Revista Bioética
ISSN: 1983-8042
ISSN: 1983-8034
Conselho Federal de Medicina

Góis, Andrea Carolina Lins de; Rabelo, Daniela Amado; Marques, Tiago Félix; Sá, Natan Monsores de
Equidade em situações-limite: acesso ao tratamento para pessoas com hemofilia
Revista Bioética, vol. 30, no. 1, 2022, January-April, pp. 181-194
Conselho Federal de Medicina

DOI: https://doi.org/10.7440/res64.2018.03

Available in: https://www.redalyc.org/articulo.oa?id=361570858019

Revista Bioética
Print version ISSN 1983-8042 | On-line version ISSN 1983-8034

Rev. Bioét. vol.30 no.1 Brasília Jan./Mar. 2022

Equity in limit situations: access to treatment for people with hemophilia

Andrea Carolina Lins de Góis [1], *Daniela Amado Rabelo* [1], *Tiago Félix Marques* [1], *Natan Monsores de Sá* [1]

1. Universidade de Brasília, Brasília/DF, Brasil.

Abstract

Hemophilia is a rare hematological condition and its treatment is the target of therapeutic innovation. In the meeting between patient needs, clinician conducts and guidance from the health manager, a conflict arises: is the protocol a therapeutic minimum or maximum? Clinical decisions under discussion with the allocation of resources lead to the discussion about equity in such limit situations. The method of the present study is a comprehensive bioethical analysis of 14 legal decisions about the access to hemophilia treatment. Decisions to guarantee access to treatments presuppose ethical link with the patient; the clinic retains a dimension of equity by allowing the treatment to be unique and the doses provided for in the protocol are suggestions and not limits. From an ethical point of view, these are expressions of justice, precaution and consideration of a patient's interests.

Keywords: Rare diseases. Hemophilia A. Bioethics. Equity.

Resumo

Equidade em situações-limite: acesso ao tratamento para pessoas com hemofilia

Hemofilia é uma condição hematológica rara e seu tratamento é alvo de inovação terapêutica. No encontro entre necessidades do paciente, condutas do clínico e orientação do gestor de saúde, surge o conflito: o protocolo é um mínimo ou um máximo terapêutico? As decisões clínicas em debate com a alocação de recursos levam à discussão sobre equidade nessas situações-limite. O método do presente estudo é compreensivo, mediante análise bioética de 14 decisões judiciais acerca do acesso ao tratamento de hemofilia. As decisões de garantia de acesso aos tratamentos pressupõem vinculação ética com o paciente; a clínica conserva uma dimensão de equidade ao permitir que o tratamento seja singular e as doses previstas em protocolo sejam sugestões e não limites. Do ponto de vista ético, estas são expressões de justiça, de precaução e de consideração dos interesses do paciente.

Palavras-chave: Doenças raras. Hemofilia A. Bioética. Equidade.

Resumen

Equidad en situaciones límite: acceso al tratamiento para personas con hemofilia

La hemofilia es un trastorno hematológico raro, cuyo tratamiento es objeto de innovación terapéutica. Ante las necesidades del paciente, la conducta del clínico y la orientación del gestor de salud, surge el conflicto: ¿el protocolo es un mínimo o un máximo terapéutico? Las decisiones clínicas en debate con la asignación de recursos plantean la discusión sobre la equidad en estas situaciones límite. Este estudio se basa en el método comprensivo a través de un análisis bioético de 14 decisiones judiciales sobre el acceso al tratamiento de la hemofilia. Las decisiones para garantizar el acceso a los tratamientos suponen un vínculo ético con el paciente; la clínica mantiene una dimensión de equidad al permitir que el tratamiento sea único y las dosis previstas en el protocolo sean sugerencias y no límites. Desde el punto de vista ético, estas son expresiones de justicia, de precaución y consideración de los intereses del paciente.

Palabras clave: Enfermedades raras. Hemofilia A. Bioética. Equidad.

Research

The authors declare no conflict of interest.

Hemophilia is a genetic, chronic, and rare condition characterized by an alteration in the blood clotting system which generates a permanent risk of spontaneous bleeding [1]. It is treated by clotting factor (CF VIII or CF IX) replacement therapy to prevent bleeding and, cumulatively, sequelae affecting affected people's daily activities and quality of life [2].

The chance of severe bleeding or bleeding in vital organs leads to a permanent need for monitoring. As a result, the daily life of people with hemophilia (PWH) is characterized by the recommendation to comply with certain "physical limits" for the sake of their integrity, urging the adoption of a set of restrictive body techniques, alert strategies (the "aura" of hemorrhage), and self-care rituals [3,4].

People with rare diseases such as hemophilia report long therapeutic itineraries [5]. The journey of the illness and the search for health care establish, to its wanderers, their own language and conduct; lead to expectations about the way of life of those who are diagnosed; prescribe behaviors; institute specific codes and jurisdiction; create communities of peers who seek, in the exchange of their feeling-thinking and experiences, a good life [6]. The life of PWH is permeated with family stories of suffering, social stigma, and injustice [7,8]. Syringes, needles, cryoprecipitates, inhibitors, among so many technical procedures and artifacts, constitute a daily or weekly ritual of clotting factor (CF) application to ensure no bleeding [9].

Over recent decades, hemophilia treatment has comprised from total blood transfusions and CF replacement to the recent possibility of gene therapy [10,11]. The tendency to incorporate therapeutic innovations and changes into clinical protocols for the comprehensive health care of PWH provides peculiar historical and sociotechnical records. That offers the possibility of following part of the biotechnological revolution in health care and an overview of the relation between social movements for the right to health and biotechnoscience.

The symbolic aspects of hemophilia – its relation with blood – and concrete issues of living with this rare hematological condition refer to the need to feel-think – coordinate reasoning and feelings – the process of becoming ill since this is an important and unique aspect of human life. Putting reason and emotion into interaction can help patients to deal with the diagnosis and to process their condition, which sometimes implies being in a solitary existential place. A feeling-thinking approach can provide conditions for patients to be able to give meaning to the processes which reconfigure their body, produce experiences and memories, modify behaviors, and transform social dynamics [12].

Feeling-thinking the diagnosis situates the person between their individual perception of pain and the alterations in their body – including examining the objective determination of the nature of the lesion, and its prognosis and therapy. This process is permeated by subjective and intersubjective apprehensions of the disease either by the individual body or by the social one, and there are good introductions to the subject [12,13]. The focus of this article refers to hemophilia and rare diseases, a diverse set of conditions that have gained prominence due to the complexity of the subject [14,15].

