Vulnerability of adolescents in clinical research and practice

Débora de Oliveira Santos¹, Fabíola Alves Gomes², Kely Raspante Teixeira³, Leonardo Roever⁴, Marceila de Andrade Fuzissaki⁵, Tales Faleiros⁶, Taís de Campos Lima³

Abstract

Adolescents are considered vulnerable and exposed to different threats to health group, making it necessary discussion about ethical aspects related to their participation in research and clinical practice. The employed methodology was an integrative literature review and it was selected studies that approached the subject "bioethical matters related to vulnerability of adolescents" within the last fifteen years. Nine articles included the pre-established criteria to the study, grouped into three categories: 1) works that mentioned the psychological-cognitive comprehension of adolescent to participate in scientific research; 2) works emphasizing aspects related to medical decisions; and 3) studies approaching the issue of sexuality in adolescence. The analysis of selected studies found out it is not possible to reach a valid consensus to all situations involving adolescents in research and clinical practice.

Keywords: Health vulnerability. Adolescence. Bioethics.

Resumo

Vulnerabilidade de adolescentes em pesquisa e prática clínica

Os adolescentes são considerados grupo vulnerável e exposto a diferentes ameaças à saúde, tornando-se necessária a discussão sobre aspectos éticos relacionados a sua participação em pesquisa e prática clínica. Por meio de revisão integrativa de literatura foram selecionados estudos que abordaram aspectos bioéticos relacionados à vulnerabilidade de adolescentes nos últimos quinze anos. Nove artigos atenderam aos critérios pré-estabelecidos para o estudo e foram agrupados em três categorias: 1) trabalhos que pontuaram a compreensão psicológica e cognitiva do adolescente ao participar de pesquisa científica; 2) estudos que enfatizaram aspectos relacionados a decisões médicas; e 3) estudos que abordaram a temática da sexualidade na adolescência. Após análise dos estudos selecionados, verificou-se que não é possível chegar a consenso válido para todas as situações que envolvem adolescentes em pesquisa e prática clínica.

Palavras-chave: Vulnerabilidade. Adolescência. Bioética.

Resumen

La vulnerabilidad de los adolescentes en la investigación y en la práctica clínica

Los adolescentes son considerados como grupo vulnerable y expuesto a diferentes amenazas en el ámbito de la salud, por lo cual es necesario que exista un debate sobre los aspectos éticos relacionados con su participación en la investigación y en la práctica clínica. Por medio de una revisión integradora de la literatura, se seleccionaron estudios que abordaban aspectos bioéticos relacionados con la vulnerabilidad de los adolescentes en los últimos quince años. Nueve artículos contemplaban los criterios preestablecidos para el estudio y se agruparon en tres categorías: 1) trabajos que contemplaban la comprensión psicológica y cognitiva del adolescente al participar en la investigación científica; 2) estudios que enfatizaban los aspectos relacionados con las decisiones médicas; y 3) estudios que abordaban la sexualidad en la adolescencia. Después del análisis de los estudios seleccionados, se verificó que no es posible llegar a un consenso válido para todas las situaciones que involucran adolescentes en la investigación y en la práctica clínica.

Palabras clave: Vulnerabilidad. Adolescencia. Bioética.

1. Doutoranda debora_olivsantos@hotmail.com – Universidade Federal de Uberlândia (UFU) 2. Doutoranda fabiolagomes@famed.ufu.br – UFU 3. Doutoranda kelyraspante@gmail.com – UFU 4. Doutorando leonardoroever@hotmail.com – UFU 5. Doutoranda marceila@usp.br – UFU 6. Doutor talesfaleiros@hotmail.com – UFU 7. Mestre taiscampos@yahoo.com.br – UFU, Uberlândia/MG, Brasil.

Correspondência

Leonardo Roever - Av. Pará, 1.720, Umuarama, Caixa Postal 592 CEP 38400-902. Uberlândia/MG, Brasil.

Declaram não haver conflito de interesse.

In the development process of science, production of knowledge that contribute to improve the quality of life of people, the participation of human beings in researches generates different ethical conflicts. Some of them are related to protection against vulnerability of participants of studies and responsibility of health professionals involved in the investigation 1,2. According to Conselho de Organizações Internacionais de Ciências Médicas (Council of International Organization of Medical Sciences), quoted at "European textbook on ethics in research", vulnerable are those relatively (or absolutely) incapable of protecting their own interests³. In other words, it is related to the limited capacity or reduced freedom of deciding about acts of civil life, including consenting and participating of research or adhere to treatment. Thus, discussions about this theme are made by bioethics, so that vulnerable subjects and groups are not susceptible to exploitation 4.

