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Ethical issues in longitudinal studies: the case of ELSA-Brasil

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ABSTRACT

The debate about ethics in research with human beings has historically emphasized experimental studies because of their greater potential to harm the subjects involved. However, observational studies also include risks and relevant questions to be discussed. This article aims to present and discuss the ethical aspects involved in the implementation of ELSA-Brasil (Brazilian Longitudinal Study for Adult Health), a longitudinal multicenter study, with public funding, in which the research subjects and investigators are employees of the same institutions. The procedures adopted to meet the ethical requirements and commitments are described, as well as the casuistics that guided the actions according to their guiding principles (beneficence, autonomy and social justice). We present some moral problems that required consideration of risks and benefits at the confluence with the study's objectives, and we conclude with comments on the peculiarities and the potential benefits of a longitudinal study.

DESCRIPTORS: Ethics, Research. Epidemiologic Research Design. Multicenter Studies as Topic, ethics. Cohort Studies. Longitudinal Studies.

INTRODUCTION

The debate about ethics in research with human beings has historically emphasized experimental studies because of their greater potential to harm the subjects involved. However, observational studies also include potential risks and relevant questions to be discussed.[3]

Research involving human beings is crucial to the generation of new knowledge that improves their health. However, it must be regulated to assure that its benefits exceed possible risks to the research's subjects. In recent decades, the recognition of the social importance of epidemiological research has increased, and it has been accompanied by the development of the understanding of the ethical aspects in this field.[8,9]

In Brazil, until the 1980s, the regulation of research with human beings focused exclusively on clinical trials by means of medical ethics committees in university hospitals. In the 1990s, the ethical regulation system of health research was structured in Brazil, and its main normative instrument is Resolution 196/96 – Research Involving Human Beings.[a] It is based on international documents, on the 1988 Federal Constitution and on the correlated Brazilian legislation, aiming to ensure that the ethical principles of respect for the person, autonomy, beneficence and justice are considered in all the development stages of the studies.

This article aimed to discuss the ethical aspects involved in the implementation of *Estudo Longitudinal de Saúde do Adulto* (ELSA-Brasil – Brazilian Longitudinal Study for Adult Health), with public funding, in which the research subjects and investigators are employees of the same institutions. The procedures adopted to meet the ethical requirements and commitments are described. Then, the casuistics that guided the actions according to its guiding principles is described. Moral problems that required consideration of risks and benefits at the confluence with the study's objectives are presented, and we conclude with comments on the peculiarities and the potential benefits of a longitudinal study.

ELSA-BRASIL: A LONGITUDINAL AND MULTICENTER STUDY

ELSA-Brasil is a cohort study of 15,105 men and women aged 35 to 74 years, civil servants of six teaching and research institutions located at different regions of Brazil. The protocol for data production included interviews, measurements and examinations, besides the storage of biological material.[1] The baseline study was carried out between 2008 and 2010. The research subjects are contacted by telephone on an annual basis, and they are invited, every three years, to perform new interviews and examinations in face-to-face contacts, in order to follow up their health status and to monitor outcomes. Potential outcomes are investigated for confirmation, and it is necessary to access health records.

The study protocol complied with Resolution 196/96 [a] and with other complementary ones − Resolution CNS 346/05, Multicenter Projects, and Resolution CNS 347/05, Storage of biological materials. It was approved by the research ethics committees of the institutions involved and by the *Comissão Nacional de Ética em Pesquisa* (CONEP – National Research Ethics Committee) of the National Health Council. This process began in May 2006 and lasted a little less than five months (with an average duration of 36 days at each center) until the final approval.

The Ethics, Recruitment and Social Communication Committee was created. This committee assists the coordination in complying with the ethical and communication aspects in relation to the institutions involved in the study and to the cohort participants. In addition, it provides subsidies regarding how to disseminate the results so as to ensure confidentiality, secrecy and subjects' protection against stigmatization. This committee was responsible for the consolidation of the protocol and of the *Termo de Consentimento Livre e Esclarecido* (TCLE – informed consent document), as well as of the Recruitment and Enrollment Manual.

