Public Health

Ethical considerations in collective health

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Introduction

Since Hippocrates, the guarantee of patients' rights, dignity and safety has been the object of consideration and debate. Recently, these discussions have been directed to the understanding that these rights represent human rights, with patients being considered within the context of their humanity. That is, the patient will be thought of not only as a biological being, but as the ultimate objective of science, placed above any pragmatic instrumental reason[1]. In the context of great social inequality, such as what is observed in Brazil, meeting Ethical principles is particularly challenging, both in research as in the practice of Epidemiology.

The Greek word *ethika* comes from *ethos* and refers to an individual's character and the morality of his action. The word morality comes from Latin and means to make the best choice among the possible ones, considering all the circumstances where there are conflicts between different values[2]. These conflicts occur in all clinical and public health situations that involve decisions, either at the level of the individual, collective, institutions or legal entities.

The disclosure of experiences carried out by the Nazis, especially with the Jewish population during the World War II led to an increased pressure to guarantee the dignity of research subjects[3]. An important landmark was the Declaration of Helsinki, which established ethical principles and procedures, leading to the creation of courts in international organs such as the Council for International Organizations of Medical Sciences – CIOMS, of the World Health Organization and the United Nations Educational, Scientific and Cultural Organization – UNESCO[4-6]. For epidemiological researches, CIOMS has launched the Universal Declaration on Bioethics and Human Rights[7]. In Brazil, the regulatory organ for Ethics in Research is the National Council of Health (Conselho Nacional de Saúde – CNS) that works through the National Research Ethics Committee (Comissão Nacional de Ética em Pesquisa – CONEP), which coordinates the National System of Ethics in Research (Sistema Nacional de Ética em Pesquisa- SISNEP).

Ethics permeates all social behavior and any professional practice, but research with human subjects requires the formal appreciation of their respective protocols by a third party to verify the meeting of established ethical principles. In the healthcare scenario, this evaluation is carried out by peers that constitute Research Ethics Committees, which are particularly important in intervention researches. However, Ethics in Research comprehends all investigations with human subjects, experimental or non-experimental, qualitative or quantitative, carried out with patients or disease-free individuals.

This scope extension is the object of controversy and debate between researchers and society, especially regarding ethnographic or social studies, for which there is no tradition regarding the scrutiny of ethical aspects by the Ethics Committee. When the research is in the Public Health area, of which objective is interdisciplinary, the challenges are even bigger. Studies can involve ethnographic and intervention components, interconnected, or associated with the daily practice of subjects, distant from academic formalism and clinical experiments. However, epidemiological researches commonly require an extensive number of participants, use of questionnaires and have a limited potential risk for the subjects.

This article aims at presenting the theoretical principles and bases of Ethics in Research *employed in the Brazilian standards*, synthesizing its *fundamental principles*, regulatory landmarks, institutional structure and specificities of Epidemiology applied to the Collective Health field.

Principles of Ethics in research in human subjects

The *fundamental* principles of Ethics in Research are the autonomy, non-maleficence, beneficence and justice, within a common parameter, which is of that of respect to human dignity[8]. It is not only about following recommendations or norms, but the consideration, on the part of investigator and team, of the ethical implications of the research project.

Autonomy

It refers to the self-government or self-management that has been extended to individuals, by incorporating the rights of freedom, privacy, individual choice, free will and self-determined behavior. In the research field, that implies that the subjects have assured their rights to decide on their participation, free of any coercion or pressure. Within this principle, it is implicit that it is the investigator's obligation: 1) to tell the truth; 2) respect the privacy; 3) protect the obtained information; 4) to obtain consent for eventual interventions, collection and storage of biological material and personal information, including images, such as videos, photographs, recorded voice material, among others; 5) when requested, contribute to the decision-making, based on his or her technical knowledge.

