagnosed conditions (i.e. families from Syndromes Without A Name (SWAN) UK) also took part in the project. All conditions are represented by patient support organisations within the Genetic Alliance UK and Rare Disease UK membership network. In February 2015 an ethics application was submitted to the Social Care Research Ethics Committee (SCREC) and the study was approved in March 2015. The SCREC is hosted by the NHS Health Research

Authority (HRA). It reviews adult social care research study proposals, intergenerational studies involving adults and children or families and some proposals for social science studies situated in the NHS.

### **Stage 3: Conduct initial mapping and literature scoping exercise**

In 2015, a condition-specific mapping and literature scoping exercise was undertaken (focusing on the selected conditions). The purpose of the mapping exercise was to build a picture of how services are currently organised for patients – the types of services they access and the level of care coordination they experience. This task involved a variety of methods including desktop research, meetings with patient representatives (staff at patient groups, some of whom also had direct experience as patients) and telephone interviews with patients, family members and healthcare professionals.

The literature scoping exercise sought to identify exiting research relevant to the chosen conditions including research focused on the psychosocial impact of the condition (on patients and other family members), cost or burden of illness studies and cost effectiveness studies for specific interventions. Further detail on the search strategy is provided in section 4, Findings and Discussion.

#### **Stage 4: Define cost components and outcome measures**

Between December 2015 and May 2016 qualitative semi-structured telephone interviews were conducted with patients and family members (including parents), as well as health care professionals and commissioners involved in the care and delivery of services for rare disease patients. Data were captured from 18 participants in total. The purpose of the interviews was to identify the important costs associated with managing rare conditions, from a range of perspectives. This stage of the feasibility study was designed to identify meaningful costs and benefits that would be feasible to measure in a full scale research project.

With participants' permission, all interviews were audio-recorded, transcribed and analysed thematically with the support of NVivo software. Emerging themes from the analysis were shared and discussed with the wider research team including the steering group in January 2016. Involving a wider group of stakeholders in the data interpretation process was important in testing and validating the findings.

#### **Stage 5: Test the feasibility of various data collection tools**

There were two elements to this stage of the research project. First, an assessment was made of the feasibility of using patient medical records and existing data sets to contribute to future data collection. This work was undertaken by Dr Talitha Verhoef (Health Economist, University College London (UCL)). Second, a new data

collection tool was designed in collaboration with the steering group and patient representatives. The tool – a 'patient diary' – was designed to categorise, collect and quantify the costs identified in the interviews (see above).

The diary was tested with seven patients and parents of patients, who also provided feedback on their experience with the diary. The pilot process intended to A) validate the costs identified, B) potentially identify new costs that the interview phase did not uncover, C) begin to assess the extent of burden on patients and families and D) assess the feasibility of collecting the data items. This exercise was carried out with patients/family members representing a wider group of conditions than the project's initial selected conditions, in order to further validate the costs and the diary.

#### **Stage 6: Write up findings and develop full scale research proposal for funding applications**

The learning and outcomes of the study are outlined in this report (see section 4, Findings and Discussion), and have also been used to inform the development of further research (see appendix 5).

### 3.3 Project management

The project team consisted of Genetic Alliance UK staff Amy Hunter (project management) and Amy Simpson (research). In addition, academic oversight was provided by Professor Steve Morris (Health Economics, UCL) who was contracted through UCL Consultants.

The steering group was composed of representatives from patient organisations, the NHS, academia and other relevant bodies. The role of the steering group was to ensure the robust, fair and transparent running of the project, and specifically to:

- Represent the views and needs of a wide range of stakeholders both from its own resources and through its network of contacts.
- Maintain awareness of the relevant evolving political, social and health service environments.
- Provide expert advice and guidance on relevant aspects of the project work.
- Contribute to refining research questions.
- Review drafts of full scale research proposals, and help identify potential sources of funding.

### 3.4 Funding

This project has been undertaken by Genetic Alliance UK, funded by Shire through a Services Agreement and by Genzyme through a restricted educational grant.

Shire's support made the project possible. Genzyme's funding enabled us to study more conditions and in greater depth.



# 4. FINDINGS AND DISCUSSION

## 4.1 Condition-specific literature scoping exercise

A literature scoping exercise was completed in 2015. PubMed was used to search for relevant papers or articles for each condition. Broad search terms were used including ‘cost’ and ‘experience’. In addition to this strategy, relevant studies were also identified on an ad hoc basis. Papers were deemed relevant if they focused on the

psychosocial impact of the condition, the cost or burden of illness, or the cost effectiveness of a specific intervention. A total of 64 papers were identified as potentially relevant (after reading the title/abstract) to the feasibility study and future research in this area.

**Table 1: Search results**

Search terms	Results	Potentially relevant
Niemann AND Cost	37	7
(Spinal muscular atrophy) AND Cost	39	26
Behçet AND Cost	16	12
Alström AND Cost	7	3
(Undiagnosed genetic condition) AND Cost	27	1
(Undiagnosed genetic syndrome) AND Cost	9	0
(MPS II) AND Cost	21	4
Niemann AND experience	69	1
(Spinal muscular atrophy) AND experience	103	5
Behçet AND experience	159	1
Alström AND experience	6	1
(Undiagnosed genetic condition) AND experience	44	0
(Undiagnosed genetic syndrome) AND experience	7	0
(MPS II) AND experience	56	3

A number of observations were made based on the findings of the literature scoping exercise. These are discussed below.

The majority of studies which included a cost-analysis element were cost effectiveness studies focused on specific interventions, treatments or diagnostic tools. As Angelis et al (2015) reported, the availability of such data in the rare disease field tends to correlate with the existence of a pharmaceutical treatment (rather than the rarity or severity of the condition) and evidence relating to indirect costs is limited. Therefore, the true impact of rare diseases is not well documented. Only two (economic) cost of illness studies were identified, although they did not include the full range of costs in their analysis.

First, Sut et al (2007) conducted the first cost of illness study in Turkey focusing on Behçets Syndrome. They found that the neurological involvement had the highest annual cost, treatments were a major cost driver and that direct costs were higher than the indirect costs. They concluded that the condition represents a considerable economic burden for the health care system in Turkey. Second, Imrie et al (2009) assessed the direct and indirect costs associated with Niemann-Pick type C in the UK, using a postal survey and medical resource use questionnaire. The total annual costs (both direct and indirect costs) per patient were estimated at £39,168. 46% related to direct medical costs, 24% related to direct non-medical costs, and 30% related to indirect costs. Some methodological limitations were identified including the small sample size and authors

suggested that costs were likely to be underestimates. The researchers found that a substantial proportion of costs were shifted to the patient, family and non-medical provider. This demonstrates the importance of measuring cost from various perspectives.

A small number of studies focused on health related quality of life or the psychosocial impact of conditions. In all cases, the conditions were found to have a negative effect demonstrating the wider impact of rare conditions. In the case of MPS II, the most affected areas were found to be physical function domains, self-esteem and family cohesion (Raluy-Callado et al, 2013). Similarly, studies with those affected by spinal muscular atrophy have indicated that patients faced particular emotional and social challenges (Lamb and Peden, 2008) and quality of life was significantly lower as a result of economic factors and a lack of social support (Kocova et al, 2014). This type of data can be an important component in health economic analysis and in establishing priorities in health care spending (Raluy-Callado et al, 2013).

Only two studies, which both focused on Alström syndrome, addressed costs and benefits associated with different service configurations. The first study found that multi-disciplinary clinics are highly valued by both patients and physicians and can be run at an affordable cost (Davison et al, 2014). However, the study only looked at costs relating directly to specialists and consumables. Benefits were found to be far-reaching and included psychological and socio-economic benefits for patients, and

‘improved decision making efficiency’ and reduction in side effects. The second study found that organised, multidisciplinary ‘one stop’ clinics are patient centred and individually tailored to the patient need with a better outcome and comparable cost compared with the current standard of care for rare disease (Van Groenendael et al, 2015).

Three studies were identified which focused on the delivery and administration of enzyme replacement therapy (ERT) for MPS patients across different settings including hospital, the family home and a specialist school. Buraczewska et al (2012) found that parents experienced psychosocial burden as a result of weekly hospital visits for treatment. The authors made recommendations for home-based treatment. Research has demonstrated that non-hospital based treatment (i.e. within the home or school) has the potential to improve compliance and quality of life and

reduce the financial burden on families (Little et al, 2009; Ceravolo et al, 2013). The results of the literature scoping exercise further demonstrated the value of further research in this area. Although the exercise focused on a small number of rare conditions, a number of significant gaps in the evidence were identified – particularly for those living without a diagnosis. As such, our understanding of the full range of costs associated with managing rare conditions, and the impact of how services are organised, is limited.

