U.PORTO

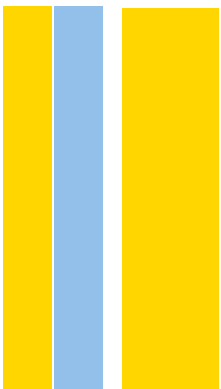
MASTER
PUBLIC HEALTH

Preferences of rare disease patients and informal carers for engagement in decision-making about health data sharing for research

Ana Francisca Carneiro Pinho

M

2024



SEDE ADMINISTRATIVA

FACULDADE DE **MEDICINA**

INSTITUTO DE **CIÊNCIAS BIOMÉDICAS ABEL SALAZAR**

Ana Francisca Carneiro Pinho

Orientadora

Doutora Cláudia Susana Soares de Freitas
Instituto de Saúde Pública da Universidade do Porto
Departamento de Ciências da Saúde Pública e Forenses e Educação Médica,
Faculdade de Medicina da Universidade do Porto

Coorientadora

Doutora Ana Lúcia Nunes Henriques
Instituto de Saúde Pública da Universidade do Porto
Departamento de Ciências da Saúde Pública e Forenses e Educação Médica,
Faculdade de Medicina da Universidade do Porto

Preferences of rare disease patients and informal carers for engagement in decision-making about health data sharing for research

Dissertação de candidatura ao grau de Mestre em Saúde Pública apresentada à Faculdade de Medicina da Universidade do Porto e ao Instituto de Ciências Biomédicas Abel Salazar.

Porto, 2024

U.PORTO
FM UP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

U.PORTO
INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR UNIVERSIDADE DO PORTO

Este trabalho foi cofinanciado pelo FEDER através do Programa Operacional Competitividade e Internacionalização e por Fundos Nacionais através da FCT – Fundação para a Ciência e a Tecnologia, I.P. (Ministério da Ciência, Tecnologia e Ensino Superior) (Ref. POCI-01–0145- FEDER-032194), no âmbito do projeto DATAGov – “Participação dos cidadãos na governança de dados de saúde: uma abordagem à proteção de dados centrada nas pessoas” (Ref. FCT PTDC/SOC- SOC/32194/2017) e da Unidade de Investigação em Epidemiologia - Instituto de Saúde Pública da Universidade do Porto (EPIUnit) (Ref. UIDB/04750/2020), Laboratório para a Investigação Integrativa e Translacional em Saúde Populacional (ITR) (LA/P/0064/2020), e dos contratos celebrados ao abrigo do Estímulo ao Emprego Científico (CEECIND/05828/2023; CEECIND/01793/2017).

ACKNOWLEDGMENTS (PT)

Com este trabalho, espero poder contribuir com conhecimento científico neste tema tão recente, mas ao mesmo tempo tão premente pelas constantes mudanças tecnológicas e desafios que se colocam à nossa sociedade, no que concerne em particular à gestão das tecnologias e dos dados em saúde e em como poderemos envolver os cidadãos nos processos de decisão. Sem dúvida, é um debate tão necessário, quanto difícil, daí ser tão desafiante e importante. Espero que este trabalho possa também contribuir para, no futuro, informar políticas públicas que se alinhem com as melhores práticas na gestão de dados em saúde, bem como para uma melhor compreensão desta questão na esfera pública e da investigação sobre o tema. Espero, ainda, que este trabalho possa contribuir para a inovação em saúde em Portugal.

Quero agradecer, acima de tudo, a todos o que estiveram comigo nesta caminhada.

Às minhas orientadoras, pela paciência, assertividade e suporte. Foi um caminho difícil, com bastantes desafios. Valeu certamente a pena esta jornada em que cultivei uma admiração por vocês e pelo vosso trabalho, pois inspiraram-me a ser uma melhor pessoa e a definir como ser uma melhor profissional no futuro.

À minha família, principalmente aos meus irmãos, que são os meus pilares. Em especial, à minha irmã Andreia, a primeira licenciada da família, a minha maior inspiração. Se não fosses tu a abrir este caminho, provavelmente eu não estaria aqui. Sou a primeira mestre da família, mas foste tu quem me abriu horizontes e acreditou que eu poderia continuar a desafiar o caminho que nos estava "predestinado". Esta conquista devo-a essencialmente a ti – é a nossa conquista. Espero ser também uma inspiração para o Pedrinho e para a Mara, a futura geração da nossa família.

Ao meu avô, que é uma força da natureza e um ser humano incrível. À minha avó, mesmo já não estando aqui para celebrar esta conquista comigo, como tanto queria. Tinhas razão, não me ias ver formada, nem com as vestes negras ou com o "canudo" na mão.

Ao meu amor maior, melhor amigo, companheiro, namorado, marido. Pedro, que estás sempre lá para apoiar as minhas conquistas e me amparar quando mais preciso. Obrigada a ti e à tua família, que sempre me apoiaram incondicionalmente.

Às minhas queridas amigas e amigos, que já são família e cuja amizade já vai em quase quatro mãos cheias. Sabem quem são.

Aos meus professores/as do básico e secundário, os que me mais me marcaram e os meus eternos mentores para a vida. Agradeço também aos meus professores/as universitários, tanto da Licenciatura, que me inspiraram e incentivaram a seguir o caminho da investigação, como aos professores/as do Mestrado em Saúde Pública, com o seu conhecimento (quase) infinito. A todos vocês, o meu obrigada. Continuem o serviço de excelência.

Ao Intituto de Saúde Pública da Universidade do Porto (ISPUP) e à Faculdade de Medicina da Universidade do Porto (FMUP), em particular na pessoa do Professor Dr. Henrique Barros e à direção do Mestrado em Saúde Pública, a todos os colaboradores, investigadores e professores, pelo ambiente acolhedor, pela excelência na produção científica, pela qualidade do ensino, pela abertura à inovação e por concederem oportunidades para aqueles cujo sonho é seguir a carreira da investigação, tal como eu.

Finalmente, aos meus queridos colegas de jornada, que estes últimos dois anos me proporcionaram vivenciar esta aventura incrível, em especial à minha querida amiga Nilza. Não há sentimento de agradecimento mais profundo por todas as boas memórias que levo deste mestrado. Todos/as vocês foram pequenas lanternas que me guiaram muitas vezes no escuro.

Agora, voemos.

A todas e todos aqui mencionados,

obrigada!

TABLE OF CONTENTS

LIST OF GRAPHS

LIST OF TABLES

LIST OF ACRONYMS

CRISPR – Clustered Regularly Interspaced Short Palindromic Repeats

DNA – Deoxyribonucleic acid

DTC – Direct-to-consumer

EC – European Commission

ESS – European Social Survey

EU – European Union

FCT – Foundation for Science and Technology

FMUP – Faculdade de Medicina da Universidade do Porto

HIC – Health Information Counsellor

IGG – Investigative Genetic Genealogy

IRDiRC – International Rare Diseases Research Consortium

ISPUP – Institute of Public Health of the University of Porto

NIH – National Institutes of Health

RCCHD – Reference Centre for Congenital Heart Diseases

RCIMD – Reference Centre for Inherited Metabolic Diseases

RDs – Rare Diseases

UHCSJ – University Hospital Centre São João

UN – United Nations

SNPs – Single-Nucleotide Polymorphisms

SPSS – Statistical Package for the Social Sciences

US – United States

RESUMO (PT)

À medida que mais aspetos da vida das pessoas são orientados através do recurso a dados, é premente garantir que as decisões sobre a partilha de dados de saúde pessoais são informadas. Tal assume especial relevância para as pessoas com doenças raras e para os seus cuidadores informais, cujos dados são mais suscetíveis a violações de privacidade e utilização inadequada, mas que, por outro lado, contribuem em grande escala para investigação biomédica, que é intensivamente informada através destes dados. Uma nova especialidade profissional poderia apoiar os doentes e os seus cuidadores informais na tomada de decisões informadas sobre a partilha de dados de saúde. Este estudo teve como objetivo avaliar como os doentes com doenças raras e os seus cuidadores informais preferem tomar decisões sobre a partilha dos seus dados de saúde para fins de investigação, incluindo a necessidade de apoio de profissionais treinados, nomeadamente *data counsellors*, e os fatores associados a esta preferência. Este estudo observacional e transversal quantitativo baseia-se num inquérito hospitalar realizado junto de 489 cuidadores informais e 162 doentes com doenças raras em dois Centros de Referência para doenças raras em Portugal, entre junho de 2019 e março de 2020. Os participantes foram convidados a selecionar um entre três modos de tomada de decisão relativamente à partilha dos seus dados de saúde para investigação: decidir sozinho, decidir com apoio ou delegar a decisão sobre a partilha de dados de saúde para investigação. A análise dos dados foi realizada através de métodos estatísticos descritivos e inferenciais. A maioria dos participantes manifestou preferência por decidir com o apoio de outras pessoas (62%). Entre estes, 60% indicaram uma preferência clara por um *data counsellor*. Aqueles com níveis mais elevados de educação, ocupações de colarinho branco superior e que estavam mais satisfeitos com a sua própria saúde preferiram mais frequentemente o apoio de um *data counsellor* para aconselhar na decisão sobre a partilha de dados de saúde ($p<0.05$). Estes resultados estão alinhados com recentes propostas que defendem a criação de uma nova especialidade médica centrada no aconselhamento de dados de saúde.

Palavras-chave: governação de dados, processos de tomada de decisão, partilha de dados de saúde, doenças raras, *data counsellors*

ABSTRACT

As more aspects of people's lives become data-driven, it is increasingly important to make well-informed decisions about whether to share one's health data and for which purposes. This is especially relevant for people with rare diseases and their informal carers, whose data are more susceptible to breaches in privacy and inappropriate use, but who may also benefit significantly from data-intensive biomedical research. A new professional specialty could support patients and carers in making informed decisions about health data sharing. This study aimed to assess how patients with rare diseases and their informal carers would like to make decisions about sharing their health data for research, including the need for support by trained professionals, namely data counsellors, and its associated factors. This observational, cross-sectional study draws on a hospital-based survey carried out with 489 informal carers and 162 rare disease patients at two Reference Centres for rare diseases in Portugal, between June 2019 and March 2020. Participants were asked to select one out of three modes of decision-making concerning the sharing of their health data for research: deciding alone, deciding with support or delegating the decision about health data sharing for research. Data analysis was conducted employing descriptive and inferential statistical methods. The majority of participants revealed a preference for deciding with the support of other people (62%). Among those, 60% indicated a preference for a data counsellor. Those with higher levels of education, upper white-collar occupations, and who were more satisfied with their own health more often preferred the support of a data counsellor to help them decide about health data sharing ($p<0.05$). The majority of participants expressed the need for support when making a decision about health data sharing for research, with more than half indicating a preference for support from a data counsellor. Our results are aligned with recent proposals advocating for the creation of a novel medical specialty centred on health data counselling.

Keywords: data governance, decision-making, health data sharing, rare diseases, data counsellors

1. INTRODUCTION

As more aspects of people's lives become data-driven, it is increasingly important to make well-informed decisions about whether to share one's health data and for which purposes (1, 2). Rare diseases (RDs), characterized by their low prevalence and high complexity, often leave patients and carers navigating a difficult path of healthcare decisions with limited resources and support (3). It is estimated that an individual has at least one connection or affiliation to someone affected by a rare disease, and due to its challenges, enhancing understanding of RDs and improving the social and healthcare support for patients and their families has posed a persistent public health challenge (4, 5).

The unique nature of RDs means that the health data of rare disease patients and their informal carers are invaluable for research, as it can offer insights that could lead to better diagnosis, faster development of medicines, and possibly tailored treatments. Given the scarcity of effective medicines and treatments, this subpopulation can benefit greatly from data-intensive biomedical research. However, this also poses relevant questions for people with rare diseases and their informal carers, since its data are more susceptible to breaches in privacy and inappropriate use. Consequently, there is a delicate balance between the potential benefits of health data sharing for research and the risks involved, often raising ethical and practical challenges, especially for vulnerable populations such as individuals with rare diseases and their informal carers (6).

Given this context, there has been a growing recognition of the need for specialised support to help individuals make well-informed decisions about sharing their health data. A new professional specialty could support patients and informal carers in making informed decisions about health data sharing. These professionals would not only be able to analyse complex information and make it intelligible for patients and research participants, but they would also have specific training and experience on advising about the benefits and risks of sharing health data for research purposes, and properly inform about all implications of their involvement. In order to guide rare disease patients and their informal carers through the complexities of health data sharing, ensuring that decisions are well informed and based on available knowledge and bearing the ethical considerations involving the process of sharing health data for research, having a specifically trained professional to advise on health data sharing meets the recent

proposals advocating for the establishment of a novel profession centred on health data counselling (7). In fact, some evidence points that individuals affected by rare diseases would like to be involved in decision-making about data sharing (8, 9), though their preferences about how best to engage in that decision-making process have not been explored.

This study aims to assess how participants would like to make decisions about sharing their health data, including the need for support by trained professionals, namely data counsellors. By understanding the preferences of rare disease patients and their informal carers, along with the factors underlying those preferences, it can inform the development of an emerging novel profession and ensure it meets the needs of those for whom this support would be greatly beneficial, such is the case for individuals with rare conditions as well as their families.

There are few empirical studies that explore individuals' preferences on what concerns the pathways of engagement in decision-making about health data sharing for research and the sociodemographic characteristics that can influence each person's preferences. It is intended that this study fills a gap in current research and contributes with new insights that can help to inform the design of new policies and approaches to sustain public participation in health research.

1.1. Rare diseases: a public health concern

The European Union (EU) considers a disease as rare when it affects less than 1 in 2 000 citizens (10). In the EU, around 36 million people live with a rare disease, and over 6 000 different rare diseases have been identified in the EU to date (10). While some RDs only affect a few patients, others can impact thousands of individuals. The National Institutes of Health (NIH), in the United States (US), have a similar but different definition considering a disease as rare if it affects less than 200 000 individuals. According to this organization, there are approximately 7 000 rare diseases affecting between 25 and 30 million North Americans, which is the equivalent to 1 in every 10 citizens (4), making rare diseases a critical public health issue. Out of the approximately 7 000 rare diseases known to date, only 5% have approved treatments (11, 12).

In Portugal, it is estimated that around 600 000 individuals are affected by a rare disease, corresponding to about 6% of the Portuguese population (13). However, prevalence data for RDs is inconsistent due to a lack of consensus on their definition and challenges in detecting and documenting them (5).

