MEDICÍNSKA ETIKA & BIOETIKA

MEDICAL ETHICS & BIOETHICS

ČASOPIS PRE MEDICÍNSKU ETIKU A BIOETIKU

■

JOURNAL FOR MEDICAL ETHICS AND BIOETHICS

ISSN 1335-0560

BRATISLAVA, SLOVAK REPUBLIC
Spring – Summer 2013 Vol. 20 No. 1 – 2

OBSAH / CONTENTS

■ **Citáty/Quotations** **1**
– *Prof. Edmund Pellegrino MD (1920 - 2013)* 1
■ **Pôvodné práce/Original papers** **2**
– Substitute Decision Making in the Czech Republic – Looking for an Interpretational Key to be Useful in the Clinical Practice. /Zástupné rozhodování za pacienta v České republice – hledání interpretačního klíče použitelného v klinické praxi. *J. Matějek* 2
– Effects of Miscarriage and Induced Abortion on Mental Health. /Účinky spontánneho a umelého potratu na duševné zdravie. *D. Serapinas, A. Narbekovas, J. Juškevičius* 5
■ **Dokumenty/Documents** **8**
– Guanajuato Declaration about *in vitro* Fertilization. /Deklarácia z Guanajuato o oplodnení *in vitro* 8
– The Ethics of Care of the Dying Person./Etika starostlivosti o zomierajúceho. *Anscombe Bioethics Centre* 9
– Medical Research for and with Older People in Europe. (Parti I)/Medicínsky výskum pre a so staršími ľuďmi v Európe. (Časť I) *GMWP EFGCP* 10

CITÁTY / QUOTATIONS[1]

On moral absolutes in clinical ethics

"Moral absolutes have little or no moral standing in our morally diverse modern society. Moral relativism is far more palatable for most ethicists and to the public at large. Yet, when pressed, every moral relativist will finally admit that there are some things which ought never be done. It is the rarest of moral relativists that will take rape, murder, theft, child sacrifice as morally neutral choices.

In general ethics, the list of those things that must never be done will vary from person to person. In clinical ethics, however, the nature of the physician–patient relationship is such that certain moral absolutes are essential to the attainment of the good of the patient – the end of the relationship itself. These are all derivatives of the first moral absolute of all morality: Do good and avoid evil. In the clinical encounter, this absolute entails several subsidiary absolutes – act for the good of the patient, do not kill, keep promises, protect the dignity of the patient, do not lie, avoid complicity with evil. Each absolute is intrinsic to the healing and helping ends of the clinical encounter." [1]

On health care

"This is not the place to design a total system of health care, nor to fill in the content of precisely what services constitute a fair share of the common good of health care, nor to speak of the costs, modes of payment, and choices among other societal goods. Obviously, those are the questions most often at issue in policy debates. But, in the end, those are second order questions. They can be answered properly only in light of the first-order questions: What is health care? What kind of good is it? What moral claim do members of a society have on this good? What are society's obligations, and what are the obligations of the health professional with reference to that good? Understanding health care to be a commodity takes one down one arm of a bifurcating pathway to the ethic of the marketplace and instrumental resolution of injustices. Taking health care as a human good takes us down a divergent pathway to the resolution of injustice through a moral ordering of societal and individual priorities. One thing is certain: if health care is a commodity, it is for sale, and the physician is, indeed, a money-maker; if it is a human good, it cannot be for sale and the physician is a healer. Plato's question admits of only one ethically defensible answer. Can we deny, then, said I, that neither does any physician, insofar as he is a physician, seek to enjoin the advantage of the physician but that of the patient? (Plato, Republic 342c)" [2]

Prof. Edmund Pellegrino MD (1920 - 2013)

[1]Texts taken from: [1] Pellegrino E. Some Things Ought Never Be Done: Moral Absolutes in Clinical Ethics. Theoret. Med. Bioeth., 2005, 26 (6): 469-486. [2] Pellegrino E. The Commodification of Medical and Health Care: The Moral Consequences of a Paradigm Shift from a Professional to a Market Ethic. J. Med. Phil., 1999, 24 (3): 243–266.

SUBSTITUTE DECISION MAKING IN THE CZECH REPUBLIC
Looking for an Interpretational Key to be Useful in the Clinical Practice

Jaromír Matějek

Institute for Ethics, 3rd Faculty of Medicine, Charles University, Prague, Czech Republic

Introduction

The emphasis on autonomous decision making of each individual patient is in the centre of contemporary medical ethics and it is to various extents present also in everyday's clinical practice in the Czech Republic (CR). However, similarly to the other European countries, the questions surrounding the *substitute decision making* (**SDM**) for the patient are far from being solved easily. In this paper, we decided to offer some reflection on these rather complex issues.

In the first part, we present an overview of the legal norms in place in CR that provide for actual SDM regulation. In particular, we refer to the *Convention on Human Rights and Biomedicine* [3] and to its Article 9, and to the new *Act on health services and the terms and conditions for the providing of such services (Health Services Act).*

In the second part, we provide some critical comments on the current CR SDM legislation. The most important question that is raised here seems to be the one of a reliable interpretation of the patient's previously expressed wishes.

In the third part, we try to inquire, whether the principle of substituted judgment and the principle of the best interest of the patient are mutually connected, and whether we could use this connection to support SDM processes in clinical practice.

Convention on Human Rights and Biomedicine (Oviedo, 1997)

The legal situation with regard to SDM in the period before the political changes started by the Velvet Revolution in November 1989 was very unclear in CR. No specific provisions existed in the law. The signing and subsequent ratification of the *Convention on Human Rights and Biomedicine* (in the year 2001) provided for some new legal structure in the field of biomedicine in CR and stimulated novel developments both in CR medical law and medical ethics.

Article 9 of the Convention is concerned with SDM. It reads: *"The previously expressed wishes relating to a medical intervention by a patient who is not, at the time of the intervention, in a state to express his or her wishes shall be taken into account."*[3]

The Convention became part of CR legislature on October 1, 2001. As an international treaty, it stands in fact above the ordinary CR laws. From this date on, it has been possible for a patient to write his/her own so-called "previously expressed wishes" document.

However, until today, it is hardly a common practice. In 2010, we asked by email 113 members of the Czech Society of Palliative Medicine, on whether they had met with patient's previously expressed wishes documents, how they had handled them, and whether they had some policy or instructions to this effect in their medical offices. Only 6 members answered. Moreover, the answers were rather unclear and uncertain. The cumulative response may read as follows: "Yes, I know the instrument of previously expressed wishes exists, but I do not know how to approach it, and in my medical office I have no instructions concerning this issue." This situation, to our knowledge, is quite similar to the one in Austria.

In Germany, the acceptance of the instrument of previously expressed wishes (in German "Patientenverfügung") is also rather low. Only about 4% of the adult German population write such texts. This is in contrast with the current situation in the United States, where the issues of advance directives, living will, and substituted judgment are included into routine questions sets at the admission of a patient to the hospital.

For better understanding of the Czech situation, however, a more comprehensive sociological study on the "end-of-life" decision making processes, factors and conditions would certainly be needed.

CR Health Services Act [5]

Rather recently, the area of SDM in CR has been regulated by the *Act on Health Services and the Terms and Conditions for the Providing of such Services.* It took effect April 1, 2012.

The issue of SDM is regulated by the provisions contained in **§ 36**, in connection with the provisions of **§ 33** and **§ 34**. Hereby, we present our own 'working translation' of these paragraphs, with some preliminary comments.

§ 36

(1) For the event the patient develops such a state of health, in which he/she is not able to agree or disagree with the provision of health services and the manner of the provision of such services, he/she shall be able to express such approval or disapproval in advance (hereinafter referred to as "previously expressed wishes") .

(2) The provider shall take into account the previously expressed wishes of the patient, if they are available, provided that at the time of provision of health services, there occurs a predictable situation to which previously expressed wishes apply, and the patient is in such a state of health when he/she is unable to express new agreement or disagreement. Only those previously expressed wishes shall be respected that have been made on the basis of written patient guidance about the consequences of his/her decisions, namely by a general practice physician, with whom the patient is registered, or any other treating physician in the field of health care related to the previously expressed wishes.

(3) The previously expressed wishes must be made in writing and shall bear a notarized signature of the patient. A written guidance in accordance with Paragraph 2 shall be part of the previously expressed wishes.

(4) The patient may make previously expressed wishes also after he/she has been received into care by the provider or at any time during hospitalization, for the provision of health services provided by this provider. The wishes thus expressed shall be recorded in the medical records of the patient; the record shall be signed by the patient, health professional and a witness; in this case the procedure in compliance with Paragraph 3 shall not apply.

(5) The previously expressed wishes

a) Need not be respected if since the time of the expression of these wishes there has occurred in the provision of health services to which the wishes relate such a development it may be reasonable to assume that the patient would give consent to the provision thereof; the decision on non-compliance with the previously expressed wishes of the patient and the reasons leading to such non-compliance shall be recorded in the medical records of the patient.

b) Shall not be respected if they encourage such practices that would result in an active cause of death.

c) Shall not be respected if the fulfilment of such wishes may endanger other persons.

d) Shall not to be respected if at the time that the provider did not have the previously expressed wishes he/she has initiated such medical services, the interruption of which would lead to an active cause of death.

(6) The previously expressed wishes shall not apply in the case of minors or patients deprived of legal capacity. [4]

This legal text aims to implement the respective provisions of the *Convention on Human Rights and Biomedicine* into the CR legal system. Unfortunately, to our knowledge, it was drafted without any serious professional or public involvement or discussion. It is difficult to understand and, even more difficult to use the provisions of this text in clinical practice (see below).

In § 33 and § 34, the provisions for appointing a "health care proxy" or a "substitute decision maker" for the patient are contained.

§ 34

(7) If the patient is unable, given his/her medical condition, to give consent to the provision of health services, and unless the concerned medical services can be provided without consent, the consent shall be required of the person designated by the patient according to § 33, Paragraph 1; if such person does not exist or is unavailable, then the consent shall be required of the spouse or registered partner; if such person does not exist or is unavailable, the consent shall be required of the parent, if such person does not exist or is unavailable, the consent shall be required of other close person eligible to perform legal acts if such person is known.[4]

This text refers to § 33, indent (1):

(1) Upon admission into care, the patient may designate persons who may be informed of his/her medical condition, and the patient may determine at the same time whether these persons may be shown medical records kept on him/her or other records relating to his/her medical condition, making excerpts or copies of these documents and whether in the events pursuant to § 34, Paragraph 7 these persons may give their consent or refuse to give their consent to the provision of health services. The patient may designate persons or express prohibition on providing health information to any person at any time after admission to care and the patient may also withdraw the designation of the person or the prohibition to provide health information at any time. The record of the statement made by the patient shall be part of the patient's medical records kept on him/her; the record shall be signed by the patient and by a medical professional. The record shall also include the statement made by the patient as to the manner in which the information on his/her health may be disclosed. [4]

In comparison to the perplexities of appointing health care proxies or substitute decision makers in other countries (usually, they have to be validated by the court), in CR – following the above given provisions – it is, in theory, surprisingly easy. It is not known to us, however, whether the patients and doctors know and make any use of this opportunity in the real clinical practice. We assume such practice is still very limited at present, if any.

