Special issue

Informed Consent, Experimentation and Emerging Ethical Problems

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ABSTRACT: Obtaining informed consent for experimentation takes on a central ethical role. This article analyses, on the basis of the historical origins of informed consent, its present role in bioethics and discusses the main ethical theories on the topic, in a pluralistic philosophical context. The author underlines the reason why informed consent should not be a detailed technical and exhaustive description of a clinical study with the exclusive aim to defend the investigators rather than protect the subjects who have been recruited. The article identifies the main ethical requirements of informed consent from the side of the researcher and of the participant, underlining the emerging ethical issues (dynamic informed consent; personalization; technological innovation; comprehension verification; physician's training in communication; health literacy for participants) and the emerging challenges (broad and flexible consent; enhanced consent; shared consent).

KEYWORDS: Bioethics; experimentation; informed consent; personalization; technological innovation

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1. Informed consent and experimentation

The specific function of 'informed consent' is to provide an instrument to guarantee the doctor-patient relationship: it is an explicit expression and authorization given by the patient to accept (consent) or refuse (dissent) treatments offered by the doctor[1].

The principle of the obligation of the investigator to ask a subject to consent to participate in a clinical study after providing detailed information regarding the purposes and methods of its execution and the possible benefits and risks inherent in participation, was introduced in 1947 from the Nuremberg Code. It derives from the sentence that the International Tribunal issued in that city on 19 August 1947 at the end of the trial against the Nazi doctors who had carried out criminal experiments in concentration camps on prisoners of war as well as women, children and persons with disabilities in a state of total unawareness[2]. This principle was later accepted by the 18th World Medical Association General Assembly held in Helsinki in 1964 in the Declaration of Helsinki (and subsequent revisions), which constitutes the ethical code of the researcher. While the Nuremberg Code still left the request for consent within the context of the direct deontological relationship between doctor and patient, the Declaration of Helsinki introduced for the first time the principle of the need for an additional external guarantee provided by the oversight of an independent committee, responsible for examining the study protocol and possibly providing feedback and suggestions to the investigator.

Even in subsequent documents, from the development of guidelines on clinical practice of the Council for International Organizations of Medical Sciences (*International Ethical Guidelines for Biomedical Research Involving Human Subjects*, adopted in 1993 with subsequent revisions) to *Good Clinical Practice* approved by the International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use in 2002 to the documents with importance at International and European level, binding to varying degrees. (*Charter of Fundamental Rights of the EU,* 2000, Article 3, Council of Europe, *Convention on Human Rights and Biomedicine,* 1997, Article 5 and *Additional Protocol concerning Biomedical Research*, 2004, UNESCO, *Universal Declaration on Bioethics and Human Rights*, 2005, Article 6, *the European Union Regulation* No. 536/2014 of 16 April 2014 on the clinical trial of medicinal products for human use, which repeals Directive 2001/20/EC), which today constitute the main regulatory reference for experimentation on humans, make explicit reference to informed consent.

Above all, it is in the field of human experimentation that informed consent has a particularly important role to play. Experimentation is essential in the context of scientific research to advance knowledge for the possible treatment of diseases. The purpose of experimentation is in itself good, as it aims to improve the conditions of human health and well-being, but the constitutive uncertainty (experimentation means 'trying' or 'testing'), the difficulty in quantifying and predicting *a priori* the possible risks balancing them with respect to the desired benefits, the certainty or probability that

[1] In clinical practice, informed consent is required with regard to treatments (for diagnosis, therapy, rehabilitation) that have a certain degree of invasiveness on the body, and is considered implicit in cases of non-invasive treatments.

[2] R.R. FADEN, T.L. BEAUCHAMP, *A history and theory of informed consent*, New York, 1986. R.R. FADEN, T.L. BEAUCHAMP, *The concept of informed consent,* in T.L. BEAUCHAMP, L.WALTERS, J.P. KAHN, A.C. MASTROIANNI (Eds.)*, Contemporary issues in bioethics*, 7th ed., 2008, pp. 166–170.

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the benefits for the subject involved in the experimentation may not be direct, but only indirect, or even only probabilities projected into the future, make this practice full of problematic elements that require adequate moral reflection, in order to protect human beings, their dignity and fundamental rights[3].