## **4.2 Mapping services for rare disease patients**

The research team undertook a number of exploratory meetings with representatives at the relevant patient organisations including Behçet’s patient centres, SMA Support UK, SWAN UK, Niemann-Pick UK, Alström Syndrome UK and the MPS Society. The purpose of the discussions was to gain a better understanding for how health services are currently organised for patients and families. This information was further supplemented using the individual experiences reported in telephone

interviews with patients, family members and healthcare professionals. A number of different health service configurations were described and are outlined briefly in the table below.

**Table 2: Service configurations**

Condition	Service Configuration
Undiagnosed genetic syndromes	<p><b>No identified service specifically for undiagnosed families</b></p> <p>Research suggests that a lack of overarching diagnosis is a barrier to accessing appropriate coordinated care and support. Typically, parents coordinate all care and services.</p> <p>However, new service developments are on the horizon for undiagnosed families. For example, a new specialist nurse post has recently been created at Great Ormond Street Hospital – this post will have a role in coordinating families’ care. In addition, the Rare Disease Centre in Birmingham (opening in 2017) will be hosting the first ever ‘SWAN’ clinic.</p>
Spinal muscular atrophy (SMA) (types 2 and 3)	<p><b>Specialised commissioned service</b></p> <p>Two major Specialist Neuromuscular Centres at Great Ormond Street Hospital for Children (GOSH) and Guy’s and St Thomas’ NHS Foundation Trust.</p> <p>Not all patients may attend the clinics due to distance so there is likely to be wide variation in experiences relating to coordination.</p> <p>Neuromuscular Advisors attached to some clinics, although the nature of their roles varies and most parents/patients are likely to be responsible for coordination of care.</p> <p>Social/community support not provided at centres, although some have psychological input.</p> <p>Historically, the transition from paediatric to adult service has been poor, but new initiatives are being set up – GOSH has recently employed a transition coordinator.</p>

Condition	Service Configuration
Mucopolysaccharidosis type II (MPS II)	<p><b>Highly specialised commissioned service</b></p> <p>Lysosomal storage disorder (LSD) services (adult and paediatric) based at Royal Free Hampstead NHS Trust, London; National Hospital for Neurology and Neurosurgery, London; Cambridge University Hospital NHS Foundation; University Hospital Birmingham NHS Foundation Trust; Salford Royal Hospital NHS Foundation Trust, Manchester; St Mary’s Hospital, Manchester; Birmingham Children’s Hospital NHS Foundation Trust; Great Ormond Street Hospital NHS Foundation Trust, London.</p> <p>Centres are predominantly for MPS patients, but patients with other LSDs attend too.</p> <p>The LSD services provide enzyme replacement therapy for patients (ERT). Those receiving treatment are required to go at least once a year for review. Long term treatment offered within homes/locally. New patients are also referred to the centres, however, many patients choose to receive their ongoing care locally.</p> <p>The level of coordination (including who and how clinics are coordinated) varies according to age of patient and location of clinic (e.g. only some centres have a clinical nurse specialist who coordinates the hospital clinic).</p> <p>Clinics normally occur once every six months or once a year and are consultation focused (rather than a ‘one stop shop’ approach).</p> <p>MPS Society has a role in helping advocate for patients in clinics and coordinating care between specialist centres and local services.</p>

Condition	Service Configuration
<p>Niemann-Pick disease (type C)</p>	<p><b>Specialised commissioned service</b></p> <p>Niemann-Pick Disease Patient Centres (5 adult and 3 paediatric) based at University College London Hospitals NHS Foundation Trust; Royal Free Hampstead NHS Trust; Cambridge University Hospitals NHS Foundation Trust; Salford Royal NHS Foundation Trust; University Hospitals Birmingham NHS Foundation Trust; Great Ormond Street Hospital for Children NHS Trust; Central Manchester University Hospitals NHS Foundation Trust; and Birmingham Children’s Hospital NHS Foundation Trust.</p> <p>A vast majority of adults and children with Niemann-Pick type C attend specialist clinics. However, a small proportion choose not to. This is likely to be because of location.</p> <p>Members of multidisciplinary team (MDT) vary according to service/patient. Aim to have all tests completed on same day. MDT clinics tend to take place every 6 months.</p> <p>Specialist nurse within metabolic team take responsibility for coordinating the clinic.</p> <p>Niemann-Pick UK provide support at clinics to improve holistic care and link to local (social/educational) services.</p> <p>Differences reported between child and adult services: big focus on improving transition from child services.</p>
<p>Behçets disease</p>	<p><b>Highly specialised commissioned service</b></p> <p>Behçets Syndrome Centres of Excellence based in Birmingham, Liverpool and London.</p> <p>MDT approach, providing clinics once a week.</p> <p>Lead nurse within centres acts as point of contact for patients.</p> <p>Behçets Patient Centres (charity) commissioned to provide non-medical support at the clinics through ‘Support Coordinator’ posts. They cover things such as employment and benefits.</p> <p>Not all patients access the specialist service, and majority will only come to be given care pathway/plan which is followed up locally. Other centres in Manchester and Cambridge (for example) which patients may attend.</p>

Condition	Service Configuration
Alström syndrome	<p><b>Highly specialised commissioned service</b></p> <p>Alström Syndrome Service provided for children and adults across 2 centres (Birmingham), and 1 outreach clinic (Leeds).</p> <p>All patients seen once a year (at least).</p> <p>MDT clinic (including input from physiotherapists, dieticians and psychologists) occurs across 2 days, with residential and social element built in. All tests, results and consultations done at ‘one stop shop’ clinic.</p> <p>Key focus of services is early prevention.</p> <p>Alström Syndrome UK commissioned to coordinate the clinics (inc. travel, accommodation etc.) and have a key role in family support and coordination between national and local services.</p> <p>At the end of the clinic, a summary report/letter is written for GP, parents and any specific local providers (decided by parents).</p> <p>Transition Coordinator funded by Alström Syndrome UK and young adults clinics held once a year for those aged 16-25.</p>

What was evident from the mapping exercise was that there was huge variation in how services are organised, and how coordinated services are, for patients and families affected by rare conditions. Even across the small number of conditions that were in focus in this study, there were differences according to the patients’ conditions, which service they were accessing, the age of the patient (paediatric or adult services), where the family lived and the capacity of the service.

For example, some felt that paediatric services were much better coordinated than adult services for some conditions. Some participants reported choosing local care providers (who they knew well and had built a relationship with), rather than travelling to specialist centres to see new doctors, even though they were available. Similarly, some specialist centres tended to focus on treatment or long term reviews as opposed

to ongoing routine care. Others reported that even where there were specialist nursing or coordinator posts in place within their service, capacity and resource demands on the professionals meant that they could not necessarily offer the same level of support to all families.

Where good examples of care coordination do exist, they appear to be provided in several different ways – through multidisciplinary teams, through care coordinators or nurse specialists, through condition specific and non-specific clinics, through patient organisation support roles, through one-stop shops and through residential or day clinics. There is no one agreed model being implemented across rare diseases and there is huge inequity in the care and support provided to patients and families.

The feasibility study focused on describing health service configurations only. Describing the complexities of service organisations (particularly when focusing on both health and social care services) is challenging – particularly when experiences differ so greatly. It requires detailed conversations with a variety of stakeholders including patients, families, patient representatives, health and social care providers, and commissioners. Future research should incorporate a stage of work to specifically focus on developing a taxonomy of service organisation/care coordination to describe the various models that exist within the rare disease community.

### **The challenges of coordinating care for rare diseases**

In describing current service configurations, patient organisation representatives and interview participants also gave us an insight into some of the issues and challenges that patients and families face in managing their conditions, and in particular, the challenges of uncoordinated care. The key challenges are outlined briefly and illustrated with quotes below, although pseudonyms are used so that participants are not identified.

- Patients with rare conditions face huge delays in getting a diagnosis. Patients and families felt that being undiagnosed acted as a barrier to receiving efficient and appropriate care, treatment and support.