Some critical remarks on current CR legislation on SDM

The current CR legislation on SDM, as given above, does leave several important issues open, or lacks clarity and precision on others. We offer some critical remarks on some of these problems below.

For example, with regard § 36, indent (2) several questions arise: What does it mean "to respect" patient's previously expressed wishes? Should I, as a doctor, fulfil these wishes literally, and even if I want to do so, is it really possible? How those previously expressed wishes of the patient should be understood, interpreted within his/her current situation? What can help us to reach a firm/er ground here?

When we consider different theories of interpretation, in particular hermeneutics, some serious doubts appear. It seems the only feasible approach to reliable understanding of a patient's text is the hermeneutical one. But where and how could we find the interpretational key to the actual text of a particular patient? It is indeed unclear, but on the other hand, it is more a philosophical than a juridical question.

When we read about "the predictable situation", what does it mean? The patient should describe this situation neither too widely, nor too narrowly. Both extreme positions could make the text invalid.

What could be the content of a written instruction? What could a doctor say in regard to the patient's future? Is he or she really interested in biological development of his or her disease? Yes, of course, but above all, the patient wants to find future meaning of his/her situation, and to this aspect the doctor has little or nothing to say.

There are many others questions, which would be worth to deal with. We have deliberately chosen those, which are more closely connected with interpretation of the patients' "previously expressed wishes" texts.

Another option on how the patient may want to arrange his/her future treatment is an appointment of the so-called health care proxy or substitute decision maker. He or she is the person named by the patient, who will make a binding decision about the patient's treatment in the future. Many questions are connected with this position seeking good decisions for the patient. Primarily, they are linked to the necessity of finding appropriate ways on how to understand, what the patient really wants (not) to be done to him/ her in the future anticipated situation.

The third alternative is to choose both of the above-mentioned options, i.e. to write the text (or fulfil a form) and at the same time to appoint a health care proxy/substitute decision maker. This alternative is anticipated and enabled by legislation in some countries, such as Austria, Germany and the U.S.A. We also find this alternative suitable for analysing and finding a possible hermeneutical approach and an interpretational key.

Proposal of a synthesizing approach to SDM

The key question is, whether and how can we connect the patient's text with the opinions of a health care proxy or a representative of the patient in general (also a doctor could be considered the representative of the patient sui generis).

The most broadly accepted principles of SDM are usually referred to the following two: a) the substituted judgment, b) the best interest of the patient, described by T. L. Beauchamp and J. F. Childress in their *Principles of Biomedical Ethics*. [1] They conclude the section on the standards for SDM as follows:

"In summary, it is presently popular in biomedical ethics to hold that an ordered set of standards for surrogate decision-making runs from (1) autonomously executed advance directives to (2) substituted judgment to (3) best interest, with (1) having priority over (2) and (1) and (2) having priority over (3) in a circumstance of conflict. We have argued that previously competent patients who autonomously expressed their preferences in an oral or written advance directive should be treated under the pure autonomy standard, and we have suggested an ***economy of standard****. That is, we have collapsed (1) and (2), as essentially identical. The principle of respect for autonomy provides their only foundation, and it applies if and only if either a prior autonomous judgment*

itself constitutes an authorization or such a judgment supports a reasonable basis of inference for a surrogate. Where the previously competent person left no reliable traces of his or her wishes, surrogate decision makers should adhere only to (3)."[2]

How could we read this conclusion? What could we use for decisions about a concrete patient? It is firstly the authoritative text of the patient alone, i.e. the advance directive; secondly, the substituted judgment based upon the previous preferences and values expressed and held by the patient. The most important sentence of the quotation given above [2] is the following: "*Where the previously competent person left no reliable traces of his or her wishes, surrogate decision makers should adhere only to his/her best interest.*" Two important issues arise, hereby, in understanding of the patient's wishes: 1) reliability of the patient's expressed wishes in the current situation, and 2) content of the best interest of the patient standard.

What are the conditions of reliability of the patient's previously expressed wishes? We believe such reliability is intrinsically connected with establishing of the compelling link between those patient's wishes and the current situation. Only those connections that can help to make good decisions for patients are to be considered reliable. However, precisely here we can see the inevitable gap between the vision of a good decision of the patient him/herself and the vision of a good decision made for the patient by a doctor, health care proxy or surrogate decision maker. Because it is still the other's conception of the good for the patient, even if the other strives to eliminate as much as possible his/her own prejudices and tries to discern and understand what is indeed this 'good for this patient' (in this particular situation). It is important to underline that we can overcome this gap only partially: by finding an understandable, verifiable connection between the previously expressed values, opinions and attitudes of the patient – and the current medical situation. It is the intellectual way, and, if you want, probably a more rational approach.

Moreover, we are probably also able to find a more personal way, how to ascertain what might be good for the patient. We mean the way of empathy and intuition. It is more a psychological approach than philosophical one. By this we may be allowed to look into the patient's situation more deeply, perhaps in a more synthesizing way. There is a valid question, however, on how much this subjective knowledge about the patient's inner is convincing or reliable to be used in subsequent SDM.

Despite the limitations given above, we may summarize that the reliability of connections of the patient's previously held values, opinions and preferences with the current medical situation could be based on a concrete, rational, verifiable proof on the one hand – and on a more subjective, largely intuitive knowledge available to the substitute decision-maker, when making important decisions for the patient in the medical situation at the end, or at the verge of that patient's life.

Another important issue in SDM is concerned with the concrete content of the so-called best interest standard of the patient. Beauchamp and Childress wrote: *"The best interest standard protects another's well-being by assessing risks and benefits of various treatments and alternatives to treatment, by considering pain and suffering, and by evaluating restoration or loss of functioning. This is, therefore, inescapably a quality-of-life criterion."* [1] Beauchamp and Childress also demanded "to adhere only to best interest standard", when there are no reliable traces of patient's previously expressed wishes.

We believe that this distinction is exaggerated. We cannot easily distinct between the patient's vision of his/her best interest standard and his/her preferences, opinions and values held during all his/her life. Conversely, the patient's preferences, opinions and values and his/her vision of the best way of life are intrinsically connected. It seems to us that Beauchamp and Childress speak more about some general vision of the best interest standard – and not about the best interest standard of the particular patient.

Certainly, no one would want to suffer (without a good reason) and probably almost everyone would want to have his/her bodily health and normal functioning maintained or restored: this seems to be undoubtedly a validly shared 'best interest' to all human persons. However, the concrete human life is much more complicated – and "only" patient's preferences and values try to catch and express the complicated nuances of a concrete, unique, single life. Thus, we should go, as much as we possibly can, for the best interest standard of the concrete patient.

We believe the only suitable and adequate measure for interpretation of the patient's previously expressed wishes and/or for understanding of the health care proxy's decision, or even of the decision of the doctor him/herself, is to take into account as much as possible the whole of the patient's previous life and his/her personality. In trying to find concrete connections (not only intellectually reflected but also emphatically felt) between relevant moments of the patient's previous life and of the current situation, we believe, there is probably the best, satisfactorily reliable way to find an acceptable solution. The one that is both anchored in the patient's former life and, at the same time, it is related to this patient's end of life. [4]

Such strongly established, mutual connections may provide for a clear sign of a synthesizing and well justified solution to be taken in the concrete situation. Certainly, we have to check for this connection repeatedly, evaluating the feedback from other relevant agents taking part in the patient's care and its management.

We are all the time operating in somewhat grey zone here, which is close to the mystery surrounding each human being and his/her inalienable dignity. Thus, we are obliged to do what we should and what we can, and to do this honestly, modestly and humbly, even if imperfectly, with the knowledge and capacities available to us in that particular case and situation. Proceeding this way will lead as close as possible to the genuine good of the patient, who is entrusted into our responsibility and care.

Conclusions

In SDM situations a reliable interpretation of both the patient's previously expressed wishes text and an understanding of the whole of the patient's previous life, his/her values, opinions and preferences, and his/her current medical situation are paramount.

In understanding reliably the whole of the patient's situation, his/her previously expressed wishes text, and/or of the decisions of the health care proxy or of the other health care decision maker, the principles of substitute judgement and of the best interest standard are intrinsically connected. The most reliable interpretational key consists not only from the assertions contained in the written patient's text, but also from our best understanding of the whole of the patient's previous life and his/her personality. Trying to find this dialogical continuity is a an important, honest and almost inescapable mission for doctors, other health care professionals, but also for all people surrounding with their attention and care the concrete suffering patient.

References

[1] Beauchamp, Tom, L., Childress, James, F.: Principles of Biomedical Ethics. Oxford: Oxford University Press, 2010, p. 98 – 104. (Abb. Beauchamp, Childress). **[2]** Beauchamp,

Childress, p. 103. **[3]** Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, [Online]. [04/10/2013]. Available at <http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm>. **[4]** Comp. Matějek, J.: *Dříve projevená přání. Výhody a rizika,* Galén, Praha : 2011, p. 49 – 59, ISBN 978-80-7260-850-6. **[5]** Parliament of the Czech Republic, Health Services Act and the conditions of their provision, Act No. 372/2011, as amended by Act No. 167/2012 and Act No. 66/2013 Coll., [Online]. [26/09/2013]. Available at < http://portal.gov.cz/app/zakony/zakon.jsp?page =0&nr=372 2F2011 &rpp = 15 # list>.

Matějek, J.: Substitute Decision Making in the Czech Republic – Looking for an Interpretational Key to be Useful in the Clinical Practice./Zástupné rozhodování za pacienta v České republice – hledání interpretačního klíče použitelného v klinické praxi. Med. Etika Bioet., Vol. 20, 2013, No. 1-2, p. 2 – 5.

