BELGIAN ADVISORY COMMITTEE ON
Bioethics

Opinion by letter No 13 on retrospective scientific studies and informed consent

Request for opinion dated 7 October 2021 from the President of the Medical Ethics Committee HIS (Hôpitaux Iris Sud)

Adoption of the opinion by letter: Committee plenary session of 8 November 2021

Preliminary Warning:
The committee's opinions are drafted in Dutch and French. Please consider these two language versions as official, even if translations in other languages are available.

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BELGIAN ADVISORY COMMITTEE ON
Bioethics

25 October 2022

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our reference
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your reference
your email dated 7 October 2021

Your request for advice regarding retrospective scientific studies and informed consent

Mr. President,

By e-mail dated 7 October 2021, you submitted the following question to us from two separate medical ethics committees, specifically, Iris Ziekenhuis Zuid (IZZ) and University Medical Centre (UMC) Sint-Pieter:
"*Following the evaluation of a study based on the data in patient records of women who had undergone medical termination of pregnancy, the medical ethics committees of the IZZ and the UMC Sint-Pieter discussed whether, in general, a retrospective study based on patient records could be conducted without seeking the informed consent of the patients involved. It was noted in this regard that if the patients concerned were asked in advance, they could object to the use of their medical data, which would also prevent their data from being made available to the researcher. The Medical Ethics Committees of the IZZ and UMC Sint-Pieter wish to seek the opinion of the Advisory Committee on Bioethics on this matter.*" [free translation]

The Committee also notes that the two Medical Ethics Committees that requested opinions came to different decisions regarding the same study.

1. Demarcation and scope of this opinion

The focus of this letter opinion is limited to the ethical dimension of the question posed for an opinion[1]. Even though this question relates to a highly sensitive topic (termination of pregnancy), the Committee only answers the question in this letter opinion in general terms.

2. General framework

The question posed concerns non-interventional retrospective studies in which the past is studied using already available data drawn from existing medical records. In general, the individuals in question are not contacted and no new health data are collected.[2] [3]

Various national opinions and codes[4] relating to medical science research in humans indicate:

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[1] It falls to the competent authorities to decide whether the ethical recommendations in this letter opinion are compatible with the applicable regulations of the General Data Protection Regulation (GDPR).

[2] "Leidraad over niet-interventionele studies" (Guidance document on non-interventional studies), Federal Agency for Medicines and Health Products and Advisory Committee on Bioethics, May 2008 (p. 15, 1.4.2. Niet-interventionele retrospectieve studies), The Ethics Committee | FAMHP: see Guidance documents section (French/Dutch only)).

[3] For information, according to art 3, § 2, of the law of 7 May 2004 on experiments performed on human subjects (hereinafter Experiments Act), *(freely translated) "the present law (...) does not apply to purely retrospective studies based on past data in existing patient records, medical records or administrative records or files, and provided that no new data relating to these patients are obtained in any way for these studies."*
(see also http://www.ejustice.just.fgov.be/eli/wet/2004/05/07/2004022376/justel)
It should be noted in this regard that in its opinion of 25 October 2008 on the draft law that led to the inclusion of paragraphs 2 and 3 in Article 3 of the Experiments Act, the National Council of the Order of Physicians considered that (freely translated) "*no relevant argument (demonstrates) that retrospective studies require less patient safeguards than prospective ones. On the contrary, by their very nature, retrospective studies merit special attention: indeed, they do not always make it possible to obtain the explicit consent of the patient, so that specific safeguards are required, such as the review by the competent ethics committee. To exclude the retrospective studies from the scope of the Law of 7 May 2004 would have the effect of eliminating the effectiveness of the procedural safeguards enshrined in the Law and would therefore harm the interests of patients.*" (Ordomedic | Retrospective Studies - Law of 7 May 2004 on...)
Paragraphs two and three were included into Article 3 of the Experiments Act by Article 84 of the Law of 19 December 2008 containing various provisions on health care.

