Global Journal of Medical Research: K
Interdisciplinary
Volume 21 Issue 4 Version 1.0 Year 2021
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

# Brazilian Patient Organizations and Regenerative Medicine: Selective Comparisons with the Experience of the United Kingdom

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*GJMR-K Classification: NLMC Code: QU 450*

*Strictly as per the compliance and regulations of:*

# Brazilian Patient Organizations and Regenerative Medicine: Selective Comparisons with the Experience of the United Kingdom

## Brazilian Patient Organizations Reg Medicine

Liliana Acero

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## I. Introduction

In recent decades public interest in the social control of health activities has increased substantively, especially in relation to new cellular and genetic therapies that form part of regenerative medicine (RM) (Webster & Wyatt, 2020; Irwin et al., 2013). Patient associations have become a global privileged locus through which to mediate state-society relations in health care (e.g. MacGowanet al., 2016). The role of these organizations has become more relevant in light of globalization and the effects of neoliberal policies in health implemented in the 1990s. These include the tertiarization of health care services and the monopolistic participation, enabled by more-restrictive intellectual property rights clauses, of the pharmaceutical industry in the market, leading to very high prices for medicines This combination of economic and social factors has left large proportions of vulnerable populations unprotected with regard to health care, especially in emerging countries (Farmer, 2005; Leach et al., 2005; Araujo Aureliano, 2018; Souza Soares & Deprá, 2012).

Consumer demands for new therapies and medicines – faced with a lack of 'solutions' to their critical health problems and in opposition to the hegemonic conventional values supported by science, medicine, and industry – has given rise to the increasing collective organization of consumers and the questioning of those previous forms of authority (Salter et al., 2015). These organizations have been able to develop their own forms of knowledge, access alternative treatments, and make political demands related to the redefinition of the rules, and values of conventional health supply models. Many are patient and family associations, that sometimes include activists; they act following 'evidence-based health' (Barbosa, 2015; Rabeharisoa et al., 2014).

Since the 1980s, new challenges to the established professions, changes in the epistemologies of the life sciences and biotechnology, and significant limitations in the perspectives of specialists in the design of therapies and medicines have produced a distrust of specialists, mainly in advanced countries. Different criteria have been applied in the definition of specialized knowledge, including experienced-based knowledge (Williams and Calnan, 1996; Nowotny, Scott, and Gibbons, 2001) and 'situated knowledges' according to age, sex, race, ethnic group, class, and sexual orientation (Haraway, 1988). Borkman (1976, 1997) was a pioneer in developing the concept of the 'experiential knowledge' of patients and he formulated an epistemological claim that patients' experiences on their own right generate knowledge. Different and sometimes controversial regulatory frameworks on health have given rise to a more pluralistic vision of knowledge, helped legitimize citizens' reflections and extend democratic participation in specialized

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knowledge fields to social groups once excluded (Irwin, 1995; Acero, 2017).

The present study analyzes the role of patient organizations in relation to RM in Brazil, and makes selective comparisons with that of patient organizations with a similar focus in the United Kingdom (UK), a global leader in RM. It intends to answer two interrelated questions:

- How can the role of patient organizations in RM best be characterized in the UK and Brazil? What are their main differences in each context?
- What are the organizational models and main activities of the different type of Brazilian patient organizations? What is their level of involvement in RM?

## II. Theoretical Reflections

This section will discuss the main frameworks in place to promote citizen participation in health care policy making, mainly in the UK, and the involvement of patient associations.

*a) Public policies regarding citizen engagement in science and health*

Different types of public policies to encourage the engagement of lay people in science and health care policy-making, including in RM, have been implemented in Europe and, up to a certain extent, in the US. They can be classified into three different types: public participation in science and health, citizen science, and patient-centered medicine.

The first type involves the strategies for citizen engagement designed by governments, such as citizen juries, public consultations, and consensus conferences and forums (Horst & Michael, 2011; Bussu et al., 2014; McGowan et al., 2016; Collins et al., 2017; Irwin et. al., 2013). In the UK, these were promoted as a governmental answer to increasing citizen distrust in science and medicine due to inadequate policies implemented to contain "mad cow disease" (bovine spongiform encephalopathy) transmitted to humans through the consumption of beef, as well as citizen resistance to the introduction of transgenics into local agriculture (Irwin & Wynne, 2003; Van Zwanenberg & Millstone, 2005).

These policies implicitly criticized the 'deficit model' used to characterize levels of scientific knowledge among lay publics, a description that led to a 'top-down' model of participation whereby citizens were considered as passive recipients to be trained in new technologies by specialists (Wynne, 1995; Collins & Evans, 2002; Collins et al., 2017). The new engagement strategies have fostered active participation, the prioritization of dialogue, and the pursuit of the gradual democratization of scientific content through the promotion of 'bottom-up' participatory activities (Irwin et al., 2013). These policies have been usually implemented as group experiments or applied to small populations where new forms of governance are being tried out.

Academic reflection on these initiatives has found a number of problems: the limited range of people involved in the activities performed, difficulties in the articulation of the impacts of the case studies developed, an excessive focus on generating consensus among participants, and a lack of analysis of participants' body language and voice tones (Wynne, 1993; Collins et al., 2017; Stirling, 2008). Studies have also noted that these practices can sometimes be used to legitimize institutional perspectives or commercial decisions previously made. In this sense, these engagement strategies can contribute to preventing plural understandings of a certain issue, instead of facilitating the processes for which they were initially designed. Alternatively, the unintended consequences of these practices can include hard-to-manage social 'overflows' (Callon et al., 2009). However, most academic studies do tend to emphasize the value of public engagement as a project of dialogical governance (Macnaghten & Chilvers, 2013), despite the drawbacks mentioned above.

In citizen science policies, the term 'citizen' refers to different types of individuals and organized social actors, including stakeholders, lay people, patients, consumers, interest groups, lobbies, and corporate groups. A good example of a citizen science endeavor is the online community, Patients Like Me. Participants share symptoms and experiences of a disease and self-management as well as the results of treatments. They use aggregate data to design new research trajectories (Wicks et al., 2018).

The European Group on Science and New Technology, in its Opinion29 (2015), describes five different models of citizen science, according to the degree and manner of citizen participation in the scientific projects. These models are the contractual, contributive, collaborative, co-created, and collegial contribution types- where citizens and specialists design initiatives and subsequent functions in research projects vary substantively.[1]Moreover, citizens can engage in projects at two different stages: 'upstream', where they participate in research agenda formulation, priority setting, and decision making on funding. In 'downstream' involvement, lay citizens engage in the evaluation, access to and decisions on data production, analysis, and result dissemination.

Research crowd sourcing[2] also tends to be adopted by citizen science projects for the purposes of information gathering, image classification, systematic revision, and funding. Participants are recruited to obtain large quantities of data over long periods of time across different environments – an impossible task for an individual scientist or a small team (Bonnie et al., 2009).