Since RDs are diseases that most providers have limited contact with within their clinical practice, they are believed to be highly under-diagnosed. Consequently, only a fraction of individuals affected by these rare conditions are aware of their specific diagnosis, making them a small minority among the larger population afflicted by the same rare disease (14, 15). A common expression that is passed along in clinical training is "when you hear hoofbeats, think about horses, not zebras", meaning that common diseases take precedence in diagnosing and rare diseases are not the first to be screened for, but rather something to consider later (16). On the other hand, patients with a rare disease have extremely frustrating experiences, going from practitioner to practitioner, from proposed diagnosis to proposed diagnosis, a litany of tests, clinical examinations, and treatments, often without any immediate benefits while they are on what is commonly termed as a *diagnostic odyssey*, since the process of diagnosing a rare disease can take months or even years, substantial financial burdens, emotional distress, and frustration (17). Patients with rare diseases often experience prolonged waiting periods when seeking a diagnosis, primarily due to the scarcity of such conditions, as the low prevalence of those diseases offers practitioners few opportunities to consider them, as well as less means or experience to draw upon collective experiential knowledge (18).

Some of the most common problems RDs patients and their informal carers face are delays in diagnosis, limited access to necessary medical treatments, difficulties financing therapy-driven biomedical and clinical research and insufficient training among health professionals to identify these diseases (19). Recent research affirms the persistence of these issues, with special emphasis on deferred diagnosis and inadequate availability of suitable treatments (5). In fact, one of the goals established by the International Rare Diseases Research Consortium (IRDiRC) for the period of 2017-2027 is to ensure timely confirmation of diagnoses within one year or less (20). The IRDiRC aims to establish a system within the coming decade that ensures patients with a suspected rare disease with a known molecular basis receive a diagnosis within one year of their initial consultation with a health professional (20).

It has been argued that overcoming challenges that undermine the identification of rare disease cases and the development of effective therapies and treatments require investment in raising awareness among the public and healthcare professionals, streamlining referrals within the healthcare system, and significantly improve the systems that facilitate health data sharing and diagnostic expertise among clinicians and researchers globally (20). Also, there are new technologies that can facilitate earlier diagnosis, holding the potential for substantial benefits, not only for the patient, but also for the healthcare system as a whole, by enabling faster initiation of treatment where available, thereby mitigating costs while optimising resources allocation (13).

The social weight of rare diseases reaches beyond patients, affecting also their families and others close to them, especially when they suffer from more serious, disabling, or difficult-to-control diseases (13). In 2021, the General Assembly of the United Nations (UN) adopted the first Resolution on the challenges of living with a rare disease, which encourages member states to strengthen health systems, namely primary healthcare, and to facilitate universal access to safe, quality, and clinically timely health services that help empower people living with a rare disease, promoting a more inclusive society. Its aim is to encourage member states to adopt strategies that can contribute to the well-being of people living with a rare disease, as well as their families (15). The European Commission (EC) has also assumed strategic objectives for rare diseases to improve patients' access to diagnosis, information, and care, and to help distribute resources across the EU, allowing patients and professionals to share knowledge and information. In this context, member states have been encouraged to promote the development of national plans and strategies for rare diseases that directly respond to the needs of patients and carers, to ensure that inequalities are not exacerbated by the country of residence, improve health outcomes, and facilitate access to innovation across the EU (21).

In Portugal, rare diseases have also been recognised as a challenge for different sectors of society, including the sectors of Health, Education, Science and Technology, Work, and the Social Sector, which must offer specific responses to the rare diseases' population who often lives in situations of greater vulnerability. Furthermore, following EC guidelines, it is assumed that early diagnosis and the follow-up of patients, especially in the most complex situations, is more effective when provided in highly specialised centres, which bring together multidisciplinary teams with high clinical, scientific, and

technological competence, allowing patients to benefit from innovative treatments and knowledge resulting from research. Reference Centres were therefore set up for the monitoring and treatment of rare diseases in the Portuguese National Health System. Reference Centres are health services, departments or units recognised as the highest exponent of competence in providing quality health care in clinical situations that require highly differentiated technical and technological resources for the management of rare diseases (7). Directive 2011/24/EU, issued on 9th March, concerning patients' rights in cross-border healthcare, has led to the official identification and recognition of highly specialised hospital services as Reference Centres by the Ministry of Health. In Portugal, these Reference Centres are governed by Ordinance No. 194/2014, dated 30th September in its updated form (7).

The Directorate-General for Health developed an Integrated Strategy for Rare Diseases 2015-2020, which is attached to Dispatch number 2129-B/2015, 27th of February, based on intersectoral and interinstitutional cooperation, that aims to bring together the contributions, skills, and resources of all relevant sectors, in order to promote a real change in the complex conditions of people affected by a rare disease. This cooperation intends to make a strong contribution improving access and quality of health care, as well as treatment conditions, based on the evidence brought from the latest research, and diversifying social responses (13). To ensure quality and safe follow-up of people with rare diseases in any health service, the Directorate-General for Health has also implemented a Card for People with Rare Diseases (Norm number 001/2018 of 09/01/2018) (13). Finally, to ensure the protection of patients with special needs or deep incapacities, a special disability social protection measure, called invalidity pension, was designed to protect the individuals in a situation of permanent incapacity for work with a prognosis of rapid evolution to a situation of loss of autonomy and negative impact professionally and throughout the life course (13).

In 2022, The Decree-Law n.º 32/2022 of May 9th determined the formation of the Intersectoral Working Group for Rare Diseases, with the objective of preparing a proposal for the upcoming National Intersectoral Plan for Rare Diseases in Portugal (22). These actions evidence a commitment towards addressing the needs of people affected by rare diseases and its understanding as a public health issue.

1.2. Benefits and risks of health data sharing for research

Approximately two decades ago, the Human Genome Project completed the identification and sequencing of all 3 billion nucleotides that make up the human genetic map (23). Following this massive accomplishment, researchers held high hopes that the genome information would provide valuable insights into numerous diseases, including rare diseases. However, it was soon discovered that aside from the genetic sequence itself, there is an additional layer of molecular information – epigenetic modifications, which are established during the developmental process and that can influence individuals' disease susceptibility (24). These variations in each single nucleotide, the basic building blocks of deoxyribonucleic acid (DNA), can be found in several locations among the entire genome, referred to as single-nucleotide polymorphisms (SNPs) (25). Since the sequencing of the human genome was completed, the research community has dedicated substantial efforts to investigating epigenetic modifications and their potential associations with various diseases, particularly with rare genetic disorders (26).

These new discoveries have paved the way for the development of new genetic therapies that can lead to important breakthroughs in biomedical sciences and clinical practice, as they are often the closest to or the only possible cure for an array of rare diseases (27). For example, a recent innovative gene therapy named Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) has been used in the US to treat sickle cell disease with success. This kind of gene editing therapies raise hope for other types of rare diseases (28). Further development and adaptation of those therapies to more rare diseases require research powered by large bulks of data including not just genomic data, but also biometric data, lifestyle information and environment exposures (29). It is imperative thus to effectively identify and engage the individuals who can derive benefits from them (30).

Rare disease patients and their family members are usually highly willing to share their data for research (6). Nevertheless, their willingness to share data appears to be subject to the presence of several data governance elements, namely: data security, assurance of privacy, the presence of consent procedures enabling participants to express preferences about data access, use and reuse and transparent provision of information about data management practices including sharing data with third parties (9, 31, 32). The need to ensure the presence of these elements is justified by concerns with database breaches, loss

of privacy and abuse of information that can lead to the discrimination of people affected by rare diseases by insurance companies or employers (27, 32). Participants also expressed fears of having to relinquish data control and ownership when their data is shared with private companies (31). These concerns may be outweighed by participants' perceived benefits of genomic research directly targeting their conditions. A recent study found that rare disease patients and their informal carers (mostly family members) selected the discovery of a cure for untreatable diseases and the development of new drugs and treatments for their diseases as the most relevant benefits deriving from sharing genomic data for research (27).

Technological advances have also contributed to the refinement of techniques and medical examinations, reducing prices and increasing access to previously inaccessible advanced technologies such as genome sequencing services that provide data for a broad range of applications (33, 34). However, because of the low prices and therefore easy access, direct-to-consumer genetic testing has proliferated as a business in countries such as the US, where regulations are less strict than in Europe and elsewhere (35).

Direct-to-consumer (DTC) genetic companies offer their customers genetic genealogical profiles that are made based on the analysis of their DNA. The genomic information collected by these companies also carries value for medical research and forensic investigations, since SNPs based profiles encompass a diverse range of individual information, including potential disease risks, physical characteristics, and ancestral origins. DTC genetic tests can be purchased by the general public from companies such as Ancestry.com, GEDmatch or FamilyTreeDNA for the purposes of knowing better their ancestry or find distant relatives (36). The accessibility and utilization of this information depend on the individuals or entities who have access to use the data stored by DTC genetic testing companies' databases, that should be restricted to companies themselves, since they are not permitted to share the data with commercial third parties without customers permission (36). However, in the past few years, Investigative Genetic Genealogy (IGG) has been a key component in more than 200 law enforcement investigations in the US, where the federal police can request DTC genetic testing companies to provide open access to their DNA databases, as has occurred with GEDmatch (36).

Critical ethical questions arise from the use of data from DTC genetic testing companies' databases for criminal investigation. These include inadvertent exposure of sensitive information to unwarranted parties, which undermines individuals' privacy or the disclosure of incidental findings (e.g. susceptibility for life-threatening disease) to customers without the support of certified genetic counsellors (37). The preservation of privacy emerges as a significant concern, particularly considering the prevailing notion that individuals generally seek to disclose minimal personal information and exercise control over the recipients of such information (38). In addition, individual privacy violation caused by the improper use or exploitation of private data poses risks to both individuals and communities, as they become subject to the influence of external entities, be that public institutions or private corporations, and as a consequence, individuals may experience limitations on their capacity to make autonomous decisions free from coercion (39, 40).

Apprehensions may also emerge regarding law enforcement authorities accessing a database that individuals had willingly contributed to without considering its access, use and reuse for other purposes (37). Pressure to obtain access to such data can be exerted also by private health insurance companies and large corporations (41). This can be especially detrimental for people affected by rare diseases, but it can also expose members of the general public to unforeseen problems, for example by sharing with them incidental or secondary findings that can potentially impact their future, such as learning about genetic predisposition for late-onset genetic diseases (42). Furthermore, they could also face the repercussions of data breaches or undisclosed surveillance, which may result in the loss of privacy and even discrimination in various domains. For instance, the disclosure of personal, social, or health characteristics deemed unfavourable by employers or health insurance companies, such as a chronic disease diagnosis, can lead to adverse consequences for individuals in the workplace or health insurance premiums (43, 44).

1.3. Decision-making about health data sharing for research

Understanding the risks and benefits involved in the sharing of genomic and health data is crucial for individuals to be both aware of their rights to data privacy, data control and

self-determination, and to be more alert, informed and empowered to enforce them. However, the consequences of health data sharing are complex and not always easy to assess or to predict by lay people, especially when sharing data for research that can yield a return of results with impact on people's future, as is sometimes the case with genomic research (e.g. results showing higher susceptibility for a late-onset genetic disease) (45, 46). This gives rise to substantial concerns regarding the necessity to obtain informed consent from individuals for participation in research that is truly informed, meaningful and free (9, 47). It also points out the need to assess potential participants' preferences and needs regarding decision-making about sharing health data for research.

Making a decision about health data sharing entails deciding which types of data one is willing to share, with whom and for which purposes. These individual-level decisions are usually enabled through different types of informed consent procedures (48). In some cases, people who have shared their data may be re-contacted to decide whether that information can be accessed by other entities, such as pharmaceutical companies, shared with other researchers, or used for previously unforeseen purposes (49).

Recent studies on public attitudes about data sharing and trust in research institutions have stressed the need for more transparency and accountability on the part of those institutions regarding the access, use, and reuse of health data previously shared for research purposes with other parties (50). It has also been argued that there should be greater efforts to provide information in an accessible way so as to empower research participants, due to the current low levels of understanding about existing practices and uses of data (51, 52).

In light of the growing value of health data, and its potential uses and consequences for the people sharing it, research participants can be expected to express different preferences when it comes to decide about data sharing. While some individuals may prefer to decide on their own, others may express a preference to doing so with the support of other people, and still others may prefer to delegate the decision to another party. Among those who prefer to decide with support of other people, this support may be provided by participants' informal networks of friends and family, or it may be delivered by researchers or health professionals. Recently, it has been proposed the creation of a new profession within medicine consisting of professionals trained to assist in the decision-making process regarding health data sharing (7).

Typically, individual control over the uses of health data information in healthcare and clinical research is not direct, but instead patients and research participants often consent to particular terms of disclosure. These terms might be explicitly outlined in informed consent forms or understood within the framework of confidentiality norms that regulate the interactions between patients and healthcare providers (49). In the following sections, literature on public views about decision-making concerned with health data sharing is discussed and the proposal for a new professional specialty on this domain is presented.

1.3.1. Public views on decision-making about health data sharing for research

Given that researchers and practitioners may lack experience with specific diseases or health services they seek to investigate, the involvement of public representatives becomes crucial. These individuals can offer valuable perspectives from a first-hand experience of a particular disease, treatment, or healthcare service (53). By sharing their views, insights and experience, the involvement of public representatives contributes to making health science research more attuned to the requirements and priorities of patients, carers, and service users, while also contributing to increase democratic input into decision-making (9). Assessing potential research participants' views about their preferred ways to decide whether to share their health data for research, as well as barriers to and facilitators of decision-making, is thus a valuable source of information to tailor consent procedures to their needs and increase the sustainability of research. Continuous engagement of rare disease patients and informal carers in research is essential for biomedical researchers to develop more precise treatments that can address the needs and challenges those conditions represent. Engaging in biomedical research is critical for enhancing comprehension of the biological and molecular processes underlying rare pathophysiological mechanisms, evaluating the effectiveness of novel medications, interventions, and devices, and advancing the field of personalised medicine (54, 55).

Moreover, quality health data from rare disease patients can not only inform biomedicine for better and more accurate treatments but can also serve the entire healthcare ecosystem with better comprehension of some rare diseases that other people, in other countries, might be on a diagnostic odyssey for (8). According to recent studies conducted in several European countries, the rare disease patients and carers community values its

involvement in individual-level health data governance processes, with many perceiving engagement in decision-making about health data sharing, access, use and reuse as a very important matter (6, 9, 27, 32, 56, 57).