[4] Excerpts from:

a. Opinion No. 40 of the Advisory Committee on Bioethics (2007) on the scope of the law of 7 May 2004 on experiments performed on human subjects, Opinion No. 40 - scope of the 'Experiments Act' | FPS Public Health (belgium.be):
"*The Committee stresses (...) the need for all research on patients, i.e. on people undergoing treatment or preventive medical monitoring and all research requiring specific medical technical expertise to be submitted to a medical ethics committee (...) This does not imply, however, for the members of the Committee, that such research must necessarily be covered by the law.*" (p. 12, 5. Decision and recommendations, second paragraph - freely translated)

b. Commentary on Article 45 of the Code of Medical Ethics of the Order of Physicians on Clinical Experiments (Ordomedic | 45):
"*1.1 Protection of the interests of participants in experiments - Clinical experiments performed on humans are necessary for the advancement of medical science. (...) The physician must always defend the interests of the subjects regardless of their role in the experiment. (...) The health and well-being of the subject are paramount. (...) / 1.2 Informed consent - (...) The subject's prior written consent to their participation in the experiment (...)*".

- the need for experiments on humans for the advancement of medical science;
- the protection of the interests of participants in experiments which assumes, among other things, that research projects are designed and implemented with the utmost care;
- the subject's informed consent is obtained;
- the positive opinion of the medical ethics committee before starting the study.

Of all these aspects, only the criterion relating to obtaining consent poses a problem in the case of retrospective studies based on records. Moreover, the Belgian law of 7 May 2004 on experiments performed on human subjects excludes from its scope purely retrospective studies based on records.[5]

Nevertheless, the guidance on non-interventional studies (May 2008)[6] recommends that (freely translated) "*out of a concern for compliance with a number of general ethical principles (...) all non-interventional studies*" (...) "*to the extent that they are conducted in the context of patient care*", (...) "*including those not covered by the law, must be submitted to a medical ethics committee for opinion*". According to this guidance, one of the concerns for a medical ethics committee when reviewing non-interventional studies is, among other things, that "*the privacy of the subject ... must be adequately protected (..)*".

Moreover, even if, in the context of a non-interventional retrospective study, former patients are generally not contacted and they have not given informed consent to access records or files containing data about them, the other criteria mentioned above are still important.

Moreover, a healthcare institution must be able to account for which individuals have been given access to patient records, medical records or administrative records or data files relating to all of its former and current patients. The researcher or research institution must therefore justify its request for access to records. In this way, a differentiation can be made between responsible access and irresponsible access. Indeed, current and former patients must be able to know who has been granted access to files or databases in which their personal data concerning their health are stored and for what purpose their data are (or will be) used. In this sense, the positive opinion of a healthcare institution's medical ethics

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c. Code of Ethics for Scientific Research in Belgium (2008) which lays down the major principles of ethically-responsible scientific practice (Publications | Belspo):
"*Despite the significant diversity of subjects and methods of scientific research, there are general principles and standards of behaviour to which researchers are obliged to adhere.*"
"*The subjects of experiments and respondents must give their informed consent: they have the right to know they are the subject of research, they must be given the most complete information possible and give their prior consent with full knowledge of the facts. Any deviation from this principle must be submitted for approval of the persons or the institutions qualified to provide an opinion on both the scientific aspects and the ethical aspects of the matter (ethics committee, programme monitoring committee, academic authorities*, etc.)."

[5] See also footnote no. 2.

[6] This guidance emerged from a roundtable organised by the Committee with the FAMHP in 2007. The quotes are from Part 2. The responsibilities of a medical ethics committee regarding non-interventional studies (p. 17) and from the second paragraph of the introduction, from the abstract (pp. 8-9). See also p. 40.

committee is a safeguard that allows both the healthcare institution and the researcher or research institution to justify access to records in the context of a non-interventional retrospective study with respect to the individuals whose data will be used.

This letter opinion also discusses the importance, on the one hand, of protecting privacy when the informed consent of the person whose health data is used is not requested, and, on the other hand, the positive opinion of the Medical Ethics Committee.

3. Protection of privacy

The answer to the question posed should be based on respect for the ethical principles of 'do no harm' and 'do good' and, to the extent possible, the informed consent of the person whose records will be used to conduct the research. Indeed, this research will necessarily involve data that are part of their privacy, since the record contains information regarding their health. The example of the subject of the research study on which the request for an opinion was submitted to the Committee is instructive in this regard both in terms of the patient's privacy and the difficulty of obtaining their consent: contacting people again several years after a medical procedure may do them more harm than good; it does not benefit the person him or herself and may even bring up painful memories. And how should former patients be contacted: by letter, phone or e-mail? At what address? Who will open the mail? The ethical principles of 'do no harm' (*primum non nocere*) and 'do good' would probably not be respected in this case.