Volunteers design protocols and develop capacities to formulate questions, collect and submit data, and contribute to online data processing and analysis (Kobori et al., 2015).

Biomedical innovations have received support from citizen science in the research and action programs of the European Commission, such as Program Horizon 2020. This program promotes the application of the theoretical and practical approach called Responsible Research in Innovation,[3] in which volunteer citizens participate in project formulation and implementation in three different roles: as knowledge producers, e.g. citizens 'making science'; as contributors, e.g. in the evaluation and feedback on new medicines; and as consumers, e.g. during online self-diagnosis and the design of healthy life programs.

'Patient-centered medicine' policies actively promote patient empowerment. They are based on a global governmental and citizen movement that has been active during almost the last 40 years. This understanding of medicine proposes new health arrangements that imply taking a wider clinical vision, whereby clinical interest is expanded to include not only the human body but also the subjective thoughts and emotional states of the patients, as well as factors in the patients´ contexts and their abilities to act within them (Gardner, 2016, p. 240).

This approach proposes a psychosocial understanding of medicine and a perspective that considers the patient 'as a person', taking into account his/her own history and disease management. The doctor/patient relationship is thereby reconfigured as more symmetrical (Mead & Bower, 2000). In the UK, this public policy has been characterized as 'the new orthodoxy' (Cribb, 2011). For example, the National Health Service (NHS) claims that one of its main objectives consists of "placing patients at the heart of everything it does. . . . NHS services should reflect and be coordinated according to the needs and preferences of patients, their families and care-takers" (NHS, 2013, p. 3).

Some academic authors have reported that at the beginning of the present decade, patients in the UK were invited to redesign health services by participating in events, interviews, and surveys as well as in the design of new hospitals (Keating & Cambrosio, 2003). However, other authors note that it has been difficult to translate this public policy into clinical routine practice and that success in its implementation has varied substantially according to the possibilities and infrastructures of each clinical setting (Dubbin et al., 2013; Liberati et al., 2015).

In the three types of policies described, patient and family social groups reformulate what Jasanoff (2005, p. 127) has called 'civic epistemologies' or tacit forms of knowing. These are defined as a mix of ways in which knowledge is produced, presented, tested, verified and used in the public arena, i.e. a collective apparatus of sense making or cultural forms of knowing that reflect specific framings of meanings.

Citizen health organizations' plural understandings and actions impact these civic epistemologies substantively. Patients/families and activists jointly produce alternative or minority narratives, socially conscious representations of health and disease based upon experience and often in contrast with hegemonic or dominant narratives.

Some properties of these contrasting epistemologies regarding RM can be described through the categories presented in Table 1.

*Table 1:* Dominant and minority civic epistemologies in Brazilian RM

| Diagnostic and analytical variables/ framing categories | Dominant narrative (Techno-deterministic) | Alternative narrative (Socially conscious) |
|---|---|---|
| Styles of knowledge making | Authoritative/excluding; interest based; top-down | Pluralistic; inclusive; service based; bottom-up |
| Public accountability (basis for trust) | Assumptions of trust Role based | Assumptions of distrust Relational |
| Technical demonstration (practices) | Empirical science | Sociotechnical explanations |
| Objectivity (registers) | Formal | Consultative |
| Main forms of expertise | Professional skills | Skills and experience |
| Visibility of expert bodies | Nontransparent | Transparent |

*Source: Reformulated by the author, following Jasanoff (2005, p. 259).*

*b) Organizational models of patient associations*

Based on a reformulation of Rabeharisoa (2003), three different models of patient organizations: the auxiliary, the emancipatory, and the partnership one, will be summarized next.

In the auxiliary model, scientific and medical functions are delegated to specialists working for the organization, who select research trajectories, support laboratories, develop new practices, and disseminate knowledge. However, the association does not participate in the decision making in relation to the research it funds. In one variant, some participants are trained to become 'lay experts' who can dialogue with specialists – an approach born within HIV/AIDS activism through the Act-Up movement (Epstein, 1995).

The emancipatory model grew out of the advocacy movement of the 1960s and 1970s that confronted the mainstream tradition of self-help groups in those decades. This model is followed, for example, by several organizations focused on breast cancer (Dresser, 2001) and by most of the community-level services in the US. Patient organizations operating this way tend to battle for the inclusion of their demands in public policy agendas; they assert their collective identity and criticize professional monopolies. Some of them also delink completely from disease definitions and treatments not based upon experience– an attitude often found among groups representing people with differential capacities, e.g. deaf people organized against cochlear implants and/or defending their right to have deaf children (Blume, 2000).

Patient organizations working in a partnership model adhere to the principle of 'follow science and medicine, but not be controlled by scientists and medical doctors'. They become specialized partners in knowledge production, treatment, and patient care. Patient and family participants relate to researchers in such a way that their objectives, hypotheses, and observations influence and improve each other. This operating model is most frequently found in rare disease patient organizations, which are trying to break the vicious cycle of scientific and social ignorance and indifference (Rabeharisoa et al., 2014). Associations often define new research trajectories and, through collective mobilization, contribute to the reformulation of the fields of competence of many research institutions. Participants often publish coauthored articles in scientific journals and/or become coinventors of patents on genes and biological materials (Callon, 2003; Nowotny et al., 2001). Examples of organizations following this model include the French Rare Disease Alliance and the French Association of Muscular Dystrophy.

The role of patients in this last model has been described by some authors as 'researchers in the wild', in reference to the fact that the patients themselves are the only ones qualified to pursue a certain kind of knowledge (Callon et al., 2001). They contribute to the reformulation of medical knowledge by the way they articulate scientific and experiential knowledges (Rabeharisoa et al., 2014). All three models are represented in RM.

To characterize patient groups, most especially those functioning within a partnership model, authors have coined the terms 'biosociality' and 'biosociability'. These are defined as the social relationships mediated by health biotechnologies that collectively democratize applications in the biosciences and recreate conventional institutional hierarchies (Rabinow, 1996; Novas, 2008). People directly interested in the resolution of a health problem become 'biosocial' in their search for answers. They organize themselves into 'expert' networks, create new framings of disease, and actively search for information on a certain disease related to research, clinical trials, and funding. Their practices are motivated by the hope of finding a cure, which in turn legitimizes the manner in which they deal with their own diseases as well as with the future of their category of disease (Mazanderani et al., 2018; Pinto et al., 2018).