A recent study about genomic data sharing revealed that, despite participants' privacy concerns, they were significantly more likely to prioritise contributing to research when required to make a choice about health data sharing, notwithstanding their privacy concerns about public genetic data access (58, 59). In another study about research participants' perspectives about DNA data sharing, results show that the absence of explicit details regarding data sharing within the informed consent forms resulted in participants' showing a range of comprehension levels and an assortment of presumptions about data sharing. Despite being subjected to the same informed consent procedures, the research participants did not exhibit a consistent comprehension concerning the entities who could access their genetic data. Numerous participants conveyed their involvement in the genetic study out of altruistic intentions, expressing eagerness to contribute their DNA data for scientific advancement. Almost all individuals engaged in focus group discussions were of the opinion that insurance companies and employers should be barred from accessing the data due to concerns of potential bias or discriminatory practices. In what concerns the aspects of wanting information about and control over the decision-making process, the majority of participants expressed that it was "very important" or "extremely important" for them to be notified about the potential scenario in which their genetic data might be disclosed to external parties (60).

In another study focusing on the impact of three distinct forms of consent regarding data release on participation in research and choices related to genomic data sharing decisions, it was found that several factors are associated with decisions about data sharing, including ethnicity (i.e. white Hispanic individuals were notably less inclined to opt for public genomic data sharing when compared to non-Hispanic white participants), marital status (i.e. unmarried participants, encompassing those who were divorced, widowed, separated, or never married, exhibited a higher tendency to select restricted genomic data sharing) and education (i.e. participants with some college education or a college degree displayed a greater likelihood of opting for restricted genomic data sharing) (61).

Two other studies showed that individuals are willing to share identifiable personal health data across various research endeavours when they have confidence in the researchers

and trust in the institutions involved. This willingness is often tied to participants receiving adequate information about the research they are contributing to, and a significant portion of individuals are more amenable to personal data sharing when they anticipate tangible benefits arising from the research, whether for their own well-being, societal advancement, or both (62, 63). In these studies, associations with sociodemographic characteristics are not further explored.

1.3.2. Data counsellors as a new medical specialty in the era of digital health

As arguments mount on the benefits of sharing health data for research purposes, it is also true that the process of transforming data into relevant information that can be used to support clinical practice, as well as determining the health data that does not serve to this purpose, demands considerable time, resources, and expertise. Some authors have argued for the need to train a new type of professional to advise both patients and healthcare professionals on how to best collect and use health data in the era of Big Data and data-driven medicine (7). This novel profession would be created as a new medical specialty: Health Information Counsellors (HICs). HICs would be trained to acquire a strong knowledge base in health data quality assessment techniques and interpretation, to be expertise in statistics, as well as interpersonal communication, health management, private and public healthcare systems, and medico-legal aspects of data privacy (7, 64). As a framework for the protection of public interests in this regard is still lacking, and challenges grow faster and ever more complex to all stakeholders involved, HICs could be a solution for supporting lay people and professionals into steering through this data jungle, giving a meaningful contribution to how increasing health data and information should inform health care (7).

A HIC program would be especially appropriate for individuals with educational backgrounds in health-related fields or the natural sciences, as well as for healthcare practitioners such as physicians, who aim to enhance their expertise in data science and health information counselling within their career advancement endeavours (7). Proficiency in clinical medicine would enable them to provide insights into the implication of various health data types for research purposes such as disease prevention, diagnosis and treatment (7). With further training and gradual practice exposure, HICs

would develop expertise in specific fields, as each HIC would possess the ability to identify situations that require specialised knowledge and would refer to specialists when faced with matters outside their own area of expertise (7). Considering the medical or health sciences background, the HIC would support patients and carers in comprehending their medical situation through evidence-based research, evaluating the suitability and pertinence of participation in a clinical trial, and deliberating between conservative and experimental treatment avenues (7). The insights gained from these consultations could be shared with the patient physician, who might also consult the HIC and through collaborative efforts, a strategic approach could be formulated. Establishing and integrating this innovative field of expertise would empower patients to make well-informed, genuinely independent decisions regarding the incorporation of these emerging healthcare data modalities into their individual health care choices (7).

This group of professionals would be different from, but complementary to, another group of professionals who also provide counselling in the area of (genetic) rare diseases, known as Genetic Counsellors. Genetic Counsellors provide counselling on genetic health conditions, tailored to the needs of patients, providing them with the necessary genomic-related information to facilitate their decision-making process and freely make their own choices, as well as support them in their choices (e.g. whether to share their diagnosis with family members; or to resort to Assisted Reproductive Medicine). These professionals contribute with their knowledge and skills to the improvement of the medical genetic services based in hospitals and clinics, promoting health education, as well as the training of other professionals and research in genetic counselling (65, 66).

The scarceness of approved treatments, let alone cures, for approximately 95% of the estimated 7 000 rare diseases recognised by the scientific community serves as a primary motivation for the participation of rare disease patients and their informal carers in research endeavours (67). Consequently, engagement has emerged as an indispensable element in nearly all initiatives related to rare diseases, driven by their strong inclination to actively participate. Present genomic research policy advocates are pressuring for the public release of data, accompanied by explicit consent for health data sharing. However, clinical researchers do not typically anticipate the use of data for purposes different from the ones it is being collected for, so details about health data access and reuse by third parties are rarely addressed within the informed consent procedures. Consequently, there

is an immediate requirement for standardised wording that can be adaptable to the needs and preferences of research participants (47). A one-size-fits-all approach to health data sharing will not serve the multiple challenges posed by the ever-fast emergence of new technologies and the pressure to access health data to better inform future biomedicine is growing. Given the numerous prospects presented by data-driven health care, HICs would bring advantages due to their capacity to elucidate data jargon into understandable and practical insights for both patients, informal carers and practitioners (7, 68).

There are many grounds and arguments for enhancing public engagement in individual-level health data governance. The literature reviewed shows that the majority of people would prefer to be involved in decision-making about data processing, rather than not be involved at all (9). Existing empirical studies have primarily focused on the levels of willingness of the general public to disclose their data (59, 69-71), the methods employed to provide comprehensive informed consent that facilitates health data sharing (60, 61, 72, 73), and the degree to which patients would share their personal health data for research purposes (74-77). HICs or data counsellors, as we refer to them hereafter, are expected to effectively translate jargon related to distinct types of data into significant knowledge for patients and healthcare practitioners (7), but also to provide counsel to anyone in need of making a decision about whether they wish to share their data about the potential impacts of doing so at various levels.

2. OBJECTIVES

The main objective of this dissertation is to contribute empirical evidence on public views about individual-level data governance processes, namely how people affected by rare diseases and their informal carers prefer to engage in decisions about sharing health data for research purposes. The specific objectives are:

1. To assess the preferences of rare disease patients and their informal carers regarding decision-making about health data sharing for research, including the need for support, and its associated factors;

2. To evaluate participants' preferred sources of support for decision-making about health data sharing for research, and its associated factors, including support by data counsellors.

3. METHODS

3.1. Study design

This is an observational cross-sectional study that draws on a hospital-based survey with rare disease patients and their informal carers. The survey was carried out at the University Hospital Centre São João (UHCSJ), and it is part of a larger project entitled "DATAGov – Public and patient involvement in health data governance: a people-centred approach to data protection and sharing in genetic diseases", whose protocol is described elsewhere (78).

3.2. Participants and procedures

Participants were recruited at two Reference Centres for rare diseases, namely the Reference Centre for Congenital Heart Diseases (RCCHD) and the Reference Centre for Inherited Metabolic Diseases (RCIMD) at UHCSJ, in Porto, Portugal. Between June 2019 and March 2020, attendants of medical consultations at the RCCHD and RCIMD that fulfilled the inclusion criteria were consecutively invited to participate in the study. Patients aged ≥12 years and informal carers, who could read and write Portuguese, and had no cognitive impairment met the inclusion criteria. Potential participants were handed a leaflet by a healthcare professional containing study information (Appendix 1) after their consultation. A member of the research team addressed them subsequently and made the invitation for participation, clarifying any arising questions about the study. Those who decided to participate in the study were then accompanied to a private setting where the researcher described the study aims and asked them to read and sign the informed consent (Appendix 2). Participants under 12 years of age were eligible to participate after they gave verbal consent, and their legal representative signed the informed consent form. All participants were asked to respond to a self-administered questionnaire.

From the 728 patients and carers invited, 651 accepted to participate, including 489 informal carers and 162 patients (response rate: 89.4%). The analyses included in this study refer to 638 participants (479 informal carers and 159 patients) with data available

on the outcome variables regarding to the preferences about decision-making about health data sharing.

3.3. Data collection

A self-report structured questionnaire was developed by the research team based on a literature review and other existing tools focusing on public and patient involvement in health data governance. Subsequently, the questionnaire was pretested by specialists in the fields of social and health sciences and then piloted with rare disease patients and informal carers. The final version of the questionnaire (Appendix 3) entailed questions about: a) positioning about health data access, sharing, use and reuse; b) opinions about public and patient involvement in health data governance; and c) sociodemographic characteristics, such as sex, age, educational level, country of origin, marital status, occupation, perceived income adequacy. Data on satisfaction with own health, involvement in patient organisations and social trust was also collected.

This study addresses specific questions regarding the topic of health data sharing. More specifically, it assesses participants' preferred modes for decision-making about health data sharing based on the analysis of answers to the following question: "If you had to decide about sharing your health data for research purposes, would you like to (please choose only one option): 1) Decide by myself; 2) Decide with the help of another person(s); 3) Delegate the decision to another person(s)". Those participants who opted for making a decision with the help of another person(s) or for delegating the decision to another person(s) were further asked to respond to the following question: "Which person(s)?" by selecting between four options: 1) Family or friends; 2) A professional specifically trained to provide health data counselling; 3) A professional not specifically trained to provide health data counselling; 4) Other. In this question, participants could select more than one response option. The response option "professional specifically trained to provide health data counselling" was used as a proxy to describe "data counsellors".

Occupations were classified according to the Portuguese Classification of Occupations (79) and grouped into four categories: 1) upper white-collar, including corporate leaders

and managers from the industry sector, high-ranking government officials, experts in their respective fields, scientists, supervisors, and technical specialists; 2) lower white-collar, including employees engaged in administrative tasks and related functions, as well as service and sales workers; 3) blue-collar, including farmers and skilled agricultural workers, fisheries sector workers, skilled workers, craftsmen or similar, machine operators, assembly workers, and unskilled workers; and 4) other, including students or participants who were unemployed, devoted to housework, pensioners or in a paid/unpaid leave, retired, and informal carers.

Social trust was measured using ten questions based on the European Social Survey (ESS) and divided in three main components: trust in national institutions, trust in international institutions and interpersonal trust. Trust in institutions was assessed through a ten-point Likert scale ranging from 0 ("No trust at all") to 10 ("Complete trust"). Participants would have to rate national institutions, such as the Parliament, Legal System, Police, Politicians and Political Parties from 0 to 10 points of confidence. To measure trust in international institutions, participants would have to rate the European Parliament and the United Nations from 0 to 10 points. To assess interpersonal trust, participants would have to rate from 0 to 10 the following statements: "Generally speaking, would you say that most people can be trusted or that you can't be too careful in dealing with people?", in which 0 corresponded to "You can't be too careful" and 10 corresponded to "Most people can be trusted"; "Do you think that most people would try to take advantage of you if they got the chance, or would they try to be fair?", in which 0 corresponded to "Most people try to take advantage of me" and 10 corresponded to "Most people try to be fair"; and finally "Would you say that most of the time people are mostly looking out for themselves or that they try to be helpful?", in which 0 corresponded to "People mostly look out for themselves" and 10 corresponded to "People mostly try to be helpful". There were also two options participants could choose if they did not want to rate a specific institution ("Refusal") or if they did not recognise it ("Do not know").

3.4. Data analysis

Participants' characteristics are presented as counts and proportions for categorical variables such as sex, age, educational level, country of origin, marital status, occupation,

perceived income adequacy, satisfaction with own health, involvement in patient organisations and preferred modes for decision-making about health data sharing. Social trust is presented as a non-normally distributed continuous variable, and it is described as median within interquartile ranges (P25–P75). The Chi-Square test or the Fisher's Exact test were used to assess the associations between the explanatory variables and the main outcomes (decide alone, decide with support of others or delegate the decision about health data sharing for research), as well as the Mann-Whitney U test, for the variables of trust in national and international institutions and interpersonal trust, for a statistical significance set at a value of $p < 0.05$.

The odds ratios (ORs) and respective 95% confidence intervals (CI) were calculated by logistic regression models to estimate the association between explanatory variables and the outcome. Logistic regression models were computed to estimate the ORs and corresponding 95% CI for the association between the sociodemographic characteristics, that were considered *a priori* potential determinants, and the preferred modes for decision-making about health data sharing. A significance level of 0.05 was considered. Analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS), version 27.0 (IBM Corp., Armonk, NY, USA).

3.5. Ethical considerations

This study is part of a larger project entitled DATAGov that received ethical approval from the Ethics Committee for Health from the University Hospital Centre São João and Faculty of Medicine of University of Porto (Ref. 99/19).

All necessary procedures were ensured to uphold that the study complied with ethical standards. All participants were provided with an information leaflet in hand, in which the details of the study were explained. Additionally, all questions regarding the study and the participation in the research were clarified with each participant. At the time of recruitment, it was again explained with detail what was intended with the participation of each individual in the research project, the objectives and data confidentiality was reinforced. Furthermore, it was assured that individuals would be able to withdraw the

research project at any time without this entailing any kind of consequence for the individual itself nor its family.

After clarifying all questions, participants who accepted to take part in the questionnaire were given a consent form and asked to sign two copies. Participants underage gave verbal consent for participation and the consent form was signed by their legal caretakers. Patients who were unable to give consent due to impairment or other reasons were not included in the study.

All research data collected was pseudo-anonymised. Questionnaires do not disclose the identification of participants and identifying information is only available to the research team.

4. RESULTS

4.1. Characteristics of the study participants

The characterisation of the study participants is detailed in *Table 1*. From a total of 638 individuals, 24.9% were patients with a rare disease and 75.1% were informal carers of a person with a rare disease. Overall, most participants were female (70.8%), had more than 30 years of age (69.5%), attained 12 years or less of education (75.6%), were originally from Portugal (94.7%), were satisfied with their own health (72.7%) and were not involved in patient organisations (94.8%). Generally, participants presented lower levels of trust in national institutions (Median [P25–P75] 3.4 [1.8–5.2]), when compared to trust in international institutions (Median [P25–P75] 5.0 [2.0–7.0]) and interpersonal trust (Median [P25–P75] 4.7 [3.0–6.7]).