Vulnerability involves three main considerations related to the individual: Lack of competence to protect their own interests; compromising volunteerism of consent; and fragility of physical and psychological condition due to age, disease or incapacity⁵. Thus, an individual can be vulnerable for over one reason, and classify him as vulnerable simply because he belongs to a certain sub population can be a mistake. It happens in different situations with adolescents, who are often excluded from occasions that involve decision making 6-11. Therefore, this work has the purpose of identifying, in both national and international literature, ethical aspects related to vulnerability of adolescents in clinical research and practice.

Method

To conduct this study, it was chosen the method of integrative revision of literature, being followed by some stages. The first of them intended to identify the theme and select the hypothesis or research matter, set out criteria to include and exclude studies, define sampling, outlining the type of information to be extracted from selected studies and categorize them. The second one involved assessment of studies included in integrative revision, and in the third stage the results were interpreted. Finally, the revision/synthesis of acquired knowledge was submitted ¹². To outline the study, it was searched answers to the following main matters: "How is it set out the scientific production about the theme 'bioethics aspects related to

vulnerability of adolescents'?"; "What is the focus given to the theme by current publications?"

The bibliographic survey was made in July 2015. The searches were made in online databases Scientific Eletronic Library Online (SciELO), Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs), Literatura Internacional em Ciências da Saúde (Medline), Science Direct, Web of Science and Highwire Press. The bibliography was based on integration of the following descriptors found in DeCS: "Bioethics"; "adolescent"; and "health vulnerability". The eligibility criteria to inclusion in the sample included studies that approached the proposed theme; had been published from January 2000 to July 2015; had been fully available and in Portuguese or English languages.

The search resulted in five articles at Lilacs, two at Medline, 294 references at Science Direct, one reference at Web of Science, eight articles at Highwire Press and three at SciELO. After reading, nine articles included the eligibility criteria and were selected. It was used an instrument to systematize data, containing title, year and publication type, detailing objectives, methodology, results, discussion, level of evidence and final considerations of works ¹³. Nevertheless, it must be clarified that one of identified limitations in analysis of this study can be attributed to selection and combination of used terms to survey works, considering they considerably limited the set of articles published at researched databases.

In addition to such distortion related to amount and diversity of works produced in scientific literature about the matter another point that must be highlighted about the depth level of analyzed articles, as they exposed ethical aspects in a superficial way. Despite limitations, it cannot be disregarded the importance of this revision of literature, as it raises different ethical aspects related to access to health by adolescents, either on clinical practice or related to research, indicating the necessity of more discussions about the subject.

Results

The selected articles were mostly (67%) written by American authors, especially from the United States. About the publication year, 22% were published in 2004 and most of them were published (78%) within last five years. From selected articles, three of them (33%) came from specific journals of medical ethics, five (56%) from medical journals

and one (11%) from nursing journal. With regard to bioethical matters, it is observed that three of them (33%) approached vulnerability of adolescents to participate in researches, three (33%) mentioned vulnerability aspects of adolescents about medical decisions and three (33%) discussed decision making of adolescents related to sex, reproduction and genre.

Thus, the publications were grouped in categories I, II and III, respectively (Table 1). The articles that are part of category I mentioned the psychological-cognitive comprehension of adolescent in participating of research, highlighting that it is a transition period that must not be simply characterized as a continuous and uniform process, requiring a multidisciplinary approach. Furthermore, it was surveyed the position of parents and responsible people within the context of research with adolescents. Thus, it was listed subjects such as informed consent, autonomy of adolescents to participate in scientific studies and vulnerability ¹³⁻¹⁶.

In this same context, but emphasizing aspects related to medical decisions, some authors of works selected in category II claimed that the autonomy of adolescents, despite relative, is not taken into consideration in different situations. It occurs even when the adolescent is considered competent and capable of making decisions related to family routines and health situations. Moreover, in certain ethical situations involving adolescents it is not possible to make a decision following strict procedures or principles. To effectively answer many ethical dilemmas, it is required to adopt a deliberative and individualized approach ¹⁷⁻¹⁹. Another aspect approached in works analyzed in category II considers that, among changes connected to adolescence, sexuality has a great impact, especially for being the phase of vital cycle when it is consolidated both individuality and sexual choices ²⁰⁻²².

Discussion

Vulnerability of adolescents who participate in researches

In bioethics, children and adolescents are considered a vulnerable group because they are not usually capable of making mature decisions or are subject to authority of somebody else. Moreover, differences between children or adolescents and

their parents can mask an underlying divergence, making their rights and interests become socially devaluated. They can equally have acute medical conditions that require immediate decisions, not consistent with informed knowledge or serious medical conditions that cannot be effectively treated ²³. However, when we talk about vulnerability and adolescence, few things are found and discussed in literature, considering their magnitude and relevance. The survey of publications for this revision can confirm this statement, observing the scarcity of works that approach this subject, especially when it was Brazilian studies ²⁴.