It is between the radical techno-scientism of a libertarian and utilitarian kind, which pushes towards experimentation 'at any cost', with a technophilic blind faith and optimism in the benefits, and extreme anti-scientism, which blocks and obstructs research in a pessimistic and technophobic manner for fear of the negative effects, that bioethical reflection has consolidated a shared stance on certain limits of licitness in human experimentation. Although the context of constitutive moral pluralism in the bioethical debate continues to give rise to theoretical discussions and various practical interpretations, reflection on human experimentation has developed some common lines, at the bioethical and bio-legal levels, allowing for the configuration of a national and international legislative framework of reference (both soft law and hard law) with some common ethical principles and criteria, deemed particularly important in the context of human experimentation. Informed consent is, specifically, among these criteria.

When reference is made to informed consent, we generally think of a document drawn up in written form that presupposes and implies the precise modalities of the relationship between doctor and patient: the doctor has the duty to inform the patient about experimental treatment; the patient has the right to be informed and express (or not express) consent to the medical act[4]. Information is the condition for the structural possibility of consent: without information, consent is not possible. Consent is the condition for the structural possibility of experimentation: without consent and against consent the researcher cannot conduct experiments.

Historically, the ethical requirement for informed consent has arisen from events that shed light on experimentation carried out only for the good of science but 'against' human beings, human beings not being adequately respected in their dignity, used in an unconscious way only as a means and not also as an end. The experiments of Nazi doctors were an extreme historical example, like other events, which stimulated the birth of bioethics.

2. A comparison of bioethical theories: doctor/patient contract and doctor/patient alliance

The binomial “information/consent” is used in different ways according to the model of medicine and concept of ethics which it makes reference to. Informed consent marks a shift from a 'paternalistic' model of medicine to a model which values patient autonomy. Paternalism was an authoritarian model of medicine which considered the doctor to be the depository of knowledge, being in a position of dominance/power and superiority, while the patient was placed in a position of subjection and inferiority. In accordance with this perspective, the doctor decided 'for' the patient, imposing his/her will without offering explanations, without listening to the needs and desires of the patient,

[3] Italian Committee for Bioethics, *Drug experimentation,* 1992. Unesco International Bioethics Committee, *Report on informed consent*, 2008.

[4] If the right not to be informed is foreseen in the informed consent related to clinical practice, this right does not exist in experimentation.

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ignoring inclinations and subjective perceptions. This model, at least in Western societies, is criticized on the ground that the doctor does not have arbitrary dominion over the patient's life and health and that the patient is not merely a passive instrument, but an active subject who must participate and be involved in a fully informed way in the decision.

The paternalistic model is opposed to the 'contractual' model that considers the doctor and the patient to be moral agents and free contractors. This model of medicine falls within a liberal-libertarian concept of bioethics, which on a non-cognitivist basis (the assertion that objective truth is not knowable) as well as on an individualistic basis (the affirmation of free subjective decision even in relation to moral values), believes that patient self-determination, whatever that may be, must be placed at the centre.

In this perspective, the doctor must inform the patient in a detailed and neutral manner, limiting himself/herself to presenting the range of alternative options, leaving the autonomy of choice to the patient or, if anything, helping the patient to interpret the best choice consistent with his/her beliefs (all deemed to be acceptable, in an equivalent manner). It is an impersonal model, which reduces the doctor to health counsellor and the patient to user, resulting in the overthrow of paternalism, attributing a prevalence to the patient's will and reducing the doctor to passive executor of the will of others. In this sense, contractual medicine re-proposes a unilateral and hierarchical model (analogously to paternalism), overturning its parts. On a contractualist view, consent is understood as a merely formal procedure for registering the patient's self-determination (whatever it may be).

This view of informed consent has been subjected to criticism, grounded, on one hand, in the supposedly unreal assumption of symmetry between doctor and patient or in the abstract condition of full mental clarity and self-referentiality of the patient in the decision, and on the other, in the unavoidable trend towards the shunning of therapeutic responsibility on the part of the doctor and the drifting towards a medicine known as “defensive medicine or defensive medical decision-making”. In this direction, a change in the meaning of informed consent would be introduced with respect to its original meaning, leading the doctor/researcher to act or not act in his/her own interest and not in the interest of the patient, in order to prevent accusations of *malpractice* and consequent legal sanctions.