When comparing informal carers and patients, the formers were more often female (78.7% vs. 47.2%, $p<0.001$), older than 30 years old (87.6% vs. 15.7%, $p<0.001$), with lower levels of education (≤ 12 years: 68.9 vs. 95.6, $p<0.001$), and were married or living with a partner (78.0% vs. 10.1%, $p<0.001$). The majority of carers were employed (74,4%), while most patients had other occupations (e.g. studying) (86.1%). More than half of the carers perceived their income as insufficient (56.5%), contrasting with 63.9% of the patients, who considered it enough to make ends meet or comfortable ($p<0.001$). More than half of the carers and patients were satisfied or very satisfied with their own health (76.2 vs. 62.3, $p=0.003$) and were not involved in patient organisations (93.7 vs. 98.1), $p=0.037$) Patients presented higher levels of trust in international institutions (Median [P25–P75]: 6.5 [3.0–8.0] vs. 5.0 [2.0–7.0], $p<0.001$) than carers (Table 1).

Table 1. ***Participants' characterisation, stratified by patients and carers***

		Total (n=638) n (%)	Patients (n=159) (24.9%)	Carers (n=479) (75.1%)	*p*
Sex, n (%)	Female	452 (70.8)	75 (47.2)	377 (78.7)	**< 0.001**
	Male	186 (29.2)	84 (52.8)	102 (21.3)	
Age (years), n (%)	<18	92 (14.5)	92 (57.9)	0 (-)	**< 0.001**
	18-30	101 (16.0)	42 (26.4)	59 (12.4)	
	>30	440 (69.5)	25 (15.7)	415 (87.6)	
Educational level (years), n (%)	≤12	479 (75.6)	151 (95.6)	328 (68.9)	**< 0.001**
	>12	155 (24.4)	7 (4.4)	148 (31.1)	
Country of origin[a], n (%)	Portugal	602 (94.7)	154 (96.9)	448 (93.9)	0.220
	Other	34 (5.3)	5 (3.1)	29 (6.1)	
Marital status[b], n (%)	Married or living with partner	388 (61.1)	16 (10.1)	372 (78.0)	**< 0.001**
	Other	247 (38.9)	142 (89.9)	105 (22.0)	
Occupation[c], n (%)	Upper white-collar	149 (24.6)	5 (3.2)	144 (32.2)	**< 0.001**
	Lower white-collar	115 (19.0)	8 (5.1)	107 (23.9)	
	Blue-collar	91 (15.0)	9 (5.7)	82 (18.3)	
	Other	250 (41.3)	136 (86.1)	114 (25.5)	
Perceived income adequacy, n (%)	Insufficient/Caution with expenses	320 (51.8)	52 (36.1)	268 (56.5)	**< 0.001**
	Enough to make ends meet/Comfortable	298 (48.2)	92 (63.9)	206 (43.5)	
Satisfaction with own health, n (%)	Very unsatisfied/ Unsatisfied	50 (7.8)	16 (10.1)	34 (7.1)	**0.003**
	Not satisfied or unsatisfied	124 (19.5)	44 (27.7)	80 (16.7)	
	Satisfied/Very satisfied	463 (72.7)	99 (62.3)	364 (76.2)	
Involvement in patient organizations, n (%)	No	601 (94.8)	154 (98.1)	447 (93.7)	**0.037**
	Yes	33 (5.2)	3 (1.9)	30 (6.3)	
Trust in national institutions, Md (P25-P75)*		3.4 (1.8–5.2)	4.4 (2.0–6.0)	3.4 (1.8–5.0)	0.060
Trust in international institutions, Md (P25-P75)*		5.0 (2.0–7.0)	6.5 (3.0–8.0)	5.0 (2.0–7.0)	**< 0.001**
Interpersonal trust, Md (P25-P75)*		4.7 (3.0–6.7)	4.7 (2.7–6.7)	4.7 (3.0–6.4)	0.756

In each variable, the total may not add 638 participants, 159 patients or 479 carers due to missing values. The proportions may not add 100 due to rounding.

[a] Other includes participants which the country of origin was Brazil (n=9), France (n=7), Angola (n=4), Venezuela (n=3), Germany (n=2), Cape Green (n=2), Mozambique (n=2), South Africa (n=1), Switzerland (n=1), São Tomé e Príncipe (n=1), England (n=1) and one did not specify the country of origin.

[b] Other includes participants who were single (n=201), widow/widower (n=5), divorced (n=38) or separated (n=4).

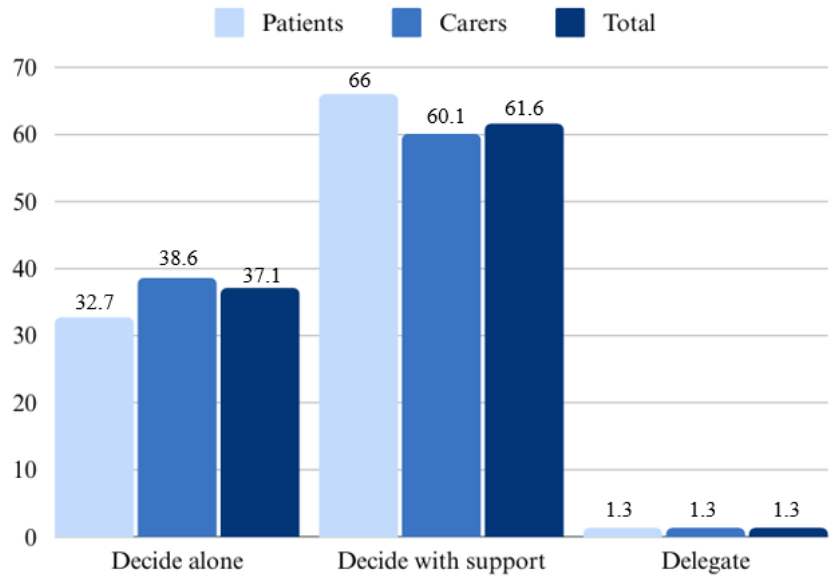
[c] Other includes students (n=122), unemployed (n=78), retired (n=11), houseworkers (n=26), informal carers (n=5), temporary leave (n=5), medical leave (n=1), disability leave (n=2), pensioners (n=3), freelancer (n=1), self-employed (n=1), and scholar (n=1).

*Md (P25-P75) represents the Median and the respective quartiles, meaning that 25% of the data falls below the first quartile and that 75% of the data falls below the third quartile.

4.2. Preferred modes of decision-making about health data sharing for research

Participants' preferences concerning decision-making about health data sharing for research according to patients' and carers' responses are presented in *Graph 1*. 61.6% of the participants preferred to decide with support, while 37.1% preferred to decide alone and 1.3% of participants preferred to delegate the decision about health data sharing for research to another person. No statistically significant differences were found between patients and carers concerning preferences for deciding alone, deciding with support of others, or delegating the decision to share health data for research (p=0.406).

Graph 1. ***Preferred modes of decision-making about health data sharing for research, according to patients and carers***



As the proportion of participants who prefer to delegate their decision about health data sharing for research is residual, further analyses were conducted considering only participants who preferred to decide alone or to decide with support. Participants' characteristics of those who chose these two response options are detailed in *Table 2*.

There were no significant differences between carers and patients when choosing to make a decision alone or with support (p=0.185). Participants with 12 or less years of education more often preferred to decide with support of others when deciding about health data sharing (79.7% vs. 68.4%), while participants with more than 12 years of education more often preferred to decide alone (31.6% vs. 20.3%). Furthermore, participants with upper-white collar occupations more frequently preferred to decide alone (32.4% vs. 20.3%), while participants with blue-collar occupations were more likely to prefer to decide with the support of others (17.6% vs 11.1%). Participants that perceived their income as insufficient/need to be cautious with expenses more frequently preferred to decide with support of others rather than to decide alone (55.2% vs. 45.9%, p=0.030). Participants that were satisfied or very satisfied with their own health were more likely to prefer to decide alone (76.8% vs. 70.4%, p=0.020).

Table 2. ***Preferences for making decisions alone or with support when sharing health data for research, according to participants' characteristics***

		Total (N=630)	Decide alone (n=237) (37.6%)	Decide with support (n=393) (62.4%)	*p*
Type of participant	Patient	157 (24.9)	52 (21.9)	105 (26.7)	0.185
	Carer	473 (75.1)	185 (78.1)	288 (73.3)	
Sex, n (%)	Female	447 (71.0)	170 (71.7)	277 (70.5)	0.786
	Male	183 (29.0)	67 (28.3)	116 (29.5)	
Age (years), n (%)	<18	91 (14.6)	24 (10.2)	67 (17.2)	0.051
	18-30	100 (16.0)	41 (17.4)	59 (15.2)	
	>30	434 (69.4)	171 (72.5)	263 (67.6)	
Educational level (years), n (%)	≤12	472 (75.4)	162 (68.4)	310 (79.7)	**0.002**
	>12	154 (24.6)	75 (31.6)	79 (20.3)	
Country of origin[a], n (%)	Portugal	595 (94.7)	223 (94.1)	372 (95.1)	0.584
	Other	33 (5.3)	14 (5.9)	19 (4.9)	
Marital status[b], n (%)	Married or living with partner	383 (61.1)	149 (62.9)	234 (60.0)	0.500
	Other	244 (38.9)	88 (37.1)	156 (40.0)	
Occupation[c], n (%)	Upper white-collar	149 (24.9)	73 (32.4)	76 (20.3)	**0.002**
	Lower white-collar	113 (18.9)	46 (20.4)	67 (17.9)	
	Blue-collar	91 (15.2)	25 (11.1)	66 (17.6)	
	Other	246 (41.1)	81 (36.0)	165 (44.1)	
Perceived income adequacy, n (%)	Insufficient/Caution with expenses	315 (51.6)	107 (45.9)	208 (55.2)	**0.030**
	Enough to make ends meet/Comfortable	295 (48.4)	126 (54.1)	169 (44.8)	
Satisfaction with own health, n (%)	Very unsatisfied/ Unsatisfied	49 (7.8)	22 (9.3)	27 (6.9)	**0.020**
	Not satisfied or unsatisfied	122 (19.4)	33 (13.9)	89 (22.7)	
	Satisfied/Very satisfied	458 (72.8)	182 (76.8)	276 (70.4)	
Involvement in patient organizations, n (%)	No	593 (94.7)	225 (95.3)	368 (94.4)	0.713
	Yes	33 (5.3)	11 (4.7)	22 (5.6)	
Trust in national institutions, Md (P25-P75)*		3.4 (1.8–5.2)	3.8 (1.6–5.6)	3.2 (2.0–5.0)	0.495
Trust in international institutions, Md (P25-P75)*		5.0 (2.0–7.0)	5.0 (2.5–7.5)	5.0 (2.0–7.0)	0.072
Interpersonal trust, Md (P25-P75)*		4.7 (3.0–6.7)	4.7 (2.9–6.7)	4.7 (3.0–6.3)	0.393

In each variable, the total may not add 630 participants due to missing values. The proportions may not add 100% due to rounding.

[a] Other includes participants which the country of origin was Brazil (n=9), France (n=7), Angola (n=4), Venezuela (n=3), Germany (n=2), Cape Green (n=2), Mozambique (n=2), South Africa (n=1), Switzerland (n=1), São Tomé e Príncipe (n=1), England (n=1) and one did not specify the country of origin.

[b] Other includes participants who were single (n=201), widow/widower (n=5), divorced (n=38) or separated (n=4).

[c] Other includes students (n=122), unemployed (n=78), retired (n=11), houseworkers (n=26), informal carers (n=5), temporary leave (n=5), medical leave (n=1), disability leave (n=2), pensioners (n=3), freelancer (n=1), self-employed (n=1), and scholar (n=1).*Md (P25-P75) represents the Median and the respective quartiles, meaning that 25% of the data falls below the first quartile and that 75% of the data falls below the third quartile.

The factors associated with participants' preferences for deciding about health data sharing for research with support are described in *Table 3*. A logistic regression with a variable that contains de groups of people who preferred to decide alone and those who preferred to decide with support was conducted taking "deciding with support" as a binary outcome (dependent variable) and "deciding alone" as the reference category to assess its association with the participants' sociodemographic characteristics (independent variables). The variables "sex" and "age" were added to the model for theoretical reasons, since their inclusion helps to improve the model accuracy and generalisability of the results by controlling for potential confounders. "Educational level" and "occupation" were both significant as determinants, however, they presented collinearity in the model. The decision to only include "occupation" to the model was made based on the assumption that the type of occupation held may determine access to a larger or smaller range of social networks and resources (i.e. social capital). The final multivariate model included only variables that remained significant ($p<0.05$). The variables included in the model were then "sex", "age", "occupation", "perceived income adequacy" and "satisfaction with own health".

Participants with 18-30 years showed lower odds of deciding with support than of deciding alone (OR (95% CI): 0.49 (0.25–0.97)), while participants with blue-collar occupations were more likely to prefer support in the decision-making process (OR (95% CI): 2.20 (1.22–3.97)). Those with a better perceived income were less likely to prefer the support of others to decide about health data sharing (OR (95% CI): 0.70 (0.48–1.00)). Although the association with satisfaction with health was not statistically significant, a strong tendency for participants who were not satisfied or unsatisfied with their own health to more frequently prefer support for decision-making about health data sharing for research was nevertheless observed (OR (95% CI): 2.02 (0.97–4.22)).