RIGHT TO AUTONOMY AND INFORMED CONSENT

Respect for autonomy is the ethical principle evoked to justify the requirement of the informed consent.[3,14,22] The autonomous choice presupposes the capacity of voluntary decision, i.e., free from coercion or manipulation by third parties, and sufficient and understandable information to support it.[14,22] The informed consent creates the opportunity for research subjects to consider, according to their perceptions, the risks and potential benefits of the research, thus contributing to reduce potential damages.[14,22]

Subjects should understand procedures, risks, discomforts, benefits and rights involved in their participation in the research.[11] However, some studies have shown limited knowledge about the research among individuals that had consented to participate,[13] which may be due to the research subjects' conscious choice to disregard information, or to failures in the communication process.[13] For communication to be effective, it is necessary to adopt a model that values both the

[a] Ministério da Saúde, Conselho Nacional de Saúde, Comissão Nacional de Ética em Pesquisa. Normas de pesquisa envolvendo seres humanos - Res. CNS 196/96. *Bioética*. 1996;4(2 Supl):11.

transmitted content and the speech act, that is, how the actors involved in the communication act transmit proposals, understand them and respond to them.[16]

Including in the TCLE all the relevant aspects in a way that is clear enough to be understood by a varied audience is always challenging. At the same time, it is desirable that the reading of the document is not tiresome, as part of its content is transmitted when the research is introduced to the eligible person.

ELSA-Brasil has great complexity, with interviews, measurements, and examinations, storage of biological material and requirement of access to secondary health data. This made the preparation of the TCLE become particularly difficult and required many discussion rounds, with the assistance of communication experts. Many pre-tests were carried out in the six centers, with outsourced employees whose profile of age, sex and level of schooling was similar to that of the ELSA-Brasil population, until all the comprehension problems had been solved and the best form to present the study and its ethical aspects had been achieved.

With this process, the aim was to achieve a clear and objective product, whose content included: introduction of the study, objectives, institutions involved, participation in the study, storage of biological material, and participants' rights. These rights comprise: not answering questions during the interviews, refusing to be submitted to examinations, asking for the substitution of the interviewer or stop participating in the research at any moment. However, minimum criteria of participation in the cohort were established and these included answering specific blocks of the questionnaire, electrocardiogram, blood sample collection and blood pressure measurement. If a person refused to perform any of these, he/she was informed that he/she could not participate in the study.

Sources of secondary health data have been increasingly used in research studies. The sensitive nature of the information raises questions related to respect for the subjects' privacy and autonomy. In this context, the requirement of consent to use identified secondary data has been a hotly debated topic.[15,18,22]

Subjects' consent to access functional and health records has been considered a fundamental condition to participate in the study, as this information is essential to investigate the outcomes[2] and, consequently, to fulfill the objectives of a longitudinal study. Therefore, the following sentence was included in the document's final statement, after the general agreement with the conditions to participate in the study:

"I state that I authorize the researchers of the Brazilian Longitudinal Study for Adult Health – ELSA-Brasil, to obtain information on my health history from health institutions, medical records at outpatient clinics, emergency services and/or hospitals, according to the specific situation."

The consent to store biological material, in turn, was considered optional, even though the researchers committed to obtain new authorizations for the future performance of genetic examinations. This motivated the inclusion of a specific space for the formal authorization, with the individual's signature:

"I state that I agree that blood samples are stored for future analyzes about the diseases being investigated in the study."

☐ Yes ☐ No

During the recruitment and constitution of the cohort, the research subjects were individually informed and expressed their agreement about reading and signing the TCLE. The participants could take this document home, to read it in detail and consult people he/she trusted, ensuring their comprehension and full agreement with its content.

Besides the individual contact, information about the study was broadly disseminated by means of printed materials, websites and in collective activities. Goldim et al,[11] using empirical data, suggest that the collective transmission of information can be effective in the recollection of information that is necessary to the informed consent.

