The Role of Informed Consent in Clinical and Research Settings

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KEYWORDS
- Informed consent
- Capacity
- Competence
- Autonomy
- Patient-physician relationship
- Decision-making
- Health care communication

KEY POINTS
- Informed consent is grounded in the principles of autonomy and respect involving a mutual understanding of the diagnosis, available treatment options, and consequences of opting for these different options.
- Informed consent should be provided by a capacitated patient or their proxy except for life-threatening emergencies where seeking consent would delay necessary treatment.
- For informed consent to be legally and ethically valid, patients must receive the necessary disclosures for decision-making, voluntarily give consent, and comprehend the information being communicated.
- Educational barriers, changing demographics, and advances in data technology are some of the most pressing challenges encountered during the process of obtaining informed consent.

Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient’s consent commits an assault, for which he is liable in damages.

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INTRODUCTION

Informed consent plays an integral role in the patient-physician relationship. In this article, the authors present the concept of informed consent in 4 parts. First, they provide a brief history of the genesis of informed consent in clinical and research settings. Second, they describe the assessment of patient’s capacity, the necessary first step in the informed consent process. Third, they explain the process of obtaining valid informed consent. Finally, the major contemporary challenges to the informed consent process are presented.

History

The foundational concepts of the informed consent process in modern medicine date back to ancient Greece. Some modern medical ethicists believe that ancient Greeks adopted a paternalistic approach to the patient-physician relationship, which entails making decisions without explicit patient consent. However, there is considerable evidence from Cos school around 400 BC including On Ancient Medicine, The Sacred Disease, Aphorisms, On Wounds in the Head, and The Oath that proves the contrary: ancient Greek physicians interacted with patients based on honesty and trust.

Several cases in the last century have shaped current widespread adoption of informed consent as the only ethical standard of care for clinicians and researchers. Fig. 1 summarizes 4 major cases that laid the legal foundation of informed consent in the United States.

Although these 4 cases established the importance of patients consenting to interventions by physicians, the notion “informed consent” as a legal duty was first mentioned in 1957 in Salgo v. Leland Stanford Jr. University Board of Trustees. The patient in this case was left paralyzed after translumbar aortography. Because the surgeon did not inform the patient about the potential risks associated with aortography, a California Court of Appeals ruled for the patient. Although consent had been obtained, the doctor did not provide the patient with the necessary information needed to make a decision; the standard of informed consent had not been met.

Informed consent is also a cornerstone of ethical medical research. One major historical event that highlighted the dangers of unethical research conduct was the USPHS Syphilis Study at Tuskegee. In 1932, 600 men—399 with syphilis, 201
without—were enrolled in a natural history study. By 1943, penicillin was the treatment of choice for syphilis, but the participants of that study were not informed that they had syphilis and were not offered treatment. This study highlights that informed consent is time specific (Box 1). Multiple advisory panels and governmental services have since condemned this unethical study and organized support for the study survivors and their families.

Another example of unethical research atrocities occurred during World War II, where German physicians conducted pseudoscientific medical experiments using thousands of concentration camp prisoners without their consent. In the 1947 Nuremberg Medical Trial, these doctors were indicted for their ruthless behavior, and 16 of 23 doctors were sentenced to death.

The Nuremberg Trial resulted in the establishment of 10 principles for conducting research on human subjects which became the famous Nuremberg Code. The Code’s first principle is that “the voluntary consent of the human subject is absolutely essential.” The Code also establishes that valid consent is voluntary, competent, informed, and comprehending. Following the Nuremberg Code, the Declaration of Helsinki was drafted to serve as a nonlegal guide to doctors in the conduct of ethical research. Although there have been multiple revisions and controversies regarding the distinction between informed consent for therapeutic and nontherapeutic research, the Declaration provided early guidance for conduct on ethical research.

In 1938, the Federal Food, Drug, and Cosmetic Act gave authority to the Food and Drug Administration (FDA) to oversee safety of food, drugs, medical devices, and cosmetics. In the United States in the 1960s, the FDA and the National Institutes of Health (NIH) established policies to protect human research subjects. In 1996, the FDA published the Statement of Policy Concerning Consent for Use of Investigational New Drugs on Humans, inspired to a great extent by the Nuremberg Code and the Declaration of Helsinki.

Similar efforts were exerted by the NIH over this period, including the establishment of review boards that are now considered an integral part of the research process. In addition, the Department of Health and Human Services Office for the Protection of Research Risks oversees all federal agencies that conduct or support human subjects research under the Common Rule.

The past century has witnessed a dramatic transformation of the importance of informed consent and the regulation of research. This tightly regulated process is predicated on the value of individual autonomy and the patient’s right to determine their medical fate.