In the case of hemophilia, its rarity and current models of health care reinforce the need to understand how the plurality of organic responses, perceptions, thoughts, feelings, sensations, and emotions in the spaces of interface between caregivers and care affect a possible objective description of itineraries. Bioethical issues concerning access to hemophilia care technologies reinforce the conceptual aspect of boundary – it is a boundary object – that can be felt-thought. The purpose of this article is to apply this conception of feeling-thinking in the analysis of equity in limit situations, particularly about the issue of singular access to preventive drug treatment for PWH.

It is important to understand that prophylactic CF replacement is the standard of care for PWH [16]. According to Ar, Baslar, and Soysal, *current weight-based fixed-dose prophylaxis regimens are effective; however, they lack flexibility and generally fail to meet the patients' individual needs and expectations, and recent developments in hemophilia treatment provide new opportunities for more personalized prophylaxis* [17]. Biotechnological advances have enabled the replacement of blood products with biological drugs but their incorporation into health

systems requires the establishment of standardized protocols whose target is the "average patient," a statistical entity derived from epidemiological measures of the forms of treatment.

Hemophilia treatments have been provided for this "hypothetical average patient," which enables planning and adjustment of the logistics of drug procurement/distribution and financial management by the health system manager. However, in the clinical space, this situation is confronted with the logic of individualized medication administration.

The customization of treatment responds to the direct need of patient, and the estimation of per capita medication doses is linked to the management logics involved in the relations between the State and the market. In this context, at least three perspectives interact: patient needs, clinician conducts, and guidelines for health managers. Thus, a limit situation is created: is the protocol a therapeutic maximum or minimum?

Method

Bioethics is ethics of life and health and it deals with *moral life as it is practiced, not (only) as it is theorized* [18]. As applied ethics, it seeks to solve practical problems in the biomedical, biotechnological, sanitary, social, and environmental fields, in persistent or emerging situations, by considering the elements that constitute a given conflict and by analyzing the assumptions and developments of the decision-making process in that situation. Considering that there is much discussion in the literature about what would be the methodological vocation of bioethics [19-25], this research seeks to harmonize assumptions of empirical bioethics with currents of thought elaborated at the Unesco Chair of Bioethics at the University of Brasília (UnB).

There are three dimensions that need to be achieved in bioethics research [18]:

1. Truthful condition: the research process should try to ensure that the ethical issue under research is genuine and authentic, framed in terms of the way it is lived and negotiated in practice by moral agents, rather than constructed in an abstract manner by a moral theorist;
2. Realistic condition: the research process should try to ensure that the analysis is consistent with the current circumstances in which the moral agents are situated and gives due consideration to factors that may constrain or limit the actions or choices available to the agents;
3. Pragmatic condition: the research process should try to produce conclusions and/or solutions to the normative problems that are sufficiently respectful and that involve the concerns and issues of the interested parties, so they can be accepted and implemented.

The methodological approach proposed here is socially situated and comprehensive, presenting knowledge, elements, perceptions, and assertions based on the proximity and experience of the felt-thought phenomenon. It is a bioethical analysis of situation – not purely casuistic/comparative or based on conscientious objections or particular moral conflicts [26] –, in which the multi-dimensions of the conflict situation are considered, safeguarding an effort of harmonization between ontologies, epistemologies, and theoretical frameworks [18].

The first step of the process refers to identifying the nature of the bioethical issue (emerging or persistent [27]), that is, the feeling-thinking observation of the situation that is put for analysis. At this point, it is assumed that a conflict of interests exists and makes sense, that is, that there is a moral conflict that can be described and for which there are possible answers or propositions (in the case of dilemmas). At this stage, it is necessary to describe the context of the moral issue raised, verifying reality (complex and concrete [28]) and available indicators (social, sanitary, epidemiological, etc.).

The research process respected the fact that discussions in bioethics have an interdisciplinary character. Thus, it was established that the elements that constitute the ethical issue to be investigated are also permeated by this characteristic, that is, they are boundary objects. The subject chosen in this research was access to hemophilia treatment. The descriptors related to bioethics are: 1) in a macrobioethical dimension: social responsibility and health justice; and 2) in a microbioethical dimension: vulnerability, justice – as fairness, assuming a certain untranslatable dimension of this word, which has commonly been understood as equity –,

the rule of rescue, and the principle of non-abandonment. The terms *hemophilia*, *prophylaxis*, *treatment*, and *bioethics* were also searched, in a concatenated manner, in English and Portuguese, in the MEDLINE and SciELO databases.

This stage has a narrative dimension, in which people, groups, institutions, and even objects or artifacts that have agency in the world can be heard. Manchola-Castillo and Garrafa [29] and Manchola Castillo and Solbakk [30] list ways to collect the narrative, and Manchola presents the perspective adopted in this work:

In several of his works, Nussbaum emphasized that narrative elements, at times generated by the Socratic method, can enrich moral judgment, by producing emotions such as empathy and compassion in the agents who decide. According to the author, *these elements can result in richer moral decisions, which take into consideration the various nuances that stories – unlike simple cases or reports – include, namely: settings, times, characters, traditions, feelings, values and various principles* [31].

To listen to other voices involved in the issue of conflicts in access to hemophilia treatment, and understanding that this issue involves the decision-making process in areas of health which transcend clinical practice, it was necessary to conduct this research with institutions focused on that purpose. Thus, we sought another space in which conflict is apparent: the judicial branch. Decisions from local and higher courts were collected, in an initial analysis of the lawsuits in the judicial system (Natjus and website of the National Council of Justice - CNJ), from documents available on the institutions' own websites.

Ordinance 725/2018 [32] of the State Department of Health of the Federal District (SES-DF) can be listed as a normative starting point. Jurisprudential research was also carried out in the database of the Court of Justice of the Federal District and Territories (TJDFT) and in the Federal Regional Court of the 1st Region (TRF1) – district of the DF –, without including the databases of the superior courts, using the keywords *hemophilia*, *medicine*, *medication*, and *supply* in Portuguese. Criminal and social security issues were excluded.

The second step of the analysis corresponds to bringing the possible answers or propositions solve the ethical conflict into the scope of feeling-thinking. *Sentipensamento* [feeling-thought] is a term collected from Colombian folk wisdom by sociologist Borda [33] and by Galeano [34], being echoed by Santos [35] and Moraes and Torre [36]:

In the culture of the Colombian Caribbean, and more specifically in the riverside culture of the Rio Grande de La Magdalena river, which transports its waters to the Atlantic Ocean, the turtle-man who knows how to endure to face setbacks in life and to overcome them, who in adversity withdraws and then returns to existence with the same energy as before, is also the feeling-thinking man who combines reason and love, body and heart, to get rid of all the (bad) *formations that break this harmony and to tell the truth, as described by Eduardo Galeano in* Livro dos Abraços [Book of Hugs], *in honor of the fishermen of the Colombian coast* [33].