The agreement of child and adolescent for research, diagnosis or treatment purposes is a complex subject and without consensus in literature. The controversies include the definition of what consent is, from which age the investigators must obtain it and who must be involved in obtainment process. It equally includes ways of solving disputes between children or adolescents and their parents, the amount and quality of information that must be provided to children or adolescents and their families and what constitutes an effective, practical and realistic decision making model ²⁵.

Article 5 of Convention on the Rights of the Child, prepared by the United Nations, affirms that responsibilities, rights and duties of parents must be respected in a consistent way with the developing capacities of the child. Moreover, in article 12 of the same document, it is set out that child's opinions must be considered according to his/her age and maturity ²⁶. Pursuant to Guidelines to Research in Health of Adolescent, those with age equal or beyond 14 years old can comprehend the investigation and have cognitive capacity similar to adults to make decisions about participation in research ⁸.

A revision of literature made by Hunfeld and Passchier ¹⁴ concluded that children and adolescents reasonably comprehended the purpose and risks of medical study in which they participated and that their comprehension increased with age. In this regard, some researchers defend that, before requesting the consent of child or adolescent, it is crucial that the investigator understands his/her comprehension level. Moreover, a second relevant aspect to be considered is what the child or adolescent would wish to know, a matter not always taken into account in researches involving this audience ^{14,27}. It must be highlighted that in matters related to vulnerability, the potential to actual and potential benefit and damages is markedly different

when the adolescents are sick or in the hospital. In addition to that, disease has been described as a distinct and extra type of vulnerability ²⁴.

Fortenberry 15 Rosenberger and Ott. conducted a study that assessed the reasons that led parents to authorize the participation of their daughters in a research about sexuality and sexually transmitted diseases. They observed that most parents who considered the participation of their daughters beneficial coincides with the quantity of those who considered them vulnerable to approached situation. On the other hand, parents' authorization can be an important source of problems if those adolescents in risk situation are being systematically excluded because parents deny their participation 28.

Chartier and collaborators ²⁹ intended to examine the participation of adolescents in a program of depression diagnosis at school upon two different procedures to obtain parents' authorization. They found out that a significantly smaller proportion of students participated when parents' informed consent was requested. The authors deduce that it probably occurred a selection problem in this work, as female teenagers and students of public schools had more consent requests signed by third parties, which, consequently, provided them a greater representation in such study ³⁰.

With that in mind, Ruiz-Canela and collaborators 16 defend that waiving an active authorization of parents could be acceptable when the risk of damage is minimum; the investigation matters are related to activities to which adolescents are not legally considered children; the risk of damage or discomfort can increase if it parents' authorization is required; and when the discomfort risk is low because the questionnaire is not potentially offensive to some adolescents and/ or parents. Thus, it can be the moment to suggest a new point of view about such important matter and develop guidelines under which the parents' consent can be waived. Thus, the voluntary participation of adolescents in intervention studies must be object of a broader debate among researchers of health area.

Vulnerability of adolescents and medical decisions

Adolescents are often not followed by their relatives or legal responsible people at the moment of medical decisions, which makes the appointment complex ³¹. In ambulatory services, adolescents are usually instructed by health practitioners to be

followed by an adult. The Ministry of Health ³² does not require the presence of a responsible person with the adolescent in health services, justifying that such presence can embarrass the adolescent and prevent the full exercise of their choices, considering his fundamental right to health and freedom. Although the absence of a responsible person is allowed in health services, the practitioner has to be aware of factors that can increase the vulnerability of this adolescent. For instance, there are situations when there is insufficient communication and bad comprehension by the adolescent, there is risk the patient feels isolated, distrustful and anxious ³³.

The article 103 of Código de Ética Médica (Medical Code of Ethics) (CEM) specifies that adolescents can decide by themselves to make appointments and exams, provided that the practitioner assesses they are able to understand their acts and conduct themselves independently, considering the principle of autonomy 34. Consequently, the practitioners must be aware of standards that assure the rights of their patients, aiming at their best interests 35. To Dickens and Cook 36, if the adolescent shows maturity to decide about the problematic of his health-disease just like adults, he can enjoy the confidentiality and right to treatment according to his wishes. In assistance practice, the doctor must respect the individuality of each adolescent, keeping a nurturing posture, grounded on values of health and well-being of the youth and also respecting the principle of autonomy 37.

If normally the legal right of consent to medical treatment and decisions is in charge of parents or legal responsible of adolescent, the literature registers that there are also many cases when adolescents can provide their own consent 35,38. In case of sexual violence, suspected or confirmed maltreatment against children or adolescents, it is mandatory to register the violence, being required a cooperation with the Child Protective Service 32. The laws also handle related subjects, such as duties of protecting medical confidentiality 39, as confidentiality with adolescents can be something ethically and professionally challenging 31,40. To Michaud and collaborators 17, it is not possible to make decisions following strict procedures or principles, but reflection and common sense must always be present. Thus, it is evident that in clinical practice directed to this audience, there is a necessity of considering ethical aspects and particularities of each situation.