In contrast to paternalistic and contractualist medicine, there are several lines of thought upholding the key importance of dialogue and the relational dimension, precisely in informed consent, recognizing - albeit the patient's constitutive asymmetry in relation to the doctor, given the former’s position of scientific incompetence and vulnerability in sickness - a 'therapeutic alliance' or 'therapeutic relationship' that is outlined in the personal encounter and common commitment to health care.

According to the relational model of therapeutic alliance, information does not end with the description of the facts, but it integrates with counselling in the form of advice that urges the patient to become aware of problems, to elaborate a reasoned and not an emotional choice, facilitating a decision-making process through dialogue as a dialectical and communicative interaction, aimed at identifying a common goal. This model places the patient at the centre as a person, considered in his/her dignity *per se*, and supports the ethical duty as well as the deontological duty of the doctor to treat and care for the sick person and respective fragility, especially in the context of experimentation, within the development of scientific research, given the condition of uncertainty in the benefit-risk

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balance. It is in this context that the bioethical relevance of the Hippocratic paradigm strongly re-emerges: it is a matter of acknowledging that the relationship with the patient is a structural part of the medical act and of the experimentation itself[5].

The individual, whether healthy or sick, male or female, adult or minor, whatever the cultural affiliation or concept of religion, who freely participates in research is not a mere object manipulated or used as a tool to accomplish goals that are to him or her unknown. Ideally, this is an individual who cooperates in solidarity to the improvement of medical treatment and to the progress of scientific knowledge that will have possible future benefits for mankind.

In this sense, informed consent is therefore a fundamental ethical requirement in experimentation; it expresses, on one hand, the therapeutic responsibility of the researcher towards the subject and, on the other, it develops a broader participation of the patient in the decisions concerning him/her. It cannot and must not be reduced to a mere "form" to be filled out with indifference by the researcher and hastily "signed" by the subject, in order to comply with purely bureaucratic requirements. A form of this kind, even if carefully prepared, could never cover all the unpredictable situations related to the experimental-clinical reality and risks impersonally proceduralising the relationship and distorting the relational and interpersonal constitutive meaning of informed consent, which is aimed at protecting the health of the subject.

In the field of bioethical reflection, both in scientific discussion and in the deliberations of international, European and national bioethics committees, several 'ethical requirements' have been elaborated, and are explicitly being refined, which set out the conditions for a practical implementation of informed consent, being more consistent with its original authentic meaning in the relational-dialogical context[6].

3. Ethical requirements for informed consent in experimentation

The existence of the patient's informed consent is not in itself sufficient to make a study "ethical": it is also a matter of verifying 'how' informed consent is given. The informed consent form *is a neces-*

[5] This is the stance of the Italian Committee for Bioethics: "The legitimation and basis of medical treatment is, at the same time, an instrument to realise the search for a therapeutic alliance - within the law and deontological codes - and the full humanisation of the doctor and patient relationship, to which today's society aspires"; "The information is aimed not at filling the inevitable gap in technical knowledge between doctor and patient, but at placing a subject (the patient) in the condition to carry out his or her rights in a correct way and hence to express a will that is in fact his or her own; in other words, to put him or her in the situation to choose" (ITALIAN COMMITTEE FOR BIOETHICS *Information and consent related to medical acts,* 1992).

[6] J.W. BERG, P.S. APPELBAUM, C.W. LIDZ, A. MEISEL, *Informed Consent: Legal Theory and Clinical Practice*, 2nd ed, New York, 2001. P.J. CANDILIS, C.W. LIDZ, *Advances in informed consent research*, in F.G. MILLER, A. WERTHEIMER (Eds.), *The Ethics of Consent: Theory and Practice*, New York, 2010; J. KLEINIG, *The nature of consent*, in F. G. MILLER, A. WERTHEIMER (Eds.), *The Ethics of Consent: Theory and Practice*, New York, 2010; N.C. MANSON, O. O'NEILL, *Rethinking Informed Consent in Bioethics*. Cambridge, 2007.

sary but not sufficient element, if it is not accompanied by fundamental requirements[7]. The elements of ethically authentic informed consent are[8]:

3.1. Information as a process of empathetic communication of the doctor/researcher

Information from the doctor/researcher and the healthcare team (on the aims of the study, methodology, risks and benefits, alternatives, revocability of consent, privacy protection) must be correct and scientifically and technically comprehensive, as well as informative and understandable, without becoming too superficial. Excessive technicality, on one hand, and excessive simplification, on the other, do not allow the subject to gain a proper understanding.