## III. Methodological Approach

The present study forms part of a wider research program developed intermittently since 2009to analyze innovation, regulation, and governance in relation to RM in Brazil (see, for example, Acero, 2010a; 2010b; 2011a; 2011b; 2019, 2020a; 2020b; 2020c). This article was based on a qualitative study that included a bibliographical and documentary analysis of academic literature and official national and international reports on the specific topic. Secondary information was gathered on the principal civil organizations which support RM in the UK – foundations, charities, and patient organizations – from their websites and online interviews were conducted with selected key informants. An in-depth analysis based on information gathered in the websites of the main patient organizations in Brazil related to RM and a total of 18 interviews with representatives of some of these organizations complement this study.

Patient organizations focusing on specific diseases that are more actively involved with RM were selected from a sample of 23 such Brazilian associations within the Latin American network called Latin Alliance (Alianza Latina). Five semi-structured hour-long online interviews were conducted that were recorded and transcribed at the beginning of 2021. In relation to rare diseases, a total of 40 national organizations were selected from a list of 470 Brazilian rare disease patient organizations compiled by the NGO Cure Tay-Sachs Brasil,[4] and relevant information was collected from their websites. The main criteria for the selection of the 40 organizations were (a) their support or interest in research/clinical trials related to the

diseases in question and (b) their interest in research in or clinical trial support for RM, which include genetic diagnosis and treatments.

Thirteen semi-structured hour-long online interviews were carried out between January and March 2021 with representatives from some of the rare disease patient organizations more active in RM. The interviews were recorded and transcribed. Interviewees were selected based on the organizations' websites or contacted through the qualitative technique snowball, in which some participants suggest new participants who in turn suggest successively new participants (e.g. Biernack & Waldorf 1981).

Content analysis was applied in the study of the narratives in the interviews (e.g. Cavalcanti et al., 2014), whereby after several systematic and in-depth readings of the answers, main categories of analysis and coding were defined. These are type of services offered to affiliates, involvement in RM research and clinical trials, role played by public agencies in relation to the disease, organization's engagement in public policy, and relationship established with national and international institutions and with the media.

## IV. A Brief Summary of the UK Experience

State agencies, scientific networks, and civil society associations of patients, foundations, and charities are involved in the three types of public policy initiatives discussed above. In the UK, they form a complex network that supports RM research activities and provides a significant percentage of the funding for the sector (Acero, 2011).

Charities are extremely relevant in the UK because they finance infrastructure, research programs, and fellowships; help define RM bioethics guidelines; and decisively influence the formulation of public policies. Two of the most active ones in RM are the Nuffield Council on Bioethics and the Wellcome Trust. The first, founded in 1991, is an independent and highly influential group that functions as a consultative body for the technical assessment of 'the publics' in relation to different subjects on bioethics in biomedicine. Its recommendations, based on periodic public consultations, tend to influence lay and professional publics views highly as well as public policy initiatives. The Wellcome Trust, an independent charity, is the main agent of nongovernmental funding of biomedical research in the world. At present, it works on a budget of approximately 29.1 billion pounds and focuses on three main areas: the financial support of researchers of excellence, the acceleration of clinical research results, and the study of key medical topics in different historical and cultural contexts. It also supports public engagement activities.

In summary, both institutions are helping to guide RM research and therapy through the evaluation of research proposals, funding, and bioethics guidelines, as well as international scientific cooperation. Their recommendations transcend the UK context and collaborate substantively to global governance of this area of medicine.

A significant number of European disease-specific patient organizations in RM participate in a total of 11 regional consortia to finance research and development of RM therapies through the European Consortium of Stem Cell Research (Eurostemcells) (see www.eurostemcell.org). It was impossible to calculate the exact number of disease-specific patient organizations in the RM universe in the UK. The Real College of Surgeons in England estimates there are hundreds of active patient groups. As of July 31, 2019, the NHS had listed more than 180 certified organizations, more than half of which had some form of RM involvement (seewww.eurostemcell.org).

The role of this type of UK patient organizations can be illustrated through a brief discussion of the activities of the larger disease-specific UK patient organizations with a long history: the British Heart Foundation (BHF), Cancer Research UK, and the Juvenile Diabetes Research Foundation (JDRF). They not only offer support to patients, public information, and treatments, but also finance national and international research projects, centers, fellowships for specialists, and public education events. For example, BHF funds three pioneering centers in RM based at well-known local universities with the aim of studying the repair of damage caused by heart attacks. Cancer Research UK, focused on immunotherapy and the cellular therapy for cancer called CAR-T, has invested 85 million pounds for research purposes, as well as approving 122 scholarships. The JDRC's global program on type 1 diabetes funds more than 500 active research projects around the world and supports more than 70 clinical trials, having invested internationally more than 1.5 billion pounds in research to date.

The World Health Organization defines a rare disease as one that affects fewer than 65 per 100,000 persons or 1.3 per 2000 and estimates that there exist more than 7,000 types of these diseases globally. These affect 8% of the global population and in Brazil that translates to between 13 and 15 million people (Domingues de Lima et al., 2018). Rare diseases are chronic and/or degenerative diseases that generate various types of deficiencies, are responsible for high morbidity and mortality rates, and mostly have a genetic and hereditary etiology that, as such, can affect families for generations. It often takes a very long time to detect these diseases and medicines/therapies tend to have very high prices (EORD, 2005). It has been estimated globally that only 10% of these health conditions have a specific treatment and that at present there exist only 400 medicines on the market (Melnikova, 2012).

Novas (2012) shows the role played by civic society organizations in the evolution of legislation on rare disease in the US, relating that American health authorities were informed of the importance of drug development for such diseases through a combination of activism carried out by a patient group coalition, Congress hearings, surveys, academic conferences, and media reports. As a result, cutting-edge legislation was approved – the US Orphan Drug Act (1983) – a policy model that was also recently adopted by the majority of European countries.

There are hundreds of rare disease patient organizations in the UK. Only some of the main umbrella organizations that act within the national territory will be mentioned here. For example, the National Organization for Rare Disorders, Inc. is an advocacy, research, and services association for patients made up of more than 300 organizations based in England and the US that pursues the identification, treatment, and cure of this type of disease. The European Organization for Rare Diseases, an NGO that represents 956 rare disease patient organizations, has the goal of improving the life of 30 million patients in Europe.

In summary, public engagement of civil society in RM in the UK is multiple, in terms of the actions and organizations involved. On the one hand, there are a number of governmental initiatives on public engagement, often related to controversial ethics and social topics on RM, for example, on gene editing techniques and the flexibilization of CT approval (Faulkner, 2016; Dickenson, Darnovsky, 2019; Acero, 2020). On the other hand, key foundations as well as patient associations contribute to the definition of research themes, research project implementation and funding and influence the design of national and international policy in RM. The UK also recruits innumerable volunteers for activities in citizen science. The NHS, already knowledgeable in the application of several types of genetic and cellular therapies, openly promotes 'patient-centered medicine' including in RM. Some of these trends will be contrasted next with the experience in Brazil.