Abstract

An overview of the current situation in 'substitute decision making' in the Czech Republic (CR) is presented. CR ratified (in 2001) the *Convention on Human Rights and Biomedicine (Oviedo Convention,* 1997). At present, the key practical question is to establish how the provisions contained in the Article 9 of the Convention "shall be taken into account". The author aims to outline the most important features of a reliable interpretational key to any patient's text authorising such (substitute) decision making. He claims this key could be found in the careful evaluation of the whole of the patient's previous life and his/her personality. Then, establishing a strong, meaningful connection between the complex personal realities of the patient and the patient's "previously expressed wishes" text may lead to satisfactory solution in a concrete situation.

Key words: substitute decision making, advance directive, living will, interpretation, law, Czech Republic

Abstrakt

Článek přináší přehled o situaci v oblasti "zástupného rozhodování za pacienta" v České republice. *Konvenci o lidských právech a biomedicíne* ratifikovala Česká republika v roce 2001. V současnosti je hlavní praktickou otázkou, jak naplnit dikci devátého článku Konvence "bude brán zřetel..." Autor se pokouší nalézt takové charakteristiky interpretačního přístupu, které zajistí co možná nejvěrnější naplnění pacientových záměrů. Tvrdí, že takový přístup lze nalézt v pečlivém vnímání celku pacientova života a jeho osobnosti. K adekvátnímu řešení, podle něj, vede nalezení silné a smysluplné souvislosti mezi pacientovým textem a celkem jeho života a jeho osobnosti.

Klíčová slova: zástupné rozhodování, dříve vyslovená přání, interpretace, právo, Česká republika

Correspondence to: MUDr. ThLic. Jaromír Matějek, Ph.D., Th.D., Institute for Ethics, 3rd Faculty of Medicine, Charles University, Ruská 87, Praha 10, CZ 100 00, Czech Republic, jaromir.matejek@lf3.cuni.cz.

EFFECTS OF MISCARRIAGE AND INDUCED ABORTION ON MENTAL HEALTH

Danielius Serapinas [1,2], Andrius Narbekovas [2], Jonas Juškevičius [2]

[1]Mykolas Romeris University, [2]Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction

Induced abortion and miscarriage are regarded serious and distressing life events for a woman [1].

Responses to miscarriage are very diverse, and 'adjusting' after miscarriage is complex. For some women, the emotional impact may be minimal, but many experience depression and anxiety, which can persist for months or years. Poor adjustment to miscarriage has been associated with psychological, social and reproductive risk factors. At a psychological level, a history of mental illness is associated with poorer adjustment to miscarriage. However, it is necessary to distinguish between the women, whose symptoms are the result of miscarriage, and those, whose symptoms are a continuation of an unrelated mental health problem. Few sociodemographic variables have been found to affect women's psychological outcomes after the miscarriage; although the limited evidence suggests that single women and those who are older may be at a greater risk of psychological distress [2].

Abortion can cause anxiety and depression and can be experienced as a traumatic life event [3]. The results of research into the psychological implications of abortion are equivocal, and this has resulted in much debate, possibly because the theme is controversial on the political, ethical and social grounds [4]. New evidence shows that anxiety symptoms are the most common adverse response and that our understanding of abortion as a potential trauma has increased [5], [6]. Few studies have compared the course of psychological response after a miscarriage with that after an abortion [7]. Induced abortion and miscarriage are similar life events in that women abort after a relatively short duration of pregnancy. However, these two life events differ in several important respects. Miscarriage happens involuntarily and suddenly to a woman, who was expecting to give birth to a child, whereas abortion is a planned and known event [8]. It may be connected with feeling of guilt, because the woman takes the decision by herself.

Calling into question the conclusions from some earlier literature reviews, a moderate to highly increased risk of mental health problems was detected after an abortion. Consistent with the tenets of evidence-based medicine, this information should inform the delivery of so-called abortion services. Symptoms may start immediately after the abortion, or appear some years later [9]. After the initial tears of despair from the emotional loss and the physical pain are gone, the decision to end the life of her child haunts the woman, sometimes even with a more concrete questions: Was it a boy? Was it a girl? How old would he or she be today? Question after question and reminder after reminder bring woman deeper into despair. Patients often deny having abortion/s due to the feeling of guilt and depression associated with these sad for them personal memories [10]. This denial sometimes makes the very diagnosis of mental disfunction difficult, or almost impossible. This may also contribute to the fact that some studies did not provide results consistent enough with the negative impact of induced abortion upon the mental health [11].

Symptoms after abortion may range from a mild depression to serious suicidal thoughts. They can also be linked to other problematic behaviours, such as eating disorders, drug or alcohol abuse, and various instances of the self inflicted harm [12]. Millions of women have had abortions only to discover subsequent emotional dilemmas that would not go away [12]. It may require a long period of recovery. An induced abortion, usually, is the result of a decision-making process taking several days of consideration. The woman, however, is usually not emotionally/mentally prepared for it, when she arrives at the hospital. Discovery of an unexpected pregnancy might have put her into the real existential crisis. The period prior to the abortion might have been for her very distressing. The process of decision-making for having an abortion could have been quite difficult. The reasons for her decision of having an abortion can affect the psychological response after it in fact takes place [12].

Despite a considerable amount of research in this area, it is still not clear which social, psychological and reproductive variables are most likely to affect a woman's adjustment after the abortion. The longitudinal analysis of a large, nationally representative cohort of young Australian women did explore, whether there were any identifiable factors associated with mental health parameters among the women who had experienced a miscarriage. Rather than focusing on the presence or absence of the clinical levels of depression or anxiety, as is common in this area of research, the authors used the measure of general mental health, designed specifically for normal populations, as their outcome measure. Specifically, this analysis did address the question, whether the trajectories of mental health among the women with a history of miscarriage did differ with regard to demographic factors, internal and external coping resources, and other measures of psychological health and well-being. The broader aim of the study was to identify the characteristics of women who had coped well – in comparison to those who did badly after miscarriage, to inform the useful interventions in assisting the women after the miscarriage [2].

Taking into account the differences mentioned above, it may be truly expected that the social, moral and psychological contexts of an induced abortion may be much more complicated than those of a miscarriage. This may result also in measurable differences with regard to the subsequent psychological responses of the woman.

Objective of the study

The objective of our study was to determine, whether there are differences in the patterns of psychological symptoms in women after having a miscarriage in comparison to women having an induced abortion.

Materials Study subjects and methods

Two comparable series of women (age, status of health, social status etc.) were included into this pilot study. The first series consisted of 20 women, who experienced a miscarriage, the other of 20 women, who underwent an induced abortion. The women were interviewed in 3 outpatient clinics in Vilnius, completing a special questionnaire in the pe-riod of a year or more after the event (miscarriage or abortion). Data were assessed by using Mann-Whitney *U* test.

In our literature evaluation study, a systematic search of the available literature was performed to collect the studies conducted on the same subject. The studies taken for further analysis had to report results of a quantitative or qualitative evaluation of mental health in women after their abrupt pregnancy termination by either a miscarriage or an induced abortion.

Results and discussion

Despite the small numbers of subjects enrolled into the pilot study, our data pointed out that the women who had experienced an induced abortion reported significantly higher counts of mental distress symptoms than those who had a miscarriage. Concretely, the differences between the two series were as follows: feeling of guilt 16 vs. 10; anxiety 17 vs. 8; suicidal thoughts 7 vs. 3; episodes of crying 15 vs. 10; anger 13 vs. 2; avoidance of social contacts 12 vs. 4 (all $p < 0.05$). The youngest woman of our series was 18, the oldest 34 years old.

After termination of pregnancy, 4 couples of 20 separated. The majority of women (n = 18) did not report changes in their sexual behaviour after miscarriage. On the other hand, 13 of women after abortion reported a decrease of the sexual desire. Studies analyzing impact of abortion on psychosexuality show, that women undergoing abortion had significantly more conflicts in their partnerships [13]. Male pressure on women to have an induced abortion has a significant, negative influence on women's psychological responses in the 2 years following the event. Women who gave the reason "have enough children" for choosing abortion reported slightly better psychological outcomes [12]. With regard to their relationship with their children the women in both groups reported mostly (17 women in each group) no effect of either induced abortion or miscarriage.

Changes in eating habits (mostly lack of appetite) were reported by 10 women in the 'abortion group' and 5 women in the 'miscarriage group' ($p < 0.05$). Sleeping disturbances were reported by 16 women of the 'abortion group' (insomnia, nightmares), and by 12 in 'miscarriage group' (n.s.). Beginning of an anxiolytic medications use was mentioned by 11 women in 'abortion group' and by 9 women in the 'miscarriage group' (n.s.). Our findings are generally concordant with the previous reports in the available literature. The pilot character of our study prevents us from making any stronger generalizations. We believe that studies using the same methodology in our conditions (Lithuania) are further warranted.

Despite somewhat controversial and difficult subject of study, i.e. abortion and miscarriage, the research in this area reveals some novel, interesting findings that point to the practical measures to be considered in general practice when dealing with the women having passed an experience of a miscarriage or of an induced abortion.

Recent studies have explored the psycho-traumatic aspects of an abortion. About 10% of women were still 'traumatized' (according to a high Impact of Events Scale [IES] score) six months after having an induced abortion [15], while more than 1% of women suffered from the Post-Traumatic Stress Disorder (PTSD) even two years after [14]. An important study dealing with quantitative estimates of mental health risks associated with abortion [16] revealed 'moderate' to 'highly increased' risk of mental health problems after having it. The finding that abortion is associated with significantly higher risk of mental health problems if compared with carrying a pregnancy to term is consistent with literature demonstrating 'protective effect' of the pregnancy delivered relative to particular mental health outcomes. For example, with regard to suicide, data reported the annual suicide rate for women of reproductive age to be 11.3 per 100 000, whereas the rate was only 5.9 per 100 000 in association with birth [16]. Several studies conducted in different countries revealed even lower rates of suicide following birth when compared with women in the general population [7, 8]. Compared to women who delivered, women who had an early or late abortion had significantly higher mortality rates within 1 throughout 10 years. A lesser effect may also be present

relative to miscarriage [17] More research is needed to examine systematically the specific nature of this 'protective effect', to determine the extent to which it holds also for unintended pregnancies delivered, and to examine possible 'protective effect' of childbirth with regard to other mental health variables [16].

Another larger study (3310 women aged 18 or more involved) [18] concluded that abortion was associated with an increased likelihood of several mental disorders: mood disorders (adjusted odds ratio [AOR] ranging from 1.75 to 1.91), anxiety disorders (AOR ranging from 1.87 to 1.91), substance use disorders (AOR ranging from 3.14 to 4.99), as well as suicidal ideation and suicide attempts (AOR ranging from 1.97 to 2.18). Adjusting for violence weakened some of these associations. For all disorders examined, less than one-half of women reported that their mental disorder had begun after their first abortion. Population attributable fractions ranged from 5.8% (suicidal ideation) to 24.7% (drug abuse)[18].