This is, therefore, the feeling-thinking-acting integration, an embodied cognitive-emotional process that is in sharp contrast to the abstract and "disembodied detachment" of Cartesian rationalism. In a way, it is a fortuitous convergence between popular wisdom and the new perspectives provided by neurosciences, showing that different epistemologies, in certain circumstances, can coexist and dialogue.

It is about revisiting the narratives and exercising understanding as to the nature of the arguments of the different agents, paying attention to which norms, virtues, principles, and values were evoked in the process. Damásio, for example, states that *we are not thinking machines, we are feeling machines that think* [37]. These thoughts are echoed in texts by other authors [30,38,39].

At this stage, symbolic, technical, political, economic, historical, and social aspects can become vectors of analysis, as they constitute the complex and concrete context in which the moral conflict takes place. It is possible to evoke instruments, regulations, and theories, such as the Universal Declaration on Bioethics and Human Rights (UDBHR), to help organize a possible response to the conflict.

In this process, one should not disregard subjective aspects of the conflict which can affect those involved, such as feelings of injustice, fear, abandonment or non-resignation in relation to the

problem, that is, the false reason-feeling duality is not assumed. Moral reasoning is always implied or situated and involves a balance between moral emotions and reason, even though certain schools of ethical thought insist on a proposal for the exclusive regimentation of reason.

Finally, theoretical elements and arguments are sought by means of which the formulated ethical decision is justified, in articulation with the concrete reality of the world-system, with a certain degree of abstract conceptualization and active experimentation. That will enable verifying whether the ethical evaluations or judgments reached are relevant in resolving the conflict.

Development

Limit situation

In 1976, in his opening speech on a world congress on hemophilia, hematologist Ilsley Ingram stated: *The history of hemophilia shows the human mind trying to define and cover a mysterious and fascinating phenomenon; and, also, the human heart, responding to the challenge of repeated adversities* [40].

These adversities are the limit situations. This is a polysemic concept, but some authors provide clues as to how it is possible to interrelate it with the issue of equity in access to hemophilia treatments. Common sense understands it as situations in which a person undergoes experiences which are different from those resulting from ordinary or commonplace situations. According to Berlinguer, as pointed out by Garrafa [41], biotechnoscientific advances lead to moral issues which are situated on the edges, that is, technological innovations in the biomedical field (emerging situations) challenge certain current conceptions and norms, constituting limit situations.

According to Freire [42], such situations refer to the historical conditions preventing people from having freedom which result in great socioeconomic asymmetries. The term *limit situation* has an existential connotation (death, suffering, struggle, guilt) stemming from certain life circumstances, as pointed out by Thornhill, Miron and Jaspers [43]. Silva, assuming that, *in terms of ethical decision, objective and subjective factors cannot be completely separated*, ponders:

> *The limit situation is always configured by the insufficiency of value, but, again, this insufficiency is not intrinsic to the value itself; it appears when the dramatic singularity of the situation in which the subject is involved leads them to question value, and to see that what value represents in terms of good does not coincide with the* best *choice* [44].

The author emphasizes that, *in terms of ethical decision, objective and subjective factors cannot be completely separated, and that we cannot choose just one of them as the grounds for the options* [44], but it is necessary to reach a third way, pondering *times when many lives are worth the sacrifice of a few; there are times when the sacrifice of a life is not justified by the salvation of many* [44]. Part of the ethical tension involved in the issue in question is related to the above: how the singular situation and the limit that a PWH lives, when trying to access treatment, becomes a conflict of distributive justice and puts identified and statistical lives in opposition [45].

Such perspectives can compose the following panorama of analysis: PWH can benefit from new treatments that have a positive impact on their quality of life but there are clinical, ethical, sanitary, social, and economic conditions and determinants that constitute the complex equation of access to the new medication [46]. Innovation cycles, resulting from biotechnoscientific advances, impose an accelerated pace on interactions between health professionals, patients, and the drug industry, generating expectations of positive effects of new drugs, demands for updated protocols and pressure on health systems, which need to readjust budgets, procurement, and dispensing processes.

In this context, managers tends to consider scarcity of resources and utilitarian metrics – cost-effectiveness, for example [47]. Patients require access to medication not only to avoid sequelae or not to die prematurely, but so they can live with quality until the end of a human life with normal duration.

We should highlight the reasons which bring the issue of quality of life to this discussion. Hemophilia is a genetic-hereditary condition which primarily affects males and, as it is a "blood disease" (with all the symbols implied in this fact), subject affected families to peculiar care dynamics. These dynamics are imposed by the "fear of bleeding," with new limits for boys who, in our society, are required to play "strong" and/or "daredevil" male roles [48,49].

Consequently, a silenced limit is established: boys with hemophilia "should not" play sports and should take care to avoid accidents during free play [3]. This is a limit that can be circumvented by current models of prophylactic treatment, which, however, are expensive.

There is an extensive literature on hemophilia, with books [50] and manuals [51], and this reflection is not focused on thoroughly describing biological events or biomedical approaches to the subject. By means of feeling-thinking, this text was built to discuss a dimension of injustice, which is, first of all, lived and felt. In other words, we intend to discuss a concrete aspect of the conflict between conceptions of justice that can be expressed in the following question: do we only seek to compensate those who are in a disadvantaged situation or do we aim to provide people with the same choices or chances, regardless of their status in the world-system?

There are currently two modes of CF replacement treatment: the first is based on demand and the second is prophylactic [50,51]. On-demand treatment is applied after a bleeding episode, whereas prophylactic treatment is applied in advance.

It seems obvious that adopting an effective prophylactic scheme, using the principle of precaution, would be the ethical choice to make. Thus, primary prophylaxis is a consensus among researchers and organizations in the field of hemophilia studies. Moreover, a study involving Brazil and Canada, for example, shows as its main finding that increasing access to CF concentrates for boys with severe hemophilia is a global imperative [52].

In Brazil, there was the establishment of clinical protocols and therapeutic guidelines (CPTG) for hemophilia treatment [53]. These are structured guidelines containing the best available evidence (efficacy, safety, effectiveness, and cost-effectiveness) for proper diagnoses, recommended treatment, available medicine in the Unified Health System (SUS), and other guidelines to be followed by health managers and professionals. The protocol enables the assignment of technical standards and guidelines to care but we must acknowledge that its character is limited (to the summary of evidence) and temporally restricted.