## V. Results and Discussion

*a) The organization of Brazilian civil society in RM*

In Brazil, state promotion of public engagement policies in science and health has been very limited and does not form part of an explicit program with assigned funding and a stable structure as, for example, in many European countries. Public engagement is solicited in relation to specific actions or in the form of internet consultations organized by specialized agencies relating laws and normative resolutions. These tend to be directed at selected stakeholders; public convocation is hardly transparent and notices of consultations are rarely disseminated by the mass media. Reports on results are restrictively distributed to selected stakeholders. The general public has little or no access to the results of consultations, even more so in the case of RM, a sector that has only recently emerged (e.g. Acero, 2011 b). In this sense, civil society remains 'free' to use its own criteria and initiative for collective organization. On the other hand, a 'patient centered' approach to medicine has not been promoted as a national policy within the public health system, *Sistema Único de Saûde* (SUS), or in the private sector (see, for example, Agreli et al., 2016 for a comparison between local and international initiatives on this subject).

Beyond the associations of scientists/medical doctors, two main forms of organizations of Brazilian civil society exist in relation to RM. These can be classified as (a) those specific to RM, like MOVITAE (Movement in Favor of Life), and some of the many rare disease patient organizations; and (b) other organizations that include a few concerns associated with RM in their agendas and are active in relation to those only during specific events. The latter include organizations focusing on legal issues or human rights (CONECTAS-DDHH), ethics and gender (Anis), civic and political rights (OABS), and NGOs within the women and racial movements (e.g. CRIOLA, Catholics for the Right to Decide, National Network of Women's Health and Sexual and Reproductive Rights).

The largest national mobilization of civil society in favor of RM took place between 2005 and 2008 during debates on stem cell research and on embryonic stem cell research (ESCR) in particular while the national Biosecurity Law was being approved. Subsequently, a claim for a Direct Action of Unconstitutionality was made that contested the legality of ESCR and the Federal Supreme Court (STF) in 2008 convened a Public Audience, after which the claim was reversed in favor of ESCR (see Acero, 2010 a; b). Some of the associations founded in that historic period remain active today.

More recently, there have been important mobilizations organized by rare disease patient groups to aid in the formulation and implementation of public policies, such as during the development of the National Program on Rare Disease, as well as in support of the approval of specific medicines (Pinto et al., 2018). Rare disease patient organizations have also been mobilizing more substantively since2016 in relation to specific cases of 'health judicialization', for example when the STF judged a legal demand on the approval of medicine for the treatment of pulmonary arterial hypertension –a high-cost treatment unregistered by the National Sanitary Vigilance Agency (ANVISA) – against the State of Rio Grande do Norte. This mobilization was named: "STF my life has no price" (Dominguez de Lima et al., 2018).

Institutional flaws in the public health sector relating to community health have contributed to the proliferation of NGOs supporting public sector activities

in science and health care (Acero, 2011).In relation to RM, a wide range of NGOs disseminates practical information on bone marrow and umbilical cord blood donations to public banks and provides access to voluntary donor registries. Some of them collaborate directly with the National Network of Umbilical Cord and Placenta Banks and with the Brazilian Registry of Voluntary Donors of Bone Marrow associated with the Ministry of Health. Among the most active groups are the Alliance for Organ and Tissue Donations, the Pro-Vita Association for Bone Marrow Transplant, and the Bone Marrow Association.

*b) Disease-specific patient organizations*

Some associations are formed by stakeholders in relation to a specific non-infectious disease. These groups tend to contest institutions and conventional norms 'from the outside' (Salter et al., 2015; Leach et al., 2005; Rabeharisoa, 2014). Most of them were founded by patients and/or relatives of patients searching for treatments of health conditions or by scientists and/or medical doctors with similar motivations.

Information collected via the internet for the present study shows that there are 23 Brazilian disease-specific patient associations that are integrated into the Latin Alliance, a Latin American network of more than 100 different patient organizations created in 2006 (https://redalianzalatina.org/pt-br/alianza-latina/membr-os).[5] Most of these associations have been formed since the 1990s; they tend to operate nationally, with representation in as many as 20 states, and to work in association with other related NGOs.

Five interviews were conducted with (a) representatives of the Brazilian Association of Amyotrophic Lateral Sclerosis (Abrale) and the Brazilian Association of Thalassemia (Abrasta) (these two associations were addressed in a single interview because they often work together), (b) the Brazilian Federation of Philanthropic Institutes of Support to Breast Health (FEMAMA), (c) the Brazilian Association of Muscular Dystrophy (ABDIM), (d) Love and Union Against Cancer (AMUCC), and (e) the Brazilian Association of Ulcerative Colitis and Crohn Disease (ABCD).

On their websites, half of the 23 organizations mention their participation in RM research and/or clinical trials, some developed at relevant public and private charity hospitals. Other organizations, like AMUCC, only use biosimilar medicines to treat women's breast and ovarian cancers. Biosimilar medicines are developed from live cells and since 2017 have been adopted by SUS.

Most associations sound very optimistic about the present and future results in CT. For example, the ABCD representative mentioned that in 2017 the first successful treatment of Crohn's disease with CT in Brazil took place: it involved only one patient and used a technique that had already been approved to treat severe cases in Europe and the US.

FEMAMA's affiliates are making a strong effort to have genetic and hereditary tests included in the treatment of breast cancer and genomic-based tumors at SUS. AFEMAMA representative who was interviewed commented, "Once regenerative medicine takes more space and becomes more important, things will change and our NGO will try to become more knowledgeable in this respect".

An Abrale/Abrasta representative reflected upon Brazil's relative backwardness in terms of CT development and application:

> In relation to the use of CT, Brazil is some steps behind the rest of the world. For thalassemia, the type of treatment that exists today is bone marrow transplant, that is still in an initial and risky phase – in spite of having been already incorporated into SUS. . . . The first transplant here took place no more than ten years ago and since then, there have been no more than 20 other transplants in Brazil. . . . Beyond transplants, there is a new CT for cancer treatment: Car-T cell therapy. It is applied for some types of leukemia and lymphoma. In Brazil, it is still in the trial and approval phase;it will be some time before it is widely available to patients.

An aspect common to all these organizations is that they recruit a wide spectrum of volunteers. In terms of offering support to patients, the organizations carry out treatments, rehabilitation, and complementary health activities; disseminate the results of national and international research; organize mobilization campaigns; provide legal support; make equipment and prosthesis donations; promote self-help groups; advocate for the passage and implementation of laws and influence the design of public policies; monitor data on the diseases represented; ease access to SUS; help with the reentry of patients into the labor market; and facilitate contact between patients and specialists.