The longitudinal study in women with a history of miscarriage [2] supports previous small-scale clinical research showing that a number of variables are associated with adjustment after miscarriage. Women who reported two life events in the past 12 months and women who reported greater levels of stress were most likely to have lower initial mental health scores. Stress has been associated with an increased risk of having a miscarriage, as well as being an outcome of miscarriage. Thus, it seems that reducing stress during pregnancy may be of public health importance, as well as enhancing the general well-being of a woman [9]. Women, who are pregnant or planning pregnancy and experiencing high levels of stress may benefit from cognitive-behavioural stress management interventions. Such interventions could potentially be incorporated into antenatal classes; alternatively, screening for high levels of stress could be a routine aspect of antenatal healthcare visits. Greater provision of information on managing stress, through PCPs and other community resources, may also be beneficial [2].

Two recent meta-analyses claimed that the induced abortion might lead to the deterioration in mental health [16, 19]. Women who underwent an abortion experienced an 81% increased risk of mental health problems, and nearly 10% of the incidence of mental health problems was shown to be attributable to abortion [19]. In terms of public health and practical implications, health education should also contain information of the potential health hazards of abortion, including very preterm birth and low birthweight in subsequent pregnancies [20].

Conclusions

The findings of our pilot questionnaire study in women who had undergone induced abortions revealed a higher frequency of various psychological symptoms in comparison with the group of women that suffered a miscarriage. However our finding of an increased risk following abortion may be due to some confounding factors that we could not have controlled. Responses of women in the 'miscarriage group' were similar to those expected after a traumatic and/or other untoward life event. Complexity of situations surrounding the experience of an induced abortion may account for the differences observed between the two groups with regard to the course and outcomes of women's psychological responses. Women in both groups may greatly benefit from receiving adequate in-formation on psychological aspects of an abrupt pregnancy termination, as well as from the professional psychological support given to them from the health care personnel.

References

1. Klier CM, Geller PA, Ritsher JB. Affective disorders in the aftermath of miscarriage: a comprehensive review. *Arch Women Ment Health*, 2002, 5: 129-149. **2.** Rowlands I, Lee C. Adjustment after miscarriage: Predicting positive mental health trajectories among young Australian women. *Psychol Health Med* (England), Jan 2010, 15(1): 34-49. **3.** Engelhard IM, van den Hout MA, Arntz A: Posttraumatic stress disorder after pregnancy loss. *Gen Hosp Psychiatry*, 2001, 23: 62-66. **4.** Kero A, Hogberg U, Lalos A: Wellbeing and mental growth – long-term effects of legal abortion. *Soc Sci Med*, 2004, 58: 2559-2569. **5.** Bradshaw Z, Slade P. The effects of induced abortion on emotional experiences and relationships: a critical review of the literature. *Clin Psychol Rev*, 2003, Dec; 23(7): 929-58. **6.** Fergusson DM, Horwood LJ, Boden JM. Reactions to abortion and subsequent mental health. *Br J Psychiatry*, 2009 Nov;195(5):420-6. **7.** Broen AN, Moum T, B_dtker AS, Ekeberg O. The course of mental health after miscarriage and induced abortion: a longitudinal, five-year follow-up study. *BMC Med*, 2005 Dec 12; 3: 18. **8.** Broen AN, Moum T, Bodtker AS, Ekeberg O: Psychological impact on women of miscarriage versus induced abortion: A 2-year follow-up study. *Psychosom Med*, 2004, 66: 265-271. **9.** Broen AN, Moum T, Bödtker AS, Ekeberg O. Predictors of anxiety and depression following pregnancy termination: a longitudinal five-year follow-up study. *Acta Obstet Gynecol Scand*, 2006; 85(3): 317-323. **10.** Kimport K, Perrucci A, Weitz TA. Addressing the silence in the noise: how abortion support talklines meet some women's needs for non-political discussion of their experiences. *Women Health* (England), 2012,Feb 9; 52(1): 88-100. **11.** Stotland NL. Induced abortion and adolescent mental health. *Curr Opin Obstet Gynecol*, 2011, Oct; 23(5): 340-3. **12.** Broen AN, Moum T, Bödtker AS, Ekeberg O. Reasons for induced abortion and their relation to women's emotional distress: a prospective, two-year follow-up study. *Gen Hosp Psychiatry*, 2005 Jan-Feb; 27(1): 36-43. **13.** Bianchi-Demicheli F, Kulier R, Perrin E, Campana A. Induced abortion and psychosexuality. *J Psychosom Obstet Gynaecol,* 2000, Dec; 21(4): 213-217. **14.** Major B, Cozzarelli C, Cooper ML, Zubek J, Richards C, Wilhite M, Gramzow RH. Psychological responses of women after first-trimester abortion. *Arch Gen Psychiatry*, 2000, Aug; 57(8): 777-784. **15.** Perrin E, Bianchi-Demicheli F. Sexual life, future of the couple, and contraception after voluntary pregnancy termination. Prospective study in Geneva (Switzerland) with 103 women. *Rev Med Suisse Romande*, 2002, May; 122(5): 257-260. **16.** Coleman PK. Abortion and mental health: quantitative synthesis and analysis of research published 1995-2009. *Br J Psychiatry*, 2011, Sep; 199(3): 180-186. **17.** Reardon DC, Coleman PK. Short and long term mortality rates associated with first pregnancy outcome: Population register based study for Denmark 1980-2004. *Med Sci Monit*, 2012; 18(9): PH71-76. **18.** Mota NP, Burnett M, Sareen J. Associations between abortion, mental disorders, and suicidal behaviour in a nationally representative sample. *Can J Psychiatry*, 2010 Apr; 55(4): 239-47. **19.** Kendall T, Bird V, Cantwell R, Taylor C. To meta-analyse or not to meta-analyse: abortion, birth and mental health. *Br J Psychiatry,* 2012; Jan; 200: 12-14. **20.** Klemetti R, Gissler M, Niinimäki M, Hemminki E. Birth outcomes after induced abortion: a nationwide register-based study of first births in Finland. *Human Reproduction,* 27(11): 3315-3320.

Serapinas D, Narbekovas A, Juškevičius J.: Effects of Miscarriage and Induced Abortion on Mental Health./Účinky spontánneho a umelého potratu na duševné zdravie. Med. Etika Bioet., Vol. 20, 2013, No. 1 – 2, 5-8.

Abstract

Miscarriage and an induced abortion are life events that can potentially cause a strong mental distress in the woman. The paper reports findings of a pilot study conducted in two comparable groups of women, who underwent either a miscarriage (20 women) or an induced abortion (20 women) and were willing to fill in a questionnaire on their mental health status. Significantly higher proportion of women in the 'abortion' versus 'miscarriage' group reported having various mental health problems (especially the feeling of guilt, anxiety, anger, episodes of crying etc.), as well as conflict situations with their partners. Women in both groups may greatly benefit from receiving adequate information on psychological aspects of an abrupt pregnancy termination (by a miscarriage or induced abortion), as well as from the professional support given to them from the well trained health care personnel.

Key words: abortion, mental health, miscarriage

Abstrakt

Spontánny aj umelý potrat sú nepriaznivé životné udalosti v živote ženy, ktoré môžu spôsobiť závažný psychický stres. Práca uvádza výsledky pilotnej štúdie u skupiny 20 žien, ktoré podstúpili umelý potrat, a skupiny 20 žien, ktoré mali spontánny potrat, a boli ochotné zúčastniť sa dotazníkového výskumu zameraného na hodnotenie ich psychického zdravia. Významne vyšší podiel žien zo skupiny, ktorá podstúpila umelý potrat, než zo skupiny, ktorá mala spontánny potrat, vo svojich odpovediach uviedlo rozličné psychické problémy (najmä pocity viny, anxiozity, zlosti, epizódy plačlivosti atď.), ako aj konfliktné situácie v partnerských vzťahoch. Ženy z oboch skupín by mohli mať podstatný úžitok z informácií o psychologických aspektoch náhleho predčasného ukončenia tehotenstva (spontánnym alebo umelým potratom), ako aj z profesionálnej podpory zo strany správne vyškoleného zdravotníckeho personálu.

Kľúčové slová: umelý potrat, spontánny potrat, duševné zdravie

Correspondence to: Assoc. prof. Danielius Serapinas, Medical Academy, Lithuanian University of Health Sciences, Eiveniu 2, Kaunas LT 50009, Lithuania, e-mail: dserapinas@gmail.com

DOKUMENTY / DOCUMENTS

GUANAJUATO DECLARATION ABOUT „IN VITRO“ FERTILIZATION

April 20th, 2013

Background

In Guanajuato City, Mexico, April 20th 2013, various experts in bioethics, medicine, philosophy, biology, law, academia and the general sciences, came together with the purpose of subscribing the Guanajuato Declaration, a set of interdisciplinary reflections in connection with the sentence brought about by the Inter-American Court of Human Rights of the case *Artavia Murillo and others* (*"in vitro* Fertilization") vs. *Costa Rica* from 28 of November 2012.

Objectives

In this Declaration we aim to show some deficiencies on the sentence of the Inter-American Court of Human Rights and to postulate several principles or relevant ideas that should be considered by any national or international institution that has the responsibility of interpreting, promoting and defending human rights. The persons, whose signatures appear at the end of this Declaration ("subscribers"), accept and support each one of the points enlisted in the same, and submit them to the international scientific community so that those who agree with its content might express their acceptance of its terms ("adherents").

The subscribers of the Declaration regret the scientific and legal imprecisions of the sentence and consider those imprecisions a reason why the sentence should not be considered a relevant precedent in the ruling of further matters on *in vitro* Fertilization, and other topics related to it.

Principles

1. Human dignity is the foundation of human rights. There is no value that has the foundational ultimacy of dignity. Not even freedom, equality or justice are capable of supporting by themselves the full normative system that human rights suppose. In consequence, every organ with judicial functions at a national or international level, when deciding issues related to a possible violation or affectation of human rights, must turn before anything else to human dignity, since it is the only element of the juridical system that allows, on the one hand, to sustain correctly a resolution based on the respect owed in every moment to human beings and, on the other hand, to guide the hierarchy of rights, which supposes finding the best way to exercise them. A judiciary practice that undermines the importance of human dignity by substituting it with another value or norm, anticipates a partial resolution that will translate into the defenselessness of human beings and contradict the inherent vocation of human rights.