‘... I went probably in excess of fifteen/sixteen times... it is such a simple urine test to test for a metabolic condition...

he could have been diagnosed a hell of a lot earlier... which would have changed things massively for him’. **[Parent]**

‘... we spent 27 weeks in hospital, we couldn't access any support at all... we're sat there going “right, you can't help us but you can help the family across the way... because they've got a diagnosis... they can access everything” and it's so frustrating.’ **[Parent]**

‘I suppose the most difficult thing was it was such a long time waiting for a diagnosis... it felt the longest time, you know, and to be so unwell and so disabled after being so fit was very difficult.’ **[Patient]**

‘... because I only had a probable diagnosis, I didn't really get started on a treatment pathway, which was very, very difficult.’ **[Patient]**

- Rare conditions are often severe, disabling and affect multiple parts of the body. As such, patients and families require care and input from a range of various specialities and providers – across both health and social care sectors. Patients and families described the challenges of navigating the fragmented system.

‘... sometimes it's quite fragmented and we don't quite know where to go... you're never quite sure who covers what really... I



think it's more about budgets . . . instead of looking at the needs of the child.' **[Parent]**

- Those with rare conditions need effective local care, especially in emergency situations when their specialist centres are a long distance from their home. Patients and families reported poor communication and coordination across the two levels of care.

'I don't think professionals quite get it, they see you for half an hour at an appointment every three months but they're not there like last night when we had to get an ambulance and rush Henry into hospital, they're not there at that point and the impact then that has on my twelve year old . . . ' **[Parent]**

' . . . we had an incident a couple of years ago where he had . . . [an] infection and we really didn't feel confident with him being at our local hospital, we wanted to be at Great Ormond Street . . . we felt like we just weren't listened to . . . I think we spent more money phoning up the doctors at Great Ormond Street and going up and down to our local hospital and having to re-explain to every new sister and nurse that came on about Ben's condition . . . ' **[Parent]**

- When the range of specialities and services are not provided in a coordinated or rationalised manner, patients and families reported facing an excessive number of appointments.

' . . . usually we'll get like a barrage of appointments come through from Great Ormond Street all at the same time . . . and unfortunately a lot of those clinic appointments are on different days . . . So we may be going up and down to Great Ormond Street for three days over the period of one week or two weeks . . . '

**[Parent]**

- Similarly, patients and family members described a lack of communication between providers and between services and families. As such, it was often left to families to facilitate.

'The number of agencies and people that we were starting to deal with and learn about was extensive and we learned very, very early on that they didn't talk to each other. So what we had to do was become project managers, if you like.' **[Parent]**

' . . . the doctors are wonderful, I mean, you're talking about the best doctors in Europe . . . and you get to see one, you get a plan and then it falls into the black hole of admin.' **[Patient]**

' . . . we repeat ourselves constantly . . . if it was better coordinated they would have a better understanding of Henry so when we did go to see new consultants I wouldn't be sat there discussing my pregnancy [and] what happened from birth.' **[Parent]**

- As reported by some, even if care coordination initiatives are in place, the resources and capacity within some services means that not all patients and families will necessarily receive the same level of care and support.
- Patients and families felt particularly anxious about transitioning from paediatric to adult services. Many services did not provide transition support for families who were required to move on from a service which they knew so well.

‘I just think there’s just been so many budget cuts and . . . that it’s just been so hard to implement probably what was going to be a good system and it just seems to fall apart really. I think all departments are making cuts and I think the children are suffering really.’ [Parent]

These findings are important context for understanding the full range of costs associated with managing rare conditions, and in demonstrating why coordinated care might be particularly important for those affected by rare conditions.

### 4.3 Defining cost components and outcome measures

Qualitative interviews were undertaken to better understand the costs of managing a rare condition and to identify meaningful costs and benefits (or outcomes) that would be feasible to measure in a full scale research project. Interviews were conducted with patients, family members, health care

professionals and commissioners in order to get a range of perspectives. In total, data was captured from 18 individuals (9 patients/parents; 8 healthcare professionals and 1 commissioner). The table below gives the numbers of participants for each of the conditions:

**Table 3: Qualitative interviews**

	Patient/Parent	Healthcare Professional	Total
Undiagnosed	2	1	3
MPS II	2	1	3
SMA	1	0	1
Niemann Pick type C	1	1	2
Behcets syndrome	2	3	5
Alström syndrome	1	2	3
Total	9	8	17

Participants identified a wide range of costs. The costs can be divided into two groups: the costs incurred by patients and families (often referred to as the 'hidden costs') and the costs incurred by the NHS and other services (or wider societal costs). Although the section is sub-divided into costs for the patient/family and costs to the NHS, it is important to note that all participants were able to identify a range of important costs (not just those that they incurred themselves). The costs identified are discussed in detail below. Quotes have been used to illustrate key points made by patients, parents and healthcare professionals (HCP).

### **Costs to patients and families: Financial**

Patients and parents provided many examples of how their/their child's rare condition impacted on them financially. The financial impact on families related to both medical appointments and wider condition management costs.

'Financially it's heinous . . . the unseen costs of having a disability, you know, like well it just costs more . . . in so many ways that you wouldn't think about.' **[Patient]**

'The financial impact that's had on our family has been huge, absolutely massive.' **[Parent]**

Families described the financial costs associated with attending medical appointments including trips to see the GP, outpatient appointments, clinical research and inpatient hospital stays. Firstly, travel was expensive. Whilst some participants

were able to claim back travel expenses (e.g. if they were in receipt of benefits), many could not. One participant noted that the cost of a train fare can sometimes be equivalent to a week's food bill. Some patients reported having to rely on more accessible (and expensive) modes of transport:

'I pay for a taxi if I need to go anywhere on my own . . . they provide an ambulance free of charge, however coming home you can be waiting from 1 to 4 hours and each ambulance journey . . . takes 1-2 hours which can be tiring, depressing and having to put a sock in it if you want the loo!' **[Patient]**

Patients and families also talked at length about the cost of petrol and parking:

'I'm sure everybody will raise the topic of hospital car parking when . . . you're at different hospitals every week, you can't even buy the season car park tickets because you're at different hospitals.' **[Patient]**

Travels costs were particularly high for those travelling to specialist centres, which were often a long distance away from home. Because of the time away from home, families regularly incurred additional costs such as taking time away from work, childcare for siblings, accommodation costs and subsistence.

'We have been seriously financially impacted . . . we have to go up the evening before . . . we have to fund everything ourselves like the petrol, the food, sundries,

subsidies, everything, and then we claim for it back. So we're down a day's money each month with my husband who's self employed and then we have to find about £140/£150 a month on top of everything else that we've got going on and our usual hospital appointments . . . it's very difficult, it's made a massive impact on our lives and we've had to, kind of, re-evaluate everything.' **[Parent]**

Not only did patients and parents report taking days off work for appointments, many had made the decision to leave employment altogether. This was often due to the sheer volume of medical management required each week:

'The appointments come through, everything's just put into a diary, we also have lots of appointments with social services . . . school nurses . . . there's nobody else to do it, there isn't anybody else who coordinates it . . . the impact of it is that I've had to give up work.' **[Parent]**

Parents of children with rare conditions described the burden placed on them as coordinator and full-time carer, which was all encompassing and not always compatible with paid employment. This had a huge impact not only financially but psychosocially (see below). Families described having to re-evaluate their lifestyles as a result of the vast change in their financial circumstances.

Such costs were found to be accentuated by two factors. First, the costs incurred did not always relate to one individual. Quite often,

two parents would need to attend a medical appointment with their child, or a patient might take a friend or carer for support. This was particularly important in supporting patients with complex medical needs and providing emotional support for carers. As a result, the costs reported above could double or triple with each appointment. Second, participants reported that uncoordinated care increased the financial costs that they incurred. For example, it would be considerably cheaper (from the patients' perspective) for a family to see a range of doctors within one multidisciplinary clinic on one day, as opposed to having to attend multiple appointments on different days, in different departments. Some participants reported having to attend two or three different appointments each week, some of which might turn out to be unnecessary. Third, in addition to medical appointments, families often had to factor in costs associated with social care and local appointments (e.g. trips to pick up prescriptions and physiotherapy appointments).