Information must not be the mere technical and cold transmission of data and news in a detailed way, but it must redress the inevitable difference in knowledge between researcher and research participant, placing the subject in a position not only to receive information but also broaden knowledge and gain awareness. In this sense, information is and must also be a *dynamic process* of interpersonal communication, which is achieved through the modality of interaction between doctor/researcher and patient/research participant, certainly not reducible to a single encounter but achievable through a regular, constant and continuous relationship, called for by the doctor/researcher and requested by the patient/research participant, in order to create a relationship of trust suitable to facilitate communication. It is seldom possible to provide full information in a single meeting[9]. A new consent is indispensable, especially if the research continues in different directions.

Communication must also be *humanly sensitive*, ethically aware with regard to sick subjects, who face uncertainties and risks in participating in research. Information calls for a substantial understanding of the experiences, hopes and fears of those who suffer and therefore the doctor/researcher is required to possess and cultivate certain human qualities or empathic virtues (the ability to listen and dialogue, psychological sensitivity, the trait of delicacy) which enable them to perform their professional duties giving special attention to the subject, who must always have a central role.

It is necessary to reconcile the subject's right to know what participation involves in terms of potential benefits and risks with the amount of available knowledge (which is often scarce in the early stages of development of a new drug) and with the patient's real possibility of understanding, and avoiding fuelling unjustified and excessive/unreasonable expectations or unnecessary anxieties and fears in the subject, not commensurate with the real benefits and risks.

[7] President's Commission For The Study Of Ethical Problems In Medicine And Biomedical And Behavioural Research, *Making Health Care Decisions: A Report on the Ethical and Legal Implications of Informed Consent in the Patient-Practitioner Relationship*. Washington, D.C., 1982.

[8] C. Grady, *Enduring and emerging challenges of informed consent*, in *The England Journal of Medicine*, 26, 2015, pp.855-862.

[9] S. Joffe, R.D. Truog, *Consent to medical care: the importance of fiduciary context*, in F. G. Miller, A. Wertheimer (Eds.), *The Ethics of Consent: Theory and Practice*, New York, 2010. F. G. Miller, *Consent to clinical research*, in F. G. Miller, A. Wertheimer (Eds.), *The Ethics of Consent: Theory and Practice*, New York, 2010. F.G. Miller, A. Wertheimer, *Preface to a theory of consent transactions: beyond valid consent*, in F.G. Miller, A. Wertheimer (Eds.), *The Ethics of Consent: Theory and Practice*, New York, 2010.

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3.2. The personalization of information

Informed consent must not be reduced to a standard form with few variations depending on the context, instead, it should be thought out in an appropriate manner (tailored consent) with regard to the different specific needs of patients and subjects, or at least of homogeneous groups of patients.
The theory of the "reasonable person standard"[10] (distinct from professional practice and the patient's subjective standard), that is, assuming a reasonable standard person as a useful model adaptable to the prevailing circumstances in which a reasonable person can find himself/herself, is difficult to apply in specific situations of particular vulnerability or cultural difference.
There is increasing awareness, in bioethical and bio-legal reflection, of the need for specific attention to be paid to the differentiation of subjects on the basis of age (minors, the elderly), sex (men, women during fertility, pregnancy, breastfeeding), ethnic group (according to cultural and/or religious diversity), conditions of awareness in relation to pathologies that compromise *consciousness* (e.g. people with dementia), emergency conditions (we talk about deferred consent).

3.3. The understanding of information by the patient/research participant

Information must be neither excessive nor minimal, but sufficient for the patient/research participant, and above all it must be *fully understood*. The information communicated to the subject must make him/her aware of the significance of the experimentation and what participation actually entails (also in terms of commitment and responsibility) and verify the subject's critical awareness of the potential/possible benefits and risks, as well as the possible consequences of non-participation. It should also be considered that understanding involves not only the rational and intellectual dimension, but also the emotional dimension, connected to individual psychological experience closely related to the pathology.
To ensure the conditions of understanding, it is essential that the information/communication is "adapted" to the specific needs of subjects, with reference to age, sex, cultural and/or religious affiliation. The appropriateness and adequacy of the information is to be evaluated *case by case*, based on the existential, social and cultural context.
It is obviously difficult to say whether it is possible to define the universal characteristics of a "reasonable man" and the breadth of information that he/she would like to receive. It is more logical to think that information must be adapted to the individual subject or at least to groups of subjects, taking into account the numerous personal, social and cultural factors.