These organizations are sometimes substantively involved in the recruitment of patients for RM clinical trials, either via the dissemination of news, promoting the sponsorship of local clinical trials– often drawing upon the support of regional or international associations – or via direct patient recruitment, as the following three narratives relate:

> When there are research projects that need dissemination and are suitable, we disseminate them through our communication channels. But patients get in contact with them directly. (representative of ABCD)

> ADB [Brazilian Dystrophy Alliance], together with other Latin American NGOs, are trying to persuade TREAT-NMD [Neuromuscular Network – an international patient association] to promote a Latin American clinical trial. As this is only in an initial

> negotiation, I cannot tell you on what specific subject the trial will focus.(representative of ABDIM)
>
> There is a Brazilian organization called Institute to Defeat Cancer (IVOC). They have a platform that maps all the local clinical research projects that are taking place for cancer treatment. In this way, they are able to handle the recruitment of patients. Abrale sends to them the patients interested in participating in clinical trials. . . . Normally, our organization gives preference to the dissemination of national level clinical trials because it is very difficult to create expectations in a patient when something is far from taking place locally. (representative of Abrale/Abrasta)

As the last narrative suggests, these local organizations try not to generate false hope in patients regarding treatment possibilities and cures – a phenomenon known as RM 'hype' that is often present in media reporting – and also to avoid widespread use of risky, unproven treatments and medical tourism, which is a global concern in the sector (see Caulfield & McGuire, 2012; Acero, 2014; McMahon, 2014). These patient organizations often provide the public information on the experiences of patients with the different treatments. For example, a representative of Abrale/Abrasta stated, "Practically in all the reports published we include a real case, usually interviewing a patient or family member".

Most of these organizations are funded by donations from individuals and/or private hospitals and research centers related to their topics of concern; almost half of them, receive some level of international funding and/or are integrated into international patient organizations and a third of them receive donations from private national enterprises and the large international pharmaceutical firms. Few receive any form of financial support from the public sector.

Most of the organizations have entered into long-term informal collaborations with researchers affiliated to public universities/hospitals. Some of these partnership are aimed at providing benefits to their members in terms of the use of health care services, as is the case with ABCD and FEMAMA. They also often develop their own printed or online publications (e.g. *RevistaJeito de Viver* of ADJ- Diabetes Brasil) regularly where they disseminate, for example, cases of successful treatments and scientific and medical world news on the diseases represented, as well as run YouTube channels (e.g. *TV Abrasta*), for public education regarding their diseases of concern.

The majority of these associations are not directly involved with scientific research either in their disease area or in RM. But some of their members participate in mixed study groups with disease specialists and these frequently include discussions on RM. However, more than half of the organizations do conduct research on the evolution of the health of their affiliated patients. For example, AMUCC has two qualitative/evaluative research projects underway that are taking this approach to different treatments being evaluated. Two other patient organizations work in four interrelated subareas: education and information, public policies, research, and support to patients. Representatives from Abrale/Abrasta reported that "the research axis can be divided into two areas: research on the patient trajectory (primary research). There is a database where patients are registered and followed up. And research on data mining (secondary research) where information from the DataSUS platform [ a platform on health care of the public health system] on a certain disease is organized". Abrasta also operates a nationwide Cancer Observatory and in its research projects compares local and foreign patient trajectories to establish differences and trends.

Larger patient organizations or those with a longer history tend to point out that, though there exist plenty of public participatory venues, the representation of patient organizations in them is quite minimal. For example:

> In relation to government, there are different and important settings for deliberation: CONITEC, ANS, CNS, Cosinca, and many others. Some of these institutional spaces are occupied both by government and civic society. Seats for civic society members may be sometimes occupied by representatives of patient organizations. However, the patient organization representation in these settings is still limited. In the Chamber for Supplementary Health (CAMSS), for example, there are only two chairs for associations on pathologies out of almost forty. Abrale and Abrasta have already participated in this venue and today we are fighting to win more chairs.[6] (representative of Abrale/Abrasta)

The associations recognize that some measures taken by the Ministry of Health (MS) have been beneficial for their affiliates, such as the approval of the Program for Assisted Non-Invasive Ventilation (MS, decree N$^{o}$ 1.370, of July 3rd 2008), which has saved lives through the free provision by SUS of respiratory equipment. However, they are critical of the scant recognition the federal and state governments have given to their efforts to increase patients' access to treatments and of public agencies' unresponsiveness to their demands for meetings with policy makers.

Opinions are divided between those who consider the mass media very helpful and supportive of their public campaigns and those who avoid all media exposure, because of the low quality of the reporting: "ABDIM has already been invited to present in different media but did not accept, because it tends to be very sensationalist, instead of dealing with our problems

seriously. Some patients from our NGO participate in interviews but at a personal level, not as organizational representatives" (representative of ABDIM).

Variations in media representations can be partially explained by the marked differences between the characteristics of national-level news channels and those of state and local news coverage. The latter tend to be more supportive of these patient organizations.

In summary, unlike their counterparts in the UK, Brazilian disease-specific patient associations do not provide any financial resources for research centers, let alone for RM research. Given structural and social constraints related to health care in Brazil, these organizations specialize in supporting the improvement of patients' health in different ways and compensate for crucial gaps in public health care delivery.

*c) Patient organizations focused on rare diseases*

There are approximately 470 rare-disease patient organizations in Brazil, most of which are developing digital activism intensely and thus expanding identity frontiers and geographical boundaries (Souza, 2006). The category 'rare disease' entered the public consciousness in a significant way in Brazil in 2009 with the organization of the First Brazilian Congress on Rare Disease; the next major step was the formation of a working group for the formulation of the National Policy of Integral Treatment of People with Rare Disease (Brasil, 2014).This policy had as its precedent the National Policy of Integral Treatment on Clinical Genetics, implemented in 2009 (MS, 2009). More recently, the Health Ministry in 2016 invested in the modification of seven preexisting health establishments so that they are now endorsed as genetic services of excellence (Nunez Moreira et al., 2018).

However, in most cases where specific therapies and medicines have been approved for use in a substantial number of countries, patients in Brazil have no access to them. They either have not been incorporated into SUS or have not received commercial authorization locally (Meira & Acosta, 2009). For example, out of a total of almost 400 rare diseases identified in the country in 2018, only 34 of them were mentioned in the official resolution on Clinical Protocols and Therapeutic Guidelines (PCDTs) and thus had medicines/therapies available within SUS (MS, 2015).

Analysis of the information collected via the internet shows that the 40 rare disease patient associations researched for this study are engaged in tasks that are very similar to those of disease-specific patient organizations. At the same time, they have undertaken some specific tasks due to the characteristics of the diseases on which they focus being less well known clinically, their late social acknowledgement in Brazil, and their involvement in gene therapy.