A wide range of financial costs associated with general condition management were identified by families. For example, families discussed the cost of private healthcare. In the absence of a diagnosis, one family was forced to seek a second opinion in the private sector:

'I had a very good package that covered 80% of our healthcare but we still had to fund 20% of that and I think that ended up costing us in the region, somewhere in the region of about £4,000.' **[Parent]**

Many of the participants interviewed were affected by disabling conditions. As a result, they faced significant costs associated with accessing specialist equipment and activities, many of which were not covered by health or social care budgets:

‘You do worry about money at times and particularly when your child needs a piece of equipment that might benefit them . . . She has a standing frame at school so it was suggested that it might be useful for her to have one at home because it’s much better for her to be upright . . . But that isn’t a statutory piece of equipment and it costs £2000.’ **[Parent]**

‘We pay . . . to have disabled riding and he also goes to a sensory cafe once a week that we pay privately for too, because he can't go to the local play area and he can't go to the local soft play because there’s too many children and it’s too noisy and he doesn't cope.’ **[Parent]**

Other financial costs included those associated with organising and managing aspects of the condition, childcare, respite care and prescriptions:

‘It’s not cheap. How much does toner cost, how much does paper cost, how much does it cost to have access to the internet?’ **[Parent]**

‘ . . . arranging childcare for a night out is expensive and then having a night out itself . . . you're ending up spending about £150 for

one night . . . you don't feel like you've got any respite whatsoever from it.’ **[Parent]**

Although the focus of this study is on the coordination of health services, it is important to understand the wider context and to have an awareness of the full financial impact facing families affected by rare conditions: the costs of uncoordinated care are in addition to the other day to day hidden costs associated with living with a rare condition.

### **Costs to patients and families: Other (non-financial)**

For patients and families living with rare diseases, the cost implications go beyond the financial. During interviews, participants described a wide range of other types of costs and impacts which they faced in managing a rare condition – many of which can be directly attributed to how health and social care services are organised and coordinated.

‘Time’ was a frequently reported cost. Parents in particular described, at length, the time burden of caring for someone with a rare condition. This included time spent making telephone calls to various providers and services, attending appointments, attending meetings, working with support groups, undertaking nursing or clinical tasks, and researching information:

‘So once the girls are at school you kind of have a list of things that you need to do that day . . . You know it might be . . . organising her medicines, chasing up the chemist, there might be a problem at the surgery with a prescription . . . researching things

like her wheelchair . . . once one thing is sorted there's another item that you need to sort as well.' **[Parent]**

In the absence of efficiently coordinated services (and in particular in the case of undiagnosed conditions where there is so little evidence of coordinated services), parents devoted huge amounts of time and resources organising, managing and coordinating their child's care themselves. Due to the often complex nature of rare conditions, there is often a wide variety of services, professionals and providers to coordinate at any one time. Parents described themselves as 'project managers':

' . . . we learned very quickly how complex our lives . . . [were] going to be . . . when you go into a meeting, you leave your personal feelings outside the room and you treat [your child] as an individual and a project, something that needed to be done . . . you have to look at the practical aspects of management.' **[Parent]**

As one healthcare professional stated, care for patients with rare conditions should be holistic in nature, it requires strong leadership and communication between clinicians – it should absolutely not be the patient or parent's role:

' They almost lose being a parent . . . becoming a manager or a carer . . . it's very difficult for them and having to tell the story time and time again is exhausting for them, frustrating . . . ' **[Healthcare Professional]**

Some described the role as full-time:

'When somebody does say to you 'well what do you do all day', when Toby is sick . . . it's just a 28 hour a day job, it means that certainly two of us have to do it because you can't do 28 hours in a 24 hour window.' **[Parent]**

As a result of the time burden, participants reported wider impacts on employment, relationships and well-being.

The wider psychosocial and health costs associated with living with and managing a rare condition are vast. It is not the intention to provide a full account of all of these costs in this report. Such costs are likely to differ between conditions, and individuals. However, patient and family interview data provided an insight into the breadth of costs and their relative importance. The interviews also revealed the specific impact of uncoordinated care on patients and families, physically, psychologically and socially.

As mentioned previously, participants reported disruption to employment as a direct result of managing the condition. Not only does this have an obvious financial impact, it also affects individuals' sense of self, identity and mental well-being. This is demonstrated in the quotes below:

'I had to give my job up, [my son] had the worst year health wise he'd ever had and I was having the best year of my career after going back to work . . . it's quite difficult actually because I really miss my me time I guess, I miss being an individual as well as a



mum and a wife, you know, and a carer.'

**[Parent]**

'I mean, I liked working, that was part of me, part of what made me me, I miss that . . . being ill does erode at your confidence.'

**[Patient]**

Schooling was also found to be disrupted to some extent, for patients and siblings of patients:

'Sheffield for me is a good 40 minute drive plus a good half an hour to find somewhere to park and sometimes I can have three appointments a week. There is no consideration for the impact that has or the fact that [he] is missing huge amounts of time at school.' **[Parent]**

Participants (both patients and family members) frequently reported the impact of managing a rare condition on their own mental and physical health. They described a wide variety of challenges which they felt had a negative impact on their mental and physical health including financial worries, uncertainty relating to the condition, stressful treatment decisions, and isolation. The quotes below help illustrate the wide and varied impact of living with a rare condition:

'I see how stressed out my husband gets with regards to money and it breaks my heart because we can't plan for the future, we're just kind of living month by month at the moment . . . ' **[Parent]**

'I don't know if [I'm] going to need surgery or something . . . if there's very few of you then you can't always have that sort of reassurance . . . So that can be slightly emotionally draining . . . it can play on your mind a bit.' **[Patient]**

'I know it's had an impact on my health from a stress perspective . . . I developed severe migraines and . . . I have beta blockers and blood pressure tablets every day now . . . What's that cost?' **[Parent]**

'I ended up on antidepressants first time in my life, I put on a huge amount of weight just through comfort eating, my . . . marriage was literally on the rocks for about two years because I was so nervous of Henry all the time, we went from having quite an active social life to never going out.' **[Parent]**

'We don't go out anymore. We used to go to the pub every week . . . it's not an option. So you become isolated . . . You're relying on Facebook, Twitter and email to do a lot of your work.' **[Parent]**

Such costs were also found to be directly associated with receiving uncoordinated care. For example, parents and patients reported that travelling to and attending an excessive number of appointments was physically tiring. This was particularly difficult for those with physical disabilities or those suffering from fatigue relating to their condition. Participants described the

intensity and burden of daily condition-management tasks and having to 'fight battles' to get access to appropriate care and services:

'You're fighting battles all the time really to get things, which should be sort of quite easy and it does have an impact on your health and wellbeing.' **[Parent]**

All participants made reference to the impact on the wider family. They felt that these costs were particularly hidden. First and foremost, as described above, parents and full-time carers faced huge costs.

Quite often different members of the family take on the caring role. The costs and impacts are therefore not just felt by one parent or one carer. Other parents and grandparents also support the day to day condition management. As such, a ripple effect is felt and costs can be seen to multiply further. More than one individuals' work is disrupted and more than one individuals' time is taken up.

'Every three months in Birmingham we have to go up for two days . . . We simply can't do it just one of us on our own, Ben is very big, very strong . . . I couldn't dream of doing it on my own.' **[Parent]**

'For things like heart or seeing the specialist to review all the results we tend to take our Mum with us so it's quite good to have another point of view.' **[Patient]**

Second, participants reported disruption to family time as a result of living with and managing a rare condition. One interviewee even stated that hospital appointments were a rare opportunity to spend time together as a family:

' . . . the worst part of my husband having all time off to attend appointments is that he has to work all weekend . . . the only real good quality time that we get to spend together as a family is when we go to hospital.' **[Parent]**

'I would say that we actually haven't had a holiday . . . for ten years.' **[Parent]**

Similarly, some mentioned that relationships (e.g. relationships with partners) were affected:

'personal relationships, that's another one that can be a stretch . . . in some cases you will have a sick child but dad still goes off to work and mum has to take the burden . . . sometimes there's a lack of empathy in the family as well.' **[Parent]**

The impact on siblings of patients was noted by parents during interviews. For example, siblings would often be required to spend long periods of time away from their parents (as a result of frequent appointments or hospital stays). As the quote below demonstrates, support for young siblings in this context is particularly important:

'When . . . in hospital for any length of time, I've got a twelve year old at home who



worries and panics . . . we've had paramedics here doing things . . . it doesn't matter how much you try to keep [them] away, he's aware that they're in the house, he's aware that there's . . . it's that fear as well.' **[Parent]**

### **Costs to the NHS and wider societal costs (of uncoordinated care)**

The narrative and quotes above have described the costs faced by patients and their families – both financial and psychosocial. The section below reports on costs from a different perspective – costs to the NHS and other wider societal costs. It focuses on the costs implications of uncoordinated care. The majority of the data are from interviews with health care professionals.