The participation does not mean only "entering" the research, but the right to remain or leave, at any phase. This is important, when there is a restriction in the capacity of making decisions or individual freedom, such as cases with consciousness level or cognitive capacity impairment, institutionalized individuals or inmates. In these cases, the authorization of the legal, institutional or individual tutors is necessary, as well as of family members. Researches with military personnel or other institutions with a strong hierarchic organization require extra care regarding decision to participate, which must be separated from the discipline and structure of the institutional power.

As the decision to participate in researches must be the result of the individual's exclusive choice, it is mandatory that the individual knows about the research purposes, reason for the selection, procedures, potential risks, benefits and harms, and especially, to whom the research interests. This information and participation decision process is called "consent". Therefore, the subjects are contacted, informed about the research and invited to participate. If they agree to do so, the Free and Informed Consent Form (FICF) must be presented to them, which must be written in a language and style that is appropriate to the target population. On the one hand, this is not always easy to do, due to the nature of some researches which are complex and unusual, difficult to comprehend even in the academic environment. On the other hand, consent may sometimes be difficult to obtain, as in clinical emergency situations, or in multicentric international studies, in which the FICF, appropriate for the headquarters, might not be adequate for the requirements of other countries.

Cultural differences about the understanding of protocols and even inconsistencies in the translation of instruments can occur, limiting the effectiveness of their use. It is important to remember that declared and formal institutional agreement is always required when the research involves institutions, either at the recruiting of individuals or data collection phase.

In Brazil, the participation of Native Brazilians requires the approval of the tribe, through its chief representative and of the National Native Brazilian Foundation (Fundação Nacional do Índio).

Population-based researches or those developed in communities can benefit from the project presentation to discuss it with their members and thus, carry out adjustments in their strategies to meet the collective and individual expectations. Visual material and wide discussions in workshops and seminaries can be used to allow a better understanding and comprehension by the subjects, and therefore, more conscious decisions. That represents a higher level of quality regarding individual consent, both regarding the operational aspects and the potential impact of results. That is the core of the "genuine consent" concept, which appeared in 1995 at the Nuffield Council on Bioethics, and puts the perfectly informed consent into perspective, substituting it by the idea of an effort to achieve the best possible communication and transparency[9]. Ways to employ this concept have been increasingly discussed, such as the broad dissemination of the research in the media, i.e., its objectives, methods, scope and expected impacts[9].

The individual, classic, formal, identified and signed consent is relativized in researches carried out by phone or the internet, and the electronic form of the FICF might be used, with a digital signature or not. Interviews carried out by phone allow, almost exclusively, obtaining the FICF through verbal authorization, except when personal contacts are complementary involved.

The FICF must not be too extensive and has to include the main investigator's data, its institutional affiliation, address, telephone and alternatives for contact. The effectiveness of the FICF is questionable when the study population is within survival thresholds, has limited reading or understanding capacity. When the subjects are illiterate, someone trusted by the interviewee can be included as a witness to collaborate in their decisions.

Beneficence

Researches that are aimed at the participants' benefits are ethically acceptable. Examples of such benefits are the improvement of the knowledge on diseases, cures and rehabilitation. Less evident, especially for the lay public, are the benefits of basic research, on procedures or methods. Benefits can have a stronger impact on the collective and not exclusively on the individual plane, as in Public Health researches aimed at collective risks and public policies.

It is noteworthy to consider the association between the public and the private, and between the research financial support and objective. Although, in many countries, the health research has significant financial support from the public sector, either institutions or workers, the manufacturing and commercialization of products

are commonly the responsibility of the private sector[10]. Hence, the knowledge and technologies produced with public resources are not always available to the population, whose contribution through taxes made the research possible. As evidence of that fact is the lack of medications for AIDS in African countries, which have broadly participated in researches that allowed drugs to be manufactured and commercialized. Some therapeutic assays were interrupted when the treatment effectiveness was acknowledged, leaving the participants without access to the drugs used in the research itself[10], stirring up the public opinion that called attention for the need to guarantee the treatment[11]. Thus it is the investigator's responsibility, when formulating the investigation question, to consider to whom the results interest and how the participants will potentially benefit, either individually or collectively.