At the beginning of the study, a broad dissemination was carried out to ensure the right to participate of potentially eligible individuals. The aim was to clearly explain the eligibility criteria – age limits and formal employment at the teaching institutions – and the sampling goals, as not everybody that enrolled would be summoned to participate. In spite of this, after the goals had been achieved, in all the centers, it was attempted to summon all the enrolled individuals, exceeding the sampling goals that had been previously established.

Indications of potential volunteers by superiors were avoided, so as to ensure free decision and that the employees were not pressured by their bosses to participate in the study.

The right to information is guaranteed by a permanent policy of social communication, with production of printed materials, the updated maintenance of a page in the internet[b] and information in the institutional websites. Thus, research subjects have access to all the explanations they need, whenever necessary and at any time.

[b] ELSA-Brasil [cited 5 oct 2011]. Disponível em: www.elsa.org.br

PRESERVATION OF THE CONFORT AND SECURITY OF THE RESEARCH SUBJECTS

Every research involves some degree of risk of physical, psychological, social or economic damage. Observational studies have fewer risks, but they can cause physical and psychological discomfort, which should be avoided or minimized. Risks in epidemiological studies are, generally speaking, lower than in other areas of biomedicine.[3] However, failures in data protection at workplaces can, for example, cause damage through the stigmatization of subjects.

In the ELSA-Brasil, human and material resources were guaranteed in order to maintain the comfort of research subjects, starting with the premises. Care was taken in relation to people with disabilities, concerning accessibility (for example, wheelchair users), staff training (interviews with individuals with hearing losses), and the production of informative material in Braille.

One of the initial challenges was to establish the profile of the operational team due to the institutional bond shared by the main researchers and the research subjects. The *Comitê de Ética em Pesquisa* (CEP – Research Ethics Committee) of the *Instituto de Saúde Coletiva* of *Universidade Federal da Bahia* recommended that students and ex-students could not interview or examine teachers and technicians of their courses of origin and that the field teams could not include employees from the same institution. These recommendations were followed in all the centers, thus avoiding that acquaintances were involved in interviews and examinations, which might cause embarrassments. There was the possibility of substituting the interviewer in cases in which he/she was already acquainted with the person he/she was going to interview.

During the training of the team, the ethical aspects were emphasized and simulations of the application of the TCLE were performed, in order to minimize damages and embarrassments in the interviews and examinations. On this occasion, it was especially emphasized that the team members should adopt a posture of respect for cultural, moral, and religious values, and to habits and customs.

Care was taken to minimize the discomfort generated by venipucture and the intake of dextrose (a substance used in the glucose tolerance test), including team selection and training, comfortable premises and the distribution of these examinations in the data production flowchart during the visit.

Problems identified during the permanence at the Investigation Center that required urgency-emergency care had their assistance assured at a unit that had been previously specified.

Preservation of confidentiality and secrecy

The guarantee of data confidentiality is a crucial aspect of protection of research subjects' privacy due to the risk that third parties access personal information and the consequent possibility of stigmatization and social or economic losses.[3,9] Ensuring confidentiality is essential in epidemiological studies because of the very large number of participants, large teams and the production of a huge amount of data of a private nature.[3] In studies of this type, privacy protection is essentially a question of protection of confidential information about the person.[3]

During the training of the team, the need to respect the research subjects' privacy was emphasized, as well as the necessity of confidentiality of the collected information and of compliance with the norms aiming at data security.[4,17] In the present study, in which subjects and researchers are employed in the same institutions, special care was taken to avoid the direct access of colleagues from the team to private information about the research subjects.

Data production was performed in soundproof rooms. All the information obtained with interviews and examinations is stored without nominal identification, only through a numerical code. The biological samples are identified by means of barcodes.

Only a restricted group of researchers has access to the information obtained in confidence or, exceptionally, health professionals who provide urgency/emergency care for clinical complications detected during the examinations, upon the subjects' authorization. Access is not allowed, under any circumstance, to employers or superiors, and the information is used exclusively for the purpose of scientific research, without nominal identification.

The team members are forbidden to make any comments about the interviews' content or the examinations' results, which can only be discussed with the field supervision to clarify doubts.