The anticipated benefits of coordinated care were consistently raised by participants. They argued that specialist and coordinated care could (and should) achieve the following:

1. Timely access to diagnosis, effective treatment and other relevant services.
2. Proactive and not reactive care.
3. Standardised care across patient community.
4. Personalised and holistic care.
5. Effective communication across specialisms and providers.
6. Education and awareness amongst health care professionals (at all levels) and patients.

7. Research and innovation (including access to research studies).

Not only would these factors improve health outcomes for patients, they could also lead to cost savings within the NHS. Two examples are provided below. From a commissioning perspective, evidencing that the costs associated with hospital admissions can be reduced is particularly valuable.

' . . . our ambition . . . is to reduce the number of people who go blind . . . from a wider perspective, that will reduce costs. Because . . . a person who goes blind avoidably would be a huge cost to the system. They wouldn't be able to work necessarily as . . . they'd be consuming resources in the health system because of that. So that's costs we can avoid.'  
**[Healthcare Professional]**

' . . . a lot of patients with Behçet's needed frequent admission because they were never really sorted out properly, so our aim is to minimise the number of hospital admissions and minimise the duration of admission for the disease and that has a major saving to the NHS.'  
**[Healthcare Professional]**

It was argued that uncoordinated care has cost implications for the NHS. As shown in the quotes below, health care professionals identified a number of different costs associated with excessive appointment schedules including administration costs, transport costs and staff time. They argued

that such costs could be reduced if consultations and tests were arranged for a single appointment:

‘If a patient needed a fibroscan, an ultrasound, a CT scan, lung function, a six minute walk test, psychology appointment, a dietetic appointment, they would be coming in at a separate time for all of those investigations . . . we would be paying for transport for every single appointment . . . they would need to have lots of people available . . . to accompany them or the hospital would have to provide that so they can get to all these appointments, I mean, that’s massive.’ **[Healthcare Professional]**

A more coordinated system would also potentially reduce the duplication and repetition of appointments and tests:

‘It means the care is more efficient and effective and there’s not unnecessary duplication of attending multiple hospitals, multiple consultants effectively for the same problem. So to the NHS that’s going to be less cost because there’s less appointments needed.’ **[Healthcare Professional]**

In the case of undiagnosed families, where there is often no clear care pathway in place, families and the NHS incur the costs associated with inappropriate, repetitive tests and overlapping care.

Potential savings associated with care coordinator posts and the use of technology/remote consultations were explored with participants. Both were expected to have potential benefits and savings for both the families and the NHS.

For example, if families had one point of contact for any questions or concerns, and/or they could easily access care and advice without attending the hospital, then costs associated with appointments could be reduced for all parties:

‘I do a lot of phone calls to these patients . . . But I think that’s possibly cost saving because I think . . . he would come into hospital a lot more if he didn’t have that.’ **[Healthcare Professional]**

It was argued that effectively coordinating care could reduce ‘Did Not Attend’ (DNA) rates, and therefore reduce NHS costs (at the same time as improving health outcomes). For example, one healthcare professional argued that many families give up trying to navigate the system – they struggle to coordinate their care and become disengaged with health care services. In addition, during crucial periods such as transition between paediatric and adult services, coordination is even more important in avoiding DNA rates:

‘. . . also tracking youngsters when they transfer from paediatric to adolescent service if you haven’t got somebody whose role it is to support them through that transfer and also track that they’re attending at least for their first two adult appointments, the cost for young people dropping out of the service.’ **[Healthcare Professional]**

Interviewees also noted the potential cost savings in relation to treatment. Where treatments are available for rare disease

patients, they are often expensive. Quick and effective management is required to ensure that patients are treated appropriately:

‘By focusing treatment more effectively that means that . . . the high cost drugs are being used appropriately . . . it’s possible that patients would have been having a high cost drug when they didn’t really need it and to have the care optimised by the low cost, simpler treatment. So all of those have got big savings for the NHS.’ **[Healthcare Professional]**

The complexity of NHS costs savings should also be considered here. Whilst some examples provided above may result in overall NHS budget cost savings, some trusts or departments may benefit from the cost saving more than others. What might be a saving for one, may be a cost implication for another. There are many different budgets within the NHS (and in other sectors) which may be impacted differently as a result of different service configurations.

Finally, interviewees identified the wider societal consequences of managing rare conditions – particularly the implications of

having patients and family members out of work and reliant on benefits:

‘We are really not contributing to the economy as much as we were ten years ago . . . we’re probably a burden on society now as well because of Disability Living Allowance and Carers Allowance and Working Tax Credits and so and so forth.’ **[Parent]**

### **Meaningful costs and benefits: a summary**

As demonstrated in the introduction, the full impact and costs associated with managing rare conditions are currently unknown. However, the qualitative interviews carried out for this report demonstrated that costs are varied and incurred by not only health and social care providers, but also patients and families themselves. These costs are both financial and psychosocial. These can be thought of as ‘hidden costs’. It can be argued that future research evaluating services for rare diseases should take into account a broader range of costs and benefits. These costs are summarised below, in tables 4 and 5.

**Table 4: Costs for patients and family members of managing a rare condition**

Financial	Other
<p><b>Costs associated with appointments:</b> Time off work and reduced income; childcare; travel including petrol, public transport and taxis; parking; food and refreshments; accommodation; sundries; accessible vehicles and transport options.</p> <p><b>Other financial costs associated with wider condition management:</b> Private healthcare; childcare and respite; specialist activities and equipment; IT, internet and telephone costs (including paper and printing cost); prescriptions; fees for informal helpers and carers; disruption to employment and income.</p>	<p><b>Time:</b> Time off work; time spent coordinating ('project managing') care and the various agencies and appointments involved; time spent fighting to access care and support.</p> <p><b>Psychosocial, health and well-being:</b> Disruption to schooling, employment and personal time; impact on relationships and social life; isolation; impact on identity and sense of self; living with uncertainty; mental health; fatigue; confidence and self esteem; anxiety and stress associated with appointments.</p>
<p><b>Wider family:</b> Costs identified above related to patients, parents and grandparents; siblings and wider support networks.</p>	

**Table 5: Costs to the NHS (and wider society) of uncoordinated care**

<p><b>Wider societal costs:</b> Patients/parents out of work; benefits; implications for social care budgets</p>
<p><b>NHS costs:</b> Duplication of efforts and unnecessary appointments (healthcare professional and secretarial time, tests and interventions, administration (e.g. appointment letters)); missed appointments (Did Not Attend (DNA) rates) and non-compliance with medication; higher rates of hospital admissions; poor patient outcomes.</p>

## 4.4 Testing the feasibility of data collection

### Using existing data sources

As part of this work, we commissioned a health economist at UCL to assess existing datasets on the use of services for the selected rare diseases and their potential

usefulness in providing data on contact with services (including primary care); use of diagnostic tests; medication use and other interventions; and hospital visits.

A brief report has been produced outlining what data exist and in what form including: Hospital Episodes Statistics (HES) data, Clinical Practice Research Datalink (CPRD) data, rare disease registries, publicly available datasets (or aggregated data) and data available on application (such as patient level data). The report suggests that existing data sets for the rare conditions we have chosen are not sufficient and any future research project would need to use new tools to collect relevant data. A summary of the findings of this work are provided at appendix 3.

### **Diary development**

One aim of the feasibility study was to consider how new data about costs (and outcomes) can be collected in a full scale research project. As demonstrated in appendix 3, existing data sets for rare conditions are not sufficient to collect the different types, and full range, of costs that were identified in the qualitative interview stage – particularly the costs incurred directly by patients and families. For example, what emerged from patients and families as important and often ‘hidden’ costs associated with managing a rare condition (particularly in the context of uncoordinated care) were financial costs associated with appointments, and time.

Patient-reported resource-use measures (RUMs) are important in economic evaluation. They are developed in many different formats, and might include questionnaires, diaries or interviews, administered by post, in person or by telephone (Thorn et al, 2013). As part of the study, we developed a ‘patient diary’. The purpose of the diary was to categorise,

collect and quantify some of these important costs identified by patients and families.

The diary was developed in collaboration with steering group members including health economist, Professor Steve Morris. The Database of Instruments for Resource Use Measurement (DIRUM) is an open access database of resource-use questionnaires and diaries for use by health economists in trial-based economic evaluations. We searched the website (<http://www.dirum.org/instruments/all>) to identify useful examples of questions and formats to inform the diary development. The majority of the tools in the database were found to be condition-specific or were not related to rare conditions.