Decision making of adolescents related to sex, reproduction and gender

It is highlighted in this category the matter of gender identity disorder or transsexuality ^{21,22}, characterized as psychiatric disorder where the subject has a divergence of sexual identity and gender with regard to his/her biological gender, being diagnosed in any phase of life ⁴¹.

Some authors approached the requirement of advising and following up the adolescents in this circumstance. It is equally highlighted that a definitive treatment, such as sex reassignment surgery, must be postponed until adulthood (as of 18 years old), because it includes actions that impact future rights of minor and his/her life choices. It is indicated to undergo partially irreversible surgeries, such as feminization treatment (implanting breast prosthesis) or masculinization (mastectomy and hysterectomy) as of 16 years old with parents' consent²¹.

A study with the objective of exploring the matter of adolescent's capacity of consenting health care related to transsexuality was made in Colombia and the United States. The former stood out for having enacted a law that limits the inclusion of parents in medical decision making in those circumstances and the adolescent is considered an active subject of process. It occurs by obtaining qualified consent, which considers the following parameters: Requirement and urgency of procedure; risk and how intrusive the procedure is; age and autonomy degree of child/adolescent ²².

This matter was recently approached in Brazil in ordinances of Ministry of Health. It was started with Ordinance 1.707/2008⁴², which described minimum steps to follow up and human treatment of transgender, as well as it acknowledged the requirement of regulating reassignment procedures by Sistema Único de Saúde (Unified Health System) (SUS). The Ordinance 859/2013⁴³, which extended the access to health care to transgenders, allowing the beginning of hormonal therapy at 16 years old, with authorization of parents and after multidisciplinary follow up, was suspended. Nowadays it is in effect Ordinance 2.803/2013⁴⁴, which regulates the beginning of hormonal therapy as of 18 years old and surgical procedures can be started at 21 years old, provided that there is specific indication and previous follow up for two years in specialized service. It also approached the matter of reassignment procedures on trial basis by SUS.

The Conselho Federal de Medicina (Federal Council of Medicine), upon Resolution 1.955/2010⁴⁵, also discusses the subject and set out minimum conditions to carry out the procedure. Answering the doubt of Defensoria Pública do Estdo de São Paulo (Public Defender's Office of State of São Paulo), the Opinion 8/2013 of such body ⁴⁶ is favorable to hormonal treatment of adolescents of 16 years old, in addition to support the assistance in specialist center with required resources to correct diagnosis and integral attention.

Therefore, it is observed that the discussions and laws about the subject are recent in Brazil and it is identified the necessity of deepen the discussion, considering it is a complex subject that involves different points of view. The discussion has been especially intricate because it approaches two delicate topics: transsexuality and adolescents, in other words, vulnerable subjects due to psychiatric condition and age. Moreover, there is the fact that health care practitioners increasingly face situations like this and need clear guidance and grounded on specific and consistent laws.

Another item that was evident in articles that include the category discussing here was both sexual and reproductive health, specifically the confidential treatment of sexually transmitted diseases (STDs), abortion and contraception 21,22. According to international standards of human rights, adolescents have the right to confidentiality and access to services of sexual and reproductive health, and he can consent the care or not, especially in cases of STDs and pregnancy. Nevertheless, the legislation often considers that adolescents are incapable of making decisions in an autonomous way, thinking it is appropriate the participation of parents and/or legal representatives in the process. It is observed a violation of rights to privacy and self-determination 22.

To Romero and Reingold ²² and Beh and Pietsch ²¹, there are many discussions aiming at the balance between rights of adolescents to make autonomous and confidential decisions related to their health and parents' rights. Those authors also claim that, according to clinical experiences, youths have the capacity of making decisions just like adults. But they warn that laws continue to limit their capacity in different situations related to health care. Consequently, it is identified a dichotomy related to adolescents, as it is expected they are responsible for their acts and lives, but there is no legitimacy of their rights.

Recently, it has been observed an effort by Brazilian government in developing policies that consider them subjects of rights, citizens capable of making responsible decisions in this field. However, it is also identified inconsistency in legislation ⁴⁷. Pursuant to Brazilian Civil Code, the adolescent is of age at 18 years old, an age that is discrepant with the permission to vote as of 16 years old ⁴⁸. The national guidelines of Integral Attention to Health of Adolescents and Youths are grounded on human rights, being children and adolescents acknowledged in those documents as social subjects, bearing their own rights and guarantees, regardless of parents and/or relatives ⁴⁹.