Box 1
The two pillars of an informed consent

<table>
<thead>
<tr>
<th>Informed consent is case specific.</th>
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<tbody>
<tr>
<td>• Informed consent given to perform a particular procedure does not automatically give consent to perform another intervention, even if the physician is operating in the patient’s best interest.</td>
</tr>
<tr>
<td>• Two main scenarios would render this condition not applicable:</td>
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<tr>
<td>o in cases of emergencies</td>
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<tr>
<td>o when patients give a broad consent</td>
</tr>
<tr>
<td>Informed consent is time specific.</td>
</tr>
<tr>
<td>• Informed consent given for a particular procedure once does not automatically make it valid for later use.</td>
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<tr>
<td>• A patient’s values and beliefs might change over time.</td>
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The informed consent process is grounded in principles of autonomy, respect, and good faith. Informed consent is not limited to a signed agreement to a particular treatment plan. Informed consent includes an understanding between physicians and their patients of the risks or consequences associated with a health care management plan or research-related activities. The first essential requirement of informed consent is a competent patient with the capacity to make decisions. Physicians must ensure that they are communicating with competent patients or competent proxies. The evaluation of a patient’s mental capacity is necessary to balance respect for autonomy and protection of those with cognitive impairment.

**Competency Versus Capacity**

Competency is a legal term that describes the mental capability to rationalize, understand one’s circumstances, weigh risks and benefits, and voluntarily communicate a decision in a legal setting. Capacity, on the other hand, is a functional determination that an individual is capable of making a medical decision within a given situation. The court is the only authority that can determine a patient’s competency; however, not every case requires determination of competency from the court, as this would drain both the medical and judicial systems. Instead, physicians can evaluate a patient’s capacity to make an informed consent.

Observational studies offer several predictors of incapacity. Patients with dementia tend to have high rates of incapacity that is more pronounced with severe disease, as these patients suffer from progressive cognitive decline impairing their decision-making abilities. Hospitalized patients with psychiatric disorders often demonstrate incompetency, most commonly those with acute schizophrenia compared with those with depression. In these patients, lack of awareness and need for treatment of psychiatric disorders are the strongest predictors of incapacity.

Conditions that limit cognition may also render patients incapacitated to make medical decisions, such as pharmacologic sedation or acute intoxication of an illicit substance. Medical conditions may also affect decision-making capacity, including unstable angina or diabetic ketoacidosis. As expected, incapacity is more apparent in inpatient settings, with increasing age and cognitive impairment being the strongest predictors of mental incapacity.

In a medical setting, physicians assume patients are competent unless they exhibit otherwise. This assumption is of practical importance, allowing health care professionals to focus on providing necessary diagnostic and therapeutic interventions without delay in patients who seem to have decision-making capacity on a standard initial evaluation.

**Clinical Assessment of Capacity**

When health care professionals suspect incapacity, they should perform a complete assessment to determine cognitive abilities and capacity to consent. The first step in evaluating capacity is to set the right climate. Then, proceed to a clinical interview to assess its 4 criteria. It is important in the case of an incapacitated patient to seek a surrogate decision-maker who may consent on behalf of the patient except in cases of life-threatening emergencies.

**Objective Tools for Cognition and Capacity**

If there is a concern regarding the patient’s cognition, formal cognition assessment may be performed. There are several online tools for assessing cognition, including...
the Mini-Mental Status Examination (MMSE) and the Montreal Cognitive Assessment (MOCA). MMSE scores less than 20 to 24 increased the likelihood of incapacity by 6.3 times. The MOCA questionnaire has 94% sensitivity and at least 90% specificity for detecting incapacity at a threshold score of 22. If the assessment of capacity is still not clear, the use of systematic formal tools is indicated. Table 1 outlines a few examples of the most commonly used systematic approaches to capacity assessment. Of note, the major downside of these systematic tools is the significant time commitment involved to administer them, and for this reason, these tools are not often used in general practice but are more commonly used in clinical research.

THE INFORMED CONSENT PROCESS

After establishing the capacity of a patient or finding a surrogate in the case of an incapacitated patient, the next step is the informed consent process. Valid informed consent is based on a true understanding and clear physician-patient communication rather than just a signed form. In the Belmont Report, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research claims that the informed consent process is predicated on 3 foundational elements: information, voluntariness, and comprehension. These elements can occur in any order,
although it is customary to provide information, emphasize the voluntariness of the decision-making process, and then assess comprehension. The opportunity for voluntariness may vary depending on the urgency of the clinical situation, but clinicians should emphasize that patients may adjust their decision as they learn more about the indications, benefits, risks, and alternatives of a given intervention (Fig. 4 and Box 3).