Some of the principal differences in tasks are that rare disease patient organizations encourage more intensely than do disease-specific organizations the participation of their members in the public consultations on clinical protocols developed by the National Commission for the Adoption of Technologies (CONITEC) at SUS –even though no representative of the former organizations can serve on the commission– and also in the consultations by the National Commission of Research Ethics (CONEP). They take action in tandem with local health agencies to verify the availability of medicines and demand that state authorities purchase them; they also participate in the organization of patient and medicine registries as well as in the distribution of medicines and even help hospitals with the scheduling of patient appointments. They frequently pay some or even all of the lawyers' fees for the many instances of litigation in progress; help patients access genetic diagnostics; find referrals to specialists; lecture within specialized trainings on rare diseases; offer and often cover some portion of the cost of complementary treatments for long-term diseases, as well as connect patients with researchers to access adequate diagnostics within the public health network. Associations also promote the 'value of being rare' to develop affirmative actions that bring in other informed social sectors to participate in networks that can increase the visibility of their demands (Nunez Moreira et al., 2018).

Rare disease patient groups tend to be smaller in size than those concerned with specific diseases, even though they differ substantively in the number of participants in their directing bodies (between 3 and 120 active individuals) as well as in their membership ; they range between 59 ( e.g. DII|) and 7,000 (e.g. Retina Brasil) affiliates.

Thirteen interviews were carried out with representatives of the following organizations: Brazilian Group for the Study of Cystic Fibrosis (GBEFC), the Multiple Sclerosis Association from the State of Rio de Janeiro (APEMERJ), Multiple Sclerosis Carriers Association (APEMBS), Brazilian Association of Assistance to Mucoviscidosis (ABRAM), Retina-Brazil, Brazilian Association of Huntington (ABH), Brazilian Association of People with Crohn Disease and Ulcerative Retro Colitis (DII Brasil), Association of Volunteers, Researchers, and Carriers of Pathologies Involving Clogs (AJUDE-C), Maria Vitória Association of Rare and Chronic Disease (AMAVI), Hunter House, Carioca Association of Assistance to Mucoviscidosis (ACAM-RJ), Retina Brasil, Brazilian Association of Rett Syndrome (Abre-Te) and Tay Sachs-Brazil. Approximately 75% of these organizations have patient members who are taking medicines of a biological/cellular nature, making use of genetic diagnostics, or participating in RM clinical trials.

*d) The narratives of the interviewees on rare disease*

Rare disease organizations tend to participate actively in patient recruitment for existing local clinical trials related to the diseases on which they focus. For example, a representative of Retina Brasil reported that,

> the University of the State of São Paulo (UNIFESP) has a research group on hereditary retina diseases and one of the scientists involved, Dr. Juliana Sallum, created a laboratory that performs clinical tests on medicines, the only laboratory in Brazil and it is affiliated to a public university. . . . In the State of Minas (Gerais), Dr. Fernanda Porto has turned her clinic into a laboratory: Clinic and Research Centre (INRET). . . .Retina Brasil helps Dr. Juliana and Fernanda [by] sending patients for the clinical trials they carry out. . . . Recently, patients have been referred for a research project on Stargardt disease, for a clinical trial on Lebercongenital amaurosis . . . and for a new trial, called "Natural History" . . . Beyond this, we [Retina Brasil] try to raise consciousness among patients on the need to carry out genetic tests".

However, the majority of the interviewees observed, in contrast with the citizen science experiences in Europe already discussed, that "what we try to do is to follow research development and invite researchers to events whenever we can. Beyond this, medical doctors form a 'closed up' community and tend not to share much of their information with our associations" (representative of AMAVI).

Interviewees estimated that there were more than 15local clinical trials on genetic/cellular therapies for rare diseases at different phases running at the time, but they complained that this was insufficient:

> The only reason why Brazil is behind the rest of the world in relation to treatments is the fact that there are many more clinical trials taking place in other countries. In that case, there are more opportunities for foreign patients to be treated in those research projects, if they do not take placebos (representative of ABH).

> There is a genetic therapy, approved by the FDA since 2017, that was only recently approved by Anvisa, in 2020. It involves eye surgery, whereby a modified gene is injected into the patient's eye. At present, Retina Brasil is trying to have it incorporated into SUS's treatments. Though very expensive, there would be few patients who could try this therapy. . . . In cellular therapy, there is an ophthalmologist at Ribeirão Preto [São Paulo State] who tried to develop an experiment with stem cells for the retina to treat pigmentary restenosis. . . . But it was rejected by the medical community. This new type of technology is called optogenetics. . . . At present, genetic and cellular therapies are beginning to converge, and optogenetics is one of its expressions (representative of Retina Brasil).

A representative from ABRAM reflected that it was not an easy matter even in advanced countries to implement CT and gene therapy and that the process had also demanded constant activism from patient associations.

Some of the associations' representatives described RM treatment as very expensive and commented that "in Brazil, it is only being applied when other forms of therapy (such as, medication with antibiotics) are ineffective. I do not know of cases of RM performed by SUS – the few cases I know of here are financed by private health plans" (representative of APEMERJ).

In some cases, public resistance to CT treatments is justified by medical doctors' not recommending these therapies and their associated risks – though the specialized literature shows CT risks do not tend to be higher than those of genetic therapies (e.g. Webster & Wyatt, 2020). Other interviewees explained this resistance as being based on dominant social assumptions that make their affiliates reject participation in CT clinical trials. They observed that "there is a very great prejudice in relation to these procedures here in Brazil, people are afraid in relation to cellular therapy" (representative of APEMBS).

It could be some of these negative public opinioms can be partially attributed to remnants of the influence on public representations – especially of embryonic stem cell research – as expressed by some social sectors during the long public debate that took place between 2005 and 2008 mentioned above (Acero, 2010 a; b), as well as the local exclusion of medical doctors from the initial stage of stem cell research development (Acero, 2011). But it could also partially reflect public disinformation on RM, often influenced by the poor quality of local media reporting on RM scientific, ethical, and social controversies (Acero, 2020 a;b; c).

Eleven of the representatives interviewed emphasized that in Brazil many cases of rare diseases are only treated after legal settlements are reached. They explain that their organizations had to get involved in political battles so that patients could simply access medicines and treatments, even when they had already been approved by ANVISA. They characterize policy agents as not being very proactive in demanding that the pharmaceutical industry price medicines affordably and/or make a stronger effort to sponsor clinical trials: for example, "There is scarce information on why these medicines are so expensive. A good negotiation between the pharmaceutical industry and the Federal government is required to reduce prices. The universe of patients with cystic fibrosis is big enough (almost 6 to 8 million patients in Brazil). The government needs to

listen more closely to our organizations. . . .Beyond this, it would be important to rethink the 2012 law in order to make it more flexible, so that it could attract pharmaceutical firms to sponsor these trials in the country"[7](representative of ABRAM).