Table 3. ***Factors associated with the preference for deciding with support about health data sharing for research***

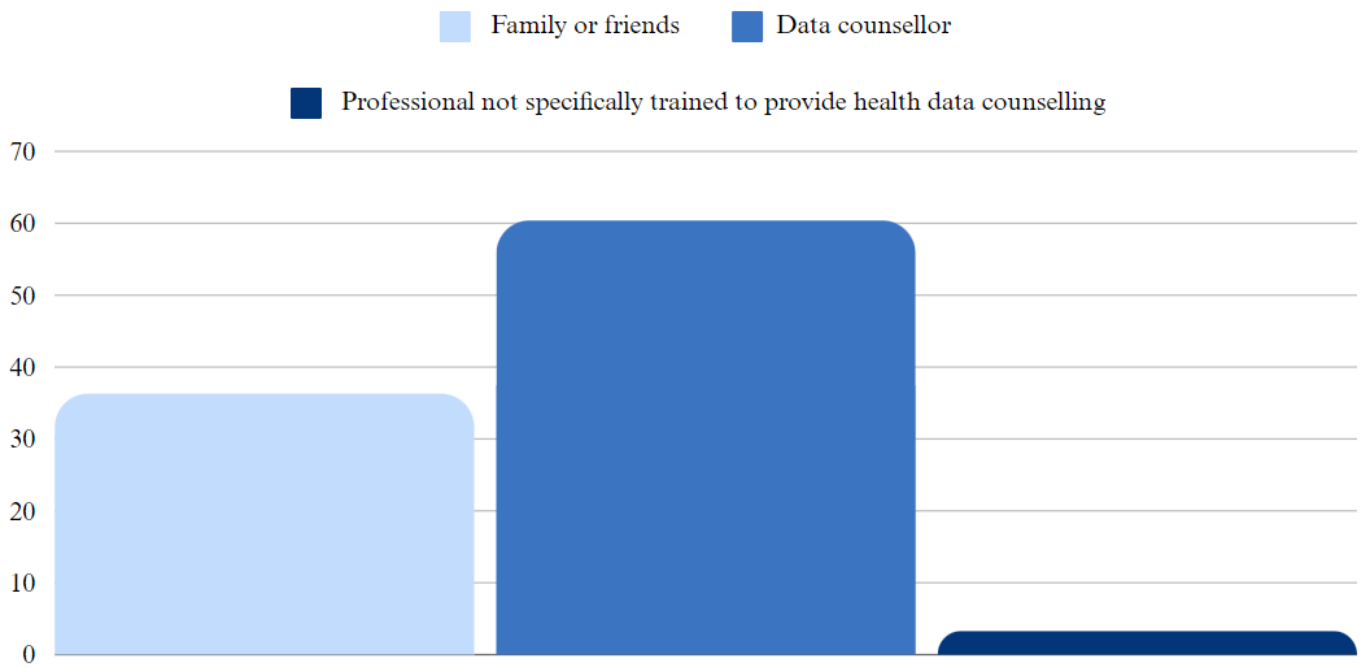
		Decide with support **Adjusted* OR** (95% CI)**
Sex	Female	1.00 (REF)
	Male	1.04 (0.70–1.54)
Age (years)	<18	1.00 (REF)
	18-30	**0.49** (0.25–0.97)
	>30	0.60 (0.31–1.15)
Occupation	Upper white-collar	1.00 (REF)
	Lower white-collar	1.24 (0.74–2.07)
	Blue-collar	**2.20** (1.22–3.97)
	Other	1.55 (0.94–2.55)
Perceived income adequacy	Insufficient/Caution with expenses	1.00 (REF)
	Enough to make ends meet/Comfortable	**0.70** (0.48–1.00)
Satisfaction with own health	Very unsatisfied/ Unsatisfied	1.00 (REF)
	Not satisfied or unsatisfied	2.02 (0.97–4.22)
	Satisfied/Very satisfied	1.36 (0.71–2.58)

*Adjusted OR represents the odds ratio that controls for other predictor (independent) variables in this model (*Sex*, *Age*, *Occupation*, *Perceived income adequacy* and *Satisfaction with own health*).
**95% confidence interval.

4.3. Preferred sources of support for decision-making about health data sharing for research

The preferred sources of support for decision-making about health data sharing for research selected by participants who opted to decide with support (n=391) are shown in *Graph 2*. The majority of participants (60.4%) preferred to decide with support of a data counsellor, while 36.3% chose to decide with the help of family or friends. A much smaller proportion of participants expressed a preference for deciding with the support of a professional who was not specifically trained to provide health data counselling (3.3%).

Graph 2. Preferred sources of support for decision-making about health data sharing for research



To analyse the sociodemographic characteristics associated with the preference for choosing a data counsellor to support decision-making, the responses indicating a preference to decide with the support of "family or friends" and to decide with the support of a "professional not specifically trained to provide health data counselling" were re-categorised as a single variable, hereinafter referred to as "Other". The results are presented in *Table 4*.

There were significant differences between patients and carers regarding their preferred source of support ($p<0.001$). Carers preferred the support of a data counsellor to decide about health data sharing more frequently than patients (carers: 68.5% vs. patients: 38.1%, $p<0.001$;). In addition, older participants and participants with higher levels of education and who were married or living with a partner were also significantly more likely to prefer to decide about health data sharing with support of a data counsellor (>30 years: 70.1% vs. <18 years: 37.3%, p<0.001; >12 years of education: 74.4% vs. ≤12 years of education: 57.0%, $p=0.006$; married or living with partner: 66.8% vs. other: 51.3%, $p=0.003$). A similar trend was also observed among participants with upper white-collar occupations (75.7%, $p<0.001$), followed by participants with other occupation classes.

Table 4. ***Preferences for data counsellors as a source of support for decision-making about health data sharing, according to participants' characteristics (n=391)***

		Total (n=391) n (%)	Data Counsellor (n=236)	Other** (n=155)	*p*
Type of participant	Patient	105 (26.9)	40 (38.1)	65 (61.9)	**< 0.001**
	Carer	286 (73.1)	196 (68.5)	90 (31.5)	
Sex, n (%)	Female	276 (70.6)	175 (63.4)	101 (36.6)	0.069
	Male	115 (29.4)	61 (53.0)	54 (47.0)	
Age (years), n (%)	<18	67 (17.3)	25 (37.3)	42 (62.7)	**< 0.001**
	18-30	59 (15.2)	26 (44.1)	33 (55.9)	
	>30	261 (67.4)	183 (70.1)	78 (29.9)	
Educational level (years), n (%)	≤12	309 (79.8)	176 (57.0)	133 (43.0)	**0.006**
	>12	78 (20.2)	58 (74.4)	20 (25.6)	
Country of origin, n (%)	Portugal	370 (95.1)	220 (59.5)	150 (40.5)	0.099
	Other	19 (4.9)	15 (78.9)	4 (21.1)	
Marital status, n (%)	Married or living with partner	232 (59.8)	155 (66.8)	77 (33.2)	**0.003**
	Other	156 (40.2)	80 (51.3)	76 (48.7)	
Occupation, n (%)	Upper white-collar	74 (19.9)	56 (75.7)	18 (24.3)	**< 0.001**
	Lower white-collar	67 (18.0)	45 (67.2)	22 (32.8)	
	Blue-collar	66 (17.7)	41 (62.1)	25 (37.9)	
	Other	165 (44.4)	82 (49.7)	83 (50.3)	
Perceived income adequacy, n (%)	Insufficient/Caution with expenses	208 (55.5)	133 (63.9)	75 (36.1)	0.241
	Enough to make ends meet/Comfortable	167 (44.5)	96 (57.5)	71 (42.5)	
Satisfaction with own health, n (%)	Very unsatisfied/ Unsatisfied	26 (6.7)	15 (57.7)	11 (42.3)	0.059
	Not satisfied or unsatisfied	88 (22.6)	44 (50.0)	44 (50.0)	
	Satisfied/Very satisfied	276 (70.8)	177 (64.1)	99 (35.9)	
Involvement in patient organizations, n (%)	No	367 (94.6)	219 (59.7)	148 (40.3)	0.065
	Yes	21 (5.4)	17 (81.0)	4 (19.0)	
Trust in national institutions, Md (P25-P75)*		3.8 (1.6–5.6)	3.8 (2.0–5.1)	3.2 (1.8–4.8)	0.117
Trust in international institutions, Md (P25-P75)*		5.0 (2.5–7.5)	5.0 (2.4–7.0)	4.5 (2.0–6.5)	0.103
Interpersonal trust, Md (P25-P75)*		4.7 (3.0–6.7)	4.5 (3.3–6.7)	5.0 (2.7–6.3)	0.671

In each variable, the total may not add 391 participants due to missing values. The proportions may not add 100 due to rounding.

*Md (P25-P75) represents the Median and the respective quartiles, meaning that 25% of the data falls below the first quartile and that 75% of the data falls below the third quartile.

** Other includes "Family and friends" and "Professional not specifically trained to advise on health data sharing for research" as preferred sources of support for decision-making about health data sharing.

The descriptive analysis suggests distinct choices from patients and informal carers regarding the preferred source of support for decision-making about health data sharing for research, suggesting that, at least on a first phase, further inferential analysis should be conducted separately for these two groups. However, given the sample size, both groups would not be robust enough to conduct a logistic regression. Additionally, even to compute a single multivariate model, the data does not exhibit sufficient variability or separation among the groups, leading to concerns about the model fit and potential overfitting. Assuming these issues, to proceed with a logistic regression would likely result in an unreliable model with poor predictive power.

5. DISCUSSION

This study explores public views about individual-level data governance processes by inquiring into the preferences of rare disease patients and their informal carers regarding decision-making about sharing health data for research purposes. One of its main findings is that the majority of participants prefer to make decisions about sharing health data for research with the support of other people (62%). Another important finding is that most of the participants who prefer to decide with support would rather receive the support of professionals specifically trained to provide health data counselling, i.e. data counsellors (60%). At present, there is a scarcity of empirical studies exploring these preferences and assessing the sociodemographic factors associated with data donors' preferred modes of decision-making concerning health data sharing. The present study contributes relevant empirical evidence to start closing this gap.

This study shows that participants with blue-collar jobs were significantly more likely to opt for decision-making about health data sharing with support from third parties, while those aged 18-30 and who perceived their incomes to be comfortable or sufficient to make ends meet showed a significantly lower tendency to prefer support. People engaging in blue-collar work are more prone to have lower levels of education, and potentially less access to the resources needed to make informed decisions about health data sharing (e.g. information, time, health and digital literacy). This may lead them to feel more confident to make decisions with the support of others. Moreover, people with blue-collar jobs may experience less work and financial security and thus be less prepared to invest time and energy in seeking information about the implications of sharing health data or even perceiving that as an additional burden (80). Previous studies have highlighted how low levels of public understanding about health data sharing and use for research purposes (51, 52, 81) may contribute to reduce willingness to share health data, particularly when that data is intended to be used by multiple researchers or organisations (82). This is in line with a previous study that showed that participants with lower levels of education place less importance on being involved in decision-making about health data sharing, potentially because they are not sufficiently equipped to assess the risks and benefits that may derive from its use (27).

Our results also point to a strong preference for the support of data counsellors (60%). This preference underscores the importance of tailored support mechanisms that address the unique needs and challenges faced by people affected by rare diseases and their informal carers. Furthermore, it also supports recent proposals in the literature suggesting the creation of a new professional specialty dedicated to assisting potential data donors in decision-making processes regarding the sharing, access, use and reuse of health data for research and clinical purposes (7). The significantly lower preference for support from family or friends (36%), or untrained professionals (3%) suggests that participants highly value expert guidance.

Carers (69%) and older participants (>30 years: 70 %) who were married or living with a partner (66%) were significantly more inclined to seek support from data counsellors than patients and younger individuals. This tendency may result from the accumulated experience associated with care responsibilities and age, which can influence the perception of the need for professional guidance in complex decision-making processes (5) that may have a significant bearing in advancing translational research and care for their family members. However, it also points to the need to approach young people with rare diseases and inquire into their specific needs and preferences regarding individual-level decision-making about health data sharing. Although rare disease diagnostics are improving, many patients have faced long diagnostic odysseys (18, 20) and late interventions, and in some cases the absence of therapies, which often result in low life expectancies. As a result, the community of rare disease patients tends to be young, as observed also in our sample. Thus, further qualitative research is needed to understand whether young peoples' preference for sources of support other than data counsellors (i.e. friends and family) is due to personal reasons or less ability to foresee the type of support that can be provided by those professionals. In addition, participants with higher levels of education (>12 years: 74.4%) and qualified occupations (upper white-collar: 75.7%; lower white-collar: 67.2%) were also significantly more likely to prefer support from data counsellors. These results suggest that educational level and socioeconomic position play a role in shaping preferences for decision-making support, with participants from more socially advantaged groups potentially showing greater awareness and ability to participate in complex debates about health data (12). A previous study conducted with this same group of rare disease participants found that those participants with higher levels of education were more likely to value involvement in decision-making about the

purposes for which their health data can be used (9). By providing personalised guidance and addressing arising concerns (e.g. about data security and privacy), data counsellors can serve as key intermediaries in navigating the intricate landscape of data sharing by facilitating the information data donors need to consent to health data sharing fully informed of its potential uses and implications. This is likely to strengthen data donors' sense of agency and autonomy, while at the same time promoting transparency and trust in research initiatives (15, 16). Furthermore, it may increase willingness to participate in individual-level health data governance, which has been associated with trust in research institutions (9).

As noted earlier, this study shows that younger participants and those with lower levels of education are less likely to set a preference for the support of a data counsellor. Ensuring equitable access to expert support across diverse socioeconomic backgrounds is a critical challenge. Shall this new profession be created in the future, it will be crucial to produce educational materials that illuminate on their competences, roles and responsibilities, preferably in co-design with patients and their carers (81). This will be essential to prevent inequalities and to balance the potential benefits of data sharing with the need to capacitate data donors to make informed decisions that can protect the sensitivity of health information while enabling its use for the common good (9). Involving stakeholders in health data policy development and promoting transparency in data processing practices are also crucial steps to build a robust framework that respects individual rights while advancing research objectives (52, 82). Recent studies in several EU countries show that the rare disease patients' community values involvement in health data governance both at an individual-level (i.e. in decision-making processes regarding health data sharing, access, use, reuse) and at a collective level (6, 8, 9, 39, 56, 57, 83). It is important to acknowledge these aspirations and to encourage the creation of participatory initiatives and spaces linked to data processing organisations that can supplement the efforts made by the rare disease patients' organisations. Consulting beforehand with representatives of the rare diseases community, including young people, about their preferences for and expectations of distinct types of participatory initiatives (e.g. one-off exercises vs. continual participatory spaces), as well as about social and ethical aspects such as providing potential participants with the resources needed for meaningful and long-term participation, is essential to promote inclusive participation

and to strengthen institutional commitment towards public involvement in health data governance (80, 84, 85).

Finally, approximately a third of the participants preferred to decide alone whether to share their health data for research (37%). Among these, participants with white-collar jobs were significantly more likely to select this option. Perhaps this can be explained by people with qualified occupations typically having more access to social capital, which can afford both broader networks and the resources needed to inform decisions, since access to health services has been suggested as a key mechanism through which social capital exerts its influence on health outcomes (86, 87). Thus, even if these participants are not in the hold of all the information required to make an informed decision, they may experience greater ease in obtaining it through their networks, and thus feel they can decide autonomously. However, it is important to note that our study also shows that participants with white-collar jobs were also significantly more likely to choose the support of data counsellor when preferring to decide about data sharing with support of a third party. While seemingly contradictory, this finding may be explained by this sub-group of participants being more aware of the risks associated with health data sharing and the need to seek expert advice. For example, a recent study carried out among this same group of participants found that informal carers with higher levels of education were more likely to identify the possibility of extraction of information that goes beyond the research objectives for which it was shared (e.g. misappropriation and use by insurance companies to match premiums to the expected expenses deriving from complex rare diseases) as a significant risk associated with genomic data sharing (27). When perceiving a gap within their networks to seek out answers to these concerns, these participants may be more straightforward in acknowledging the advantages of benefiting from the advice of trained professionals, namely a data counsellor.