Finally, it must be observed there are always risks and these must be considered in relation to potential benefits, seeking to maximize the latter, while minimizing damage and risks, guaranteeing that maleficence and beneficence are equally shared between the participants.

Non-maleficence

It comprehends the participant's guarantee that he or she will not suffer any damage during the research, i.e., guarantee that predictable risks are prevented. Desperate situations, of depletion of available therapeutic resources and hope of cure with treatments still in experimental phases can lead to the search and even pressure on the part of patients to participate. The expectation of treatments that are not available in the market and free of costs has attracted many volunteers[12].

In addition to the physical effects, but not less severe, there are psychological, intellectual, social or spiritual discomforts. It is important to consider that damages to the image can be caused simply by disclosing the participation in the investigation.

Questions on past traumas can cause suffering by being recalled. Participants can also be emotionally touched or feel embarrassed by sensitive themes, such as religious beliefs or sexual behaviors.

Mental illness sometimes occurs without the awareness of the patient or is the object of denial. The identification and disclosure of a diagnosis, within a research context, can cause discomfort or embarrassment. It is important to pay attention to researches conducted in multiple phases, when the progression between the phases results from diagnoses, which can compromise their confidentiality. It is worth remembering that the risks for the participants caused by the research can be at the population level, such as in environmental interventions, or individuals ones, such as the collective stigma caused by the participation in the research itself[13].

It is noteworthy that the pharmaceutical industry has a large participation in the economy. When the research is carried out in poor countries and the responsibility of the initiative and performance belongs to other countries, the consequences can be disastrous. Therefore, the need to keep the poor populations safe[10,14,15].

Justice

The principle of justice means that the research subjects must have guaranteed their equality of rights. Still, under the perspective of equity, relative to unequal treatments, but compatible with individual or social inequalities to overcome them.

The concept of equity broadens that of equality, which considers all subjects equal. In addition to the concept of equity, the concept of merit – what is deserved – and that of prerogative – that what someone is entitled to, are important. Therefore, the principle of justice implies in just, equal and appropriate treatment, taking into consideration what is due to people. Thus, the research must minimize the onus for vulnerable subjects.

Every subject must have, in principle, the same chance to be selected, obviously guaranteeing coherence with the objectives and the methodology of the research. Any exclusion must have a justification in the investigation, without reflecting discrimination or negligence. The FICF must contain the reason for the choice of the individual, and what the individual represents in the study population. One example of injustice in research in Brazil was a study on malaria, in which the participants, who belonged to the lower socioeconomic classes, received remuneration. The project was approved by CONEP and Ethical Committees of the institutions in charge of the project in Brazil and another country, but the protocol did not mention the remuneration to the participants[16].

Other principles and guidelines have been the object of discussion by several authors, such as the specific respect to ethnical[17] and religious[18] diversity, scientific validity and social value[19], among other aspects, such as informed consent, non-exploration, essentiality, privacy and confidentiality, risk precaution and minimization, professional competence, responsibility and transparence, distributive justice, institutional arrangements, public domains and adherence[20].

Regulatory landmarks and institutions related to Ethics in Research in Brazil

First, the investigators must follow the dispositions contained in the Ethical Codes of their respective professional categories and the specific norms of Ethics in Research, of which main document in Brazil is Law 196 of the National Council of Health – CNS, which created CONEP, responsible for monitoring Research Ethics Committee (REC). Several other complementary laws followed Law 196 and can be consulted at the electronic address of CONEP.