In 2007, Manco-Johnson and collaborators [54] conducted a clinical trial which showed the protective effect of prophylaxis, especially on joint injuries, a recurrent problem for people with hemophilia. However, this implies higher costs than the on-demand therapeutic regimen, which complicates the entire process of accessing the technology. The authors also point out that the technological transition – from the use of blood-derived CF to the use of recombinant factor – has provided safety to patients haunted by HIV and hepatitis, in the same way that, today, they would be haunted by viruses such as those that cause covid-19, dengue, zika or chikungunya.

Since 2007, the use of recombinant CF for hemophilia treatment has become widespread and, in Brazil, its adoption depends on agreements between the State and companies in the sector. Thus, the Brazilian Ministry of Health, despite numerous difficulties, recognized this possibility by updating – in development after consultation with the community [55] – the clinical protocol and therapeutic guidelines for prophylaxis of severe hemophilia A [53]. However, the PWH community already signals demand for long-lasting recombinant CF with individualized treatment.

The coexistence of four different generations of therapeutic approaches to hemophilia can lead to confusion as to the choices available as it establishes the need to compare them: the first generation (1970s) corresponds to plasma-derived CF; the second generation (1990s) corresponds to recombinant CF; the third generation (2010s) corresponds to long-lasting recombinant CFs; and, currently, there is ongoing research with gene therapies and molecular approaches which are more complex, corresponding to the fourth generation. There are variations between them as to costs, safety, efficacy, and outcomes [56].

This complex situation must be carefully analyzed as it leads to conflict between choices (best treatment option) and values (duties or consequences), that is, between the options for the best treatment or for the best cost-effectiveness estimate, for example. This type of analysis seems to have emerged from the myth of the bed of Procrustes or the allegory of the bed of Sodom and can be translated as follows: must patients adjust to the protocol or must the protocol be adjusted to patients?

However, this analysis cannot be carried out exclusively within a health economics model without considering the diversity of other criteria, including human rights. The literature has already pointed to paths, such as multi-criteria-based decision analysis [57].

In the process of translating knowledge, that is, in its practical application, clinical researchers and managers need to reach consensus on how to apply new knowledge and incorporate new technologies into health systems. The equation for treating hemophilia – even though the goal has always been to treat people... – is expressed in terms of direct and indirect costs, the burden of living with hemophilia (burden of disease), the type of technology (blood-derived or recombinant CF), and the means of access (demand or prophylaxis in their different degrees) [52,58-61].

Having obtained these pieces of information, often produced by evidence summarization strategies, hematologists organize panels to establish goals for the treatment of people with hemophilia. In general, the health system manager is compelled to convert these goals into protocols, from a utilitarian perspective, which optimizes resources and standardizes treatments. Such standardization assigns per capita IU of CF for treatment and estimates per capita treatment costs.

Logically, these calculations are required so as to enable the planning of public procurements or purchases, which, in turn, need to be provided for in a budget. Therefore, a "good manager" is expected to prioritize economy and contain costs since there are frequent complaints of overpricing by the pharmaceutical industry [62]. However, once the drug pricing rounds have been overcome and an average cost per patient and purchase plans have been defined, another question arises: are the doses provided for in the protocol suggestions or limits?

Systematic reviews and meta-analyses, recognized as robust evidence, work with estimates (odds ratio, relative risk, homogeneity/heterogeneity measures, etc.) and, despite being necessary technocratic approaches, are based on controlled conditions [63]. Moreover, these studies, which support the formulation of protocols, are time-limited and the academic world is not stationary. Reviews are retrospective and cover specific time intervals. Therefore, from time to time it is necessary to revise the reviews.

Another important point refers to the outcomes and to the magnitude of the effects of treatments described in the protocols. Again, it is necessary to observe that randomized clinical trials distance the clinician from anecdotal evidence, that is, from everyday impressions about treatments or conducts, which can be biased. However, despite the risk of bias, we must consider that the expression of a genetic condition or disease has singular aspects, whether biological or psychosocial.

According to Greenhalgh, Sackett – one of the fathers of Evidence-Based Medicine (EBM) [64] – argues that, before putting a patient on treatment with a drug, the physician should:

Define the ultimate goal of treatment for this patient (cure, prevention of relapse, limitation of functional disability, prevention of late complications, tranquility, palliative effect, symptom relief, etc.);

Select the most appropriate treatment using all available evidence (which includes assessing whether the patient really needs to take any medication);

Specify the treatment target (how will you know when to stop treatment, change its intensity or switch to another treatment?) [65].

In another excerpt, Greenhalgh reflects:

Thus, while the original protagonists of EBM are sometimes mistakenly presented as having crossed out the poor patient from the script, they were actually very careful to introduce EBM as determined by patient choice (and hence as dependent on clinical reasoning). The "best" treatment is not necessarily that which has been shown to be more effective in randomized clinical trials, but rather that which that best fits a given set of individual circumstances and aligns with the patient's preferences and priorities [66].

These excerpts allow two considerations: 1) treatment must always be singular; and, consequently, 2) the doses provided for in the protocol are suggestions and not limits. Therefore, clinicians must manage the best evidence in the literature and examine it considering the evidence patients show (and clinicians observe) and the preferences patients express. From an ethical

point of view, these are expressions of justice, precaution and consideration of the patient's interests. The therapeutic act is not limited to the technocracy of the dose established in the protocol but depends on the appropriate formulation of a conduct based on the best available evidence which indicates the dosage that will meet the singularity of the case.

Singular access

The choice of treatment presupposes an ethical link with the patient, who accepts treatment as a gesture of trust and necessity. Thus, the clinical decision retains a dimension of equity, in which physicians consider whether they are giving all patients what they need to have their health restored. A clinical action objectively adduced from the protocol will operate with another moral vector, that of equality, that is, everyone will receive the same treatment.

In this case, the same treatment means the denial of the patients' biopsychosocial singularity, without giving any effect to their needs or requirements. Acting within an egalitarian parameter of justice in this type of situation can paradoxically create inequity or increase injustice. Thus, patients who need a higher dose of medication, for being outside the parameters established in the protocol, may find themselves unassisted or insufficiently assisted.

To determine whether the justifications shown above are consistent with the reality of the limit situations for PWH, we searched for the arguments presented in judicial decisions (JD) on hemophilia treatments at the CNJ, TJDFT, and TRF1 – DF district websites. This analysis enabled reflections on singular access in limit situations focusing on the real conflicts brought to the Brazilian courts.

In total, we found 14 JDs (named JD-1 to JD-14) in the Brazilian capital, the focus of this research. Data were arranged with the categorization of arguments available in these documents (from the Government, physician, and magistrates). Of this total, 13 were favorable and one was unfavorable to drug access, the latter being related to a person with severe hemophilia B. As a parameter for data organization, we used the model of Marques [67] with adaptations. We analyzed arguments of representatives of the State, health professionals invited to speak, and judges.