The data system of ELSA-Brasil includes routines that aim to preserve data secrecy and security and guarantee information integrity. The system has the following features: use of a safe connection (HTTPS), access to the system is restricted to registered users with passwords, specific profiles of access according to distinct functionalities, use register system, and timeout after a period without interaction. The participants' personal identifiers are stored separately from the system's other data.

The databases are stored by the Datacenter of ELSA-Brasil in servers of the *Centro de Processamento de Dados* (CPD – Data Processing Center) of *Universidade Federal do Rio Grande do Sul* and they can be accessed

only by machines authorized by the CPD itself. Data extraction from the system to generate bases for analysis is performed only by users with permission.

Data processing is performed without personal identifiers and the same occurs with database distribution. The identification numbers on the bases distributed to the researchers are different from those used in data collection. Security copies of the system's base are encrypted. The bases distributed by the Internet, e-mail or DVD are protected by passwords.

All the teams' members and users of the system and of the databases sign a document in which they commit to data confidentiality.

UNFORESEEN AND ETHICALLY RELEVANT SITUATIONS: THE CASUISTICS OF ELSA-BRASIL

The main argument that justifies epidemiological research is that its social benefits are substantial and overcome possible risks of physical, psychological or social damage.[8]

ELSA-Brasil is a solid research, constructed in successive stages of peer review, conducted by researchers who have a tradition in scientific investigation, to generate nationwide scientific knowledge about the health of adult populations.

The research subjects have, as an immediate benefit, access to results of measurements and examinations that are useful in clinical assessments. They are informed about incidental diagnoses,[23] with guidance and referral to the adequate assistance within what is offered by the institutions and by the *Sistema Único de Saúde* (SUS – Brazilian Unified Health System). Despite the existence of a protocol for the most common findings, the implications and circumstances in which they must be directly communicated to the research subjects have been the object of permanent debate in the study. A great ethical challenge involves the need to deal with the clinical findings that are relevant to the health or reproduction of the researched subject.[23]

Besides immediate benefits, a strong motivation for the participants' adherence, which had been previously identified in focal groups and confirmed by explicit statements at the end of interviews and examinations, was the opportunity to contribute to the generation of new knowledge about health in Brazil. These results are in accordance with studies carried out in the United States that show that the majority of the North Americans value health research and would accept an invitation to participate in clinical studies.[18]

However, preliminary discussions about the ethical questions that surround the study, although careful and exhaustive, do not foresee all the situations that arise as the fieldwork develops. Based on such a presupposition, we tried to enhance, during the teams' periodical discussions, an adequate rationality to the best actions (or omissions) concerning the ethical challenges that emerged all the time.

Based on intra-teams debates and reflections, it was possible to develop an appropriate casuistics to the decisions. It is important to emphasize that, unlike the meaning attributed when used by physicians, "casuistics" – as it is presented here – is not limited to learning through isolated experiences of an experienced professional in order to make a prescription of precepts. The intention was to articulate the universality of a norm with the particularity of an action.[7]

According to precepts that are common both to moral philosophy and to juridical sciences,[20] "casuistics" refers to the rationalization of unforeseen events and the recognition of the inescapable weight of contingencies. The challenge in the ethical evaluation of a study like ELSA-Brasil is not limited to fitting it into the analysis matrixes that are already consecrated and duly regulated. The statements based on philosophic precepts that involve a poor understanding of the essential distinction between ethics and morals, taken as principles, are more similar to action rules[19] and perhaps do not explain fully the questions raised by studies in their methodological particularities. The genuine challenge would concentrate, therefore, on the understanding that each peculiar situation that emerges requires the identification of new questions to debate. Therefore, ethical sensitivity is needed to identify and answer them with the most informed interventions.[10]

In view of these considerations, some examples of emblematic situations were selected (Table), duly included in ethical contexts that are briefly explained, based on which we attempted to extract guiding principles that are more adequate to the peculiarities. The discussion about the casuistics and ethics of situations surpasses the dimensions of the format in which it is inserted. In spite of this, the aim of the present article is to describe a process and the derived debates about the "ethical sensibility"[10] that supports the study. The imperative of editorial limitations restricts spaces that are minimally sufficient to such discussions, which will unfold into more adequate formats, in due time.