The protection of research subjects' rights is one of the attributions of CNS, which, through CONEP, have strengthened and consolidated the performance of public organs in establishing norms and monitoring them. CONEP is a collegiate subdivision of CNS, which has consultation, deliberative, normative and educational characteristics and administrates SISNEP, an online system that records researches involving human beings. The planning of a research requires explicit disclosure of the ethical aspects and thus, the investigator must have, as part of his formation, the knowledge of principles and recommendations contained in international instruments and regulatory landmarks of the country. This must be contained in a section entitled *Ethical Aspects* (Box 1) and be the object of discussions and reflections on the part of the entire team. It is unfortunate that this section is usually limited to information that a REC has approved the study. In Box 2, some questions are presented that can be employed in these discussions. When there is a great social interface of the research, the reading of the questions in Box 1, which were adapted from Jesani & Barat[21], is recommended.

Box 1 – Examples of "Ethical Aspects of Research Project" sections based on questionnaires

Inclusion by gender, age groups and ethnicity

Participants of the present study will not be excluded by gender, ethnicity or skin color. The exclusion of the unemployed or other categories not formally defined as workers, such as students and family members that are not working or looking for a job, is justified by the study objective and is detailed in the specific Methods section.

Human subjects

This project was reviewed and approved by the Ethics Committee of the INSTITUTION (Prot. N. xx, date), as well as of the collaborative INSTITUTIONS, INSTITUTION A (Prot. No. xxx date) and INSTITUTION A (Prot. No. xxx date). The investigators have considered the question of using kindness when handling sensitive aspects such as sexual harassment, psychiatric symptoms and ethnicity that are evident at the FICF regarding the language employed in the questionnaires and instructions for the interviewers contained in the Manual of the Interviewer.

Research material to be obtained

It consists only of data obtained through questionnaires applied by interviewers, containing family, social, occupational and health-related information.

Subject recruiting

It has been shown in the Methods section that all residents of houses located in the studied areas will be selected for the research, a strategy that has been successfully employed in previous studies. The voluntary nature of subject participation and the procedures to guarantee data confidentiality will be described to the participants. Verbal consent will be obtained by interviewers and the FICF will be signed. Witnesses' signatures will be provided for those who refuse to sign the FICF. Permission to access medical records and verbal permission will also be obtained, and information regarding further visits at future phases of the study will be given.

Potential risks

There is no indication that the study procedures offer any risk to the participants. However, reports of past disagreeable experiences, such as O AGRAVO EM ESTUDO, can cause some psychological discomfort, although it can increase the awareness of danger in the workplace. This discomfort can be minimized by acknowledging that this can be a relevant contribution for the community and can support the adoption of work protection measures. Previous experiences with the population of this city have demonstrated a high degree of receptiveness regarding this type of research.

Procedures against risks

Participants' individual names shall be employed only for logistic purposes when conducting the study, such as identifying people's addresses in order to apply questionnaires and re-visits at the follow-up. Once revised and processed, the names shall be removed from the questionnaires and filed separately. A single number of identification will be attributed and used throughout the analysis. The study code shall be kept in locked cabinets, of which keys shall be under the responsibility of the main investigator. Individual identifiers shall not be employed for typing, analysis and generation of reports.

Box 2 – Questions on Ethics in Research with human subjects in the social science scenario, aiming at the investigator's consideration when creating projects.