The legal discourse on health in this sample is based on the principles and guidelines of the SUS: universality, equality, comprehensiveness, gratuitousness, community participation, decentralization, regionalization, and hierarchy of health care actions and services [68]. In Moreover, it shows certain elements of Rawlsian influence [69], *the same that states that it is obvious that a concrete society is rarely well-ordered, since "what is fair and what is unfair is usually under dispute* [70].

This dispute comprises some people with real, ordinary lives in extraordinary situations: the experience with a rare disease, imperceptible at first glance, but felt by this extended patient [71] such as the *"child of a tender age who needs treatment to have a dignified life"* (JD01 and JD07).

The reading of the two decisions apparently points to a prophylactic demand for treatment in these cases. However, there is express consensus in all of them from both hematologist specialists and the legal staff: the severity of bleeding events with the possibility of injuries and sequelae compromising health and life.

Biological and human rights arguments are repeated in specialist discourses (medical and legal) to such an extent that there is an argument pattern indicating homogeneity and similarity, but which escapes singularity, prevailing the limit to the detriment of suggestion. In a general view: the State is focused on the cost and availability of treatment; health professionals are focused on clinical outcomes; and, finally, courts are focused on the issue of rights guaranteed by the State. The three discourses are legitimate but conflicting, and are based on different ethical conceptions, which alternate between utilitarianism and deontologism.

It is known that today the system of legal decisions on health relies on the assistance of a technocratic apparatus (Natjus and e-NatJus) which, ultimately, must not accommodate a limited or caricatured view of evidence-based medicine which implies a risk of accentuation of certain characteristics of the ethical-normative frameworks guiding the positions of the parties involved in the conflict. It should be considered that the preparation of opinions by health professionals will serve as expert evidence in the

demands. This means that professionals who issue opinions need to have an adequate and critical view of the use of evidence. This is an incipient but necessary discussion [72].

In the case of hemophilia, treatment aims at a hard outcome – preventing bleeding – and it is necessary to consider that the condition mainly affects boys, who, in Brazil, for cultural reasons, like to run outdoors, climb trees, play soccer, and practice contact sports – and girls can do the same, if they want to. However, boys with hemophilia live contained or indirectly limited lives by the per capita cost of CF, that is, by the limitation of the prescription of rescue doses that they must take when they have bleeding episodes resulting from the "undisciplined imperative" of wanting to play freely, for example.

Thus, they cannot enjoy a full life because they have a disadvantage caused by the biological lottery – since they did not choose to be born with hemophilia – and the social lottery – because they did not choose not to have access to effective treatments. Nevertheless, they are compensated for by treatments that limit bleeding and enable them to live, and current protocols establish the means and dimensions of the biopolitical management of these lives. In a just society, trade-offs are necessary but perhaps insufficient to provide PWH with the same choices or chances, regardless of their status in the world-system.

The prophylaxis currently provided for in the protocols available in the SUS is at a limit and the possible use of blood products is not risk-free. The availability of second-generation CF, which is safer, depends on technology transfer or import agreements, whereas the third-generation CF has high costs but provides gains in terms of quality of life.

In lawsuits, in general, access to the second-generation and third-generation CF is requested due to its qualitative effects and gains. Singular access to CF, that is, according to individual needs and lifestyle, guarantees equal opportunities and the exercise of the capabilities described by Nussbaum, such as bodily health or playful interactions [73].

Currently, there are 13,000 Brazilians affected by hemophilia who can live in relatively good quality, provided they receive treatments planned according to singular therapeutic protocols, in which prophylaxis regimens are implemented with individual pharmacokinetic studies being carried out and with assessment of the reaction of the organism to doses of anticoagulant factor, as new studies have shown [74].

Perhaps it is necessary to recall the perspective of patient-centered care and the set of humanization actions established in the SUS to ensure the singularity of care. However, it is obviously understood that singular treatment cannot be provided to the detriment of the treatment of other groups of people, in the same way that an individual cannot be deprived or abandoned without having received proper care. Nevertheless, it should be noted that this is a false dilemma or a conflict that can be reconfigured in other terms, since it is assumed that, within SUS, all care is comprehensive and access is universal.

Financial resources are finite but the ability to manage health systems can always be optimized to ensure adequate treatment for people. Again, we recognize that this is a difficult discussion and must be taken seriously. Notwithstanding, the purpose of this research is to draw attention to the fact that, invariably, a polarization is established between providing care to a person with a rare disease or disability and the willingness of the State to pay for that, which is hidden in (shallow) arguments of the type "If I give the expensive medicine X to a person, a thousand children will be without vaccines."

To avoid conflicting perspectives, it is necessary to look carefully into the issue of financing treatments for rare diseases by conducting, for example, in-depth theoretical studies based on UDBHR articles or on equity-based approaches [75]. In the collected judicial decisions, the utilitarian argumentation – with its considerations about advantages, disadvantages, risks, costs, and outcomes – has been contrasted with a model that points to pragmatic solutions based on the impact of new drugs on the quality of life of PWH, with more Rawlsian characteristics. In a country that has a universal health system, such as Brazil, but which has persistent inequalities, this discussion is necessary and urgent.

Final considerations

The discussion on equity in limit situations of singular access to preventive drug treatment for PWH has become a constant factor in the courts.

This subject is shared with several rare diseases, which are the target of pharmaceutical innovations based on a logic of personalized and high-cost medicine. To (not) conclude, we return to the three conditions proposed in the methodology:

1. True condition: we present elements of the bioethical issue on the value of a life *versus* the cost of treating a rare genetic condition which – in utilitarian conceptions permeating the economic conjuncture of public health care – is mistakenly framed as the cost of treating one *versus* the cost of treating many. There is the possibility of other ethical-political approaches to the matter, but there is a practical and immediate repercussion, negotiated by moral agents in the courts, which has visible effects on the conditions of access to limit treatment or treatment which ensures quality of life;
2. Realistic condition: the financial resources available for the provision of treatments within a health care system are finite; withal, this same system, if universal and equitable, must guarantee equality of opportunity in access. The guarantee of "the greatest good for the greatest number of people" within the system should not mean providing minimum treatment, but rather, providing the necessary treatment. We can resume the reflection that this system should not only provide offsets to those who are at a disadvantage but also guarantee the same chances to persons regardless of their status;
3. Pragmatic condition: access to (high-cost) medicine is a limit situation which implies a reflection on the value of statistical lives *versus* the value of identified lives. Thus, it is necessary to feel-think about the possible responses or propositions to be presented based on concrete experience, that is, on the regulatory and judicial consequences of the process of access to hemophilia treatment, seeing this subject as a person who should have access to proper treatment which ensures quality of life, not just a borderline life. The opposition of the access of one *versus* the access of many should not be a moral conflict restricted to the physician or the patient but a permanent reflective exercise of the manager who needs to provide the mechanisms for this conflict to be felt less intensely in the most sensitive moral space: that of PWH care. In a heterogeneous country like Brazil, understanding the therapeutic itineraries and the costs involved in the lack of access – that is, knowing how much it costs for the health care system to leave a patient without proper treatment – can be one of the mechanisms to meet the specific demands of patient groups and to mitigate resource allocation conflicts.