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**Box 2**
The role of the surrogate decision-maker

- Ethically and legally, valid informed consent must be given by a capacitated individual. If the patient does not have capacity to make decisions, a surrogate decision-maker must be assigned.
- A surrogate decision-maker becomes unnecessary during an emergency or life-threatening condition.
- If a patient does not have an authorized decision-maker, a family member or intimate associate may be considered per state laws or any individual who has a durable power of attorney.
- Physicians have a moral duty, to the best of their abilities, to ensure that the surrogate decision-maker is operating in the best interests of the patient and based on the patient’s values.
- If the physician believes that the proxy is acting in bad faith, an ethics consultation may be required; legal consultation is usually a last resort.
- Physicians should inform conscious incapacitated patients about their plans and interventions even if consent is given by the surrogate decision-maker.

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**Box 3**
Clinical case: information, voluntariness, and comprehension.

Sample Case
Mr M, a 76-year-old patient with a history of dementia, was rushed to the emergency department after a syncopal episode. After being resuscitated in the emergency room, his electrocardiogram revealed a third-degree AV block with a heart rate of 32 BPM and a blood pressure of 89/67 mm Hg. His physical examination, laboratory tests, and imaging results confirmed the need for a pacemaker implantation. How would you proceed with the process of obtaining informed consent?

Suggested approach with the patient (if has capacity) or the surrogate decision-maker

**Disclosing medical information:** “Your fainting spell occurred because your heart rate was too slow, which can happen with age. A pacemaker can be implanted to protect you from a low heart rate and prevent fainting spells. There are risks of infection, bleeding, and injury to blood vessels. However, the risks are small and without the pacemaker, you could suffer serious injury from future fainting spells.”

**Inquiring about patient preferences for information:** “I can provide more detail about the reasons for pacemaker implantation and the benefits and risks of the procedure. What questions do you have?”

**Emphasizing voluntariness:** “While my medical recommendation is to proceed with a pacemaker, this is not an emergency. You are currently monitored and temporarily protected against episodes of low heart rate. We should decide within the next 1 to 2 days about whether or not you will have the pacemaker. Would you like to give this more thought and discuss more later today?”

**Assessing comprehension:** “To make sure I’ve explained this correctly, can you tell me the reason I am recommending a pacemaker? What about the risks of the procedure? What could happen if you decide not to have a pacemaker?”
<table>
<thead>
<tr>
<th>Test</th>
<th>Authors &amp; Date</th>
<th>Time to Administer</th>
<th>Patient Population</th>
<th>Capacity Criteria Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of Consent Capacity for Treatment (ACT)</td>
<td>Cea and Fischer (2003)</td>
<td>45 min</td>
<td>Adults with or without mild-to-moderate mental retardation</td>
<td>Understanding, appreciation, reasoning, and communicating a choice</td>
</tr>
<tr>
<td>Hopkins Competency Test (HCAT)</td>
<td>Janofsky et al (1992)</td>
<td>10 min</td>
<td>Neuropsychiatric and medical inpatients; outpatients with psychotic disorders; patients with Alzheimer’s disease; nursing home residents.</td>
<td>Understanding</td>
</tr>
<tr>
<td>MacArthur Competence Assessment Tool for Treatment (MacCAT-T)</td>
<td>Grisso and Appelbaum 1998)</td>
<td>15–20 min</td>
<td>Medical inpatients</td>
<td>Understanding, appreciation, reasoning, and communicating a choice</td>
</tr>
</tbody>
</table>
Informed Consent for Research

Although the foundational concepts of the informed consent process in research settings are similar to those in clinical settings, the former requires a higher standard of consent because the patient would be susceptible to the risks of unapproved interventions. Participants in clinical research should provide informed consent after the full disclosure of necessary information. This information includes a written summary of the study design along with possible consequences of the tested intervention or the control group in understandable language.

The institutional review board (IRB) provides legal protection to human research subjects involved in clinical research. The IRB is governed by the Code of Federal Regulations Title 21, Part 45 (21 CFR 56). The main roles of the IRB are to verify that valid informed consent was obtained, ensure that the potential benefits of the research exceed the possible risks, and protect participants’ integrity and autonomy. In addition, the NIH Office for Human Research Protection issues guidelines on protecting human subjects involved in federally funded research. Nevertheless, the current standard of practice in clinical research is far from the theoretic ideal. Some researchers may use complex documents in the consent process with legal and medical jargon to minimize their risk of exposure to litigation.

FUTURE DIRECTIONS

There is a well-documented gap between the current application of the informed consent process and the ideal theoretic framework that promotes patient’s autonomy and bodily integrity. Many challenges arise during the consent process between a physician or investigator and the patient or study participant. Some of the most pressing challenges encountered during this process include (1) educational barriers, (2) changing demographics, and (3) advances in data technology.