SPECIFICITIES OF LONGITUDINAL STUDIES: FINAL COMMENTS

Longitudinal studies constitute the ideal non-experimental design to detect cause and effect associations, to understand the etiopathogenesis of chronic diseases and, consequently, to propose prevention and control measures, improve diagnostic criteria and treatment protocols.

Table. Casuistics of unpredicted events, their contexts and the actions taken.

Facts	Ethical Context Considered	Resolution
Many participants used to go to the Investigation Center to ask for medical consultations or opinions related to past clinical situations.	ELSA-Brasil was subsidized by public fostering agencies to produce research. The complete assistance support would be redundant, in view of what is offered by the institutions, and it would require a much more complex structure. In addition, it would make costs become prohibitive. The principle of "Social Justice" (which guides the project) antecedes the principle of individual Beneficence (provided that it is not an urgency situation).	After the results of the examinations, the doctors involved in the study only instructed the individuals about the need (or not) of consultations with specialists or gave them any other kind of support related to the problem.
Some participants refused to submit to certain examinations or to be interviewed. Others refused to provide blood samples for storage.	ELSA-BRASIL complies with a protocol that aims to obtain, from each participant, measurements and information that are sufficient to the project's objectives. If the participant refused or could not offer a "minimum set" of information, his/her contribution could not be include in the project. Again, the principle of Social Justice (which guides the project) antecedes the principle of individual Beneficence in such cases.	The study could not have the participation of individuals who refused (or were not able) to submit to the "minimum set" of examinations Such interdiction does NOT apply to refusal to provide biological material for storage.
Examination results raised doubts and anxiety because of information that was not clinically contextualized (generally obtained through the internet or third parties).	The principle of "non-maleficence", in view of information that generates anxiety, implies responsibility for the full clarification of the released results.	All the doubts were directly and fully clarified by the doctors involved in the project.
In some cases, the deadline established to release results was not met, mainly because of technical and logistic difficulties.	The omission of information concerning the nature of delays might be considered as maleficence – some participants, perhaps symptomatic, might be waiting for the results to consult their doctors.	The contingencies that generated delays were explained to the participants. The limitations deriving from the project's structure, which is multicenter and not targeted at providing care, were also clarified. The participants who were symptomatic, but duly informed, could perform updated examinations outside the ELSA-Brasil.
The results of some examinations informed severe conditions (uremia, myocardial ischemia that was still unknown, severe anemia) which, if not informed immediately, would expose the participants to risks of severe complications.	In this case, the principle of non-maleficence – related to omission concerning the participant's health status – anteceded the privacy and confidentiality related to the principle of autonomy.	The alarm conditions were previously stipulated. Upon arriving at the Investigation Center, the set of examinations was assessed by the doctors, who contacted the participants directly and immediately to guide them about their problems.
Participants who confided suicide ideation (identified by the CIS-R questionnaire) would need immediate psychiatric support.	The confidentiality of the interview should be overruled. The principle of non-maleficence – related to omission – antecedes privacy and confidentiality, which are related to the autonomy principle.	The specialists instructed the team on how to recognize the most urgent cases, which would require immediate psychiatric support. Such support was immediately contacted whenever necessary.
Electrocardiographic changes were identified in some participants, suggesting a disease with risk of sudden death. They should be immediately referred to the cardiac support, breaking the process' confidentiality.	Likewise, individual beneficence and security antecede privacy and confidentiality.	The technicians were trained to recognize such changes and immediately contacted the cardiologist who supported the Investigation Center, so that he guided the participant and the team itself.