2. The life of the embryo is, since its beginning, human, because its nature is not modified or perfected by reason of its growth, development or sufficiency; in consequence, it deserves, from the beginning, the protection of human rights, in the same way in which the rights of children, women and disabled people, etcetera, are recognized. Today scientific developments in the area of embryology force us to pose and defend embryo's rights, especially the right to life by reason of its condition of vulnerability.

3. The term "conception" that has been used by the 41st article of the American Convention on Human Rights, must be understood in the same way in which it was considered when it was subscribed in 1969; this is, as the union of an ovum with a spermatozoon. The argument that argues that implantation is the element which defines conception is false; implantation closes the cycle of conception that, amongst other things, allows the diagnose of a pregnancy. The practice of ART (Assisted Reproductive Technologies) proves by itself that the development of the embryo begins with fecundation.

4. The main international instruments of human rights, such as the Universal Declaration of Human Rights, the American Convention on Human Rights and the International Covenant on Civil and Political Rights establish clearly the right to non-discrimination, a right that also holds for the embryo; hence, there's no reason that justifies the distinction that, in the use of ART, is made between embryos whose implantation has been attempted and those that are discarded or cryopreserved. These actions are considered by us as morally reproachable and they need decisive intervention from the authorities.

5. Human rights are independent norms, which means that the legitimacy, existence, validity and belonging of each one inside the juridical system does not depend on the legitimacy, existence, validity and belonging of the other. Henceforth, we cannot and should not confuse correlation with independence. In this way, reproductive rights are related, amongst other rights, with the right to a private life, but this does not mean that the first is conditioned by the second. If we cannot accept the independence of human rights then we would have to forcibly admit a hierarchy between them; which is something that cannot be accepted in a truly free and democratic society.

6. The normative system of human rights does not admit that one of them, whichever it might be, overimposes or imposes itself a priori over the others, because each one of them has the same hierarchy and obligatory force. This does not preclude the possibility of a weighing between them in a case of conflict. Considering the right to a private life as foundation of other rights like, for example, reproductive rights cannot be admitted on the abovementioned logic.

7. The history of the contemporary world can be explained in terms of a frontal struggle between authority and freedom, giving birth to the irreconcilable division between public life and private life as if human rights could be located exclusively in one of these two spaces. Reality implies that human rights do not exclusively belong to

the realms of private or public life. If human rights, and especially reproductive rights, where rooted only in the public sphere, these would not be anything else but concessions or prerogatives provided by the State to the people. On the contrary, if they were rooted only on the private sphere, these would be a set of norms or starting points emanating from social convention or consensus. Both positions are discredited today. In consequence, everything relative to human rights, and in particular to reproductive rights, has a public part and a private part. In their exercise there's undoubtedly an intervention from personal freedom, but the fact that the State worries about their recognition, protection and promotion, proves that in them there's an element of the public sphere; that is, of justice.

8. Society expects that any national or international institution in charge of the protection of human rights would gather the scientific data provided by scholars and researchers from universities and research centers necessary to build an adequate appreciation of facts and circumstances. In this sense, we notice several errors, scientific imprecisions and methodological deficiencies in the Court's sentence. Some of them are: a) Excessive weight of non-scientifically supported references for the definition of "conception"; b) It is affirmed, incorrectly, that: "Before the IVF (*In Vitro* Fertilization) there was no scientific possibility of accomplishing fertilizations outside the body of a woman" (No. 179), while since 1934, Dr. Gregory Pincus achieved this on rabbits; c) It is argued that all of the 2-week embryos' cells are identical (No. 184, footnote No. 280), when in reality there are hundreds of cells and different structures so different from each other such as placental membranes, and the embryo's complex structures like the ectoderm, endoderm and mesoderm; d) the fertilized egg is confused with the blastocyst (No. 180), because it is asserted that the fertilized egg is the one that gets implanted in the endometrium and; e) It is affirmed that the 8-cell embryo has identical cells (Pg. 59, quote 280, assessor Escalante), when it is well known that from the two-cell embryo there is a directionality: the development of the embryo is defined primarily, yet not exclusively, by one cell, while the other one becomes the foundation for the development of the placenta and the placental membranes.

9. The minimal protection that a just society can offer to embryos since fertilization is the respect to its human rights. Otherwise, or by doing it from the moment of implantation, reproachable actions could arise such as illegal embryo trafficking, trading or their disposition on behalf of laboratories without the permission from their biological or adoptive parents.

10. Subscribers and adherents to this Declaration are moved by their academic and scientific goal of searching for the truth and doing good in their work, and postulate these principles so that they can guide any reflection that is made in connection with human rights and, especially, reproductive rights.

The text taken from the web page http://declaraciondeguanajuato.org/english.php, where additional information can be obtained.

THE ETHICS OF CARE OF THE DYING PERSON

Anscombe Bioethics Centre, Oxford, United Kingdom

A Catholic Ethical Framework

1. The Catholic tradition has developed, through many centuries of reflection, a rich strand of thought and practice on what constitutes a good death and on the ethics of care for people who are dying. In recent times this been articulated by popes and by Vatican documents including: *Declaration on Euthanasia* (1980); *Evangelium Vitae* (1995); *The Catechism of the Catholic Church* (1997); and 'On Life-Sustaining Treatments and the Vegetative State' (2004). This autho-ritative teaching provides guidance for Catholics on the ethics of treatment and care towards the end of life.

2. The same teaching is presented in several documents of the Catholic Bishops' Conference of England and Wales including: *Cherishing Life* (2004); *The Mental Capacity Act and 'Living Wills': a practical guide for Catholics* (2008); and *A Practical Guide to The Spiritual Care of the Dying Person* (2010).

The Governing Principle

3. The life of every human being, as made in the image of God, possesses an intrinsic worth or dignity which must be given strict respect in accordance with the fundamental requirements of justice.

Basic Guidelines

4. The governing principle means we should not refuse medical treatment or ordinary care motivated by the thought, 'I no longer have a worthwhile life'. Such refusals deny the intrinsic worth of life and they make death the object of the refusal. They are suicidal. If a refusal by a proxy decision-maker is based on the judgment, 'he/she no longer has a worthwhile life', this is euthanasia.

5. Euthanasia is 'an action or omission which of itself and by intention causes death, with the purpose of eliminating all suffering' (*Evangelium Vitae*, 65). Euthanasia (sometimes euphemistically termed 'assisted dying') involves the unjust and morally unacceptable killing of a human person, it endangers and fails to respect the equality of people with disability and it harms the common good of society.

6. Due respect for my life generally obliges me to accept ordinary care and nonfutile, non-burdensome medical treatment. However, due respect for my life is compatible with the judgment, 'this medical treatment is no longer worthwhile',

- either because it no longer serves its purpose (is **futile**),
- or because it is excessively **burdensome**: the burdens may be physical, psychological, social, or economic,
- or because it promises **too little benefit relative to the burdens it entails** (even if those burdens are bearable).

Note that judgments about what counts as excessively burdensome are relative to my sensitivities, sensibilities, physical condition and social situation, so they are necessarily made by me if I am competent. In the case of previously competent but now incompetent patients, judgments about what is excessively burdensome should take account of reliable testimony to their previously expressed statements about what they would find burdensome. In the case of patients who have always been incompetent account should be taken of reliable testimony to their sensitivities.

7. In 2004, Pope John Paul II made it clear that clinically assisted nutrition and hydration is ordinary care and 'in principle obligatory'. In contrast, since the 1993 Bland judgement, the law in the United Kingdom has permitted some profoundly disabled patients to be deprived of clinically assisted nutrition and hydration even if it is successfully sustaining their life and is not burdensome to them. This withdrawal of basic sustenance, without overriding reason, amounts to unjust killing. Nevertheless, the in-principle ethical obligation to provide clinically assisted nutrition and hydration may not apply in some dying patients if it would not succeed in prolonging life or in alleviating their symptoms relative to the burdens it entails.

8. Our responsibilities and relationships with others and the central importance of our relationship with God require that we should seek to remain conscious throughout the process of dying, where we would normally be conscious. There are appropriate reasons for use of sedatives, even though this may lead to some clouding of consciousness/drowsiness. Exceptionally, for example, if someone were in severe intractable pain that could not be alleviated in any other way, it would be permissible to sedate that person to the point of unconsciousness. Given advances in palliative medicine, this should rarely be necessary. It is quite common that people slip into unconsciousness naturally as part of the process of dying, but it is not right deliberately to deprive a dying person of consciousness without a serious reason.

This statement of ethical principls relevant to any plan or framework to support the care of the dying was agreed by the Anscombe Bioethics Centre on 12 July 2013.

The text taken from the Anscombe Bioethics Centre's web page: http://www.bioethics.org.uk/images/user/TheEthicsofCareoftheDyingPersonwebsite.pdf

MEDICAL RESEARCH FOR AND WITH OLDER PEOPLE IN EUROPE

(Part I)

European Forum for Good Clinical Practice,
Geriatric Medicines Working Party

Coordination: Hugonot-Diener Laurence, MD. MSc, Hopital BROCA-APHP CMRR Paris sud, France and co-chairman of EFGCP GMWP

European revision coordination: Diener Lilly, REGATES, London, UK

Participants: Alvino Simonetta, MD, inVentiv Health clinical, Milan, Italy; Baeyens Jean-Pierre, MD, University of Luxembourg; Bone Michael P., MD, South Tyneside NHS Foundation Trust, UK; Chirita Denisa, MD, Grünenthal, Germany; Hirsch Francois, PHD. INSERM, Paris, France; Husson Jean Marc, MD, Former Chairman of EFGCP GMWP, Paris, France (+ in 2011); Maman Marianne, MD, Novartis, Switzerland; Piette Fran_ois, MD, Pr. of Gerontology, Paris Hopital Charles Foix (Ivry), France; Tinker Anthea, Pr. Institute of Gerontolgy, King's College London, UK; Vetel Jean-Marie, MD, CNSA, Paris, France; Von Raison Florian, MD, Chairman of EFGCP GMWP and Novartis, Switzerland

Reviewers: Borg John J, BPharm, PhD, Medicines Authority, Malta; Crome Peter, DSc, UCL, London, UK; Corvol Aline. MD, German Reference Centre for Ethics in the Life Sciences DRZE, Germany; Dal Lago Lissandra, Institut Jules Bordet, Belgium; Ferry Monique , MD, PHD, INSERM, France; Franco Alain, MD, Vice president of IAGG and Professor, Nice, France; Frühwald Thomas, MD, Prof. Department of Geriatric Acute Care, Hietzing Hospital, Vienna, Austria; Ivanow Frederic, MD, Janssen R&D, UK; Miller Ram R, MD, GSK NC, USA; Marquet Thierry, MD, Eisai, France; O'Mahony Denis, MD, UCC Medical School, Cork University Hospital, Wilton, Cork, Ireland; Pallis Anthanasios, MD, PhD, University of Heraclion, Greece; Petrovic Mirko, MD, EMA Geriatric Expert Group and Prof. Ghent University, Belgium; Rohou Solange, MD, AstraZeneca, France; Sass Gretel, MD, medac, Germany; Van Den Noortgate Nele, MD, PhD, University Hospital Ghent, Belgium; Vellas Bruno, MD, President of IAGG and Prof., Toulouse, France

Editorial note: Editor of this journal finds the following guidelines particularly interesting both because of their subject and superb scholarship. Part II of the text will appear in the next issue of the journal.
The full text available at the EFGCP webpage at: www.efgcp.be

EXECUTIVE SUMMARY

This document provides recommendations, primarily on ethical aspects of clinical trials performed in older people, who may belong to a vulnerable patient population. Older people experience a higher incidence of disease-related morbidities, take more medicines, are subject to more multiple medication regimes, and account for more adverse drug related events than their younger counterparts. Therefore, it is important to conduct more research and clinical trials in this patient population to further knowledge in the understanding and management of their conditions and treatment. Medicines used by the older people must be of high quality, appropriately researched and evaluated throughout their life cycles.