It was important to draw upon good practice guidelines in the development of the data collection tool. First, it has been argued that questionnaires should be as short as possible and identify the main costs from the chosen perspective (Rolstad et al, 2011 cited in Thorn et al, 2013). Secondly, the most relevant questions should be placed first (Thorn et al, 2013). Third, there is some evidence to suggest that the use of resource-use logs (e.g. diaries completed by patients in real time) could be useful in reducing the amount of missing data in RUMs (Thorn et al, 2013).

As argued by Ridyard and Hughes (2015), RUMs should be described more accurately and thoroughly in order to increase transparency of reporting. The characteristics of the diary developed during the feasibility study are summarised in table 6.

**Table 6: A description of the data collection tool**

<b>Source of data</b>	Patient or family member
<b>Who completes it?</b>	Patient or family member
<b>How is it administered?</b>	To the self (the patient or family member)
<b>How is it recorded?</b>	Diary
<b>Medium of recording</b>	There were various options available for participants of the pilot including: electronic Excel spreadsheet, electronic word document (both completed on the computer and returned via email) or printed word document (completed on paper and returned by post).

DIRUM note that methods for collecting economic data are rarely validated or piloted prior to their use. In fact, under a third of studies funded by the UK Health Technology Assessment (HTA) programme described a RUM validation process (Ridyard and Hughes, 2010 cited in Thorn et al, 2013). It has been argued that questionnaires and RUMs require validation ‘to ensure the appropriateness of the response categories, the clarity of the instructions, and the layout, format and length of the questionnaire’ (Thorn et al, 2013: 158). Yet, currently, there is a lack of consensus on whether, or how, tools should be validated.

Early content validation was carried out in this study, through the use of qualitative interviews with a range of stakeholders including patients and family members. This data informed the content of the diary. The diary was also piloted with a small number of patients and family members (parents). Participants were both previous interviewees and new study participants. They represented both the conditions

selected as the focus for the feasibility study and a wider range of rare conditions. The purpose of the pilot was to:

- Further validate the costs identified
- Potentially identify new costs that the interview phase did not uncover
- Help assess the extent of burden on patients and families
- Assess the feasibility of collecting the data items – including identifying where poor response exists, identifying ways to reduce the length of the diary, identifying ways to improve the diary or the process of completion, identifying the most appropriate format or medium of recording for patients.

A copy of the Word/print formatted diary which was piloted is shown in appendix 4.

In total, seven participants piloted the diary during the feasibility study including two adult patients and five parents of patients. The participants represented a wide range of conditions including mal de

debarquement syndrome; Alström syndrome; Behçets syndrome; SMA type 2; idiopathic intracranial hypertension; Chiari malformation; Niemann-Pick type C and undiagnosed conditions. Participants piloted the diary over 2 to 4 weeks. Following the pilot period, participants took part in follow up telephone interviews to give their feedback on their experience of completing the diary. A summary of their feedback is provided on the following pages.

### **Format of diary**

The diary was tested in a variety of formats – Word, Excel and paper.

Some participants chose to complete the diary in paper format. For them, this had the advantage of being able to complete ‘on the move’; for example, in the waiting room at the hospital. Carrying the diary on their person gave them the flexibility to complete the diary as and when they had a spare moment. However, in its current format, the paper version is over 30 pages long and not easy to carry. This is because it includes several tables for participants to complete, depending on the number of health visits they attend in that time period. Although in the pilot period families did not necessarily attend this many appointments, if participants were to complete a diary over a long period of time (months as opposed to weeks), they may well need a large number of tables to complete. Thought should be given as to how this can be condensed in paper format. One further issue experienced in the piloting of paper versions of the diary is that some participants missed tables towards the end of the document (e.g. tables focusing on other types of costs). They were lost within the length of the

document. Future versions should provide a contents page, or some other system to help patients and families navigate the various fields.

The electronic versions were more suitable for some participants who had access to laptops/computers. These formats were found to be easier/cheaper to transfer between the research team and the participant. Careful consideration would need to be given in future research as to how such data can be transferred securely and confidentially. The electronic formats also gave participants the option to expand text boxes, tables and cells as appropriate, depending on how much information they wanted to provide. Participants were able to see all fields and types of costs, which reduced the amount of missing data. Some participants suggested that future data collection tools like this should be available in a format which can be viewed and completed on a mobile phone or tablet such, as an app.

What emerged as most important in relation to the format of the diary, was that participants felt a range of formats should be available to patients and families taking part in a full scale research project to ensure maximum engagement and accessibility.

### **Burden and time associated with completion**

Most participants reported that the diary took them less than 20 minutes per week to complete. Some completed it on an ad hoc basis at convenient times during the week and others set aside a small amount of time at the end of each week to write up their key costs. All felt that this was an acceptable



and manageable task – not one that was too burdensome. Some participants reported spending longer on the diary completion, especially those who focused on providing an in-depth account of the psychosocial costs they faced. For example, one participant was keen to include historical psychosocial costs. This participant had not taken part in a previous interview and so this was their first opportunity to record such information. In fact, during interviews, many participants reported verbally other historical costs which they couldn't include in the diary because the costs weren't incurred during the piloting time frame. It is anticipated that future use of the tool will lead to the inclusion of more costs as participants complete the diary over a longer period of time. However, thought should be given as to whether participants should have the option to include other retrospective/historical costs, to be included as further evidence.

### **Missing data**

All participants were asked to identify any costs that they felt weren't included in the diary. Very few were reported, suggesting that the content of the pilot version covers both a wide range of important and valid costs. However, a few suggestions were made which should be considered for future data collection tools. First, participants should be encouraged or asked explicitly to include costs (financial or otherwise) incurred by other family members. Second, it was felt that future versions of the diary should keep a qualitative element to them. For participants, this was crucial in capturing the nature of psychosocial impacts.

A suggestion was also made to ask participants 'what is this cost equivalent to?' So, for example, if a participant reports that a train fare cost them £50, they should be given the opportunity to report whether this was equivalent to a week's food bill for their family. This type of information would help assess the scale of cost impact on families. Thought should be given as to how this question is framed in future research projects, as it may be intrusive or sensitive to ask questions about family income/salaries. Instead, researchers could ask questions focused on identifying how families live their lives differently as a result of managing a rare condition (e.g. How does this alter how you live your life? Are you managing on your normal income? How easy is it to meet household needs?). A multiple choice question might also be useful here and could flag up where families are accessing additional income support such as loans, financial help from family members, and accessing savings. A suggestion was also made to ask participants whether the costs associated with the appointment were worth it – a 'was it worth it?' (and 'if not, why not?') question might help identify where appointments are inefficient, duplicated or unnecessary (due to poor coordination). Finally, participants felt that the diary should include 'other' options as far as possible to enable participants the flexibility to add further detail.

### **Benefits of collecting data**

Interestingly, participants reported a number of benefits to themselves associated with the diary completion exercise. First, participants described the



process as therapeutic, particularly those providing detail on the psychosocial costs associated with managing a rare condition. Very rarely do patients and family members have the opportunity to think through and record such challenges. One participant described the process as 'a good way of releasing it'. Second, participants reported feeling shocked at the extent of costs during the pilot period. The diary process gave them a unique opportunity to record and count the actual costs (financial and time) that they incur on a weekly basis. Taking part had made them think about how the small costs mount up and for some it was a shock to see the true scale of costs they incurred over time. This indicates that the costs associated with managing a rare condition can also be 'hidden' to some

extent from the patients and families themselves. One participant also felt that the record would be a useful tool to take to doctors and others to evidence the impact of the condition on them.

As well as the potential benefits of completing the diary, it is also important to acknowledge the potential risks to future research participants (for example, the burden of seeing the full impact of the rare condition on them). This must be considered in future research and research ethics applications. Safeguards should be in place such as: acknowledging the risk; making patients and families aware of the potential burden in the participant information sheet; and offering participants someone to talk to after their involvement as part of the debrief process.

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## Appendix 1: Steering Group terms of reference

### Role of Steering Group

The role of the Steering Group is to ensure the robust, fair and transparent running of the project. More specifically the role of the group is to:

- Represent the views and needs of a wide range of stakeholders both from its own resources and through its network of contacts
- Maintain awareness of the relevant evolving political, social and health service environments
- Provide expert advice and guidance on relevant aspects of the project work including:
  - o Literature review
  - o Ethics committee approval
  - o Testing feasibility of proposed full scale project methods
  - o Refining research questions
  - o Reviewing drafts of full scale research proposals, and helping to identify potential sources of funding.