This situation, and in particular the fact that it is difficult and often impossible to apply the principle of informed consent, is still also valid for any non-interventional retrospective study on any medical problem. Indeed, in non-interventional retrospective studies, it is often the case that informed consent cannot be requested because it is impossible to contact and inform the patient, or this may require disproportionate effort or risk making the achievement of the study objectives impossible or seriously compromising them.

When consent is requested in the context of scientific research, whether for an experiment or a study on file, all information regarding the research must be made available to the person who is invited to participate in the research: the specific research question and the concrete purposes of the study must be known to this person and clearly explained to him or her. That is why it is clearly not possible to seek consent from every patient for research that is not yet known, whether interventional or retrospective. In the context of a retrospective study, the same rule applies and the patient's informed consent therefore cannot be requested in advance.

It is sometimes considered asking each patient admitted to the hospital if they accept that their patient records can be used for scientific purposes, with the aim of improving the quality of care, provided that all conditions regarding the confidentiality of their patient data are guaranteed. This idea conflicts with the need for obtaining targeted consent. Moreover, if the patient, for example when admitted to the hospital, has already indicated his or her objection to a study or a certain type of study, his or her refusal must be respected and his or her data will not be processed.

In summary, the Committee believes that the principle of obtaining a former patient's consent must be adhered to unless it undermines the principles of 'do no harm' and 'do good', or requires disproportionate effort.

4. Role of the medical ethics committee

Submitting non-interventional retrospective studies to medical ethics committees is not required by law[7], but it is generally assumed that such scientific research based on personal health data is preceded by a favourable opinion from the medical ethics committee of the institution where the research is planned[8]. Moreover, the Committee notes that this is the case in practice.

This committee will primarily watch over the scientific relevance of the project and its design, the ethical principles of do no harm and do good, the protection of the patient's privacy and anonymising or pseudonymising their personal data. It will also assess whether the exemption to inform the patient does indeed apply in this particular research proposal, which presupposes that the researcher or research institution provides an explicit justification for why informed consent is not requested.

Some members of the Advisory Committee start from the observation that the personal data required for a retrospective study are often not available in anonymised or pseudonymised form. The researchers must then obtain access to patient records to collect this data and then anonymise or pseudonymise it. These same members believe that this should then ideally only be done by researchers who are part of the team that has or had a care relationship with the patient, especially if informed consent is not requested for the study. These members see it as incumbent on medical ethics committees to include this element in the assessment of whether or not an exemption can be granted to inform the patient and seek their informed consent.

The Committee notes that a medical ethics committee may not always reach the same conclusion as another committee on the same question. Even if uniform decisions are still preferred, analysing a problem from an ethical standpoint may lead to a different conclusion depending on the medical ethics committee reviewing the case. As regards the ethical basis, when data are weighed against each other, one value may be more decisive for one medical ethics committee than another, and therefore lead to a given conclusion that is not shared

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[7] See reference above to Art. 3, § 2, of the Experiments Act.

[8] See also 3. Ethical principles.

by another committee. The decisions or binding opinions of medical ethics committees must state the arguments on which they are based.

5. Conclusion

The question asked for guidance concerns the familiar problem that for non-interventional retrospective studies, patients are not always asked for their informed consent to the use of their data in the context of a specific research project based on records. The Committee confirms that on an ethical level, such studies should be submitted to the respective medical ethics committees of the healthcare institutions involved, tasking them with assessing these research projects. In particular, these committees should judge the relevance of the reasons for the request for exemption from the strong recommendation to obtain the former patient's consent to the use of their medical records in the planned research. The Committee expects medical ethics committees to justify their decision in each case with specific arguments for each research proposal submitted.

Yours Sincerely,

Paul Cosyns
President of the Advisory Committee on Bioethics

This letter opinion was drawn up by Paul Cosyns, Etienne De Groot, Thérèse Locoge and Jules Messinne.