

INFORMED CONSENT IN PSYCHIATRIC RESEARCH – CONCEPTS AND CHALLENGES

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SUMMARY

Research involving vulnerable population of mentally impaired persons is raising considerable controversies from its very beginnings. These controversies are created around everlasting tensions between two positive duties: the duty to protect vulnerable subjects, and the duty not to deny them potential benefits. Most of the contemporary ethical guidelines and regulations, including most recent revision of the Declaration of Helsinki, permit these researches under certain ethical conditions. The notion of informed consent as a cornerstone of bioethics emerges as essential requisite of moral research. We are presenting some key concepts and safeguards regarding informed consent that researcher needs to be aware of when conducting a research involving mentally impaired persons. Theoretical and practical challenges that are arising from these safeguards are discussed with an overview of most recent scientific data. Lastly, we briefly address the most important legal standings that will be introduced in 2015, by new Croatian Law on the Protection of Persons with Mental Disorders.

Key words: *clinical research - clinical trials - research ethics - informed consent – psychiatry - mental capacity*

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Introduction

Fifty years of World Medical Association's Declaration of Helsinki, a critical statement of ethical principles for physicians doing medical research, will be marked in July 2014 (Carlson et al. 2004). The level of scrutiny of medical research with human subjects, necessary for improving the therapy outcome, has risen over the last few decades when numerous legal protective measures have been implemented. Last October, ethical issues in psychiatric practice, as well as in psychiatric research, have again received the attention of Croatian psychiatrists after new Law on the Protection of Persons with Mental Disorders had been presented by Ministry of Justice. Such legal protection is necessary, considering the fact that psychiatric patients are more vulnerable than others because their mental disorders can impair their cognition, social interaction, critical judgment or understanding of the reality (Capron 1999, Roberts 2002). A clearer understanding of research ethics, announced in the new law that goes into effect on January 1st 2015, is necessary when clinical investigators plan to conduct the therapy research on potentially cognitively diminished participants. In this paper the authors will investigate some procedural challenges considering the implementation of written informed consent to clinical research, a basic safeguard for human subject protection, to clinical psychiatric practice.

Historical Emergence

The discourse of informed consent was built primarily through the languages of law and moral philosophy. It's history can be traced back to US

Supreme Court case of *Schloendorff v. Society of New York Hospitals* in which Justice Benjamin Cardozo stated that "every human being of adult years and sound mind has a right to determine what shall be done with his body" (Schloendorff 1914.). In these earliest stages of "the doctrine of informed consent" emphasis was put on traditional duty to obtain consent to invasive treatment what gradually evolved to duty to disclose certain types of information, meaning that consent should not only be free, but also informed. In its last stage of development the quality and standards of disclosed information are stressed, requiring that information is presented in the way that reasonable person would find it material for making autonomous treatment decision that is consistent with his or her values and preferences (Faden et al. 1986, Berg et al. 2001). Its historical evolution is still reflected throughout two different meanings of informed consent: the autonomous authorization, and legally and institutionally effective approval (Faden et al. 1986).

The first attempt to reconcile insatiable scientific ambition with the protection of human subject's rights is the Nuremberg Code, the key document in the history of the ethics of medical research (Shuster, 1997). Formulated in 1947 after the horrors of World War II, it is the starting point of all subsequent ethical and legal documents covering the experiments with human subjects. Among the 10 research principles in the Code, centered not on the researcher physician but on the research subject, the crucial elements of the first three should be emphasized:

- The voluntary consent of the human subject is absolutely essential;
- The experiment should yield necessary results unprocurable by other means of study; and

- The experiment should be based on knowledge of the natural history of the disease or other problem (Pincus et al. 1999).

The principle of informed consent regarding medical research was elaborated and expanded in World Medical Association's (further in text WMA) Declaration of Helsinki, a document that has risen to a guiding statement of ethical principles for medical researchers (Carlson et al. 2004). The biggest contribution, at that time, of the Declaration was the differentiation between therapeutic research, one that can "promote the health of the group represented by the potential subject" or the subjects themselves, and other research (non-therapeutic) in which no health benefits of the subjects are to be expected. In the latter case, personal informed consent is mandatory, while in the former case it can be given by a legally authorized representative if the subject "is incapable of giving informed consent." (Berg et al. 2001)

Declaration of Helsinki has been extensively revised several times, with the last important changes being adopted in Fortaleza in October 2013. In the introduction Declaration defines the research on human subjects emphasizing the obligation of physicians to hold the subject's health a priority: "It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research." Physician must take special care of groups or subjects "that are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm." (WMA, 2013).