While the protection against the risks of research in such a vulnerable population is paramount this should not lead to denying them the benefits of research. In many instances, older people can consent to participation in research. Should their capacity to consent be impaired for any reason, it may be advisable to make an assessment while always ensuring a supportive and caring environment respecting their dignity and rights. Whenever older people are unable to consent, their assent should be sought systematically using age appropriate information, in addition to seeking the consent of their legal or authorised representative.

Research ethics committees need internal and/or external geriatric expertise to balance the benefits and risks of research in older adults. The lack of legal ability to consent has implications on the design, analysis and the choice of comparators. Clinical trials should only be performed by investigators trained in Good Clinical Practice with experience of older patients or in collaboration with a geriatrician. Pain, fear and distress should be prevented and minimised when unavoidable. People suffering from dementia represent one of the most vulnerable geriatric populations and require even more careful review. Finally, various other aspects relating to the performance of trials in older people are discussed.

In Europe the population is ageing rapidly. Older people are daily taking many medicinal products not necessarily suitable for them. Publications show that older patients are underrepresented in clinical trials. Extrapolation from clinical trials (CT) to daily life is very difficult due to polytherapy which may lead to safety issues and iatrogenic disorders. The absence of the proper recruitment of adequate number older patients in the clinical development plan of new medicinal products not specifically devoted to an ageing population is not ethical. The aim of this guidance is to improve this situation.

1. INTRODUCTION - RATIONALE FOR THE DEVELOPMENT OF THE RECOMMENDATIONS

The reasons why medicinal products need to be studied in older people have been detailed in various publications. Differences in pharmacokinetics and pharmacodynamics, and in adverse reactions, are more common in older people compared to adults as a whole. In comparison with younger adults, older people are characterized by age-related changes in pharmakinetics and pharmacodynamics which, in addition to multi-morbidity and polypharmacy, increase the risk of adverse drug reactions and drug interactions.

In those cases where it is advisable to include older people in a clinical trial, the choice of subsets of the geriatric population to be included should be made on the basis of the likely target population for the medicine being tested and, the possibility of extrapolation, The scientific validity of research is not valid if the extrapolation is made from the data of younger adults. All medicines, which may be used in very old, frail or patients with multi-morbidity, should be evaluated in such patients.

Trials are necessary and should aim at progresing well-being and the treatment, prevention and diagnosis of ill health (WHO definition (1)) including for older patients.

The 1993 E7 ICH guidance from (2) Studies in Support of Special Populations: Geriatrics provides recommendations that apply for that population with the guiding principle: "Drugs should be studied in all age groups, including the elderly, for which they will have significant utility. Patients entering clinical trials should be reasonably representative of the population that will be later treated by the drug".

In 2008 experiences from the implementation of the guidance in the ICH regions were analysed and published in a concept paper which raised requests for clarification. In 2010 ICH published (3) a question and answer document (Q&A) intended to clarify key issues.

"With the increasing size of the geriatric population (including patients 75 years and older) and in view of the recent advance in pharmacokinetics and pharmacodynamics since ICH E7 guidance was established in 1993, the importance of geriatric data (from the entire spectrum of the geriatric patient population) in a drug evaluation program has increased."

Certain specific diseases are unique to older people. Specific consequences of medical interventions may be seen in older participants. Unfortunately, this has been demonstrated by previous significant incidents with the use of medicinal products. Because of the special protection they deserve, legally incompetent older or vulnerable people should not be the subject of clinical trials when the research can be done in legally competent subjects (i.e. adults capable of informed consent). When research with older people proves necessary, the inclusion of the least vulnerable amongst them should be encouraged.

2. SCOPE

Medicinal products may be used with a view to treating, preventing or diagnosing a disease or condition. This document is also intended for all stakeholders involved in any stage of a clinical trial, including sponsors, research ethics committees, regulatory authorities, pharmaceutical companies, insurance companies and investigators (including all trial-related staff) of clinical trials conducted in older adults of all ages, their families and patient representatives. This document is applicable to interventional and non-interventional studies, and focuses specifically on geriatric clinical trials; it should therefore be read in conjunction with relevant legal texts and guidelines. Its recommendations should contribute to the promotion and protection of the dignity, the well-being and the rights of older people, who may be vulnerable and in some circumstances unable to give informed consent. Clinical trials performed in the older population should be carried out under conditions providing the best possible protection for this vulnerable population whilst recognising their right to benefit from research.

3. ETHICAL PRINCIPLES, LEGAL CONTEXT AND FUNDAMENTAL RIGHTS

Ethical principles referred to in this document are those expressed, for example, in the Declaration of Helsinki published by the World Medical Association (2008) (4), the Charter of Fundamental Rights of the European Union (2000(5)), the Universal Declaration on Bioethics and Human Rights (UNESCO, 2005 (6)), the Universal Declaration on the Human Genome and Human Rights (UNESCO, 1997 (7)), the International Declaration on Human Genetic Data (UNESCO, 2003 (8)), the Universal Declaration of Human Rights (1948 (9)), and the Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (1997 (10)).

These principles are also echoed and referred to in the ICH E6 guideline on Good Clinical Practice (11). For the purpose of research, three ethical principles should be adhered to: **autonomy** of the participant, **beneficence** and **justice**, where autonomy means respect for a patient's autonomy and rights of dignity and privacy, beneficence is defined as the ethical obligation to do good and avoid harm, and justice is a fair distribution of burden and benefits of research. These are fully applicable to clinical trials in older patients.

3.1 LEGAL CONTEXT

The legal framework under which clinical trials are conducted in older patients includes regulations and guidelines. Research in and with the older person should comply with all relevant legal, regulatory and ethical guidelines; this includes the ICH E7 and its related Q&A document.

3.1.1 Legal context

- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 (12) on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (herein the 'Clinical Trials Directive'), as amended by
- Directive 2001/83/EC of the European Parliament and of the Council of 6 November products 2001(13) on the Community code relating to medicinal for human use, as amended by
- Directive 2003/94/EC of the European Commission of 8 October 2003(14) laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use.
- Regulation (EC) No 726/2004 of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use an establishing a European Medicines Agency. (15)
- Directive 2005/28/EC of the European Commission of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products.(16)
- Pharmacovigilance regulations (EMA 2 /07/2012 (17) is comprised of Directive 2010/84/EU and Regulation (EU) No 1235/2010. (17))

3.1.2 Relevant guidelines

- Guideline for Good Clinical Practice (E 6), CPMP/ICH/135/95(11)
- Choice of Control Group in Clinical Trials (E10), CPMP/ICH/364/96
- ICH E7 guidelines, 1993, E7 (2) 2008 Final Concept Paper (18), Q&A 2010 (3)
- CHMP Guideline clinical trials in small populations (20),
- CHMP/EWP/83561/2005
- CHMP Guideline on conduct of Pharmacovigilance for medicines used by the geriatric population (June 2006) EMEA/ CHMP/PhVWP/235910/2005- rev. 1(21)
- Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use (revision 2) as required by Article 18 of Directive 2001/20/EC.(22)

- Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use (revision 1) as required by Article 8 of Directive 2001/20/EC (23).
- Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of amendments and declaration of the end of the trial (revision 2), as required by Article 9 (8) of Directive 2001/20/EC. (24)
- Detailed guidance on the European clinical trials database (EUDRACT Database) as required by Article 11, 17and 18 of Directive 2001/20/EC, CT 5.1 Amendment describing the Development of EudraCT Lot 1 for 1 May 2004 and CT 5.2 EudraCT core dataset.(25)
- Revised Questions and Answers on Clinical Trials (Notice To Applicants, Volume10, April 2006 (26))
- World Health Organization, Operational Guidelines for Ethics Committees That Review Biomedical Research (Geneva, 2000 (27))
- Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). International Ethical Guidelines for Biomedical Research Involving Human Subjects (Geneva 2002 (28)).
- Management of Safety Information from Clinical Trials. Report of CIOMS Working Group VI.WHO ed. 2005 (29)

3.2 DEFINITIONS/GLOSSARY

3.2.1 Ethics committees (and research ethics committees)

Article 2 (k) of the Clinical Trials Directive defines an ethics committee as: "An independent body in a Member State, consisting of healthcare professionals and non medical members, whose responsibility it is to protect the rights, safety and wellbeing of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, expressing an opinion on the trial protocol, the suitability of the investigators and the adequacy of facilities, and on the methods and documents to be used to inform trial subjects and obtain their informed consent." The term 'research ethics committee' is ncreasingly used to differentiate between ethics committees specifically dealing with the onduct of research and those dealing with medical ethics in general.

3.2.2 The geriatric population

An European consensual definition of geriatric medicine may help to understand who the geriatric patients are.

Geriatric Medicine UEMS-GMS definition

(accepted in Malta and modified in Copenhaguen in 2008)

Geriatric Medicine is a specialty of medicine concerned with physical, mental, functional and social conditions in acute, chronic, rehabilitative, preventive, and end of life care in older patients.

This group of patients are considered to have a high degree of frailty and active multiple pathology, requiring a holistic approach. Diseases may present differently in old age, are often very difficult to diagnose, the response to treatment is often delayed and there is frequently a need for social support.

Geriatric Medicine therefore exceeds organ orientated medicine offering additional therapy in a multidisciplinary team setting, the main aim of which is to optimise the functional status of the older person and improve the quality of life and autonomy.