There is also controversy with regard to sexuality. The Estatuto da Criança e do Adolescente (Child and Adolescent Statute) 10 claims that basic rights of health and freedom prevail over any other that may prejudice them. The doctor is allowed to define with the adolescent contraception methods, including emergency contraception, if there are no evidences of sexual abuse. It is also grounded on CEM, when it mentioned that it is the right of patient (...) to freely decide about contraceptive method 50. Pursuant to Código Penal Brasileiro (Brazilian Penal Code) 51, to have a sexual intercourse with minors of 14 years old is a crime of rape, being the violence related to age and, especially, to vulnerability of victim. However, this is discrepant with current social reality, as most adolescents start their sexual activity before this age 47.

Thus, it is observed that there are discrepancies between legal premises and social practices. Considering such disparity, it is crucial that matters related to adolescent sexuality are equated and solved considering the bioethics principles (beneficence, not maleficence), aiming at pleasurable and safe sexuality, respect and confidentiality, provided that it does not cause harm. Finally, another complex and specific theme approached in this category was implanting oocytes and collecting ovarian tissue, intending to restore fertility of adolescents with cancer who underwent different treatments that often culminate in infertility.

Some mentioned ethical considerations were related to safety of procedure. The medications used to stimulate oocytes can increase the seriousness of tumor and postpone chemotherapy and storing oocytes entails risk of chromosomal abnormalities. On the other hand, the risks are justified by benefits of positive psychological effect to the adolescent, who sees, with this technique, a possibility of resurgence of fertility.

It is evident the necessity of more researches and creating policies that approach future rights of patient, about availability of gametes and actions related to it, such as the procedure in case of death ²⁰. Technical matters, such as feasibility of procedures to preserve fertility, are approached in literature ^{52,53} to the detriment of ethical matters. This can be justified by incipience of subject, being many techniques related to it still being tested. Nevertheless, upon discussing ethical aspects related to the subject, this study intends to contribute with the state of art and indicate the necessity of intensifying discussions about it.

Final considerations

This study identified, by means of analysis of scientific literature, three categories about bioethics aspects related to vulnerability of adolescents: With regard to participation in researches, medical decisions and decision making related to sex, reproduction and gender. In this first category, it was evident the necessity of considering the psychologicalcognitive comprehension of adolescent and his autonomy to participate in researches. In the second one, most studies discussed that adolescents, although considered competent and capable of making decisions related to routines in family and health situations, do not have autonomy in situations related to medical decisions. Finally, in the category related to decision making about sex, reproduction and gender, it was identified matters related to gender identity disorder or transsexuality; discrepancies between legal premises and social practices related to sexuality; and aspects related to decision making about different procedures aiming at maintenance of fertility in adolescents with cancer.

It is also observed a lack of consensus and definitive laws that set out accurate criteria about participation of adolescents in research and clinical practice. Each individual and situation is different and require a contextualized approach. Consequently, the health care practitioners, in addition to managers of right, teachers, pedagogues and society in general must encourage the discussion about different aspects related to reflection between respect to autonomy and protection against vulnerability of adolescents, aiming at assuring their rights and strengthen their citizenship.