The Steering Group will be composed of representatives from patient organisations, the NHS, academia and other relevant bodies.

It is envisaged that the Steering Group will convene three times during the feasibility phase project (either face to face or via internet/teleconference), however additional meetings may be called if necessary. Between meetings the Steering Group will be consulted by email and telephone for input on specific matters that may arise through the lifetime of the project.

Travel and subsistence expenses will be covered for all activities in line with Genetic Alliance UK's expenses policies.

## Steering Group members

Name	Role
Renata Blower	SWAN UK Parent Representative
Kay Parkinson	Founder of Alström Syndrome UK. Chief Executive Officer for Cambridge Rare Disease Network.
Dr Peter Corry	Paediatrician (retired). Member of the Rare Disease UK management committee.
Professor Eamonn Maher	Professor of Medical Genetics and Genomic Medicine, University of Cambridge. Former Academic Lead for the Centre for Rare Diseases and Personalised Medicine, University of Birmingham. Advisor to Myrovylitis Trust.
Professor Steve Morris	Professor of Health Economics, University College London.
Duane Schulthess	Managing Director of Vital Transformation, a consultancy specialising in measuring the impact of policies and interventions in medicine.
Dr Celine Lewis	Research Psychologist, University College London. Former researcher at Genetic Alliance UK.
Professor Heather Skirton	Professor in Applied Health Genetics, Plymouth University.
Corinna Alberg	Project Manager, Public Health Genetics Foundation. Observer on Genetic Alliance UK Board of Trustees.  Corinna stood down from the steering group in early 2016 when she moved jobs.
Dr Mike Knapton	Medical Director for Prevention and Care at British Heart Foundation. GP. Non-executive Director, Cambridge University Hospitals NHS Foundation Trust.
Dr Amy Hunter	Senior Research Manager, Genetic Alliance UK.
Amy Simpson	Research Associate, Genetic Alliance UK.

## Appendix 2: Sampling frame

Type of Condition	Blood				
	Renal				
	Gastrointestinal				
	Cardiovascular and respiratory				
	Skin				
	Bone connective tissue				
	Endocrine and reproductive				
	Vision or hearing	X			
	Metabolic				
	Central nervous system and mental function				
	Neuromuscular	X			
	Rare cancer				
Onset of Condition	Congenital				
	Adult onset	X			
Rarity of Condition	Child onset				
	Very Rare (i.e. fewer than 500 in England)				
Treatment	Rare (affecting less than 5 in 10,000)	X			
	No treatment/only symptom management	X			
Variability (severity)	Treatment available to target the underlying pathology				
	Consistent level of severity across cases				
Chronic/ Acute	Variable levels of severity	X			
	Chronic	X			
Diagnosis	Acute (inc. Susceptibility to acute)				
	Difficult to diagnose				
Sampling Unit (Condition)	Straight forward to diagnose	X			
	Example - Name of condition				

## Appendix 3: Existing datasets for rare diseases

The information provided below is based on the work undertaken by Dr Talitha Verhoef, Health Economist, UCL.

### Coding systems for rare diseases

Several existing codification systems were identified. Among them the most important are:

- The World Health Organisation's International Classification of Diseases (ICD). The current version is ICD-10. This system is under revision and the next version (ICD11) is expected to be released in 2017. Nearly 500 rare diseases have a specific code in the ICD10. However, there are thought to be between 6000 and 8000 rare conditions. So, it is only possible to use ICD-10 codes for a small proportion of rare conditions and it is not possible to use a code for the undiagnosed community. For some conditions there may be a specific code (e.g. Behçets Syndrome). However, for others there is more than one code available or the ICD-10 code includes other conditions as well.
- The Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) is run by the International Health Terminology Standards Development Organisation and is available in over 50 countries. It has been adopted as the standard terminology for the National Health Service in the UK and includes not only disease classification but also other medical terminology areas. Nearly 3000 rare diseases have a specific SNOMED CT code.
- Orphanet is the most comprehensive online database of rare diseases. The Orpha codes system is designed based on Orphanet data. Each of the nearly 7000 rare diseases listed on the Orphanet website has an Orpha code - a larger number than those rare diseases that have either an ICD or SNOMED CT code.

### Hospital Episodes Statistics (HES)

HES data includes detail of all NHS admitted patient care, outpatient appointments and A&E attendances in England. It includes private patients treated in NHS hospitals, patients living outside of England, and care delivered by treatment centres (including those in the independent sector) funded by the NHS. Each HES record contains a wide range of information about an individual patient admitted to an NHS hospital including: clinical information about diagnoses and operations; information about the patient, such as age group, gender and ethnicity; administrative information, such as time waited, and dates and methods of admission and discharge; and geographical information such as where patients are treated and the area where they live. It contains admitted patient care data from 1989 onwards, outpatient attendance data from 2003 onwards and A&E data from 2007 onwards.

The following aggregated data (for 2013/14) is publically available via the Health and Social Care Information Centre (HSCIC) website:

- A&E attendances per diagnosis: Diagnoses do not include the rare conditions this feasibility project is focussing on (not specific enough).



- Adult critical care per Health Resource Group (HRG): HRG groups are not specific enough to find the rare conditions that this feasibility project is focussing on.
- Hospital admissions per diagnosis: Diagnoses based on ICD code only.
- Outpatient activity per diagnosis: Diagnoses based on ICD code only.

Data may also be extracted on application at the patient level (with or without personal confidential data) on hospital visits. Anonymised data for a specific patient group using NHS numbers might be possible, but there is a risk of identification due to small sample sizes.

In summary, there are many possibilities for the use of HES data. However, the process for accessing and working with personal confidential data can be difficult and is often a lengthy process. In addition, HES does not offer data in relation to primary care attendances or social care use – it would only offer an insight in to one aspect of rare condition management.

The process to request data is described on <http://www.hscic.gov.uk/dars>.

### **Clinical Practice Research Datalink (CPRD)**

All CPRD datasets contain coded data. The CPRD supply the necessary coding dictionaries and links to dictionaries to develop code sets and understand the variables used. The key coding schemes and dictionaries used in the NHS are: ICD-10, READ, OPCS4, SNOMED CT and the British National Formulary (BNF). In the near future, the CPRD will include ATC drug coding and MedDRA for adverse event reporting in clinical trials. Patient level data is available on:

- Primary care: records of clinical events (medical diagnoses), referrals to specialists and secondary care settings, prescriptions issued in primary care, records of immunisations/vaccinations, diagnostic testing, lifestyle information (e.g. smoking and alcohol status), and all other types of care administered as part of routine GP practice.
- Prescriptions in primary care: generics and/or branded products issued in primary. Information on formulation, strength and dosing instructions will also be available.
- Secondary care: HES data will be made available as separate modules of hospitalised care, outpatient visits (visiting a consultant), maternity care and augmented/critical care. In this data source each patient has a line of data for each "consultant" episode of care; this is best understood as a line of data for each ward in which the patient is treated.
- Prescriptions in secondary care: data for drugs administered in hospital or day care. This dataset does not cover all drugs as some drugs are provided from a ward trolley. New drugs will however be in this dataset, as will cancer drugs given in the day care setting.

The CPRD Data Team will extract datasets for researchers against a query specification. The query and its output content will be agreed with the researcher prior to generation of the data sets. CPRD has a market pricing structure for access to data and services. Service costs are priced based upon time of staff and use of specific IT systems. Data costs are charged at a fixed rate depending upon which data sources are required and the complexity of linkage. Access to the CPRD data and services can be highly tailored to your specific needs. The CPRD Knowledge Centre ([kc@cprd.com](mailto:kc@cprd.com)) offer information on pricing arrangements to suit the needs of

researchers. Pricing arrangements are formalised within the legal agreement covering all aspects of the use of the CPRD data and services.