Strengths and Limitations

A primary strength of this study lies in its exploration of public views about data counselling, which remains an understudied topic. This study provides valuable insights that point to the complexities involved in making decisions about health data sharing, and the factors associated with them, and that can inform policy by addressing a significant

gap in health data policy implementation. This study thus presents relevant empirical evidence and lays the groundwork for developing tailored interventions that can enhance patient-centred care and optimise the decision-making process in the context of health data sharing for research. Furthermore, this exploratory study also presents objective and systematic observations that can be reliable sources of information for further studies on this matter, contributing with valuable insights to a field that is still unheeded.

However, this study has some limitations that need to be acknowledged. Participants were recruited in one reference academic hospital centre that receives patients from the Northern Health Region of Portugal and therefore does not represent the general population of rare disease patients and informal carers in Portugal, which can limit the generalisability of the findings. Furthermore, recruitment was carried out in the academic hospital where participants are cared for. Despite full assurance that the decision not to participate in our study would not amount to any negative repercussions, the setting may have influenced research participation. Undertaking a similar study in non-academic hospitals and in private organisations across the country would likely offer a fruitful ground for comparison.

The cross-sectional design of the study captures preferences at a single point in time, which may not consider changes in attitudes over time or as a result of evolving data governance practices. Furthermore, a small sample size reduces the statistical power to detect significant associations and may limit the generalisability of the findings. Additionally, the lack of variability within the sample may have constrained the ability to identify meaningful relationships between variables, indicating a need for further quantitative research. Finally, conducting a qualitative study could offer relevant insights into participants' motivations and expectations regarding health data sharing decision-making and, in particular, about their preferences of support by a data counsellor.

6. CONCLUSION

This study offers valuable insights into patient and public participation in individual-level data governance within the context of rare diseases. When asked to make a decision about health data sharing most of the rare disease patients and informal carers surveyed in our study expressed a clear need for support, with the majority indicating a data counsellor as their preferred source of support. The results of this study can contribute to address both research and data policy implementation gaps, since our results provide backing for the proposals advocating the establishment of a novel profession centred on health data counselling. This also represents a proposal aligned with the values of innovation and cross-sector collaboration promoted by central governing bodies that act as catalysts for innovation and the integration of care within a patient-centred approach in Portugal. As a potentially new professional specialty, data counsellors hold the potential to help sustain public participation in health research, fostering improved practices within healthcare, and facilitating the expansion of research opportunities.

Further research is needed to better understand the relationship between the preferred modes of decision-making and its associated factors, as well as to assess the unravelling implications of the establishment of data counsellors within the Portuguese National Health System, and in other countries.

APPENDICES

Appendix 1: Information leaflet for participants.

Informação sobre o estudo

Estamos a desenvolver um estudo sobre as opiniões de doentes, cuidadores informais, profissionais de saúde, gestores, técnicos e pessoal administrativo quanto aos benefícios e riscos associados à partilha de informação de saúde e à participação dos cidadãos na sua governação, no âmbito das doenças raras.

Gostaríamos de contar com a sua participação.

Antes de decidir, é importante que saiba mais acerca deste estudo e do que lhe é pedido se aceitar participar.

Por favor, leia atentamente este folheto informativo e coloque todas as perguntas que achar necessário.

Por que queremos falar consigo?

A finalidade deste estudo é perceber de que forma as necessidades, preferências e valores das pessoas com doenças raras, cuidadores informais, profissionais de saúde, gestores, técnicos e pessoal administrativo podem ser incluídas na governação de informação de saúde.

Quando falamos de informação de saúde estamos a referir-nos a todo o tipo de informação direta ou indiretamente ligada à saúde de uma pessoa e à sua história clínica e familiar (por exemplo, registos clínicos, resultados de análises e outros exames complementares, intervenções e diagnósticos).

Serão convidadas a participar pessoas com mais de 12 anos de idade seguidas nos centros de referência para as Doenças Hereditárias do Metabolismo e de Cardiopatias Congénitas do Centro Hospitalar Universitário de São João (CHUSJ), e seus cuidadores informais, assim como profissionais de saúde, gestores, técnicos e pessoal administrativo da equipa alargada.

Em que consiste a sua participação?

Gostaríamos que respondesse a um questionário num local reservado nas instalações do CHUSJ, com uma duração prevista de 20 minutos. Estamos disponíveis para esclarecer todas as dúvidas e questões que possam surgir.

Quais serão os benefícios da sua participação?

Será participante de um estudo inovador que procura compreender os benefícios e os riscos associados ao envolvimento dos cidadãos na governação de informação de saúde, contribuindo para:
- Identificar os desafios inerentes à partilha de informação no âmbito das doenças raras e seus benefícios;
- Incentivar o debate em torno das respostas aos desafios que enfrenta a proteção de informação de saúde;
- Adaptar a governação de informação de saúde às necessidades, preferências e valores de todas as pessoas envolvidas.

A informação é confidencial?

Sim, nos termos exigidos pela lei. Toda a informação que partilhar connosco será vista somente pelos membros da equipa de investigação.
A informação será armazenada de forma segura. Sempre que as informações recolhidas forem utilizadas, nunca será usado o seu verdadeiro nome.

Sou obrigado/a a participar?

Não. Caso decida não participar, esta decisão não terá quaisquer desvantagens nem influenciará os cuidados de saúde. Mesmo depois de aceitar, poderá desistir em qualquer altura e sem justificação.

Quem coordena o estudo?

A coordenação é da responsabilidade do Instituto de Saúde Pública da Universidade do Porto (ISPUP), sendo a investigadora principal Cláudia de Freitas.

Este estudo é financiado pela **Fundação para a Ciência e a Tecnologia.**

Como será usada a informação?

Os resultados deste estudo serão divulgados de diversas formas (relatórios, artigos científicos e comunicações orais), junto da comunidade científica e de pessoas que podem tomar decisões em relação às políticas que regulam a proteção de dados de saúde.

Obrigado por ter lido este folheto!

A sua participação será muito valiosa.

A aplicação do questionário apenas prosseguirá depois de colocadas todas as questões pelo participante e após assinatura do consentimento informado.

Ser-lhe-á dado este folheto informativo e uma cópia do consentimento informado.

Para qualquer dúvida, sugestão ou comentário, por favor entre em contacto connosco:

Investigadoras:

Cláudia de Freitas | Susana Silva

Instituto de Saúde Pública
Universidade do Porto
Rua das Taipas, 135
4050-600 Porto
Tlf: 222 061 820 | 912 371 276
E-mail: datagov2018@gmail.com

Este trabalho é financiado pela Fundação para a Ciência e a Tecnologia (FCT/OE) (POCI-01-0145-FEDER-032194) e pelo Programa Operacional Competitividade e Internacionalização promovido pelos Fundos Europeus de Desenvolvimento Regional (FEDER/FNR), no âmbito do projeto DATAGov (AAC nº 02/SAICT/2017 - projeto nº 032194) e da Unidade de Investigação em Epidemiologia - Instituto de Saúde Pública. da Universidade do Porto (EPIUnit) (POCI-01-0145-FEDER-006862; Ref. UID/DTP/04750/2013).

ISPUP
INSTITUTO DE SAÚDE PÚBLICA DA UNIVERSIDADE DO PORTO

FOLHETO DE INFORMAÇÃO AO PARTICIPANTE

Participação dos cidadãos na governação de informação de saúde: partilha e proteção de dados em doenças raras

Appendix 2: Informed consent survey for participants.

CONSENTIMENTO INFORMADO, ESCLARECIDO E LIVRE

PARA INVESTIGAÇÃO CLÍNICA

Considerando a "Declaração de Helsinquia" da Associação Médica Mundial (Helsinquia 1964, Tóquio 1975, Veneza 1983, Hong Kong 1989, Somerset West 1996, Edimburgo 2000, Seoul 2008, Fortaleza 2013)

SÃO JOÃO

Designação do Estudo *(em português)*

Participação dos cidadãos na governação de informação de saúde: partilha e proteção de dados em doenças raras (DATAGov)

Confirmo que expliquei ao participante/representante legal, de forma adequada e compreensível, a investigação referida, os benefícios, os riscos e possíveis complicações associadas à sua realização.

Informação escrita em anexo: ☐ Não ☒ Sim (Nº de páginas 2)

O Investigador responsável

Nome: Cláudia Susana Soares de Freitas _____
legível

_____
assinatura

Identificação do participante

Nome: _____

BI/ CC nº: _____

Participante/ Representante legal

· Compreendi a explicação que me foi facultada acerca do estudo que se tenciona realizar: os objetivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto.

· Solicitei todas as informações de que necessitei, sabendo que o esclarecimento é fundamental para uma boa decisão.

· Fui informado da possibilidade de livremente recusar ou abandonar a todo o tempo a participação no estudo, sem que isso possa ter como efeito qualquer prejuízo na assistência que é prestada.

· Declaro não ter sido incluído em nenhum outro projeto de investigação nos últimos três meses.

Concordo com a participação neste estudo, de acordo com os esclarecimentos que me foram prestados, como consta neste documento, do qual me foi entregue uma cópia.

Data: ___ / ___ / ___ _____
assinatura

Nome *(Pais/Representante legal)*: _____

BI/ CC nº: _____ Grau de parentesco: _____

Data: ___ / ___ / ___ _____
assinatura

△ Nº4 CES-IM014.0

Appendix 3: Self-report structured questionnaire applied to participants.

ID ☐☐☐☐☐

QUESTIONÁRIO

Governação de informação de saúde

Este estudo pretende conhecer as opiniões de doentes, cuidadores informais e profissionais ligados à saúde quanto à participação dos cidadãos na governação de informação de saúde, no âmbito de doenças raras. A governação de informação de saúde refere-se às políticas, procedimentos e práticas relacionadas com a recolha, proteção, partilha e uso de informações de saúde.

Não há respostas certas nem erradas. Interessa-nos conhecer a sua opinião sincera. Agradecemos a sua colaboração e o tempo que irá disponibilizar para responder a este questionário.

Data de preenchimento: |__|__|/|__|__|/|__|__|__|__|
(dia) (mês) (ano)

1. **É portador de alguma doença rara?**
   - Não ☐0
   - Sim ☐1 Qual? _____

2. **É cuidador informal de uma pessoa com uma doença rara?**
   - Não ☐0
   - Sim ☐1 Qual a doença da pessoa de quem cuida? _____

3. **Neste momento, está a preencher este questionário na qualidade de:** (por favor assinale apenas uma opção de resposta)
   - Doente ☐1
   - Cuidador Informal ☐2
   - Profissional de saúde ☐3 Categoria profissional: _____
   - Outra ☐4 Qual? _____

4. O Regulamento Geral sobre a Proteção de Dados (RGPD) da União Europeia entrou em vigor a 25 de Maio de 2018. **Como se sente em relação à informação que tem acerca desse Regulamento?**

- Nada informado ☐0 (por favor passe para a pergunta 6)
- Pouco informado ☐1
- Mais ou menos informado ☐2
- Informado ☐3
- Muito informado ☐4

5. **Indique, por favor, quais foram as <u>duas principais fontes</u> onde obteve informação acerca do Regulamento Geral sobre a Proteção de Dados?**

- Televisão ☐1
- Jornais ☐2
- Rádio ☐3
- Internet ☐4
- Profissionais de saúde ☐5
- Associação de doentes ☐6
- Familiares, amigos ou colegas ☐7
- Outra
  Qual?_____ ☐8

Predisposição para partilhar informação, com quem e com que finalidades

6. Há diversas informações de saúde que podem ser usadas em investigação científica. **Em que medida estaria disponível para <u>partilhar</u> as seguintes informações para fins de investigação:**

	Não disponível				Sempre disponível
- Dados pessoais (ex. nível de escolaridade, idade)	☐0	☐1	☐2	☐3	☐4
- História clínica individual	☐0	☐1	☐2	☐3	☐4
- História clínica familiar	☐0	☐1	☐2	☐3	☐4
- Amostras biológicas (ex. sangue, urina)	☐0	☐1	☐2	☐3	☐4
- Informação genética (ex. ADN)	☐0	☐1	☐2	☐3	☐4

6.1. É importante para nós compreender melhor a sua resposta. **Explique-nos, por favor, a sua posição.**

_____

_____

_____

7. **Para si, em que medida é importante poder decidir sobre a <u>partilha</u> das suas informações de saúde para fins de investigação?**

- Nada importante ☐0
- Pouco importante ☐1
- Mais ou menos importante ☐2
- Importante ☐3
- Muito importante ☐4

8. A investigação científica pode ser realizada por diversas instituições. **Em que medida estaria disponível para partilhar as suas informações de saúde com as seguintes <u>instituições</u>:**

	Não disponível				Sempre disponível
- Instituições de saúde onde recebo cuidados	☐0	☐1	☐2	☐3	☐4
- Universidades portuguesas	☐0	☐1	☐2	☐3	☐4
- Universidades fora de Portugal	☐0	☐1	☐2	☐3	☐4
- Empresas comerciais portuguesas (ex. farmacêuticas, seguradoras)	☐0	☐1	☐2	☐3	☐4
- Empresas comerciais fora de Portugal (ex. farmacêuticas)	☐0	☐1	☐2	☐3	☐4
- Associações de doentes portuguesas	☐0	☐1	☐2	☐3	☐4
- Associações de doentes internacionais	☐0	☐1	☐2	☐3	☐4

9. **Para si, em que medida é importante poder decidir <u>com quem</u> as suas informações de saúde são partilhadas?**
   - **-** Nada importante ☐0
   - Pouco importante ☐1
   - Mais ou menos importante ☐2
   - Importante ☐3
   - Muito importante ☐4

10. **Em que medida estaria disponível para partilhar as suas informações de saúde para as seguintes <u>finalidades</u>?**

	Não disponível				Sempre disponível
- Investigação sem fins lucrativos	☐0	☐1	☐2	☐3	☐4
- Investigação com fins lucrativos	☐0	☐1	☐2	☐3	☐4
- Bases de dados nacionais	☐0	☐1	☐2	☐3	☐4
- Bases de dados internacionais	☐0	☐1	☐2	☐3	☐4
- Uso de companhias de seguros	☐0	☐1	☐2	☐3	☐4
- Uso de empresas farmacêuticas	☐0	☐1	☐2	☐3	☐4

11. **Para si, em que medida é importante poder decidir as <u>finalidades</u> para as quais as suas informações de saúde são partilhadas?**
   - **-** Nada importante ☐0
   - Pouco importante ☐1
   - Mais ou menos importante ☐2
   - Importante ☐3
   - Muito importante ☐4

12. Suponha que autorizou o uso das suas informações de saúde em projetos de investigação. **Se as suas informações forem utilizadas para esse fim, gostaria de <u>ser notificado/a</u> sobre isso?**
   - Sim, sempre ☐1
   - Sim, uma vez por mês ☐2
   - Sim, uma vez por ano ☐3
   - Não ☐4

13. Existem alguns aspetos que as pessoas podem considerar importantes para decidir se vão partilhar as suas informações de saúde para investigação. **Se tivesse que tomar essa decisão, qual o grau de importância que atribuiria aos seguintes <u>aspetos</u>:**

	Nada importante				Muito importante
- Conhecer os objetivos da investigação	☐0	☐1	☐2	☐3	☐4
- Garantir a privacidade das minhas informações	☐0	☐1	☐2	☐3	☐4
- Garantir a segurança das minhas informações	☐0	☐1	☐2	☐3	☐4
- Confiar na organização que acolhe a investigação	☐0	☐1	☐2	☐3	☐4
- Confiar na equipa que vai realizar a investigação	☐0	☐1	☐2	☐3	☐4
- Poder retirar o consentimento a qualquer momento	☐0	☐1	☐2	☐3	☐4
- Ter acesso aos resultados após a conclusão do estudo	☐0	☐1	☐2	☐3	☐4

14. As informações de saúde recolhidas para tratamento médico ou para fins de investigação podem ser reutilizadas para outras finalidades (por exemplo, avaliação da qualidade e planeamento de serviços ou políticas). **Para si, em que medida é importante poder decidir se as suas informações de saúde podem ser <u>reutilizadas</u> para finalidades diferentes daquela para a qual foram recolhidas inicialmente?**

- Nada importante ☐0
- Pouco importante ☐1
- Mais ou menos importante ☐2
- Importante ☐3
- Muito importante ☐4

Posições sobre consentimento

15. A partilha de informações de saúde para investigação só pode ocorrer mediante consentimento prévio dos seus titulares. **Por favor indique qual a modalidade de <u>consentimento</u> que prefere relativamente à partilha de informação genética e não genética:**

15.1. Um **<u>consentimento geral</u>** (dado uma única vez para qualquer projeto de investigação) ou um **<u>consentimento específico</u>** (dado para cada projeto de investigação específico).