Referências

- Maders AM. Investigação biomédica e vulnerabilidade: um estudo acerca da responsabilidade dos profissionais da saúde nas pesquisas envolvendo seres humanos. Mundo Saúde. 2014;38(2):228--36
- 2. Barchifontaine CP. Vulnerabilidade e dignidade humana. Mundo Saúde. 2006;30(3):434-40.
- 3. European Commission. European textbook on ethics in research. [Internet]. Brussels: European Commission; 2010 [acesso 15 jul 2015]. p. 51. Disponível: http://bit.ly/2lh9tVP
- Scarpelli AC, Ferreira EF, Zarzar PMPA. Vulnerabilidade socioeconômica versus autonomia na pesquisa em saúde. Rev. bioét. (Impr.). 2007;15(2):298-307.
- 5. European Commission. Op. cit.
- Santos ML, Emmerich A. O consentimento livre e esclarecido e a vulnerabilidade do sujeito de pesquisa. Rev. bioét. (Impr.). 2011;19(2):553-61.
- Lange MM, Rogers W, Dodds S. Vulnerability in research ethics: a way forward. Bioethics. 2013;27(6):333-40.
- Santelli JS, Rogers AS, Rosenfeld WD, Durant RH, Dubler N, Morreale M et al. Guidelines for adolescent health research: a position paper of the Society for Adolescent Medicine. J Adolesc Health. 2003;33(5):396-409.
- 9. World Health Organization. Young people's health: a challenge for society. Geneva: WHO; 1986.
- Brasil. Estatuto da criança e do adolescente: Lei nº 8.069, de 13 de julho de 1990 e legislação correlata. [Internet]. 12ª ed. Brasília: Câmara dos Deputados; 2014 [acesso 15 jul 2015]. Disponível: http://bit.ly/1UTs708
- 11. Eisenstein E. Adolescência: definições, conceitos e critérios. Adolesc Saúde. 2005;2(2):6-7.
- 12. Mendes KDS, Silveira RCCP, Galvão CM. Revisão integrativa: método de pesquisa para a incorporação de evidências na saúde e na enfermagem. Texto Contexto Enferm. 2008;17(4):758-64.
- 13. Ursi ES, Galvão CM. Prevenção de lesões de pele no perioperatório: revisão integrativa da literatura. Rev Latinoam Enferm. 2006;14(1):124-31.
- Hunfeld JAM, Passchier J. Participation in medical research: a systematic review of the understanding and experience of children and adolescents. Patient Educ Couns. 2012;87(3):268-76.
- 15. Ott MA, Rosenberger JG, Fortenberry JD. Parental permission and perceived research benefits in adolescent STI research. J Empir Res Hum Res Ethics. 2010;5(2):57-64.
- Ruiz-Canela M, Lopez-del Burgo C, Carlos S, Calatrava M, Beltramo C, Osorio A et al. Observational research with adolescents: a framework for the management of the parental permission. BMC Med Ethics. 2013:14:2.
- 17. Michaud PA, Berg-Kelly K, Macfarlane A, Benaroyo L. Ethics and adolescent care: an international perspective. Curr Opin Pediatr. 2010;22(4):418-22.
- 18. Bluebond-Langner M, Belasco JB, DeMesquita WM. I want to live, until I don't want to live anymore: involving children with life-threatening and life-shortening illnesses in decision making about care and treatment. Nurs Clin North Am. 2010;45(3):329-43.
- 19. Manson NC. Transitional paternalism: how shared normative powers give rise to the asymmetry of adolescent consent and refusal. Bioethics. 2015;29(2):66-73.
- 20. Dudzinski DM. Ethical issues in fertility preservation for adolescent cancer survivors: oocyte and ovarian tissue cryopreservation. J Pediatr Adolesc Gynecol. 2004;17(2):97-102.
- 21. Beh HG, Pietsch JH. Legal implications surrounding adolescent health care decision-making in matters of sex, reproduction, and gender. Child Adolesc Psychiatr Clin N Am. 2004;13(3):675-94.
- 22. Romero K, Reingold R. Advancing adolescent capacity to consent to transgender-related health care in Colombia and the USA. Reprod Health Matters. 2013;21(41):186-95.
- 23. Kipnis K. Seven vulnerabilities in the pediatric research subject. Theor Med Bioeth. 2003;24(2):107-
- 24. Brasil. Conselho Nacional de Saúde. Resolução nº 466, de 12 de dezembro de 2012. Aprova as diretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos. [Internet]. 2013 [acesso 20 ago 2015]. Disponível: http://bit.ly/20ZpTyq
- Unguru Y, Coppes MJ, Kamani N. Rethinking pediatric assent: from requirement to ideal. Pediatr Clin North Am. 2008;55(1):211-22.
- 26. United Nations. Convention on the rights of the child. [Internet]. Geneva: ONU; 1990 [acesso 15 ago 2015]. Disponível: http://bit.ly/1HthiYh
- 27. Feitosa HN, Ricou M, Rego S, Nunes R. A saúde mental das crianças e dos adolescentes: considerações epidemiológicas, assistenciais e bioéticas. Rev. bioét. (Impr.). 2011;19(1):259-75.
- 28. Rojas NL, Sherrit L, Harris S, Knight JR. The role of parental consent in adolescent substance use research. J Adolesc Health. 2008;42(6):192-7.
- 29. Chartier M, Stoep AV, McCauley E, Herting JR, Tracy M, Lymp J. Passive *versus* active parental permission: implications for the ability of school-based depression screening to reach youth at risk. J Sch Heath. 2008;78(3):157-64.
- 30. Geluda K, Bisaglia JB, Moreira V, Maldonado BM, Cunha AJ, Trajman A. Third-party informed consent in research with adolescents: the good, the bad and the ugly. Soc Sci Med. 2005;61(5):985-8.