## Rare disease registries

There are several rare disease registries in Europe. For the diseases selected for this study, the following registries exist in the UK:

- Registry for patients with Niemann-Pick Type C Disease
- UK and Ireland Spinal Muscular Atrophy (SMA) Patient Registry (part of the TREATNMD network): 525 patients in this registry with information on personal details, clinical information (motor function, how person is fed, if person had spinal surgery, respiratory function, use of ventilation (invasive/non-invasive)) and genetic information
- EURO-WABB: A European rare disease registry for Wolfram syndrome, Alström syndrome, Bardet-Biedl syndrome and other rare diabetes syndromes
- The Alström Syndrome UK (ASUK) Clinical Research Database
- English Mucopolysaccharidosis Registry

However, for some of the registries listed above it is unclear what information is included. A full list of registries in the UK as well as other European countries can be found at

<http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf>

## The National Congenital Anomaly and Rare Disease Registration Service (NCARDRS)

Public Health England's National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) aims to:

- Provide a resource for clinicians to support high quality clinical practice;
- Support and empower patients and their carers, by providing information relevant to their disease or disorder;
- Provide epidemiology and monitoring of the frequency, nature, cause and outcomes of these disorders;
- Support all research into congenital anomalies, rare diseases and precision medicine including basic science, cause, prevention, diagnostics, treatment and management;
- Inform the planning and commissioning of public health and health and social care provision;
- Provide a resource to monitor, evaluate and audit health and social care services, including the efficacy and outcomes of screening programmes.

Patient data can be collected without the need to seek consent from individual patients, as agreed under Section 251 of the NHS Act 2006. Further information can be found at:

<https://www.gov.uk/guidance/the-national-congenital-anomaly-and-rare-disease-registration-service-ncardrs>. Researchers are encouraged to use the data and contact NCARDRS early on in a project to make sure that the data collected is able to answer the research question and that the

research is novel. Whilst it is currently in its infancy, NCARDS may offer opportunities for data collection and extraction in the future.

## Appendix 4: Patient diary

### Instructions for participants

Thank you for agreeing to take part in this stage of the Hidden Costs Feasibility Project. In the past few weeks we have been interviewing patients and family members to find out about the sorts of costs families face in managing a rare condition. We have used this information to develop a new data collection diary. The diary is for families to make a record of the costs they incur on a daily and weekly basis. We now wish to test the diary to check that we are capturing the correct types of costs, and that we are capturing them in the best way (Is the diary easy to use? Is there anything that would make it easier for participants?). It is important that any tool used in future research has been road-tested with participants. It will also start to give us a better idea for how much cost families face.

We are asking participants to keep a log of the time and costs they face over a four week period. We are particularly interested in capturing the costs associated with each scheduled visit to a health care provider (for example an outpatient appointment, or a trip to see the GP) and the amount of time you spend arranging or coordinating the care (for example, phone calls and emails to arrange appointment times).

Before you start completing the diary, you should have had a phone conversation with the researcher who will have gone through the project information with you, given you the opportunity to ask any questions, and asked for your consent to take part.

Instructions for completing the diary:

1. Please enter the date (below) that you start logging information in the diary. This date will have been agreed with the researcher.
2. From this date, please count a total of four weeks (28 days). This is your data collection period.
3. During this period, each time you visit a health care provider, or you have a scheduled visit to see a health care provider, please complete one 'visit' table with as many details as you can. If you do not know an exact cost, please provide your best guess. Not all the costs will be relevant to you, and so you may leave some boxes blank. Please only log those visits which are related to you or your child's rare condition. For example, do not include details about a trip to see the GP if it is for something unrelated. We know that there may be many other types of visits that you make in relation to your/your child's condition, but at this stage our diary can only record visits to the NHS or other health care providers (e.g. not those provided by your local council's social care department or education authority). You may have a visit scheduled that gets cancelled at the last minute. If you incurred any costs, despite the appointment being cancelled (e.g. advance train tickets), please complete the table anyway. Health care visits might include:
  - a. An outpatient clinic appointment

- b. An inpatient hospital stay
  - c. A trip to see the doctor or nurse in your local general practice
  - d. A physiotherapy or occupational health appointment outside of the home
  - e. A trip to your pharmacy to pick up medication
  - f. Something else... if in doubt, please include it!
4. Interviewees told us that they spend a lot of time managing their condition. This included time spent on the phone, and time spent emailing different health providers, to arrange appointments and coordinate their/their child's care. Please make your best guess as to how much time you spend on these activities each week. Again, we are most interested in the time you took organising things related to health care at this stage.
  5. The final two sections in the diary give you the opportunity to make a note of any other costs you face in managing your/your child's condition. These may be in relation to health or social care or educational needs. They may be financial costs, or other types of costs (e.g. emotional or psychological impacts). Please include as much detail as you can here.
  6. You may want to set some time aside each week to update the diary. We anticipate that it will take 15-20 minutes to update per week, but this is one of the things we are not sure about yet and need to test.
  7. At the end of the four week period, a researcher will schedule a short telephone interview with you to talk through your experience of completing the diary. We are keen to get your feedback on a number of things including:
    - a. How easy was the diary to complete?
    - b. In your opinion, was there anything missing from the diary?
    - c. How long did it take for you to complete each week?
    - d. Was it easy to remember all of the different costs and details?
    - e. Can you think of any way the process or diary could be improved?

If you have any questions or queries at all during the data collection period you can call or email Amy Simpson. In fact, the more feedback we get from you the better!

Thank you for your support in the project so far.

<b>Unique participant code:</b>	
<b>Starting date:</b>	

### Visits to health care providers

Please record details of all visits to see NHS healthcare providers during this period. All visits should be made in relation to your condition (which is the focus of this study). If a visit was cancelled at the last minute, but you still incurred costs as a result (e.g. pre-paid train tickets), please include this detail and tick the 'was this visit cancelled or rearranged?' box. Please complete one table per visit.

Visit details and costs associated with visit	Visit 1
Date of visit	
Was this visit cancelled or rearranged?	
Type of visit (e.g. GP appointment, outpatient appointment, trip to the pharmacy)	
Name of provider (e.g. name of hospital)	
Reason for visit and details of visit (who did you see and what tests did you have?)	
Who attended the visit? (e.g. patient/parent(s)/siblings)	
Did anyone have to take time off work (paid or unpaid) or school? If so, please provide details.	
Time spent at visit	
Time spent travelling	
How did you travel? (e.g. car, taxi, train)	
If car, what was your mileage for the return journey?	

Cost of all public transport (including taxis)	
Cost of parking	
Costs of food/subsistence	
Cost of accommodation (if relevant)	
Did you have to arrange child care for your visit? If so, who with, how many hours, and at what cost?	
Were there any other costs associated with visit? Please provide details.	
Where you reimbursed any of the above costs? If so, please provide details.	

*(This table was duplicated for participants, so that they could complete one for each visit)*

### **Time spent managing and coordinating care**

Please make a log of the time you spend 'project managing' or coordinating your/your child's care. This may include making telephone calls to various services, sending emails etc. It may be difficult to be exact – an estimate of time is fine!

<b>Details</b>	<b>Week 1</b>	<b>Week 2</b>	<b>Week 3</b>	<b>Week 4</b>
Total time spent making telephone calls to various services				
Total time spent on the internet or emails				
Other (please specify)				
Other (please specify)				
Other (please specify)				

### Other financial costs

Please record any other financial costs you have had to meet during this period (as a result of your/your child's condition). This might include home help, prescriptions, specialist food, activities or equipment, courses or events.

Brief details	Total cost

### Other costs

Please tell us about any other costs that you or your family has faced as a result of your/your child's condition during this period. This may include non-financial costs, such as emotional or psychological costs.



## Appendix 5: Draft research proposal (for discussion at final steering group meeting – July 2016)

### Aims and objectives

The aims of the proposed research are to use quantitative and qualitative research methods to investigate the benefits and costs of different types of co-ordinated care (including no co-ordination) for people diagnosed with rare diseases, to identify the barriers and facilitators for implementing co-ordinated care in this group, and to make recommendations as to how care should be co-ordinated in this group.

The objectives of the proposed research are as follows:

1. To understand how care of people with rare diseases is currently co-ordinated in the UK.
2. To develop a taxonomy of how care for people with rare diseases may be co-ordinated.
3. To analyse the impact of different models of co-ordinated care on processes (characteristics) of care (e.g. waiting times for treatment, expertise of staff) and patient physical health and psychosocial outcomes.
4. To analyse the costs (pecuniary and non-pecuniary) and cost-effectiveness to the NHS, social services, third sector and families of different models of co-ordinated care.
5. To analyse preferences for different models of co-ordinated care by patients and families, and health care professionals.
6. To investigate the barriers and facilitators for implementing different models of co-ordinated care.
7. To make recommendations on if and how care should co-ordinated, including how this ought to be implemented, plus disseminate findings.