We thank the Coordination for the Improvement of Higher Education Personnel (Capes) for supporting this research.

References

1. Blanchette VS, Srivastava A. Definitions in hemophilia: resolved and unresolved issues. Semin Thromb Hemost [Internet]. 2015 [acesso 9 set 2021];41(8):819-25. DOI: 10.1055/s-0035-1564800
2. Timmer MA, Pisters MF, de Kleijn P, de Bie RA, Fischer K, Schutgens RE. Differentiating between signs of intra-articular joint bleeding and chronic arthropathy in haemophilia: a narrative review of the literature. Haemophilia [Internet]. 2015 [acesso 9 set 2021];21(3):289-96. DOI: 10.1111/hae.12667
3. Marques TF. Princípio da autonomia e a atividade física: influência dos profissionais de saúde nas práticas físicas de pessoas com hemofilia [tese] [Internet]. Brasília: Universidade de Brasília; 2018 [acesso 99 set 2021]. Disponível: https://bit.ly/3IlfyYw
4. Blanchette VS, Key NS, Ljung LR, Manco-Johnson MJ, van den Berg HM, Srivastava A. Definitions in hemophilia: communication from the SSC of the ISTH. J Thromb Haemost [Internet]. 2014 [acesso 9 set 2021];12(11):1935-9. DOI: 10.1111/jth.12672
5. Aureliano WA. Trajetórias terapêuticas familiares: doenças raras hereditárias como sofrimento de longa duração. Ciênc Saúde Colet [Internet]. 2018 [acesso 9 set 2021];23(2):369-80. DOI: 10.1590/1413-81232018232.21832017

6. Sulser E. A patient's perspective on hemophilia. Semin Hematol [Internet]. 2006 [acesso 9 set 2021];43(2 supl 3):S13-6. DOI: 10.1053/j.seminhematol.2006.02.005
7. Schramm W. The history of haemophilia: a short review. Thromb Res [Internet]. 2014 [acesso 9 set 2021];134(supl 1):S4-9. DOI: 10.1016/j.thromres.2013.10.020
8. Orsini M. Reframing medical injury? Viewing people with hemophilia as victims of cultural injustice. Soc Leg Stud [Internet]. 2007 [acesso 9 set 2021];16(2):241-58. DOI: 10.1177/0964663907076533
9. Wiedebusch S, Pollmann H, Siegmund B, Muthny FA. Quality of life, psychosocial strains and coping in parents of children with haemophilia. Haemophilia [Internet]. 2008 [acesso 9 set 2021];14(5):1014-22. DOI: 10.1111/j.1365-2516.2008.01803.x
10. Makris M, Hermans C. A golden age for Haemophilia treatment? Haemophilia [Internet]. 2018 [acesso 9 set 2021];24(2):175-6. DOI: 10.1111/hae.13411
11. Batty P, Lillicrap D. Advances and challenges for hemophilia gene therapy. Hum Mol Genet [Internet]. 2019 [acesso 9 set 2021]. DOI: 10.1093/hmg/ddz157
12. Czeresnia D, Maciel EMGS, Oviedo RAM. Os sentidos da saúde e da doença [Internet]. Rio de Janeiro: Editora Fiocruz; 2013 [acesso 9 set 2021]. Disponível: http://books.scielo.org/id/8s5m4
13. Helman CG. Cultura, saúde e doença. 5ª ed. Porto Alegre: Artmed; 2009.
14. Huyard C. How did uncommon disorders become "rare diseases"? History of a boundary object. Sociol Heal Illn [Internet]. 2009 [acesso 9 set 2021];31(4):463-77. DOI: 10.1111/j.1467-9566.2008.01143.x
15. Huyard C. What, if anything, is specific about having a rare disorder? Patients' judgements on being ill and being rare. Heal Expect [Internet]. 2009 [acesso 9 set 2021];12(4):361-70. DOI: 10.1111/j.1369-7625.2009.00552.x
16. Rosendaal FR, Smit C, Briët E. Hemophilia treatment in historical perspective: a review of medical and social developments. Ann Hematol [Internet]. 1991 [acesso 9 set 2021];62(1):5-15. DOI: 10.1007/BF01714977
17. Ar MC, Baslar Z, Soysal T. Personalized prophylaxis in people with hemophilia A: challenges and achievements. Expert Rev Hematol [Internet]. 2016 [acesso 9 set 2021];9(12):1203-8. p. 1203. Tradução livre. DOI: 10.1080/17474086.2016.1252670
18. Ives J, Dunn M, Cribb A, editors. Empirical bioethics: theoretical and practical perspectives. Cambridge: Cambridge University Press; 2016. (Cambridge Bioethics and Law).
19. Davies R, Ives J, Dunn M. A systematic review of empirical bioethics methodologies. BMC Med Ethics [Internet]. 2015 [acesso 9 set 2021];16:15. DOI: 10.1186/s12910-015-0010-3
20. Zeiler K, De Boer M. The empirical and the philosophical in empirical bioethics: time for a conceptual turn. AJOB Empir Bioeth [Internet]. 2020 [acesso 9 set 2021];11(1):11-3. DOI: 10.1080/23294515.2019.1708515
21. Huxtable R, Ives J. Mapping, framing, shaping: a framework for empirical bioethics research projects. BMC Med Ethics [Internet]. 2019 [acesso 9 set 2021];20(1):86. DOI: 10.1186/s12910-019-0428-0
22. Dunn M, Ives J. Methodology, epistemology, and empirical bioethics research: a constructive/ist commentary. Am J Bioeth [Internet]. 2009 [acesso 9 set 2021];9(6-7):93-5. DOI: 10.1080/15265160902874403
23. Ives J. A method of reflexive balancing in a pragmatic, interdisciplinary and reflexive bioethics. Bioethics [Internet]. 2014 [acesso 9 set 2021];28(6):302-12. DOI: 10.1111/bioe.12018
24. Ives J, Draper H. Appropriate methodologies for empirical bioethics: it's all relative. Bioethics [Internet]. 2009 [acesso 9 set 2021];23(4):249-58. DOI: 10.1111/j.1467-8519.2009.01715.x
25. Ives J. "Encounters with experience": empirical bioethics and the future. Heal Care Anal [Internet]. 2008 [acesso 9 set 2021];16(1):1-6. DOI: 10.1007/s10728-007-0077-1
26. Spielthenner G. The casuistic method of practical ethics. Theor Med Bioeth [Internet]. 2016 [acesso 9 set 2021];37(5):417-31. DOI: 10.1007/s11017-016-9382-8
27. Garrafa V. Reflexões bioéticas sobre ciência, saúde e cidadania. Rev. bioét. (Impr.) [Internet]. 1999 [acesso 9 set 2021];7(1):13-20. Disponível: https://bit.ly/36mqaIZ
28. Garrafa V. Multi-inter-transdisciplinaridade, complexidade e totalidade concreta em bioética. In: Garrafa V, Kottow M, Saada A, editores. Bases conceituais da bioética: enfoque latino-americano [Internet]. São Paulo: Gaia; 2006. p. 67-86.