3.4. The time and ethical space of information/communication

Information must be provided in a suitable place for communication and the subject must be given adequate and sufficient time to reflect on the contents of the information and decide whether to participate in the study, in *situations of no urgency*.

[10] R.R. FADEN, T.L. BEAUCHAMP, *The concept of informed consent,* cit., pp. 166-170. J.D. MORENO, A.L. CAPLAN, P. ROOT WOLPE, *Informed consent*, in R. CHADWICK (Ed.), *Encyclopedia of applied ethics*, Vol. 2, London/ Sydney/New York, 1998, pp. 687-697.

Informed consent in this sense should also become the place and time of communication and education of the patient to make conscious and responsible choices regarding his/her own health and collective health.
Obviously in cases of emergency, the lack of time for information and communication is to be respected. In these cases, informed consent is unethical; the only possible solution is deferred consent.

3.5. Assessment of the patient/researcher's competence and decision-making capacity

The subject must be in the physical-psychic-social and cultural conditions to be able to decide in a conscious and personal way. Being under age, having a physical and/or mental illness, being in a particular social-cultural condition are factors that can affect the concrete ability and aptitude to make a particular decision. The decision-making competence of a subject should therefore be verified on an individual basis, before, during and after a decision concerning experimentation that is deemed to be significant, particularly those experiments encompassing greater risks and uncertainties.
In order to recognize the capacity of a subject, it is important to examine how the deliberative process takes place. By virtue of this criterion, it is necessary to ascertain whether the subject is truly able to communicate with the doctors, showing outward signs of having understood the information and being ready to decide, with an understanding of the alternatives and their related nature, (alternatives that must be envisaged without the encumbrance of operant conditioning) as well as providing responses endowed with coherence, and persisting in the conclusions expressed.

3.6. Freedom of decision-making and the absence of direct/indirect inducement/coercion

For informed consent to be valid, it must be freely expressed, as far as possible. Freedom with which a subject adheres to a proposal to take part in experimentation can be subjected to external influences and pressures, and at times downright direct/indirect coercion coming from the family or social context, facilities, researchers, sponsors, even through incentives. One of the forms of direct incentive can be given by payment or compensation for the risk taken: this modality is not ethically acceptable, because it would make adhesion to research not authentic. The very statement that those who participate in the study will receive more attention from the doctor or researcher and better opportunities for consideration/treatment, constitutes an 'indirect incentive', especially for particularly vulnerable persons, such as minors, pregnant women, immigrants.
In order to guarantee the free voluntariness of participation, it is essential to exclude relationships of dependency or hierarchy between investigator and research subject that could result in a possible element of psychological coercion. However, it cannot be denied that a patient has a strong psychological dependency on the doctor treating him: patients expect from their doctors a recovery or at least relief from their suffering. Faced with the request to participate in a study, it is inevitable that the patient may fear upsetting the person who is responsible for his/her health and, therefore, the patient can feel somehow obliged to accept.
As a matter of fact, investigations carried out on patients who had participated in clinical trials have shown that the fear of displeasing the doctor, or in any case undermining confidence in their proposals, had been a determining factor in accepting to participate in a very high number of cases, while the real understanding of the study was scarce or had weighed very little on the decision. It is

therefore incontrovertible that in obtaining valid informed consent, a correct and transparent relationship between patient/research subject and doctor-researcher remains the basic element. However, the revocability of consent without adverse consequences for patient care and the possible discontinuation of experimentation for justified reasons by the researcher should always be made explicit.

3.7. The responsibility of the researcher

Researchers should not forget that the personal integrity and well-being of the subjects in the study fall within their main responsibility. The researcher's responsibility must be proportionate to the research risk.
However, the obligations of the researcher towards the research subject are not limited to providing information and obtaining consent. He/she must also, on a regular and continuous basis, share with the subject the data and facts that come to his knowledge during the course of the study, which could modify the subject's willingness to continue to participate (for example: toxicological test results, major adverse events, doubtful therapeutic effects).
The doctor may have a double role: as both treating physician and researcher, with the ensuing possibility of a conflict between ethical obligations, both to treat patients with the treatments he/she considers most appropriate, as well as to perform his/her work with methodological and scientific correctness, in order to contribute to the progress of knowledge. No doctor/researcher should agree to participate in a trial where he/she is required to administer a treatment he/she deems harmful. Doctors/researchers should immediately suspend a study if they are convinced that it is harmful to patients/research subjects[11].