Continue

Continuation

Facts	Ethical Context Considered	Resolution
The complete list of examinations and measurements was previously provided for the participants. Only the results of measurements that were useful to clinical assessment were handed. The "experimental" measurements, which have not been consecrated by clinical practice yet, were not handed to everybody. Some participants demanded integral access to all examinations.	Full access to examination results (related to beneficence and autonomy), even those that are not used in clinical practice yet (without evident normal ranges and, therefore, without evident correlation with pathological conditions) might generate doubts among participants, as well as among their doctors. It was decided that non-maleficence anteceded autonomy in this context.	Whenever requested, the measurements that were not used in clinical practice were handed – which would comply with the principle of autonomy. Supplementary explanations were also provided, which could avoid the maleficence derived from doubts between participants and their doctors.

CIS-R: Clinical Interview Schedule – Revised

Both data production and analysis have a continuous nature, and some future analyses cannot be anticipated. In this way, it is necessary to perform a constant evaluation of the pertinence of the repeated obtention of informed consent for new examinations, measurements and interviews.

The main challenge of maintaining the participants' adherence and minimizing losses over time brings with it the need of ethical and methodological decisions that are deeply intertwined. The reason for this is that changes can occur in the subjects' motivation concerning both a definitive and a temporary abandonment of the research, which poses the question: to what extent can we insist in the invitation to participation without harming the right to refuse (which sometimes is not expressed in an explicit way)?

Data security and confidentiality is a great challenge in studies that produce data continually, in which the inclusion of individual identifiers, such as name and address, is indispensable to monitor the participants' health status.

Although it is not adopted exclusively in longitudinal studies, the storage of biological material is currently considered an essential element to test a series of hypotheses. It is employed in the main studies with this design and represents new ethical and legal challenges.[5,6,12]

In the ELSA-Brasil, the storage of genetic and cellular material, enabling access to DNA codes and to expression patterns of RNA and proteins, will allow testing associations between cellular and molecular alterations that precede the emergence of a series of diseases. New science fields that have just started to develop, called genomics and proteomics, will enable, in a future that is not so distant, a better prediction of chronic diseases that constitute public health problems in many countries, including Brazil.[21] The advances in these areas may enable the treatment of certain diseases in preclinical stages.

Due to the project's nature, the stored samples can only be destroyed after five years. Their utilization must be in accordance with the procedures described in the protocols originally approved by the CEPs and by the National Research Ethics Committee (CONEP), and it must be approved by the Steering Committee. Any study whose questions are not included in the original objectives must be submitted again to the CEP/CONEP system.

By definition, epidemiological research should advance scientific knowledge, but also contribute to the protection and recovery of the health of populations through the application of this knowledge.[3] Because it is the first large cohort study about adult health in Brazil, ELSA-Brasil has great potential to generate scientific knowledge about the development and progress of non-communicable chronic diseases whose importance has increased due to the population's aging. The public funding of the research is a strong reason for the wide dissemination of its findings, above all in the scientific community through presentations in congresses and publication in indexed journals. However, when one produces knowledge that considers the biological, ethnic, cultural and social characteristics of Brazilian populations, it is possible to enrich the national and international scientific debate. The dissemination of the results to managers will enable to support policies and actions for the prevention, diagnosis, treatment and control of diseases that are adequate to the country's reality. Last, but not least, it is necessary to maintain a permanent diffusion of knowledge to society itself so as to guide decision-making in daily life and the social control of public policies.