They add that the situation is different in other countries, where gene and cellular therapies are available and frequently applied:

> In the rest of the world, there are already some countries that apply these therapies for cystic fibrosis systematically, especially in England, Scotland and the US. . . . At present, the few cases treated with these therapies in Brazil required winning legal cases. In those cases, the government purchased the medicine for a specific patient through the retail market (representative of GBEFC).
>
> Cellular and gene research on therapies to treat hemophilia are quite advanced – phase II or III – and look very promising [elsewhere in the world]. . . . Research is generally not so advanced in Brazil. We do not have advanced clinical trials in gene and stem cell therapies. In this sense, other countries in the world are very much ahead of us (representative of AJUDE-C).
>
> There are two main types of treatments for Rett syndrome: one with gene therapy that has the aim of curing the disease and others that try to reduce symptoms. In Brazil, there is still no medicine tested on either of these two fronts. . . . In the rest of the world there are at least three ongoing research projects that use gene therapy; one by Novartis will start human trials by the end of this year and all sound very promising. Rett Syndrome Research Trust (RSRT) has a consortium to finance research and it is looking for other genetic solutions in the near future. (volunteer from Abre-Te).

Two of the interviewees mentioned that ANVISA has only very recently approved new cellular/gene therapies and that the necessary authorizations have already been granted for their incorporation into SUS, as illustrated by the following narrative: "After the approval of the resolution by ANVISA, just a few months later, the first gene therapy registered in the country was announced: Luxturna. This medicine is for hereditary retina dystrophy. Novartis is the pharmaceutical firm producing it and it had to wait for the resolution mentioned to be able to register the drug in Brazil. . . . Very soon afterwards, the most expensive genetic therapy in the world was also registered locally: Zolgensma, for spinal muscular atrophy (SMA)" (representative of Casa Hunter).

According to several interviewees, the main hindrance to local advancement in gene treatments is the low availability of genetic diagnostics and/or their poor quality, as well as the concentration of these services in the South and Southeast regions of Brazil – an obstacle already documented by pioneering academic studies (e.g. Horovitz et al., 2013). This situation also leads to anunder- representation of the number of patients registered.

Representatives of the various organizations held very different positions in relation to the 2014 National Plan on Rare Disease. The most common critique was that the law's ruling jointly on diseases of very different kinds is a major flaw. Interviewees also mentioned that some diseases have mistakenly been defined as rare diseases due to national under-reporting. Representatives complained about the lack of a public registry for the identification of the number of Brazilian cases of each type of rare disease.

However, other representatives shared a more positive opinion of the national plan, explaining that it has facilitated a number of breakthroughs: "The 199 resolution from 2014 helped, in the sense of building a framework for the visibility of rare diseases. Moreover, it was responsible for the creation of diagnostic and treatment centers of reference. It allows the Federal Government to distribute the funding needed by the centers. . . . However, the implementation of these norms, at the state and municipal levels, has proved a difficult task" (representative of ABH).

A minority position stated that aggregating the different type of rare diseases into one national program makes sense because the communities, though heterogeneous, are rather small and their demands are similar. Representatives of most organizations expressed the view that, though beneficial, "there are still many challenges in the regulation of this resolution. The establishment of the centers of reference has not yet taken place adequately in all states" (representative of AMAVI). Another interviewee added that for the specific disease they represent, there is still no center of reference – though this has been demanded by the Brazilian Federation of Rare Disease (representative of AJUDE-C).

The majority of the interviewees reported their institutions were participating directly in key international associations on their topics of interest. From the latter, the Brazilian associations primarily obtain scientific information, support for participating in and organizing events, and often even medical assessment. For example, they mentioned being affiliates to the International Huntington Association (IHA), the European Federation of Crohn's and Ulcerative Colitis Association (EFCCA), the International Cystic Fibrosis/ Mucoviscidosis Association (ICFMA), and EURORDIS (The Voice of Rare Disease Patients in Europe) and Retina International. They emphasized that, unlike Brazilian patient organizations, international associations charge membership fees, which they use to fund research, a practice the interviewees considered unthinkable in Brazil, mainly due to their members' much lower income levels.

Most of rare disease patient organizations tend to be affiliated to the Brazilian Federation of Rare Disease (FEBRARARAS), an umbrella organization for 58 national associations, which has a lot of political strength, and advocates for the development of adequate public policies for rare disease.

Universities, like the University of Campinas (UNICAMP), research centers and hospitals are rare disease patient organizations´ main partners in research and treatment and associated NGOs occupy the second place in terms of partnerships. Collaboration with the pharmaceutical and biotechnology industries has had less importance up to now, except in some of the existing clinical trials with RM. For example, AzidusBrasil is testing the medicine Cellavita HD for Huntington disease in phases I and II clinical trials.

All interviewees complained about the lack of dissemination of their work by policy agencies, most especially by ANVISA. They also reported that their organizations have sometimes been excluded from participating in key public events on rare diseases organized by the government. A volunteer from Abre-Te who was interviewed offered the following suggestions: "We have a lot of public demands: SUS should cover expenses of genetic testing, ANS [the National Agency of Supplemental Health] should include a wider range of therapies etc. There should be a structured channel for associations to present their demands publicly on these subjects".

On the other hand, representatives of a few organizations did praise the work carried out on their behalf by state-level legislative chambers: "We have had support from the courts and the legislative assembly. The courts disseminate the work of DII Brasil through intranet [a local online platform for state employees] .But the support of these institutions would be wider if we had a national law regulating inflammation and intestinal disease treatments. When a state-level law was approved in the State of Minas Gerais, the courts became much more responsive and supportive" (representative of DII Brasil).

Interviewees differed substantively more on their representations of the role played by the mass media than on other issues. Many of them value state- and municipal-level media highly, because they invite members of their organizations in order to publicize specific events – like the 'Orange August' in the case of multiple sclerosis or the 'Purple May Campaign' on intestinal disease. In contrast, other interviewees commented that access to the media largely depended on personal contacts and complained about the media's lack of interest in obtaining quality information on treatments, as has been documented in previous studies by the author (e.g. Acero, 2020 a; b). A representative of ABRAM commented, "The media adores denunciation, but it does not try to reveal the real progress the country has had in relation to rare diseases. It could do better in portraying scientific knowledge and reporting updated information".

In summary, these recently formed rare disease associations are extremely active on the national scene and have also many international partners. They fill up vacuums in local health practices, advocate for the formulation of new regulations, and help with public administrative work. They seek to empower their members, participate in the generation of alternative forms of understanding of rare diseases, and offer their patients and families the means of access to existing diagnostics and treatments.