Geriatric Medicine is not specifically age defined but will deal with the typical morbidity found in older patients. Most patients will be over 65 years of age but the problems best dealt with by the speciality of Geriatric Medicine become much more common in the 80+ age group.

How to define a "geriatric patient" in clinical trials

(UEMS-geriatric section, 2008 (30)).

To be operational in clinical trials, this definition should be as simple as possible, reliable and pragmatic.

Five main aspects that are dominant in this definition are age, gender, function, the number of medicines prescribed and possible exclusion criteria

a. Age

"The geriatric population is arbitrarily defined, for the purpose of this guideline, as comprising patients aged 65 years or older. It is important, however, to seek patients in the older age range, 75 and above, to the extent possible. Protocols should not ordinarily include arbitrary upper age cut offs. It is also important not to exclude unnecessarily patients with concomitant illnesses; it is only by observing such patients that drug-disease interactions can be detected. The older the population likely to use the drug, the more important it is to include the very old" [e.g. 85 and older]. (ICH E7)

b. Number of patients

"To the extent possible the enrolled patient population in clinical development program should be representative of the target patient population. As stated in the current ICH E7 guideline, estimates of the prevalence of the disease to be treated by age or examination of the age distribution of usage for other drugs of the same class or for the same indication. Given the increasing prevalence and a growing recognition of the complexity of the geriatric population, it would usually be appropriate to include more than 100 geriatric patients in the Phase 2 and 3 databases and include patients over the entire spectrum of the geriatric patient population. As single trials may not have sufficient number of geriatric patients to allow such analyses, these will often need to be carried out on pooled data." ICH E7 Q&A 2010 (3)

The collection of necessary data may not always be possible pre authorization; in which case real life data should be collected afterwards.

c. Gender

In the group of patients with a geriatric profile, there are generally more women than men, due to the higher life expectancy of females. If there are no exclusion criteria there will automatically be more women, except for Phase 1 trials and some special cases (for example prostate problems). The proposal should be that the majority of subjects included may be women (except for specific cases, when specific "male pathology").

d. Functionality/Frailty

The practical identification and definition of frailty or functional status with figures for statistical purposes, is much more complex, and there is currently no universal definition. Additional research is needed before an operative definition of frailty can be established' (31).

The proposal should be that there is agreement on the usefulness of defining frailty in clinical settings as well as on its main dimensions, aiming at uniformity of regulatory requirements.

e. Number of medicines prescribed

As polypharmacy is the consequence of multiple co-morbidities, the registration of the number of different medications taken is a good indicator of the number of important co-morbidities. In many protocols the fact that a patient is taking 6 or more different medications may be seen as an indicator of risk of loss of autonomy and may reflect on frailty as well.

A relatively recent overview of the literature indicates that the two most common indicators of polypharmacy were the use of inappropriate medicines or the use of 6 and more medications at the same time (30). The number of forbidden concomitant medicines should be minimized and limited to the number of drugs that really interact with the study drugs.

f. Exclusion criteria

Many trials include an extended list of exclusion criteria, which may not be fully justified. In fact many trials are unrealistic and do not reflect the reality of everyday practice in medicine today. The proposal is to provide justification when an exclusion criterion is proposed.

g. The vulnerable patient

This concerns a small part of geriatric patients including frail patients: Vulnerability is a condition, which represents 'Those who are relatively (or absolutely) incapable of protecting their own interests'. (CIOMS. 2002 (28))

3.3 THE PROCESS OF INFORMED CONSENT

3.3.1 The definition of informed consent

Article 2(j) of the Clinical Trials Directive defines informed consent as follows: "A decision, which must be written, dated and signed, to take part in a clinical trial, taken freely after being duly informed of its nature, significance, implications and risks and appropriately documented, by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative; if the person concerned is unable to write, oral consent in the presence of at least one witness may be given in exceptional cases, as provided for in national legislation." The witness referred to in this definition should be formally independent of the sponsor and the investigator. There is a need to clearly record the names and sufficient details of their relationship to the older patient of all persons involved in informed consent. In these recommendations, "consent" refers only to the legal definition of consent.

Of course, informed consent must be sought in all older people who are able to consent. A simple, short and easy-to-understand information sheet and consent form will contribute to improving the readability and understanding of the older participant, especially if it is adapted to those with a visual or other sensory impairment and is supplemented with visual and hearing aids and cartoons as applicable.

Using a simple tool or questions to check if the participant has understood the given information is recommended. Under these conditions, If this tool is used, additional informed consent is not required from a legal representative (if any), although an older patient may still be vulnerable and require additional discussions and explanations.

3.3.2 Informed consent from the legal representative, surrogate, caregiver or "personne de confiance" as in France, or "Consultee" as in the UK

When a patient is suffering from dementia for example, and is unable to provide consent, informed consent must be sought from the legal representative. Information should be given by an experienced investigator, or an adequately trained delegate, to the legal representative, on the purpose of the trial and its nature, the potential benefits and risks, and the name of the investigators(s) who are responsible for conducting the trial with background professional information (such as training and work experience) and direct contact details (telephone and e-mail) for further information regarding the trial. The legal representative should be given sufficient time and necessary information to consider the benefits and risks of involving his protected patient in the clinical trial.

When providing such information, it is important to take into consideration all the concerns of such a legal representative, especially if inexperienced with respect to the older patient's condition. The legal representatives might therefore need more detailed and explicit information, and hence more time, to reflect on the implications of consenting, especially since they bear full responsibility for the older patient, unlike in other trials where one takes the responsibility for oneself.

Regarding the information given to the legal representatives, items for review by the research ethics committee are set out in Annex 2.

The investigator when seeking informed consent should not put undue pressure on the legal representative. For example: In the complex relationship between legal representative and physician(s), especially in the case of chronic diseases, but also in acute serious illnesses, or in the situation where the legal representative is unfamiliar with the pattern of disease, or research into its better treatment, there is the risk that the legal representative might not fully appreciate the implications of giving consent. However, the investigator should not take part in the decision-making, but should ensure that the information has been understood and that there has been enough time allowed to come to a decision.

It is particularly important that there is no therapeutic misconception.

3.3.3 Informed consent of a patient or his/her legal representative (if any) from a patient from a different cultural background

Where appropriate, a cultural mediator, familiar with medical terminology, independent from the sponsor and investigator, experienced in the language, social habits, culture, traditions, religion and particular ethnic differences should be available in the process of obtaining informed consent.

If research takes place with patients/groups of patients with limited command of the local language, the consent form should be translated into their mother tongue. For those with poor literacy, the use of pictorials and/or relevant communication support might be useful.

It is also important to be aware of potential cultural coercion either in a positive or negative direction and to respect the participants' privacy and dignity at all times.

3.3.4 Consent at the beginning of a trial and continued consent and assent during a trial

As for all participants, investigators should devote sufficient time to provide information and seek the older patient's assent, in accordance with legislation. It is important to realise that consent is a dynamic, continuous process, and should therefore not only be obtained prior to enrolling an older patient into a trial but should be maintained during the trial on a continuous basis. This could be done for example, by a brief discussion during each repeat visit. This process should be documented in the medical records or equivalent. The discussion is part of the ongoing dialogue between the older patient, the legal representative and the investigators and should focus on all aspects of the trial but in particular on any new information that arises in relation to the trial and that might affect the willingness of the older impaired patient or his legal representative if any to continue. Especially in long-term trials, the investigator should check the understanding of the older patient and the ability for assent. In the rare event of a change of legal representative during the trial, informed consent should be sought again as soon as possible.

3.3.5 Withdrawal of consent

Older research participants/patient and legal representati-

ves (when applicable) should be made aware of their right to refuse to take part in a clinical trial. They should be reassured that the withdrawal from the trial will not prejudice their future treatment in any way. In addition, refusal to give consent or withdrawal of consent to participation in research must not lead to any liability or discrimination (e.g. with regard to insurance) against the person concerned.

Older patients/participants and legal representatives (when applicable) should have the opportunity to follow research as it proceeds (unless it is clinically inappropriate or it breaches the participant's right to privacy), so as to be able to decide whether to withdraw the older patient from the research at any time. In the event of withdrawal from a blinded trial, if the patient/participant or his legal representative wishes to continue to follow the progress of the trial, information should be given that the actual data will not be available until the trial has ended. When consent is withdrawn during a procedure, for example, during anaesthesia, it may not always be possible to stop the procedure immediately, as this might jeopardize the health of the older patient.

It must be emphasised that after an older patient/research participant withdraws from a trial, the investigator is still responsible for reporting trial-related events, in accord with pharmacovigilance legislation.

3.4 ASSENT FROM OLDER AND VULNERABLE PARTICIPANTS

3.4.1 Definition of assent

The notion of assent is recognised in the Declaration of Helsinki: "When a potential subject who is deemed legally incompetent, is able to give assent to decisions about participation n research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected."

3.4.2 The legal representative of older participants

In this document, therefore, the notion of legal representative should be understood to be the legally authorized representative(s), as defined in Member States' national laws, who consent(s) on behalf of older patients recruited for research when applicable. The exact role and responsibilities of the representative in a research setting will be country specific, which needs to be recognised in the clinical trial protocol and is especially important in multinational studies.

Some authors use **'knowing agreement'** to reflect the outcome of the process of providing appropriate information, obtaining assent, and whenever possible obtaining written confirmation from the older subject. The capacity of an older patient to make voluntary, informed decisions, i.e. to assent, depends on the current mental capacity of the patient and his or her previous experience of life and illness.

The notion of **"presumed will"** enables legal representatives to express their duty to protect the interests of older persons, based on their experience with such persons during that person's life up to that time.

The evaluation of whether or not an older patient can give assent should never be based on chronological age, but should depend on other factors such as intellectual capacities. This needs to be made after discussion by the legal representative with the investigator, but the legal representative will normally know the older patient better than will the investigator and hence is usually in a position to decide on whether the older patient has understood the information as much as is possible.

Older patients must participate in the consent process together with the family, caregiver and legal representative.

Involving older persons in discussions and the decision-making process respects their dignity and life experience. This process should be conducted with enough time and with a clear and short information note.

At the same time as obtaining consent from the legal representative (if any), the assent or willing agreement of the older patient must be sought. The central role of the legal or authorised representative in the protection of the older patient should be recognised. The family or proxy or the legal representative (if any) might also wish to discuss with the older patient on their own, after having been informed about the trial, and before meeting with the investigator.

If the older patient's assent is not obtained, it is recommended that this be documented with justification in the consent form, which is signed by the legal representative and the investigator.