3.8. The rights and obligations of the participant

Informed consent must explicitly clarify the rights and guarantees to protect research subjects, notably the right to refuse to participate and the right to withdraw from a clinical study, at any time, without any resulting detriment and without having to provide any justification. Research participation must be understood as a commitment by the participant who, despite the possibility of revocation, is obliged to meet research conditions, to show loyalty to the researcher. The possibility of discontinuation of the research by the researcher must be made clear and explained.

3.9. The role of the ethics committee

Therefore, the moment in which the relationship between doctor/researcher and patient/research subject also assumes aims of general interest that go beyond the advantages of the single individual, it is inevitable to feel the need for an external, public guarantee, constituted by a third impartial actor, who is the expression and guarantor for the behaviour of the doctor/researcher towards the patient/research subject and the consent of society.

[11] The choice of randomization is particularly complex; this method of experimentation seems in fact incompatible with the possibility of providing the patient/research subject with complete information and therefore of acquiring informed consent. The question becomes even more difficult in the case of comparison with placebo, which is also considered of crucial importance for the evaluation of the pharmacological effect.

This is the concept of "renewal of consent" which expresses the oversight that an Ethics Committee must exercise on the progress of the study, in order to verify that the judgment of ethicality and feasibility given at the beginning does not undergo modifications during conduct of the clinical study.
The recourse to the patient's signature or that of one or two witnesses and approval of the informative material by the Ethics Committee represent the tools that should provide public guarantee that a fair balance between the factors mentioned has been achieved. A copy of the informed consent must always be given to the subject.

4. New modalities and challenges to improve informed consent in experimentation

4.1. Training of the doctor/researcher in communication

Researchers must be able to inform, and at the same time possess sufficient capacity for psychological introspection and empathy, as mentioned above, to enable them to adequately address a variety of complex situations, adapting the communication to the specific condition of research subjects. In order to verify the latter's understanding and effective decision-making capacity, to identify whether consent is given with full conviction and awareness, a capacity, in addition to technical and scientific competence, is required by the doctor/researcher: it presupposes also the willingness to listen, dialogue, and empathize.
The acquisition and development of this skill requires adequate educational programs, even specialized ones, with respect to particular situations that allow doctors/researchers to pursue the goals of their profession and build the therapeutic relationship on trust and mutual respect, beyond specialist fragmentation, so as to allow the recovery of a holistic vision of the patient/research subject, moving beyond technical competence towards human receptiveness.
In this context, there is also the need for the doctor/researcher, who is oriented towards clinical research activities, to receive adequate training in the field of bioethics, aimed at fostering the values of personal relationship with the patient/research subject and allowing the doctor/researcher to understand the authentic meaning of informed consent beyond the merely formal and procedural dimension.

4.2. Information for the sake of education and participation (health literacy)

Proper reception of the information that the doctor/researcher has to convey, requires a level of cultural competence of the patient/research subject that not all subjects necessarily have. In addition, research participants often have to make decisions in difficult psychological conditions, on a personal level, and in these cases not even cultural and/or scientific preparation can be sufficient to use the information received, in order to develop appropriate choices.
The decision to offer patients/research subjects all available information, can hinder or even block the ability to choose, because it may induce in them defensive attitudes when faced with what may seem the prospect of risk, or patients can be induced to demonstrate and experience symptoms or illnesses generated only from knowing of their possibility.
In this sense, the doctor/researcher must know how to assess the quantity and quality of the information to the patient/research subject, tailoring it to the patient/research subject's cultural level,

trying to communicate the information by inserting it in the context of health training and education of the patient (health literacy).
This is an aspect that is becoming increasingly important in our society, due to the emergence of the patient's *responsibility* towards his/her own health[12] and the subject's increasingly essential *participation* in health[13].