Informed Consent in Concept and in Practice

The issue of informed consent becomes a priority in contemporary research ethics with the specially concern over vulnerability of certain groups of subjects (Welie & Berghmans 2006, Gupta & Kharawala 2012). Last 20 years the number of ethical, legal and medical papers concerning obtaining informed consent in psychiatry and psychiatry research grew exponentially. So, in only two decades this issue became the greatest present challenge, unfortunately, with no universal concept. Under current Croatian statute, the possibilities for research involving subjects with diminished cognitive capacity are limited, but not completely excluded. Article 3, Paragraph 2 of the Law on the Protection of Persons with Mental Disorders says: "Consent is freely given approval by a person with mental disorder, for conducting the medical procedure [research], based on the appropriate knowledge of the purpose, nature, consequences, benefits and risks of medical procedure and other treatment options." (Republic of Croatia Ministry of Justice 2002)

Valid informed consent is considered to be a procedure that ensures direct communication, enabling

patient's (human subject) autonomous decision whether to take part in therapy (research). It is both, verbal description and discussion of all the details of the research process, as well as written information form with all the relevant, understandable information.

Informed consent must have the following elements:

- A statement with an explanation of the purposes of the research and description of the procedures to be followed / of the medicine that is going to be tested, and an identification of any procedures which are experimental.
- A description of any reasonably foreseeable risk, discomfort or disadvantages to subjects.
- A description of any benefits to the subject or to others which may reasonably be expected from the research avoiding inappropriate expectations.
- A disclosure of appropriate alternative procedures for treatment/diagnosis if any, that might be advantageous to the subject.
- A guarantee of a certain level of confidentiality.
- If research goes beyond the level of minimal risk to subjects, description of the available compensation or treatment in case of damage of any sort.
- Contact details if more information regarding the research or subject's rights are needed, including contact details in the event of damage suffered.
- A statement that participation is voluntary, that the refusal to participate or withdrawal of consent will bring no consequences regarding patients' treatment. (US Code of Federal Regulations, 1993).

Therefore, informed consent can be defined as researcher's obligation to inform potential participants about possible risks, the importance of research for the advancement of knowledge and the human welfare, and about the risks to the human subject, based on his/hers best knowledge and conscience. In short, informed consent implies researcher's most sincere effort to honor the autonomy of human subjects while considering possible participation in the research having in mind that welfare and rights of a subject participating in research are always above the pursuit of scientific and social interests.

To be legally and morally valid informed consent has to be based on the disclosure of appropriate information to a competent subject who is in a position to make voluntary choice. In other words, it has to be premised on three essential components including: decisional capacity (competence), voluntarism, and information disclosure (Dyer & Bloch 1987). The one of our special interest is related to the presence or the absence of decisional capacity. The decisional capacity is consisted of understanding the relevant information (factual understanding), rational manipulation the information (logical reasoning), communication or evidencing a choice, and appreciating the significance and meaning of the decision made (Appelbaum & Grisso 1988). One's mental abilities should be

considered preserved until serious medical reasons bring that to question (“assumption of competence”). We must add that no diagnostic category implies mental incapacity, although it is clear that certain disorders are connected with more frequent cognitive impairment. The recent studies have shown that there is much stronger and consistent correlation between cognitive impairment and decisional capacity than there is with psychopathology (Carpenter et al. 2000, Kovnick et al 2003, Palmer et al. 2004). It could be summarized, although there are some heterogeneous data, that among psychiatric disorders schizophrenia and bipolar disorder have a stronger correlation with impaired decisional capacity than depression (Grisso & Appelbaum 1995, Vollmann et al. 2003, Palmer et al. 2007). The lack of insight has been reported to be the strongest predictor of decisional incapacity among psychiatric patients (Cairns et al. 2005, Capdevielle et al. 2009).

Although there are no clear guidelines regarding assessment of decisional capacity, many authorities have recommended its evaluation, particularly when dealing with clinical studies involving greater (“more than minimal”) risks (American Psychiatric Association 1998). Policies and classification criteria about acceptable risk in proportion to impairment are implemented elsewhere, and such rules should be transferred and applied (American Psychiatric Association 1998). Generally speaking, it is proposed, that the principle of proportionality (“sliding scale”) should be applied: the higher standards of decisional capacity are needed as the risks of potential participation increases, and potential benefits decreases (Drane 1984). Therefore the costly and time-consuming evaluation by the independent forensic expert should be reserved for the vague cases and for the research with potentially high risks to potential subjects, and the criteria for diminished mental capacities must be in proportion with risks. These tendencies, steered to uniform and objectify task-specific assessment methods in scope of informed consent in research, gave rise to the MacArthur competence tool (MacCAT) as having the most empirical support and the most representative psychometric characteristics (Sturman 2005, Dunn et al 2006b). We must add that the current provisional “gold standard” regarding categorical capacity determination still are clinician judgments, especially in terms of ethical validity. The reliability of clinician judgments are scientifically unproven as produced data is showing mixed results (Marson et al. 1997). The education for psychiatric forensic experts needs to address these specific issues in more depth.