Where it is doubtful that the older patient has fully understood the purpose and implications of involvement in a clinical trial or research project, according to GCP recommendation, **it will be useful to use a simple tool to check** the patient's capacity to consent (e.g. UBACC (31) or Newcastle +85) (32).

Then if there is a failure to understand, the older patient's assent will not be sufficient to allow participation in that research unless it is supplemented by the informed consent of a proxy or of the legal representative if any. This is especially important in long term studies where changing intellectual function may occur with time and other comorbidities.

The assent information sheets and assent forms should be appropriate and should include provision of information on the purpose of the trial, and potential benefits and harms, in terms that are honest. See also Annex 3 for recommended contents.

As discussed above, assent, like consent, is a continuous process and should be sought during the trial as well, e.g. during repeat trial visits. The wishes of older patients should be respected and they should not be expected to provide reasons for refusing to assent. They should be informed that they may freely withdraw from the trial, at any time and for any reason, without any disadvantage or prejudice.

The processes for informing the older patient and seeking assent should be clearly defined in advance of the research and documented for each such patient. While assent may not be possible in all patients or in all research conditions (e.g., research in emergency situations), the information process provided to older patients and their response should be documented.

Every effort should be made to understand and respect differences of opinion between an older patient and his/her legal representative. Objections by an older patient must be respected.

During the Study

It is advisable to **produce a "Participant guide"** with simple instructions in concise sections and a diary with dates of visits with appropriate information and reminders; such as:

- Tests and procedures to be carried out (medication given, examination, blood tests, etc.) but avoid information overload.
- The need to fast or not.
- The need to take study medication or not on a consultation day.
- The presennce of a carer or not.
- The return of bottles or packaging (empty or not).
- The phone number of the study assistant or secretary.
- An explanation about what will happen at the end of the study or in case of premature topping, adverse event, new safety details, publication of results etc.

[*Continued in No. 3-4/2013 of the M&B Journal.*]

References

1. WHO definitions: World Health Organisation: Ottawa charter for health promotion. J Health Promotion 1986, 1:1-4. **2.** ICH Topic E 7 Studies in Support of Special Populations: Geriatrics, current Step 4 version. 24 June 1993. **3.** ICH Studies in Support of Special Populations: Geriatrics, Questions and answers (July 6, 2010). Web site: http://www.ich.org.: 1-5. **4.** Declaration of Helsinki published by the World Medical Association (2008): 59th General Assembly, Seoul, South Korea, October 2008. **5.** The Charter of Fundamental Rights of the European Union. 2000. Official Journal of the European Communities. **6.** The Universal Declaration on Bioethics and Human Rights (UNESCO, 2005). **7.** The Universal Declaration on the Human Genome and Human Rights (UNESCO, 1997). **8.** The International Declaration on Human Genetic Data (UNESCO, 2003) http://www.unesco.org/) **9.** The Universal Declaration of Human Rights (1948), http://www.un.org/ **10.** The Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (1997). **11.** ICH Guideline for Good Clinical Practice (E6), CPMP/ICH/135/95 (www.ema.europa.eu/ pdfs/.../ich/013595en.pdf). **12.** Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. OJ L 121, 1.5.2001: 34 **13.** Directive 2001/83/ec of the European Parliament and of the Council of 6 November 2001 n the community code relating to medicinal products for human use. Official Journal L – 311, 28/11/2004 : 67 – 128. **14.** Directive 2003/94/EC of the European Commission of 8 October 2003, laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for uman use and investigational medicinal products for human use. Official Journal of the European Union. 14.10.2003. L. 262: 22-26. **15.** Regulation (EC) No 726/2004 of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. 2004R0726-EN-06.07.2009-004.001. **16.** Directive 2005/28/EC of the European Commission of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products. Official Journal of the European Union 9/04/2005. L 91: 13-19. **17.** Pharmacovigilance regulations (EMA 2/07/2012, comprised of Directive 2010/84/EU and Regulation (EU)1235/2010. http://ec.europa.eu/health/documents/new_en.htm **18.** ICH 2008. Final concept paper E7 (R1). Studies in support of Special Populations - Geriatrics. Revision of the ICH E7 Guidelines. 23/10/2008: 1-5. **19.** Choice of Control Group in Clinical Trials (E 10), CPMP/ICH/364/96 **20.** Guideline on clinical trials in small populations, CHMP/EWP/83561/2005 **21.** CHMP Guideline on conduct of Pharmacovigilance for medicines used by the geriatric population (June 2006) EMEA/CHMP/PhVWP/235910/2005 - rev.1. **22.** Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use (revision 2) as required by Article 18 of Directive 2001/20/EC. **23.** Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use (revision 1) as required by Article 8 of Directive 2001/20/EC.Feb. 2006: 1-34. **24.** Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial (revision 2), as required by Article 9 of Directive 2001/20/EC. Oct. 2005: 1-56. **25.** Detailed guidance on the European clinical trials database (EUDRACT Database) as required by Article 11, 17and 18 of Directive 2001/20/EC, CT 5.1 Amendment describing the development of Eudra CT Lot 1 for 1 May 2004 and CT 5.2 EudraCT core dataset. EMA. **26.** Revised Questions and Answers on Clinical Trials (Notice To Applicants, Volume 10, April 2006, Chapt V.: 20-33). **27.** World Health Organization, Operational Guidelines for Ethics Committees That Review Biomedical Research (Geneva, 2000). **28.** Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). International Ethical Guidelines for Biomedical Research Involving Human Subjects CIOMS ed. (Geneva 2002). **29.** Management of Safety Information from Clinical Trials. Report of CIOMS Working Group I. WHO ed. 2005. **30.** The definition of a "geriatric patient" for use in clinical trials (UEMS-geriatric section, 2008: www.uemsgeriatricmedicine.org/) **31.** Rodriguez Manas L. et al. Searching for an Operational Definition of Frailty: A Delphi Method Based Consensus Statement. The Frailty Operative Definition-Consensus Conference Project. J. of Gerontol. 2012. doi:10.1093/gerona/gls119) **32.** Bushardt RL et al, Polypharmacy : misleading but manageable. Clin. Interv.Aging, 2008; 3(2), 383-389. **33.** Jeste DV, Palmer BW, Appelbaum PS, Golshan S, Glorioso D, Dunn LB, Kim K, Meeks T, Kraemer HC. A new brief instrument for assessing decisional capacity for clinical research. Arch Gen Psychiatry. 2007; 64: 966-974. **34.** Newcastle 85+ study: Collerton J. Biological, clinical and psychosocial factors associated with healthy ageing: study protocol. BMC geriatrics 2007, 7:14, doi:10.1186/1471-2318-7-14) **35.** Freedman, B. (1987) 'Equipoise and the ethics of clinical research'. The New England Journal of Medicine, 317, (3):141-145. **36.** Tinetti ME, Studensky SA. Comparative Effectiveness Research and Patients with Multiple chronic Conditions. NEJM. 2011, 364; 26: 2478-81.

Medicínska etika & bioetika - Medical Ethics & Bioethics. Medzinárodný, dvojjazyčný, vedecko-odborný časopis pre otázky medicínskej etiky a bioetiky. Je určený najširšej medicínskej a zdravotníckej verejnosti v Slovenskej republike a v zahraničí, zvlášť členom etických komisií. Má za cieľ napomáhať medzinárodnú výmenu informácií a dialóg na poli medicínskej etiky a bioetiky. Prináša informácie o aktuálnych podujatiach a udalostiach v oblasti medicínskej etiky a bioetiky, pôvodné práce, prehľady, významné materiály a dokumenty, kurz pre členov etických komisií, listy redakcii a recenzie. Pôvodné vedecké a odborné práce publikované v časopise sú recenzované a musia zodpovedať obvyklým medzinárodným kritériám. Založený v roku 1994 Nadáciou Ústav medicínskej etiky a bioetiky. Počas prvých rokov existencie tvorba časopisu nadväzovala na vedecko-odborné aktivity Ústavu medicínskej etiky a bioetiky, spoločného pracoviska Inštitútu pre ďalšie vzdelávanie zdravotníckych pracovníkov (IVZ) a Lekárskej fakulty Univerzity Komenského (LF UK) v Bratislave.

Medicínska etika & bioetika - Medical Ethics & Bioethics. International, bilingual, scientific – professional journal for medical ethics and bioethics. It is devoted to the broadest medical and health care professional public in the Slovak Republic and abroad. Journal pays special attention to the informational and educational needs of ethics committees' members. It aims to foster international exchange of information and dialogue in the field of medical ethics and bioethics. The journal publishes information on actual activities and events in the field of medical ethics and bioethics, original papers, review articles, important materials and documents, continuous course for ethics committees' members, letters to the editor and book reviews. Original research and review papers published in the journal are peer-reviewed and they must abide to the usual international standards. The journal was founded in 1994 by the Institute of Medical Ethics and Bioethics Foundation. During the early years of its existence, editing of the journal was related to the scientific and professional activities of the Institute of Medical Ethics and Bioethics, the joint centre of the Institute for Postgraduate Education of Health Care Professionals (IPEHCP) and the Faculty of Medicine of the Comenius University (FM CU) in Bratislava.

ISSN 1335-0560

Included into Medline ™ and Bibliographia medica slovaca
www.bioetika.sk, www. bioethics.sk

PRINTED IN SLOVAKIA

SANOFI,

DIVERZIFIKOVANÝ GLOBÁLNY LÍDER V OBLASTI ZDRAVOTNEJ STAROSTLIVOSTI SO ZAMERANÍM NA POTREBY PACIENTOV

Naša stratégia je založená na troch kľúčových princípoch: **nárast inovácií v oblasti výskumu a vývoja, využitie externých príležitostí umožňujúcich rast, adaptácia modelu spoločnosti na budúce výzvy a príležitosti.**

Silné stránky spoločnosti Sanofi spočívajú v nasledovných siedmich platformách rastu: **liečba diabetu, humánne vakcíny, inovatívne lieky, zdravotná starostlivosť o spotrebiteľa, nové perspektívne trhy, zdravie zvierat a nový Genzyme.**

Naša spoločnosť, s viac ako 110 000 zamestnancami v 100 krajinách, koná spolu so svojimi partnermi tak, aby **chránila zdravie, zlepšovala život a odpovedala na potenciálne potreby v oblasti zdravotnej starostlivosti siedmim miliardám ľudí po celom svete.**

Vydané: jún 2013

Viac informácií nájdete na: **www.sanofi.com**
www.sanofi.sk

sanofi-aventis Pharma Slovakia, s.r.o.
Einsteinova 24 - 851 01 - Bratislava - Slovenská republika
Tel.: +421 2 33 100 100 - Fax: +421 2 33 100 199

SANOFI