## VI. Conclusions

In the newly emerging sector of RM in Brazil, there are a number of key steps that need to be taken to enable an expansion in testing and the approval of CT and gene therapies, and patient organizations are at the forefront of the efforts to bring this about Their participation seems crucial to mobilize government towards an acceleration of the present translational phase in RM locally, to support and bring in patient recruits to local and international trials in the short term within the country, to speed up the approval of medicines/therapies by local agencies and the expedited free introduction of those medicines/therapies into SUS, thus helping to achieve greater health equality in RM. They work from 'alternative civic epistemologies' to science and health care that are service-oriented, inclusive and pluralistic.

Coming back to the analytic categories in the opening theoretical reflections, Brazilian patient organizations of both the types analyzed operate according to a hybrid mix of models. Organizational differences also partially reflected the associations' variety in terms of size and access to funding – a characteristic of this universe.

The organizing model most common to specific-disease patient associations can be considered a hybrid between the auxiliary and the emancipatory models discussed. On the one hand, they only have control of the research they carry out internally with their own patients and, in those projects in which they associate with scientists and medical doctors from other institutions, they do not contribute substantively to research design or implementation, participating solely in an auxiliary function. These organizations are mainly concerned with helping their patients deal with their often-chronic diseases (Pierret 2003).

On the other hand, some participants usually train with specialists in order to act as 'expert' interlocutors regarding certain diseases and the organizations advocate for the development and implementation of public policies – both of which are characteristics of an emancipatory organizational model. Some members in their directing bodies participate in

governmental institutions that represent patient demands, such as the health councils. In these senses, the organizations intend to make a substantive contribution to public policy as well as offer reformist input 'from the inside' of public institutions.

Perhaps due to the late official recognition of rare diseases and the greater scientific uncertainties in treatments, most rare disease patient organizations, by contrast, are shaped by an 'activism based in evidence' (Rabeharisoa et al., 2014). Many of them work from 'within science and medicine' to imagine policy designs in relation to the health conditions they support, putting patients and activists in contact with specialists to formulate new bases for scientific knowledge. They act within an organizational model more similar to that previously described as 'a partnership model'.

A smaller number of these organizations, however, function according to the definition of an emancipatory model: they train members to facilitate informed communication with specialists. They are dedicated to mobilizing to gain public recognition of rare disease and patient rights and influence public policy.

While neither of the two types of Brazilian patient associations fit the typical profile defined as 'citizen science', they are associated with some elements of this approach. They act more like contributors to and consumers of the existing scientific and medical knowledge than as producers of it, with the exception of some of the rare disease patient organizations. Lay participants, in general, contribute research data and aid in the dissemination of research results downstream. However, two questions deserve further research: Does 'citizen science' assume specific characteristics in emerging countries? Is the format it takes culturally and institutionally conditioned in the Brazilian case?

What can be said is that all the Brazilian patient associations directly or indirectly involved in RM are building new 'biosocialities' or 'biosociabilities' mediated by biotechnology. Rare disease patient associations in particular offer a more typical example of 'biosocial' groupings or BIO associations, as defined by Barbosa (2015). Firstly, they were generally founded by people affected by specific rare diseases and/or their families and friends, are motivated by shared biological issues that have been explored scientifically only to a limited extent, and recruit numerous activists as affiliates. Secondly, the majority of them are active participants in the national social movement in health care. Thirdly, they construct alternative civic epistemologies in science and health care that interconnect a plurality of understandings, are oriented towards community service and supporting activities based on the experiential knowledge and abilities of their lay members. Moreover, they tend to avoid hierarchies, work from a dialogical standpoint, and try to develop transparency in their relations with public agencies as well as with specialized institutions.

The information analyzed shows that, in contrast to the UK experience, there is no structured and explicit strategy of public engagement in RM at the governmental level. Moreover, the Brazilian public experience in RM, unlike that in the UK, is seeking a patient-centered approach to health care in a very limited way. The closest initiatives to this orientation being applied selectively at SUS, the analysis of which exceeds the scope of this article, are the consumer-centered work process within the interprofessional collaborative practice, the person-centered clinical method, integral care, the Amplified Clinic (CA), and the National Humanization Policy (PNH), all of them anchored in the principles of patient wholeness (Bonfada et al., 2012). However, in the newly emerging field of RM these methods and policies are nonexistent, and thus patients become more distrustful of the new therapies. Perhaps with the further expansion of RM-based therapies into SUS in the near future and, depending on political will, the integration of this patient-centered approach to health care may be considered more seriously.

## Acknowledgements

Many thanks are due to Prof. Maria Tereza Leopardi and Prof. Ana Celia Castro, Coordinator and Vice-coordinator of the Postgraduate Program on Public Policies, Strategies and Development (PPED), at the Institute of Economics (IE), of the Federal University of Rio de Janeiro (UFRJ), for their support of my work as Senior Foreign Visiting Professor and to the National Institute of Science and Technology on Public Policies, Strategies and Development (INCT/PPED) as Coordinator of a research project of the research program "Disarticulation and Reconstruction of State Policies and Capacities in a Post Pandemic World" (INCT-PPED/IPEA). I would also like to thank the IE/UFRJ graduate-level student Leonardo Bueno, for conducting most of the interviews with patient organization representatives and transcribing their responses.

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[1] In contractual projects, communities ask professionals to develop a specific project and report on its results; contributive projects are designed by scientists together with members of the lay public who contribute data; in collaborative projects, lay publics participate with information, design refinement, analysis, and dissemination of results; co-created projects are designed jointly by researchers and lay people, the latter actively engaging in all project aspects; in collegiate projects, individuals without recognized scientific credentials develop research independently.

[2] This is defined as the act of tertiarization to a big group of undefined people; this is work that used to be carried out by a specifically defined agent.

[3] This perspective anticipates and evaluates the potential social implications of and expectations concerning research and innovation with the aim of promoting the design of sustainable and inclusive research and innovation. [Available at: https://ec.europa.eu/programmes/horizon2020/en/h2020-section/responsible-research-innovation, accessed 18 January 2021].

[4] The identification of the patient organizations concerned with rare diseases was carried out by the NGO Cure Tay-Sachs Brasil (https://curetay-sachsbrasil.org) and developed by the researcher Hannah Ramos with the National Institute of Science and Technology (INCT/ PPED).

[5] The Brazilian Association of Muscular Dystrophy (ABDIM), which is not part of the Latin Alliance, carries out some of the most important activities related to RM among patient associations in Brazil.

[6] The public agencies mentioned here – the National Commission for the Incorporation of Technologies to SUS (CONITEC), the National Agency of Supplemental Health (ANS), the National Council of Health (CNS) and the Consultation Council of the National Institute of Cancer (INCA) (Consinca) – reserve seats for patient participation.

[7] This refers to the clinical resolution of ANVISA from 2012 (RDC 36), which established that the institution responsible for the clinical trial must offer financial assistance to the trial subjects even after the clinical research has ended; assistance with expenses, notably a transport and a per diem allowance, was often previously provided by patient organizations.