29. Manchola-Castillo C, Garrafa V. De la fundamentación a la intervención: una propuesta metodológica (¡narrativa!) para la Bioética de Intervención. Rev Bras Bioét [Internet]. 2019 [acesso 9 set 2021];15(1):1-18. DOI: 10.26512/rbb.v15.2019.26669

30. Manchola Castillo CH, Solbakk JH. Bioethics and imagination: towards a narrative bioethics committed to social action and justice. Med Humanit [Internet]. 2017 [acesso 9 set 2021];43(3):166-71. DOI: 10.1136/medhum-2016011079

31. Manchola C. Tres apuestas por una bioética práctica. Rev. bioét. (impr.) [Internet]. 2017 [acesso 9 set 2021];25(2):264-74. p. 271. Tradução livre. DOI: 10.1590/1983-80422017252186

32. Distrito Federal. Secretaria de Estado de Saúde. Portaria nº 725, de 5 de julho de 2018. Diário Oficial do Distrito Federal [Internet]. Brasília, nº 133, 2018 [acesso 9 set 2021]. Disponível: https://bit.ly/3we0WYj

33. Borda OF, Moncayo VM. Una sociología sentipensante para América Latina. Bogotá: Siglo del Hombre; 2009. p. 9-19. Tradução livre.

34. Galeano E. O livro dos abraços. 9ª ed. Porto Alegre: L&PM; 2002. p. 64

35. Santos BS. Epistemologías del sur. Utopía Prax Latinoam [Internet]. 2011 [acesso 9 set 2021];16(54):17-39. Disponível: http://hdl.handle.net/10316/42229

36. Moraes MC, Torre S de la. Sentipensar sob o olhar autopoiético: estratégias para reencantar a educação. Petrópolis: Vozes; 2004.

37. Damásio A. What role do emotions play in consciousness? [Internet]. 2010 [acesso 9 set 2021]. Vídeo: 5min49. Disponível: https://youtu.be/Aw2yaozi0Gg

38. Maturana HR, Varela FJ. A árvore do conhecimento: as bases biológicas da compreensão humana. São Paulo: Palas Athena; 2001.

39. Feitosa SF. O processo de territorialização epistemológica da bioética de intervenção: por uma prática bioética libertadora [tese] [Internet]. Brasília: Universidade de Brasília; 2015 [acesso 9 set 2021]. Disponível: https://repositorio.unb.br/handle/10482/18950

40. Ingram GIC. The history of haemophilia. Haemophilia [Internet]. 1997 [acesso 9 set 2021];3(supl 1):5-15. p. 5. Tradução livre. DOI: 10.1111/j.1365-2516.1997.tb00168.x

41. Garrafa V. Bioética cotidiana. Cad Saúde Pública [Internet]. 2005 [acesso 9 set 2021];21(1):333-4. DOI: 10.1590/S0102-311X2005000100038

42. Freire P. Pedagogia do Oprimido. 17ª ed. Rio de Janeiro: Paz e Terra; 1987.

43. Thornhill C, Miron R. Karl Jaspers. In: Zalta EN, editor. The Stanford encyclopedia of philosophy [Internet]. Stanford: Stanford University; 2020 [acesso 15 mar 2022]. Disponível: https://stanford.io/3Jf4KMx

44. Silva FL. Ética e situações-limite. Cult [Internet]. 2010 [acesso 9 set 2021];48-51. Disponível: https://bit.ly/3MVDOnu

45. Cohen IG, Daniels N, Eyal NM. Identified versus statistical lives: an interdisciplinary perspective. Population-level bioethics series. Oxford: Oxford University Press; 2015.

45. Cohen IG, Daniels N, Eyal NM. Identified versus statistical lives: an interdisciplinary perspective. Oxford: Oxford University Press; 2015. (Population-level bioethics series).

46. Petrini P. Identifying and overcoming barriers to prophylaxis in the management of haemophilia. Haemophilia [Internet]. 2007 [acesso 9 set 2021];13(2):16-22. DOI: 10.1111/j.1365-2516.2007.01501.x

47. Miners AH, Lee CA. Setting research priorities to improve cost-effectiveness estimations of primary prophylaxis with clotting factor for people with severe haemophilia. Haemophilia [Internet]. 2004 [acesso 9 set 2021];10(1):58-62. DOI: 10.1111/j.1355-0691.2004.00880.x

48. Kalmar L, Oliffe JL, Currie LM, Jackson S, Gue D. Men, masculinities, and hemophilia. Am J Mens Health [Internet]. 2016 [acesso 9 set 2021];10(6):22-32. DOI: 10.1177/1557988315596362

49. Reinicke K, Sogaard IS, Mentzler S. Masculinity challenges for men with severe hemophilia. Am J Mens Heal [Internet]. 2019 [acesso 9 set 2021];13(4):1557988319872626. DOI: 10.1177/1557988319872626

50. Lee CA, Berntorp EE, Hoots WK. Textbook of hemophilia. 3ª ed. Sussex: Wiley; 2014.

51. Conselho Federal de Enfermagem. Manual de hemofilia [Internet]. 2ª ed. Brasília: Ministério da Saúde; 2015 [acesso 9 set 2021]. Disponível: https://bit.ly/3tcIHk2

52. Carneiro JDA, Blanchette V, Ozelo MC, Antunes S V, Villaca PR, Young NL *et al*. Comparing the burden of illness of haemophilia between resource-constrained and unconstrained countries: the São Paulo-Toronto Hemophilia Study. Haemophilia [Internet]. 2017 [acesso 9 set 2021];23(5):682-8. DOI: 10.1111/hae.13230