	Consentimento geral	Consentimento específico
- Informação genética (ex. ADN)	☐1 (p.f. passe para a pergunta 16)	☐2
- Informação não genética (ex. dados pessoais)	☐1 (p.f. passe para a pergunta 16)	☐2

15.2. Um consentimento específico para **<u>todas as dimensões</u>** do projeto de investigação ou um consentimento específico para **<u>cada uma das dimensões</u>** do projeto de investigação (por exemplo, uso e proteção de dados).

	Todas as dimensões	Cada uma das dimensões
- Informação genética (ex. ADN)	☐1	☐2
- Informação não genética (ex. dados pessoais)	☐1	☐2

16. **Indique os <u>dois riscos</u> mais importantes que, na sua opinião, podem associar-se à partilha de informação genética para fins de investigação.**

- Falta de segurança e controlo no acesso à informação ☐1
- Restrição dos direitos à privacidade e autonomia dos cidadãos ☐2
- Possibilidade de retirar informação que ultrapasse os objetivos de investigação ☐3
- Realização de estudos genéticos que possam discriminar negativamente os cidadãos ☐4
- Outro. Qual? _____ ☐5

17. **Indique os <u>dois benefícios</u> mais importantes que, na sua opinião, podem associar-se à partilha de informação genética para fins de investigação.**
- Descoberta de uma cura para doenças sem tratamento ☐1
- Desenvolvimento de estratégias para controlar a propagação de doenças ☐2
- Desenvolvimento de novos medicamentos e terapêuticas ☐3
- Desenvolvimento de tratamentos personalizados, tendo em conta as características de cada doente ☐4
- Outro. Qual? _____ ☐5

18. **Se precisasse de tomar uma <u>decisão</u> quanto à partilha das suas informações de saúde para fins de investigação, gostaria de:** (p.f. assinale <u>apenas uma</u> opção de resposta)
- Decidir sozinho/a ☐1 (p.f. passe para a pergunta 19)
- Decidir com o apoio de outra/s pessoa/s ☐2
- Delegar a decisão noutra/s pessoa/s ☐3

18.1. **Que pessoa/s?**
- Em familiares ou amigos ☐1
- Num/a profissional especificamente formado/a para prestar aconselhamento sobre informações de saúde ☐2
- Num/a profissional de saúde não especificamente formado/a para prestar aconselhamento sobre informações de saúde ☐3
- Outro. Qual? _____ ☐4

Opiniões sobre participação

Existem diversas formas pelas quais os cidadãos podem participar na governação de informação de saúde, por exemplo, através da presença em reuniões nas quais se planeiam procedimentos para a recolha, proteção, partilha e uso de informações de saúde, em colaboração com responsáveis pela gestão de informação e outros cidadãos.

19. **Se tivesse todas as condições para participar na governação de informação de saúde no âmbito de um hospital público, estaria disponível para <u>participar</u> em**:

	Sim	Talvez	Não
- Reuniões periódicas (ex. a cada 3 ou 4 meses), dando opiniões	☐1	☐2	☐3
- Reuniões periódicas (ex. a cada 3 ou 4 meses), colaborando na tomada de decisões	☐1	☐2	☐3
- Reuniões esporádicas, dando opiniões	☐1	☐2	☐3
- Reuniões esporádicas, colaborando na tomada de decisões	☐1	☐2	☐3

20. Na sua opinião, que **<u>vantagens</u>** podem resultar da **participação dos cidadãos na governação de informação de saúde num hospital público**?

_____

_____

_____

21. Na sua opinião, que **<u>desvantagens</u>** podem resultar da **participação dos cidadãos na governação de informação de saúde num hospital público**?

_____

_____

_____

22. Supondo que deu autorização para o uso das suas informações de saúde num projeto de investigação, **indique, por favor, em que medida seria importante para si <u>participar</u>…**

	Nada importante				Muito importante
- Na definição dos objetivos	☐0	☐1	☐2	☐3	☐4
- No recrutamento de participantes	☐0	☐1	☐2	☐3	☐4
- Na recolha de dados	☐0	☐1	☐2	☐3	☐4
- Na discussão dos resultados	☐0	☐1	☐2	☐3	☐4
- Na redação do relatório do projeto	☐0	☐1	☐2	☐3	☐4
- Na disseminação dos resultados	☐0	☐1	☐2	☐3	☐4

23. A recolha de informação de saúde pode ser efetuada pela própria pessoa através, por exemplo, de uma aplicação no seu telemóvel, tablet ou computador. **Estaria disponível para <u>participar na recolha</u> da sua própria informação de saúde?**

- Não ☐1 (p.f. passe para a questão 24)
- Talvez ☐2
- Sim ☐3

23.1. **Em que medida estaria disponível para <u>partilhar</u> a informação de saúde que recolheria para as seguintes finalidades**:

	Não disponível				Sempre disponível
- Contribuir para o diagnóstico e tratamento da sua doença, tendo em conta as suas características e necessidades pessoais	☐0	☐1	☐2	☐3	☐4
- Realizar investigação sem fins lucrativos relacionada:					
1) com a sua doença	☐0	☐1	☐2	☐3	☐4
2) com outras doenças	☐0	☐1	☐2	☐3	☐4
- Realizar investigação com fins lucrativos relacionada:					
1) com a sua doença	☐0	☐1	☐2	☐3	☐4
2) com outras doenças	☐0	☐1	☐2	☐3	☐4

Características sociodemográficas

24. **Qual a confiança pessoal que tem em cada uma das instituições abaixo indicadas?**

	Nenhuma confiança										Toda a confiança	Não responde	Não sabe
- Assembleia da República	☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐
- Sistema jurídico	☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐
- Polícia	☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐
- Políticos	☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐
- Partidos políticos	☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐
- Parlamento Europeu	☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐
- Nações Unidas	☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐

25. **De uma forma geral, acha que todo o cuidado é pouco quando se lida com as pessoas ou acha que se pode confiar na maioria das pessoas?**

Todo o cuidado é pouco										A maioria das pessoas é de confiança	Não responde	Não sabe
☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐

26. **Acha que a maior parte das pessoas tenta aproveitar-se de si sempre que pode, ou pensa que a maior parte das pessoas é honesta?**

Tenta aproveitar-se de mim										É honesta	Não responde	Não sabe
☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐

27. **Acha que, na maior parte das vezes, as pessoas estão preocupadas com elas próprias ou tentam ajudar outros?**

As pessoas estão preocupadas com elas próprias										As pessoas tentam ajudar os outros	Não responde	Não sabe
☐0	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9	☐10	☐	☐

28. **Sexo:**

- Feminino ☐0
- Masculino ☐1

29. **Ano de nascimento:** |__|__|__|__|

30. **De onde é natural?**

- Portugal ☐1
- Outro país ☐2

  Qual?

_____

31. **Onde reside atualmente?** Distrito:

_____

32. **Qual é o seu estatuto marital?**

- Solteiro/a ☐1
- Casado/a ☐2
- União de facto ☐3
- Viúvo/a ☐4
- Divorciado/a ☐5
- Separado/a (casado/a mas não vive com o cônjuge) ☐6

33. **Qual o grau de escolaridade mais elevado que completou?**

- Nenhum, mas sabe ler e/ou escrever ☐1
- 1º Ciclo do ensino básico (4º ano) ☐2
- 2º Ciclo do ensino básico (6º ano) ☐3
- 3º Ciclo do ensino básico (9º ano) ☐4
- Ensino secundário (12º ano) ☐5
- Bacharelato ☐6
- Licenciatura ☐7
- Mestrado/Mestrado Integrado ☐8
- Doutoramento ☐9

34. **Neste momento, qual é a sua principal situação profissional?** (p.f. assinale apenas uma opção de resposta)

- Empregado/a a tempo inteiro ☐1
- Empregado/a a tempo parcial ☐2
- Desempregado/a ☐3
- Reformado/a ou pré-reformado/a ☐4
- Estudante/na escola/em formação profissional ☐5
- Doméstico/a/ocupa-se das tarefas do lar ☐6
- Outra. Qual? _____ ☐7

35. **Qual é a sua profissão atual?** (se na questão anterior assinalou desempregado/a, doméstico/a, reformado/a ou outra, p.f. considere a sua última profissão)

_____

_____

_____

_____

36. **Considera que os rendimentos do seu agregado familiar são:**

- Insuficientes ☐1
- Tem de ter cuidado com os gastos ☐2
- Chega para as suas necessidades ☐3
- Confortáveis ☐4

37. **Está envolvido em alguma associação de doentes?**

- Não ☐0 (p.f. passe para a pergunta 38)
- Sim, estou envolvido…
  - Numa associação local ou nacional ☐1
  - Em várias associações locais ou nacionais ☐2
  - Numa associação internacional ☐3
  - Em várias associações internacionais ☐4

37.1. **Há quanto tempo iniciou o seu envolvimento numa associação de doentes?**

- Menos de 1 ano ☐1
- Entre 1 a 5 anos ☐2
- Mais de 5 anos ☐3

38. **Até que ponto está satisfeito/a com a sua saúde?**

- Muito insatisfeito ☐0
- Insatisfeito ☐1
- Nem satisfeito nem insatisfeito ☐2
- Satisfeito ☐3
- Muito satisfeito ☐4

Agradecemos a sua colaboração!

REFERENCES

1. Patel K. The importance of data-driven decision-making in public health. IJCTT Journal. 2024;72:27-32.
2. Naeem I, Quan H, Singh S, Chowdhury N, Chowdhury M, Saini V, et al. Factors associated with willingness to share health information: rapid review. JMIR Hum Factors. 2022;9(1):e20702.
3. Faye F, Crocione C, Anido de Peña R, Bellagambi S, Escati Peñaloza L, Hunter A, et al. Time to diagnosis and determinants of diagnostic delays of people living with a rare disease: results of a rare barometer retrospective patient survey. Eur J Hum Genet. 2024;32:1116-26.
4. NORD. Rare disease day: frequently asked questions 2019 [cited 2023 Jun 26]. Available from: https://rarediseases.org/wp-content/uploads/2019/01/RDD-FAQ-2019.pdf.
5. Gimenez-Lozano C, Páramo-Rodríguez L, Cavero-Carbonell C, Corpas-Burgos F, López-Maside A, Guardiola-Vilarroig S, et al. Rare diseases: needs and impact for patients and families: a cross-sectional study in the valencian region, Spain. Int J Environ Res Public Health. 2022;19(16).
6. Courbier S, Dimond R, Bros-Facer V. Share and protect our health data: an evidence based approach to rare disease patients' perspectives on data sharing and data protection - quantitative survey and recommendations. Orphanet J Rare Dis. 2019;14(1):175.
7. Fiske A, Buyx A, Prainsack B. Health information counselors: a new profession for the age of big data. Acad Med. 2019;94(1):37-41.
8. De Freitas C, Dos Reis V, Silva S, Videira PA, Morava E, Jaeken J. Public and patient involvement in needs assessment and social innovation: a people-centred approach to care and research for congenital disorders of glycosylation. BMC Health Serv Res. 2017;17(1):682.
9. Nwebonyi N, Silva S, de Freitas C. Public views about involvement in decision-making on health data sharing, access, use and reuse: the importance of trust in science and other institutions. Front Public Health. 2022;10.
10. Nguengang Wakap S, Lambert DM, Olry A, Rodwell C, Gueydan C, Lanneau V, et al. Estimating cumulative point prevalence of rare diseases: analysis of the orphanet database. Eur J Hum Genet. 2020;28(2):165-73.
11. Haendel M, Vasilevsky N, Unni D, Bologa C, Harris N, Rehm H, et al. How many rare diseases are there? Nat Rev Drug Discov. 2020;19(2):77-8.
12. NCATS. Rare disease day at NIH 2022: shining a light on patient perspectives 2022 [updated 05-11-2022; cited 2023 Jun 23]. Available from: https://ncats.nih.gov/pubs/features/rare-disease-day-at-nih-2022-shining-a-light-on-patient-perspectives.
13. DGS. Informação de apoio à pessoa com doença rara. Estratégia integrada para as Doenças Raras 2015-2020. [updated 14-02-2019; cited 2023 Jun 1]. Available from: https://www.insa.min-saude.pt/wp-content/uploads/2020/02/Manual_apoio_doenca_rara.pdf.
14. Pai M, Iorio A, Meerpohl J, Taruscio D, Laricchiuta P, Mincarone P, et al. Developing methodology for the creation of clinical practice guidelines for rare diseases: a report from RARE-Bestpractices. Rare Dis. 2015;3(1).