Dimensions	Questions	Dimensions	Questions
1 - Essentiality and maximization of public interest and social justice	Are the investigation questions and expected answers essential for the improvement of population's health status? Will the results of this research bring benefits to society? Will they contribute to social justice?	7 - Non-exploration	Are we righteously using the time and information provided by the participants, in order not to impair their gains or dignity? Do we guarantee that unnecessary risks are not involved? Have the least-experienced investigators had their work acknowledged and justly treated and have their authorships been considered at the publications?
2 - Respect to vulnerable groups	Are vulnerable groups of subjects, such as native populations, inmates, institutionalized subjects, children, the elderly, mentally-ill individuals, individuals with limited cognitive capacity or legal custody involved in this research? If yes, have we specified the justifications in detail?	8 - Public domain	Is the research project going to be disclosed through the appropriate means of communication to the concerned subjects and participants, whether they are individuals or collectivities? Are the results going to be disclosed to the scientific community, service managers and the study subjects?
3 - Knowledge, capacity and social commitment	Does the team responsible for the investigation have the capacity, knowledge and commitment with society required to conduct this research?	9 - Public responsibility and transparency	Have mechanisms been established to guarantee complete honesty regarding resource use, financial sources, eventual conflict of interests and accountability transparency? How will this information be available to the public?
4 - Respect and protection of subjects' autonomy and privacy	Do we guarantee autonomy protection and the right to voluntary participation, with clear awareness about the objective and procedures, risks involved and the use of knowledge to all research subjects? Do we adopt procedures to guarantee the rights and dignity of the research subjects, whether they are individuals, institutions or legal entity?	10 - Authorship and disclosing of results	Have the authorship and co-authorship criteria of reports and publications been defined and agreed upon by the research team? Will co-authorship be granted to the less-experienced members of the team?
5 - Privacy, anonymity and confidentiality	Do we adopt procedures that will guarantee the participants' privacy, anonymity and the confidentiality of the information used in the research? Are all the team members aware of and committed with this guarantee?	11 - Relationship between institutions and investigators	Are the financial support institutions, sponsors, executors and co-executors aware of their role and attributions in the research? Have the team members been informed of and do they share ethical and scientific responsibility involved in the research? Has the protocol containing all relevant information been submitted to a Research Ethics Committee, when applicable?
6 - Precaution and risk minimizing	Have all possible risks been identified, with their respective degree and effects? Have these risks been clearly explained to participants, team and subjects? What has been done to minimize these risks? What measures will be adopted to discontinue the study if unexpected risks occur? What measures will be adopted to repair problems caused by the research, in case they occur?	12 - Data or material custody and sharing	Will the research data be stored, while guaranteeing the privacy of study subjects and of what is stated in the FICF? Will the biological material be adequately stored and will the institutional responsibility be defined according to the Laws of the country?

Source 1 - Based on Jesani A, Barai T. Ethical Guidelines for Social Science Research in Health. http://www.hsph.harvard.edu/bioethics/guidelines/ethical.html, 2003.
Source 2 - Adapted from Santana V & , Castilho EA, Ética na Pesquisa e Práticas Epidemiológicas. in Almeida-Filho N, Barreto ML, Roquayrol Z. Epidemiologia & Saúde: Fundamentos, Métodos e Aplicações. Rio de Janeiro: Ed Guanabara Koogan (In press).

Conflict of interest

The handling of several functions by the same investigator, as it occurs in the private sector, such as in the pharmaceutical industry or the manufacturing of substances known to be pathogenic, in addition to the private financial support given to researches or investigators, can lead to the so called conflict of interest. This means that certain results of a research are of the interest of the financial supporter, or even of the investigator. That erases or attenuates the required "neutrality" of those responsible for the research.

The interests can be financial, status-related, of authorship, commitment with advisors, heads of departments, research groups, among others[22]. But the existence of conflicts of interest does not always mean frauds or biases. In general, transparency is required related to the disclosure of connections regarding the investigators or the research, in the protocol and respective publications, specifying sources of support and funding. To overcome problems with the non-publication of clinical trials of which results are unfavorable, journals have required the protocols of these studies to be previously registered prior to their accomplishment, in systems such as CONSORT. The non-publication of negative findings impairs mainly the conclusions of the meta-analyses and consensus panels, commonly employed in the consolidation of evidence used in decision-making.

Conflicts of interest can also occur in the public sector, due to political or corporatist problems, especially regarding the disclosure of results that can have a negative impact on the prestige of politicians, technicians, managers, or interfere in the public opinion[23].