The crucial question still remains: what extent of understanding, both in qualitative and quantitative sense, is required to make a competent decision?

Another previously mentioned prerequisite that needs to be fulfilled for ethical and valid informed consent is voluntarism. Voluntarism is defined as *the ability of an individual to act in accordance with one's*

authentic sense of what is good, right, and best subjected of one's situation, values, and prior history. It involves the capacity to make this choice freely and in the absence of coercion (Roberts 2002). Subject's capacity of voluntarism can be influenced by developmental factors; illness related factors; psychological issues and cultural and religious values; and external features and pressures (Roberts 2002, Geppert & Abbot 2007).

Another notion that is important to underline, and it frequently evinces during medical research in general, is therapeutic misconception. This occurs when research subject is falling to appreciate the difference between research and usual (routine) clinical care (Appelbaum et al. 1982, Henderson et al. 2007.). Concerning general research population (not exclusively psychiatric) it is most commonly associated with lower education levels, older age, and worse self-described health (Appelbaum et al. 2004). The most commonly recorded misperceptions are regarding individual care, receiving most beneficial treatment, and procedures unique to research (e.g., randomization) (Lidz et al. 2004, Dunn et al. 2006a).

Helsinki Declaration is clear regarding including capable human subjects: “No individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.” (World Medical Association 2013) However, mentally impaired individuals are not necessary excluded in a research: “For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.” (World Medical Association 2013)

“Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.” (World Medical Association, 2013)

Informed consent may be given by patient's legal representatives or ethics committee (“surrogate or proxy

decision making”). Surrogate decision makers should, whenever possible, make their decisions based on “substituted judgment” standard (what subject would choose if he/she could). “Best interest” standard (objective standard based on community norms), should be used if the values of concerning individual are not known (Torke et al. 2008). Ethics committees are crucial for addressing these additional safeguards and monitoring research in psychiatric institutions and should be comprised of the well-educated experts that maintained high ethical standards in their professional life and acting to the best of their knowledge and belief, respecting the principal interests of subjects in the difficult cases. When the potential risk of severe violations of human rights exists, both of the institutes replacing personal informed consent must adhere to judicial decisions.

Information disclosure

Finally, we return to the information, substance of informed consent. In this case, it is more the rule than the exception that modern physicians fall into pitfalls considering the communication with patients (Lavelle-Jones et al. 1993, Scheibler et al. 2003, Vučemilo et al. 2013). After long history of paternalistic relationship (that still permeates in some aspects of medical treatments), swiftly came egalitarian principle that is in theory ethically desirable, but is seriously malfunctioning in practice. There is also a lack of consensus regarding the quality and quantity of information that should be disclosed during informed consent process (Osborn 1999). Researchers, as well as clinicians should be guided by three different and overlapping standards while disclosing information 1) professional practice standard – which requires disclosure of the information that a reasonable professional (physician) in similar situation would disclose, 2) reasonable person standard – which requires disclosure of the information that a reasonable person (patient) would find material for a decision, and 3) subjective standard – which requires acknowledgement of person’s specific informational needs during information disclosure (Beauchamp & Childress 2009).

Scientific literature shows that subjects’ understanding can be enhanced by modification of disclosure procedures such as using various educational and informational techniques (Eyler & Jeste 2006). The most commonly used techniques include education regarding the study protocol, repetition of important information, using different aids such as video-assisted presentation or explanatory tools (Wirshing et al. 2005, Dunn et al. 2001), and using interactive questioning method (Eyler et al. 2005).

New Legal Safeguards

Fifteen years after establishing the Law on the Protection of Persons with Mental Disorders, Croatian

legal experts have proposed a new one (Republic of Croatia Ministry of Justice 2014). The new law introduces establishing National Board for the Protection of Persons with Mental Disorders that will, after reviewing the ethical acceptability, approve proposed clinical research on psychiatric patients. The statute also includes another new safeguard: informed consent for biomedical research cannot be given by a legal representative or person of their trust. Although this safeguard stresses an important possible conflict, we consider it to be too rigid and regressive. The proportion of personal suffering and public health consequences of mental illness create an ethical and societal imperative to perform scientific studies on its etiology, treatment, and prevention that cannot be extrapolated by research in other groups. The legislative frame should encourage and create opportunities to decrease the burden of such diseases (Michels & Marzuk 1993a, Michels & Marzuk 1993b, Hyman 1999, Miller 1999). More elaborated discussion of these issues goes beyond the scope of this article.

In brief, many questions about informed consent in psychiatry remain open, both considering the theory and the implementation in clinical research. Psychiatric ethics is a young discipline that has to coexist with the legal system, and translating theoretical concepts to operational rules needs continuous, uninterrupted ethical feedback which is the obligation to modern times.

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