15. Isono M, Kokado M, Kato K. Why does it take so long for rare disease patients to get an accurate diagnosis? - a qualitative investigation of patient experiences of hereditary angioedema. PLoS One. 2022;17(3):e0265847.
16. Dickinson JA. Lesser-spotted zebras: their care and feeding. Can Fam Physician. 2016;62(8):620-1.
17. Bauskis A, Strange C, Molster C, Fisher C. The diagnostic odyssey: insights from parents of children living with an undiagnosed condition. Orphanet J Rare Dis. 2022;17(1):233.
18. Black N MF, Manacorda T. Diagnostic odyssey for rare diseases: exploration of potential indicators. London: Policy Innovation Research Unit, LSHTM; 2015.
19. Francisco R, Brasil S, Pascoal C, Edmondson AC, Jaeken J, Videira PA, et al. A community-led approach as a guide to overcome challenges for therapy research in congenital disorders of glycosylation. Int J Environ Res Public Health. 2022;19(11).
20. Austin CP, Cutillo CM, Lau LPL, Jonker AH, Rath A, Julkowska D, et al. Future of rare diseases research 2017-2027: an IRDiRC perspective. Clin Transl Sci. 2018;11(1):21-7.
21. European Commission. Non-communicable diseases, Expert group Public Health, Rare diseases [cited 2023 Jun 26]. Available from: https://health.ec.europa.eu/non-communicable-diseases/expert-group-public-health/rare-diseases_en.
22. Despacho n.º 5505/2023: Constitui o Grupo de Trabalho Intersectorial para as Doenças Raras, com o objetivo de elaborar o Plano Nacional Intersectorial para as Doenças Raras, Despacho n.º 5505/2023 (2023).
23. Hood L, Rowen L. The human genome project: big science transforms biology and medicine. Genome Med. 2013;5(9):79.
24. Skinner MK. Role of epigenetics in developmental biology and transgenerational inheritance. Birth Defects Res C Embryo Today. 2011;93(1):51-5.
25. Gunter C. Single nucleotide polymorphisms (SNPS) National Human Genome Research Institute [cited 2023 Oct 15]. Available from: https://www.genome.gov/genetics-glossary/Single-Nucleotide-Polymorphisms.
26. Fu MP, Merrill SM, Sharma M, Gibson WT, Turvey SE, Kobor MS. Rare diseases of epigenetic origin: challenges and opportunities. Front Genet. 2023;14:1113086.
27. Amorim M, Silva S, Machado H, Teles EL, Baptista MJ, Maia T, et al. Benefits and risks of sharing genomic data for research: comparing the views of rare disease patients, informal carers and healthcare professionals. Int J Environ Res Public Health. 2022;19(14).
28. Liu W, Li L, Jiang J, Wu M, Lin P. Applications and challenges of CRISPR-Cas gene-editing to disease treatment in clinics. Precis Clin Med. 2021;4(3):179-91.
29. Subica AM. CRISPR in public health: the health equity implications and role of community in gene-editing research and applications. Am J Public Health. 2023;113(8):874-82.
30. Braga LAM, Conte Filho CG, Mota FB. Future of genetic therapies for rare genetic diseases: what to expect for the next 15 years? Ther Adv Rare Dis. 2022;3:26330040221100840.
31. Darquy S, Moutel G, Lapointe AS, D'Audiffret D, Champagnat J, Guerroui S, et al. Patient/family views on data sharing in rare diseases: study in the european LeukoTreat project. Eur J Hum Genet. 2016;24(3):338-43.
32. McCormack P, Kole A, Gainotti S, Mascalzoni D, Molster C, Lochmüller H, et al. 'You should at least ask'. The expectations, hopes and fears of rare disease patients

on large-scale data and biomaterial sharing for genomics research. Eur J Hum Genet. 2016;24(10):1403-8.
33. Horton RH, Lucassen AM. Recent developments in genetic/genomic medicine. Clin Sci (Lond). 2019;133(5):697-708.
34. Zhang Y, Yu J, Xie X, Jiang F, Wu C. Application of genomic data in translational medicine during the big data era. FBL. 2024;29(1).
35. Hendricks-Sturrup RM, Prince AER, Lu CY. Direct-to-consumer genetic testing and potential loopholes in protecting consumer privacy and nondiscrimination. JAMA. 2019;321(19):1869-70.
36. De Groot NF, Van Beers BC, Meynen G. Commercial DNA tests and police investigations: a broad bioethical perspective. J Med Ethics. 2021;47(12):788-95.
37. Samuel G, Howard HC, Cornel M, Van El C, Hall A, Forzano F, et al. A response to the forensic genetics policy initiative's report "Establishing Best Practice for Forensic DNA Databases". Forensic Sci Int Genet. 2018;36:e19-e21.
38. Machado H, Silva S. Public participation in genetic databases: crossing the boundaries between biobanks and forensic DNA databases through the principle of solidarity. J Med Ethics. 2015;41(10):820-4.
39. OECD. Enhancing access to and sharing of data: reconciling risks and benefits for data re-use across societies: Paris; 2019.
40. European Commission. Comission Implementing Decision of 10.7.2023 pursuant to Regulation (EU) 2016/679 of the European Parliament and of the Council on the adequate level of protection of personal data under the EU-US Data Privacy Framework. 2023. p. 52.
41. EIOPA. Big data analytics in motor and health insurance: a thematic review. Luxembourg: Publications Office of the European Union; 2019 [cited 2023 Aug 22]. Available from: https://register.eiopa.europa.eu/Publications/EIOPA_BigDataAnalytics_ThematicReview_April2019.pdf.
42. Kruse J, Mueller R, Aghdassi AA, Lerch MM, Salloch S. Genetic testing for rare diseases: a systematic review of ethical aspects. Front Genet. 2021;12:701988.
43. Ganesh K, Lazar A. The work of workplace disclosure: invisible chronic conditions and opportunities for design. Proc ACM Hum Comput Interact. 2021;5.
44. Shi Z, Zhang Q, Wang X. Does the disclosure of medical insurance information affect patients' willingness to adopt the diagnosis related groups system. Front Public Health. 2023;11.
45. Milne R, Morley KI, Almarri MA, Atutornu J, Baranova EE, Bevan P, et al. Return of genomic results does not motivate intent to participate in research for all: perspectives across 22 countries. Genet Med. 2022;24(5):1120-9.
46. Xiang D, Cai W. Privacy protection and secondary use of health data: strategies and methods. Biomed Res Int. 2021;2021:6967166.
47. Graham M. Sharing genomic data for health research: institutional trust and trustworthiness, and informed consent. CMAJ Open. 2022;194(44):E1511-e2.
48. Kaye J, Curren L, Anderson N, Edwards K, Fullerton SM, Kanellopoulou N, et al. From patients to partners: participant-centric initiatives in biomedical research. Nat Rev Genet. 2012;13(5):371-6.
49. Vayena E, Blasimme A. Biomedical big data: new models of control over access, use and governance. J Bioeth Inq. 2017;14(4):501-13.
50. Shah N, Viberg Johansson J, Haraldsdóttir E, Bentzen HB, Coy S, Mascalzoni D, et al. Governing health data across changing contexts: a focus group study of citizen's views in England, Iceland, and Sweden. Int J Med Inform. 2021;156:104623.

51. Shah N, Coathup V, Teare H, Forgie I, Giordano GN, Hansen TH, et al. Sharing data for future research-engaging participants' views about data governance beyond the original project: a DIRECT Study. Genet Med. 2019;21(5):1131-8.
52. Aitken M, De St Jorre J, Pagliari C, Jepson R, Cunningham-Burley S. Public responses to the sharing and linkage of health data for research purposes: a systematic review and thematic synthesis of qualitative studies. BMC Med Ethics. 2016;17(1):73.
53. Florin D, Dixon J. Public involvement in health care. BMJ. 2004;328(7432):159-61.
54. Velvin G, Hartman T, Bathen T. Patient involvement in rare diseases research: a scoping review of the literature and mixed method evaluation of norwegian researchers' experiences and perceptions. Orphanet J Rare Dis. 2022;17(1):212.
55. Griggs RC, Batshaw M, Dunkle M, Gopal-Srivastava R, Kaye E, Krischer J, et al. Clinical research for rare disease: opportunities, challenges, and solutions. Mol Genet Metab. 2009;96(1):20-6.
56. Z. Perrin. L M. Citizens' perception of and engagement with health data secondary use and sharing in europe – a literature review 2021 [cited 2024 Jan 12]. Available from: https://tehdas.eu/app/uploads/2021/11/tehdas-citizens-perception-of-and-engagement-with-health-data-secondary-use-and-sharing-in-europe.pdf.
57. Teare HJ, Morrison M, Whitley EA, Kaye J. Towards 'Engagement 2.0': insights from a study of dynamic consent with biobank participants. Digit Health. 2015;1:2055207615605644.
58. Oliver JM, Slashinski MJ, Wang T, Kelly PA, Hilsenbeck SG, McGuire AL. Balancing the risks and benefits of genomic data sharing: genome research participants' perspectives. Public Health Genomics. 2011;15(2):106-14.
59. Boulanger V, Schlemmer M, Rossov S, Seebald A, Gavin P. Establishing patient registries for rare diseases: rationale and challenges. Pharmaceut Med. 2020;34(3):185-90.
60. McGuire AL, Hamilton JA, Lunstroth R, McCullough LB, Goldman A. DNA data sharing: research participants' perspectives. Genet Med. 2008;10(1):46-53.
61. McGuire AL, Oliver JM, Slashinski MJ, Graves JL, Wang T, Kelly PA, et al. To share or not to share: a randomized trial of consent for data sharing in genome research. Genet Med. 2011;13(11):948-55.
62. Jamal L, Sapp JC, Lewis K, Yanes T, Facio FM, Biesecker LG, et al. Research participants' attitudes towards the confidentiality of genomic sequence information. Eur J Hum Genet. 2014;22(8):964-8.
63. Kaufman DJ, Murphy-Bollinger J, Scott J, Hudson KL. Public opinion about the importance of privacy in biobank research. Am J Hum Genet. 2009;85(5):643-54.
64. Miguel Beriain I. Health information counselors help avoid automatized decisions in health care. Acad Med. 2019;94(5):610.
65. Patch C, Middleton A. Genetic counselling in the era of genomic medicine. Br Med Bull. 2018;126(1):27-36.
66. Skirton H, Cordier C, Ingvoldstad C, Taris N, Benjamin C. The role of the genetic counsellor: a systematic review of research evidence. Eur J Hum Genet. 2015;23(4):452-8.
67. Kaufmann P, Pariser AR, Austin C. From scientific discovery to treatments for rare diseases – the view from the national center for advancing translational sciences – office of rare diseases research. Orphanet J Rare Dis. 2018;13(1):196.
68. Reeves J, Treharne GJ, Ratima M, Theodore R, Edwards W, Poulton R. A one-size-fits-all approach to data-sharing will not suffice in lifecourse research: a grounded theory study of data-sharing from the perspective of participants in a 50-year-old

lifecourse study about health and development. BMC Med Res Methodol. 2023;23(1):118.
69. Gaskell G, Gottweis H, Starkbaum J, Gerber MM, Broerse J, Gottweis U, et al. Publics and biobanks: pan-european diversity and the challenge of responsible innovation. Eur J Hum Genet. 2013;21(1):14-20.
70. Lemke AA, Wolf WA, Hebert-Beirne J, Smith ME. Public and biobank participant attitudes toward genetic research participation and data sharing. Public Health Genomics. 2010;13(6):368-77.
71. D'Abramo F, Schildmann J, Vollmann J. Research participants' perceptions and views on consent for biobank research: a review of empirical data and ethical analysis. BMC Med Ethics. 2015;16(1):60.
72. Sanderson SC, Brothers KB, Mercaldo ND, Clayton EW, Antommaria AHM, Aufox SA, et al. Public attitudes toward consent and data sharing in biobank research: a large multi-site experimental survey in the US. Am J Hum Genet. 2017;100(3):414-27.
73. Ewing AT, Erby LA, Bollinger J, Tetteyfio E, Ricks-Santi LJ, Kaufman D. Demographic differences in willingness to provide broad and narrow consent for biobank research. Biopreserv Biobank. 2015;13(2):98-106.
74. Page SA, Manhas KP, Muruve DA. A survey of patient perspectives on the research use of health information and biospecimens. BMC Med Ethics. 2016;17(1):48.
75. Riordan F, Papoutsi C, Reed JE, Marston C, Bell D, Majeed A. Patient and public attitudes towards informed consent models and levels of awareness of electronic health records in the UK. Int J Med Inform. 2015;84(4):237-47.
76. Kim KK, Joseph JG, Ohno-Machado L. Comparison of consumers' views on electronic data sharing for healthcare and research. JAMIA Open. 2015;22(4):821-30.
77. Lewis C, Clotworthy M, Hilton S, Magee C, Robertson MJ, Stubbins LJ, et al. Public views on the donation and use of human biological samples in biomedical research: a mixed methods study. BMJ Open. 2013;3(8).
78. De Freitas C, Amorim M, Machado H, Leão Teles E, Baptista MJ, Renedo A, et al. Public and patient involvement in health data governance (DATAGov): protocol of a people-centred, mixed-methods study on data use and sharing for rare diseases care and research. BMJ Open. 2021;11(3):e044289.
79. INE. Portuguese Classification of Occupations: Statistics Portugal; 2010 [Available from: https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_publicacoes&PUBLICACOESpub_boui=107961853&PUBLICACOESmodo=2&xlang=pt.
80. Gjoneska B, Jones J, Vella AM, Bonanno P, Flora K, Fontalba-Navas A, et al. Citizen consultation on problematic usage of the internet: ethical considerations and empirical insights from six countries. Front Public Health. 2021;9.
81. Falcão M, Allocca M, Rodrigues AS, Granjo P, Francisco R, Pascoal C, et al. A community-based participatory framework to co-develop patient education materials (PEMs) for rare diseases: a model transferable across diseases. Int J Environ Res Public Health. 2023;20(2).
82. Middleton A, Milne R, Almarri MA, Anwer S, Atutornu J, Baranova EE, et al. Global public perceptions of genomic data sharing: what shapes the willingness to donate DNA and health data? Am J Hum Genet. 2020;107(4):743-52.
83. De Freitas C, Amorim M, Leão Teles E, Maia T, Machado H, Silva S. Public preferences for involvement in the governance of health data. Eur J Public Health. 2020;30(Supplement_5).

84. Sales CMD, Martins F, Alves MM, Carletto S, Conejo-Cerón S, da Silva LC, et al. Patient and public involvement in youth mental health research: protocol for a systematic review of practices and impact. Front Psychol. 2021;12.
85. De Freitas C. Public and patient participation in health policy, care and research. Porto Biomed J. 2017;2(2):31-2.
86. Derose KP, Varda DM. Social capital and health care access: a systematic review. Med Care Res Rev. 2009;66(3):272-306.
87. Berkman LF, Kawachi I, Glymour MM. Social epidemiology. Social epidemiology: Oxford University Press; 2000. p. pp. 174–90.