53. Brasil. Ministério da Saúde. Protocolo de uso de profilaxia primária para hemofilia grave [Internet]. Portaria nº 364, de 6 de maio de 2014. Aprova o Protocolo de Uso de Profilaxia Primária para Hemofilia Grave. Ministério da Saúde [Internet]. 2014 [acesso 9 set 2021]. Disponível: https://bit.ly/3tdSZAB

54. Manco-Johnson MJ, Abshire TC, Shapiro AD, Riske B, Hacker MR, Kilcoyne R *et al*. Prophylaxis versus episodic treatment to prevent joint disease in boys with severe hemophilia. N Engl J Med [Internet]. 2007 [acesso 9 set 2021];357(6):535-44. DOI: 10.1056/NEJMoa067659

55. Brasil. Ministério da Saúde. Relatório de recomendação: protocolo de uso profilaxia primária para hemofilia grave [Internet]. Brasília: Conitec; 2019 [acesso 9 set 2021]. Disponível: https://bit.ly/3qavjv4

56. Thorat T, Neumann PJ, Chambers JD. Hemophilia burden of disease: a systematic review of the cost-utility literature for hemophilia. J Manag Care Spec Pharm [Internet]. 2018 [acesso 9 set 2021];24(7):632-42. DOI: 10.18553/jmcp.2018.24.7.632

57. Castro Jaramillo HE, Goetghebeur M, Moreno-Mattar O. Testing multi-criteria decision analysis for more transparent resource-allocation decision making in Colombia. Int J Technol Assess Health Care [Internet]. 2016 [acesso 9 set 2021];32(4):307-14. DOI: 10.1017/S0266462316000350

58. Chen SL. Economic costs of hemophilia and the impact of prophylactic treatment on patient management. Am J Manag Care [Internet]. 2016 [acesso 9 set 2021];22(5 supl):s126-33. Disponível: https://bit.ly/3i8dckU

59. O'Hara J, Hughes D, Camp C, Burke T, Carroll L, Diego DAG. The cost of severe haemophilia in Europe: the CHESS study. Orphanet J Rare Dis [Internet]. 2017 [acesso 9 set 2021];12(1):106. DOI: 10.1186/s13023-017-0660-y

60. Pokras SM, Petrilla AA, Weatherall J, Lee WC. The economics of inpatient on-demand treatment for haemophilia with high-responding inhibitors: a US retrospective data analysis. Haemophilia [Internet]. 2012 [acesso 9 set 2021];18(2):284-90. DOI: 10.1111/j.1365-2516.2011.02623.x

61. Siddiqi A-A, Ebrahim SH, Soucie JM, Parker CS, Atrash HK. Burden of disease resulting from hemophilia in the U.S. Am J Prev Med [Internet]. 2010 [acesso 9 set 2021];38(4 supl):S482-8. DOI: 10.1016/j.amepre.2009.12.016

62. Angell M. A verdade sobre os laboratórios farmacêuticos: como somos enganados e o que podemos fazer a respeito. Rio de Janeiro: Record; 2007.

63. Greenhalgh T. How to read a paper: papers that summarise other papers (systematic reviews and meta-analyses). BMJ [Internet]. 1997 [acesso 9 set 2021];13(7109):672-5. Tradução livre. DOI: 10.1136/bmj.315.7109.672

64. Sackett DL, Haynes RB, Tugwell P. Clinical epidemiology: a basic science for clinical medicine. Boston: Little, Brown and Company; 1985.

65. Greenhalgh T. *Como ler artigos científicos*. 5ª ed. Porto Alegre: Artmed; 2015. p. 80-81

66. Greenhalgh T. Op. cit. p. 222

67. Marques SB. O direito ao acesso universal a medicamentos no Brasil: diálogos entre o direito, a política e a técnica [tese] [Internet]. São Paulo: Universidade de São Paulo; 2011 [acesso 9 set 2021]. Disponível: https://bit.ly/3u12h22

68. Paim JS. O que é o SUS [Internet]. Rio de Janeiro: Editora Fiocruz; 2015 [acesso 9 set 2021]. Disponível: https://bit.ly/3KLxZaj

69. Paranhos DGAM, Matias EA, Monsores N, Garrafa V. As teorias da justiça, de John Rawls e Norman Daniels, aplicadas à saúde. Saúde Debate [Internet]. 2018 [acesso 9 set 2021];42(119):1002-11. DOI: 10.1590/0103-1104201811917

70. Rawls J. Uma teoria da justiça. São Paulo: Martins Fontes; 2000. p. 5-6

71. Barbosa RL, Portugal S. O Associativismo faz bem à saúde? O caso das doenças raras. Ciên Saúde Colet [Internet]. 2018 [acesso 9 set 2021];23(2):417-30. DOI: 10.1590/1413-81232018232.24032017

72. Mariano CM, Furtado ET, Albuquerque FB, Pereira FHLCDAS. Diálogos sanitários interinstitucionais e a experiência de implantação do NAT-JUS. Revista de Investigações Constitucionais [Internet]. 2018 [acesso 9 set 2021];5(1):169-88. DOI: 10.5380/rinc.v5i1.56027

73. Dixon R, Nussbaum MC. Children's rights and a capabilities approach: the question of special priority. Cornell Law Rev [Internet]. 2012 [acesso 9 set 2021];97(3):549-94. Disponível: https://bit.ly/3CN6x9k

74. Dargaud Y, Delavenne X, Hart DP, Meunier S, Mismetti P. Individualized PK-based prophylaxis in severe haemophilia. Haemophilia [Internet]. 2018 [acesso 9 set 2021];24(supl 2):3-17. DOI: 10.1111/hae.13397

75. Wagner M, Khoury H, Willet J, Rindress D, Goetghebeur M. Can the EVIDEM framework tackle issues raised by evaluating treatments for rare diseases: analysis of issues and policies, and context-specific adaptation. Pharmacoeconomics [Internet]. 2016 [acesso 9 set 2021];34(3):285-301. DOI: 10.1007/s40273-015-0340-5

Research

Andrea Carolina Lins de Góis – Master – andreaclgois@gmail.com
0000-0002-4482-834X

Daniela Amado Rabelo – Master – daniela.a.rabelo@gmail.com
0000-0003-3725-0858

Tiago Félix Marques – Master – twoalief@gmail.com
0000-0001-5373-3812

Natan Monsores de Sá – PhD – monsores@unb.br
0000-0002-0293-8460

Correspondence
Natan Monsores de Sá –Universidade de Brasília. Faculdade de Ciências da Saúde. Campus Universitário Darcy Ribeiro, sala AC111 CEP 70910-900. Brasília/DF, Brasil.

Participation of the authors
All authors participated in the conception, writing and review of the article.

Received: 6.25.2020
Revised: 1.6.2022
Approved: 3.15.2022