4.3. The role of technological innovation in information, education and participation

The latest technological developments can play a substantial and decisive role in the innovation of informed consent methods, to facilitate the process of information, education and participation of the subject.
Within the context of the most recent techno-scientific developments, characterized by the speed and dynamism of the evolution, medicine is also changing. There is talk of a new paradigm of medicine: the so-called 4/5 'P' medicine, or preventive-predictive, personalized, participatory, precise medicine[14]. Medicine is geared to the citizen, with precision as regards the individual, and with an active direct involvement in knowledge. In the era of 'data intensive medicine', in the context of so-called *'big data'*[15] (expression that indicates the enormous quantity of information that can be collected at an increasingly fast speed, also in the field of medicine and health thanks to the developments of the "omics" sciences)[16], new challenges emerge for informed consent, which is beginning to take on new configurations[17].
New technologies can help the researcher to facilitate *communication and understanding* for those belonging to a lower socio-cultural level. Technologies can contribute, through the use of video or animation, to the possibility to grasp concepts and simplify the transmission of complex content through images, diagrams, figures. In this way, information can be more easily adapted to the specificity of the patients, based on their ability to understand.
Furthermore, technologies can offer *tools to verify and ascertain the effective understanding of patients.* The evaluation of the "receptivity" of the patient to the informative talk is generally entrusted to the sensitivity and experience of the doctor. It would be important to have technologies available to help the doctor to verify genuine understanding.

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[12] UNESCO, INTERNATIONAL BIOETHICS COMMITTEE, *Report of the International Bioethics Committee of UNESCO (IBC) on social responsibility and health*, 2010.
[13] EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES (EGE), *New health technologies and citizen participation*, 2015.
[14] M. FLORES, G. GLUSMAN, K. BROGAARD, N.D. PRICE, L. HOOD, *P4 Medicine: how systems medicine will transform the healthcare sector and society,* in *Personalized* Medicine, 10 (6), 2013, pp. 565-576. Medicine understood in this way has the objective of analysing individual variability in the relationship between genetics and the environment, with reference to the biography of the individual and lifestyle and increasing the effectiveness of treatments, reducing the risks in taking a specific drug.
[15] The 'volume' indicates the enormous amount of data; 'speed' refers to acceleration in data generation and data processing; the "variety" highlights the heterogeneity of the sources (computers, mobile phones, internet, sensors and mobile devices); the "veracity" underlines the possible authenticity of the data. The "value" of the data should also be added, understood as the relevance and significance in the current context.
[16] ITALIAN COMMITTEE FOR BIOETHICS, *ICT, big data and health: ethical considerations*, 2016.
[17] N.C. MANSON, O. O'NEILL, *Rethinking informed consent in bioethics*, Cambridge, 2007.

In addition, technologies can improve the *participation* of the subject in the research, through the availability of ICT platforms that provide informative material to research participants, allowing them to maintain continuous contact with the subjects in an interactive way (offering information and receiving information, being able to provide updates to subjects, modify or confirm participation in the research) and share research results with them *(benefit sharing*). This allows for the so-called *'empowerment*' of research subjects, increasing their knowledge and information (so-called *enhanced consent*) and their active participation, and it equally enables constant monitoring of the research (both by the doctor and participant), as well as pharmacovigilance during and after the study and social dissemination of results.

In this way, it is the individual himself/herself who can choose the level of complexity of the explanations and information (*tailored consent*); consent adapts to the preferences of the subject, including also the possibility to choose the type of consent preferred (broad or limited). It is the possibility to inform and educate the subject/patient to understand the paths of the research and to have the, continuously updated, tools of comprehension to be able to make an informed decision, to tackle disinformation and unconscious decisions. The opportunity for *shared consent* also opens up (sharing consent): with participation and co-sharing, or the interactive and reciprocal sharing of research results with other subjects/patients, in the same condition, and all those who may derive benefit from them. Aware of the fact that there are risks for privacy and confidentiality in giving and sharing data.

In this context, there is an emerging ethical need for digital users to control data management in general and health data in particular, in a transparent manner. Who is collecting and who will use the data, what data, how are they collected, where are they stored, for how long, for what reason and purpose (health and/or commercial purposes) should all be clearly specified, together with the possibility of revocation without negative consequences, rectification or integration or deletion of data (so-called 'right to oblivion' or right to cancellation, the right to be ignored/forgotten).

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