- 31. Duncan RE, Hall AC, Knowles A. Ethical dilemmas of confidentiality with adolescent clients: case studies from psychologists. Ethics Behav. 2015;25(3):197-221.
- 32. Brasil. Ministério da Saúde, Secretaria de Atenção à Saúde, Área de Saúde do Adolescente e do Jovem. Marco legal: saúde, um direito de adolescentes. [Internet]. Brasília: Ministério da Saúde; 2007 [acesso 15 ago 2015]. Disponível: http://bit.ly/2lODkCl
- 33. Bates AT, Kearney JA. Understanding death with limited experience in life: dying children's and adolescents' understanding of their own terminal illness and death. Curr Opin Support Palliat Care. 2015;9(1):40-5.
- 34. Conselho Federal de Medicina. Código de ética médica. Resolução CFM nº 1.931, de 17 de setembro de 2009. Brasília: CFM; 2009.
- 35. Diaz A, Neal WP, Nucci AT, Ludmer P, Bitterman J, Edwards S. Legal and ethical issues facing adolescent health care professionals. Mt Sinai J Med. 2014;71(3):181-5.
- 36. Dickens BM, Cook RJ. Adolescents and consent to treatment. Int J Gynaecol Obstet. 2005;89:179-84.
- 37. Gracia D. Fundamentación y enseñanza de la bioética. Santa Fé de Bogotá: El Búho; 1998.
- 38. Scott E, Huntington C. Children's health in a legal framework. The Future of Children. 2015;25(1):177-97.
- 39. Dickens BM, Cook RJ. Law and ethics in conflict over confidentiality? Int J Gynaecol Obstet. 2000;70(3):385-91.
- 40. Cook RJ, Dickens BM, Fathalla MF. Reproductive health and human rights: integrating medicine, ethics and law. Oxford: Oxford University Press; 2003.
- 41. Sousa CA, Ferreira BM, Barros MA. Identidade de gênero: aspectos ético-jurídicos da retificação do registro civil do transexual. Revista Eletrônica de Ciências Jurídicas. [Internet]. 2014[acesso 15 ago 2015];1(1). Disponível: http://bit.ly/2kvRVkO
- 42. Brasil. Ministério da Saúde. Portaria nº 1.707, de 18 de agosto de 2008. Institui, no âmbito do Sistema Único de Saúde (SUS), o Processo Transexualizador, a ser implantado nas unidades federadas, respeitadas as competências das três esferas de gestão. [Internet]. 2008 [acesso 8 ago 2015]. Disponível: http://bit.ly/2lOIH49
- 43. Brasil. Ministério da Saúde. Portaria nº 859, de 30 de julho de 2013. Redefine e amplia o Processo Transexualizador no Sistema Único de Saúde (SUS). [Internet]. 2013 [acesso 15 fev 2017]. Disponível: http://bit.ly/2l6UNH0
- 44. Brasil. Ministério da Saúde. Portaria nº 2.803, de 19 de novembro de 2013. Redefine e amplia o Processo Transexualizador no Sistema Único de Saúde (SUS). [Internet]. 2013 [acesso 8 ago 2015]. Disponível: http://bit.ly/1Bipb2P
- 45. Conselho Federal de Medicina. Resolução CFM nº 1.955, de 12 de agosto de 2010. [Internet]. 2010 [acesso 8 ago 2015]. Disponível: http://bit.ly/2kvU3sU
- 46. Conselho Federal de Medicina. Parecer CFM nº 8, de 22 de fevereiro de 2013. O adolescente com TIG deve ser assistido em centro especializado, de excelência e multiprofissional. [Internet]. 22 fev 2013 [acesso 8 ago 2015]. Disponível: http://bit.ly/2l6JU7Q
- 47. Moreira RM, Teixeira SCR, Teixeira JRB, Camargo CL, Boery RNSO. Adolescência e sexualidade: uma reflexão com enfoque bioético. Adolesc Saúde. 2013;10(3):61-71.
- 48. Brasil. Lei nº 10.406, de 10 de janeiro de 2002. Institui o Código Civil. [Internet]. 2002 [acesso 8 ago 2015]. Disponível: http://bit.ly/1hBawae
- 49. Brasil. Ministério da Saúde. Diretrizes nacionais para a atenção integral à saúde de adolescentes e jovens na promoção, proteção e recuperação da saúde. [Internet]. Brasília: Ministério da Saúde; 2010 [acesso 15 fev 2017]. p. 64. Disponível: http://bit.ly/1cUN6h9
- 50. Conselho Federal de Medicina; 2009. Op. cit. Art. 42.
- 51. Brasil. Decreto-lei nº 2.848, de 7 de dezembro de 1940. Código Penal. 1940 [acesso 20 dez 2016]. Disponível: http://bit.ly/2kZslzx
- 52. Castellotti DS, Cambiaghi AS. Preservação da fertilidade em pacientes com câncer. Rev Bras Hematol Hemoter. 2008;30(5):406-10.
- 53. Resende E, Ferreira M, Sá M, Abreu S. Protocolo de seguimento e revisão da literatura: sequelas endócrinas em longo prazo após tratamento de doença oncológica na idade pediátrica. Rev Port Endocrinol Diabetes Metab. 2015;10(2):175-81.

Participação dos autores

Todos os autores conceberam e planejaram o trabalho conjuntamente. Sistematizaram e analisaram resultados e redigiram e revisaram o texto.