REFERENCES

1. Aquino EM, Barreto SM, Bensenor IM, Carvalho MS, Chor D, Duncan BB, et al. Brazilian Longitudinal Study of Adult Health (ELSA-Brasil): objectives and design. *Am J Epidemiol*. 2012;175(4):315-24. DOI:10.1093/aje/kwr294
2. Barreto SM, Ladeira RM, Bastos MSCBO, Diniz MFHS, Jesus EA, Kelles SMB, Luft VC, Melo ECP, Oliveira ERA. Estratégias de identificação, investigação e classificação de desfechos incidentes no ELSA Brasil. *Rev Saude Publica*. 2013,47(Supl 2):79-86.
3. Beauchamp TL. Moral foundations. In: Coughlin SS, Beauchamp TL, Weed DL, editors. Ethics and epidemiology. 2.ed. New York: Oxford University Press; 2009. p.22-52.
4. Buckovich SA, Rippen HE, Rozen MJ. Driving toward guiding principles: a goal for privacy, confidentiality, and security of health information. *J Am Med Inform Assoc*. 1999;6(2):122-33. DOI:10.1136/jamia.1999.0060122
5. Cambon-Thomsen A, Rial-Sebbag E. Aspects éthiques des banques d'échantillons biologiques. *Rev Epidemiol Sante Publique*. 2003;51(1 Pt 2):101-10. DOI:RESP-02-2003-51-1-C2-0398-7620-101019-ART3
6. Cambon-Thomsen A, Rial-Sebbag E, Knoppers BM. Trends in ethical and legal frameworks for the use of human biobanks. *Eur Respir J*. 2007;30(2):373-82. DOI:10.1183/09031936.00165006
7. Dicionário de ética e filosofia moral. São Leopoldo: Editora da Unisinos; 2003. Casuística. p.207.
8. Coughlin SS, Beauchamp TL, Weed DL, editors. Ethics and epidemiology. 2.ed. New York: Oxford University Press; 2009.
9. Council for International Organizations of Medical Sciences. International ethical guidelines for epidemiological studies. Geneva: CIOMS; 2009.
10. Diniz D. Ética na pesquisa em ciências humanas: novos desafios. *Cienc Saude Coletiva*. 2008;13(2):417-26. DOI:10.1590/S1413-81232008000200017
11. Goldim JR, Pithan CF, Oliveira JG, Raymundo MM. O processo de consentimento livre e esclarecido em pesquisa: uma nova abordagem. *Rev Assoc Med Bras*. 2003;49(4):372-4. DOI:10.1590/S0104-42302003000400026
12. Hansson MG. Ethics and biobanks. *Br J Cancer*. 2009;100(1):8-12. DOI:10.1038/sj.bjc.6604795
13. Helgesson G, Ludvigsson J, Gustafsson Stolt U. How to handle informed consent in longitudinal studies when participants have a limited understanding of the study. *J Med Ethics*. 2005;31(11):670-3. DOI:10.1136/jme.2004.009274
14. Khan JP, Mastroianni AC. Epidemiology and informed consent. In: Coughlin SS, Beauchamp TL, Weed DL, editors. Ethics and epidemiology. 2.ed. New York: Oxford University Press; 2009. p.71-83.
15. Kho ME, Duffett M, Willison DJ, Cook DJ, Brouwers MC. Written informed consent and selection bias in observational studies using medical records: systematic review. *BMJ*. 2009;338:b866. DOI:10.1136/bmj.b866
16. Manson NC, O'Neill O. Rethinking informed consent in bioethics. Cambridge: Cambridge University Press; 2007.
17. Myers J, Frieden TR, Bherwani KM, Henning KJ. Ethics in public health research: privacy and public health at risk: public health confidentiality in the digital age. *Am J Public Health*. 2008;98(5):793-801. DOI:10.2105/AJPH.2006.107706
18. Nass SJ, Levit LA, Gostin LO, editors. Beyond the HIPAA privacy rule: enhancing privacy, improving health through research. Washington (DC): National Academies Press; 2009.
19. Neves MP. A fundamentação antropológica da bioética. *Bioetica*. 1996;4(1):10.
20. Pizzi J. Ética e éticas aplicadas: a reconfiguração do âmbito moral. Porto Alegre: EDIPUCRS; 2006.
21. Schmidt MI, Duncan BB, Azevedo e Silva G, Menezes AM, Monteiro CA, Barreto SM, et al. Chronic non-communicable diseases in Brazil: burden and current challenges. *Lancet*. 2011;377(9781):1949-61. DOI:10.1016/S0140-6736(11)60135-9
22. Sheehan M. Can broad consent be informed consent? *Public Health Ethics*. 2011;4(3):226-35. DOI:10.1093/phe/phr020
23. Wolf SM, Lawrenz FP, Nelson CA, Kahn JP, Cho MK, Clayton EW, et al. Managing incidental findings in human subjects research: analysis and recommendations. *J Law Med Ethics*. 2008;36(2):219-48. DOI:10.1111/j.1748-720X.2008.00266.x

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