Ethics in Epidemiology

Epidemiological practice is closely associated with Public Health, which reflects on the overlapping of their ethical questions. These practices involve academic research and are performed in response to service demands for the epidemiological surveillance, in auditing processes or in investigations carried out by legal requirement to investigate a complaint. In these last cases, the results will be employed as evidence. In epidemiological surveillance, some common ethical dilemmas circumscribe situations where conflicts emerge between individual rights and public interest. One example is the need to control transmissible disease outbreaks, which might require the collection of samples for laboratory assessment of information through personal interviews, but it is the individual's decision to provide them.

The consequences of a possible refusal affect not only the health of individuals, but also of the population. Quarantine is a situation in which the freedom of individuals is regarded as secondary for the common good, to prevent disease transmission and environmental damage, among others. The control of communicants of certain infectious diseases can lead to difficulties to preserve anonymity and the confidentiality of information, also causing personal embarrassment.

These examples illustrate contradictions between the guarantee of basic ethical principles, especially of autonomy, in epidemiological practice. In Brazil, the case investigation by the Epidemiological Surveillance, according to Law #6.295/75 and Decree #78.231/76, not implies in obtaining consent, because it is mandatory. The registration of the correct diagnosis and the notification to the National Notification System (Sistema Nacional de Agravos de Notificação – SINAN) are also obligatory, and is the professional responsibility of the physician. However, the aforementioned conditions regarding the respect to privacy, confidentiality and anonymity must be guaranteed. Notice that anonymity and confidentiality are not restricted to the nominal reference of subjects, but to all forms of result presentation that allows the identification of participants, either individuals or legal entities.

Another relevant situation is when the investigator identifies among the participants cases of criminal offenses, such as physical or sexual abuse of children that involves close relatives and that must be reported to the competent authorities, guaranteeing the rights of the victims and their integrity. That depends on the degree of consolidation, infra-structure and capacity of local institutions.

The epidemiological research can offer risks to the authors. The publication of results that are unfavorable to certain groups or interests can threaten the physical integrity or the rights of the investigators. Public or anonymous threats, sometimes violent ones, as psychological or economic pressure, such as dismissal, loss of functions or, indirectly by the non-approval of project funding or publication, have been described[22].

In the United States of America, laws guarantee the rights of investigators or individuals that denounce persons in charge or situations that threaten the health of the population. Some associations and social movements support those who denounce (whistleblowers), guaranteeing their safety and encouraging this practice, both in the academic community and among citizens. For instance, workers that denounce bad working conditions and how these affect their health have the legal guarantee that they will not suffer retaliations. More information can be found at www.whistleblowers.org.

The disclosure of research results, especially those that received public funds, is considered an obligation of the investigator and of ethical behavior, of responsible conduct when handling the obtained information, giving back the knowledge to those who made it possible.

This is not always possible, considering the information nature, the population dispersion, among others, but the investigators must seek ways to make it feasible. Results of interest for the participant's health must be immediately handed.

A recent discussion deals with the availability of research data to the participants and public access to databases, but it is difficult to warrant anonymity in these circumstances. The inappropriate handling of data, to skew results in the direction of the desired outcome, has also been described as one of the common ethical questions in research. Large-scale studies are especially susceptible to the manipulation of relevant information, such as the ones that reveal weak points or biases in their development.

Another relevant aspect is that of intellectual property[21], a question that arises mainly when the research results from a collective effort, common in Epidemiology.

An ethical behavior is expressed in the explicit contribution of each collaborator, in the project phases, describing the intellectual contribution of each participant and the declaration of authorship criteria for each study product. The relationship between advisor and advisee, at any level of learning, must be guided by the respect to the dignity of the professor/student[21], acknowledging the scientific contributions and authorship. This ethical behavior must be reflected in mutual solidarity and support. The participation of coauthors that did not contribute scientifically has been discouraged.

Some journals have requested the explicit description regarding the participation of each author. Moreover, as a measure of precaution, investigators must not disclose, mainly to the media, the preliminary results of a study before a peer-conducted review is carried out.

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