Attachment

Table 1. Characteristics of studies included in revision about vulnerability of adolescents related to research, medical decisions and decision making related to sex, reproduction and gender.

Author, year, category and study outline	Results/considerations
Hunfeld, Passchier; 2012 ¹⁴ Category I Literature revision	Assessment through systematic revision of level of knowledge and comprehension of children and adolescents about the research they participated. It was assessed the comprehension about purpose of study and emotional and psychological aspects. In general, the comprehension of purpose of study was reasonable and understanding increased with age. The investigation about experience of emotional load was scarce, but it was observed that whenever researches involved intrusive procedures related to sexual development, the emotional load was heavier. Only one study assessed the psychological risks.
Ott, Rosenberger, Fortenberry; 2010 ¹⁵ Category I Qualitative study	A survey among parents of adolescents about their conception of benefits of participation of their children or legal dependents in a study about sexuality. The parents reported as main benefit the scientific relevance, familiarity relationships with the team (connection) and autonomy of adolescent. Other reasons included altruism and payments.
Ruiz-Canela and collaborators; 2013 ¹⁶ Category I Literature revision	The authors intended to critically assess different factors that could be taken into account in decision making about waiving the active authorization of parents in observational investigation with adolescents. They defend that waiving an active authorization of parents could be acceptable when the risk of damage is minimum; the investigation matters are related to activities to which adolescents are not legally considered children; the risk of damage or discomfort can increase if it parents' authorization is required; and when the discomfort risk is low because the questionnaire is not potentially offensive to some adolescents and/or parents.
Michaud and collaborators; 2010 ¹⁷ Category II Literature revision	The concepts outlined in the article show that in ethical situations involving adolescents it is not possible to make a decision following strict procedures or principles, but reflection and common sense must always be present. Each person and situation is different and it is required a deliberative approach to face ethical dilemmas in health care of adolescents. The deliberative approach is a contextualized and prudent process that prevent anyone from immediately go to "obvious answers and conclusions", very based on personal, emotional and biased opinions. Instead, it is the careful assessment of role of all moral values and their relative priorities that are incorporated in each term of decision, especially in situations when there is a great conflict between different values.
Bluebond-Langner and collaborators; 2010 18 Category II Experience report	Basic premise in involvement of individuals in decision making related to health care is that they must comprehend risks, benefits and likely results. If the involved people are children, the matter is if they get to understand the options. Some practitioners use the age and development stage of child as criteria, but the development of individuals does not occur in a uniform way and age does not necessarily predict the knowledge degree of a child. Their experiences with disease have a more important role in their comprehension. Another important factor is the interaction between adults and children. The expectations of one often interfere in those of the other one, such as when children believe they must continue with the treatment because they do not want to disappoint their parents. Another point in focus is that children are not autonomous beings, in other words, any approach that involve the perspective of children in decision making must take into account the perspective of parents, as they have both legal and moral responsibility to take care of their children. But it is important to involve children in decision making about their care, allowing them to speak and listening to them.

Author, year, category and study outline	Results/considerations
Manson; 2015 ¹⁹ Category II Literature revision	The article questions that in many jurisdictions adolescents have the right of consenting the clinical treatment, but do not have the right to refuse. Thus, there is an asymmetry between consent and refusal. The asymmetry exists because, in some cases, the refusal of treatment represents a serious risk, even of death. Therefore, some scholars have been in favor of requiring a greater competence level than the one set out when the risks are low.
Dudzinski; 2004 ²⁰ Category II Normative ethic analysis	The article considers that implanting oocytes and collecting ovarian tissue, intending to restore fertility of adolescents who survive cancer is promising. However, it is discussed the necessity of more researches before adolescents being enrolled in clinical tests in an ethic way. It reflects it must be assured that the intervention does not harm the patient, does not delay the treatment of cancer and assure the informed consent of adolescent patients and informed consent of their parents or tutors. It also discusses the necessity of developing policies about future rights of patient to protect their gametes and policies that aim at the disposal of those gametes in case of death. Furthermore, it claims the necessity of policies that protect the patient from harm and assure their right to self-determination.
Beh, Pietsch; 2004 ²¹ Category III Literature revision	The article discusses the existence of conflicts between interests of children and parents or responsible people, of community or society in different aspects, being controversial, especially when it handles sex, reproduction and gender. Thus, the practitioner must always analyze the necessity of judicial approval or consider cases when the interest of State and child can replace the authority of parents.
Romero, Reingold; 2013 ²² Category III Literature revision	The article discusses the slowness of Courts of Colombia and the United States in enacting legislations that explicitly protect the decisions of transsexual adolescents, about aspects related to their sexuality. The author highlights the decision of courts in Colombia, where the jurisprudence limits the capacity of parents to make medical decisions related to gender in the name of their transgender children.