Educational Barriers

A patient’s or a research participant’s literacy level largely influences the effectiveness of the consent process, and educational barriers limit the comprehension of consent information. In a survey of 100 IRB-approved consent forms, investigators found that consent forms were relatively long with a mean readability of Grade 11.6, which is of significant concern, as the reading level of an average American layperson is
grade 6 to 8. Furthermore, in the United States, more than one-third of adults have basic or below basic health literacy and around half of the US population have basic or below basic quantitative literacy, making the proper understanding of numerical data and statistics challenging. Even though the Code of Federal Regulations states that consent information should be presented in an understandable language to the patient or study participant (21 CFR 50.20), a study at 2 urban US hospitals including 2659 patients reported that 59.5% could not understand a standard informed consent document. Furthermore, another study of informed consent forms adopted by 5 of the largest national cancer clinical trial groups found that the forms were “slightly less difficult to read and understand than medical journals, but substantially more difficult than materials from the popular press.”

Because comprehension is an essential component of the consent process, consent given by a patient who does not understand the communicated information is not valid. Furthermore, people who have lower health literacy are particularly vulnerable because they are least able to acknowledge what they do not know and are the least likely to ask questions.

There are strategies to address these issues. In a randomized study of 1500 participants, multimedia aids including simplified language and visual representations improved the informed consent process, and interactive interventions, including multimedia aids such as short clips or infographics demonstrating particular interventions or challenging medical concepts, may be superior to noninteractive interventions. Test/feedback and teach-back techniques, along with bidirectional communication, can improve the consent process. Although most informed consent interventions focus on supplementing patients’ understanding with additional materials, improving consent should focus on better communication, not just more information. Even patients with adequate reading skills and high health literacy prefer consent materials that are easy to navigate.

**Changing Demographics**

Another major contemporary barrier to a successful and effective informed consent process is changing demographics. The US population is becoming older and more ethnically diverse. The increase in awareness of the need to address social determinants of health and health inequity is apparent in the medical community, and approaches to informed consent should be tailored for different ethnicities and minority groups. It is thus essential to amend guidelines detailing the process of informed consent to embrace cultural diversity and prepare the new generation of physicians by developing comprehensive training programs that promote cultural intelligence. Furthermore, the next few decades will experience a doubling in the percentage of people older than 65 years and an even larger increase in the percentage of people older than 85 years. The number of patients with Alzheimer disease is expected to double by 2050. As such, the proportion of adult patients who are deemed incompetent for their own decision-making is likely to increase over time. It is crucial to prepare health care professionals to assess capacity in an effective and systematic manner. Besides training health care professionals, ethical and medical societies should unify guidelines that would allow physicians to involve trusted family members and friends in the decision-making process.

**Advances in Data Technology**

Advanced technologies and artificial intelligence generate data that could be used for many purposes. These technologies raise challenging ethical questions. For example, next-generation sequencing generates an unprecedented amount of data in both
clinical and research settings. These data allow not only identification of the patient or research participant but also blood relatives. Hence, providing consent for genomic sequence analysis involves more than individual autonomy per se.

Another challenge of data technology is related to biobanks containing information on patients’ vital signs or biological materials. The data stored in a biobank could be used at any time for any purpose and by different investigators. For instance, data gathered from Apple watches for the Apple Heart Study are subject to unclear consent processes that many users sign without reviewing the extent of those consents. Informed consent in these scenarios is no longer case- and time-specific, which can jeopardize patient’s autonomy and integrity.

DISCUSSION

There are nuances when addressing informed consent in one’s practice. These nuances mainly stem from the need to highly personalize informed consent processes for every patient. The need for informed consent has been codified to highlight fundamental human rights including autonomy and integrity. The modern process of informed consent is thus regarded as a legal obligation rather than an ethical duty toward patients. Medical societies should invest in decision-making algorithms that could guide physicians’ thought processes. The challenge is in providing a standardized decision-making framework that offers a certain degree of flexibility to tailor the informed consent process to every patient. The advent of artificial intelligence and machine learning allows new opportunities for the development of reliable algorithms that could provide tailored decision-making guidance for every scenario.

SUMMARY

Informed consent is an integral component of any clinical or research interaction with patients. The process of informed consent has evolved over the past century through numerous lessons learned from malpractice and unethical conduct of human research. Understanding the historical and legal framework of informed consent, as well as the process of obtaining valid consent, is crucial to navigate through current challenges brought on by educational barriers, changing demographics, and advances in data technology. In this data-driven era, bioethicists, legal advocates, and health care professionals need to modernize the informed consent process. Regardless of future challenges, the priority will always remain the same: informed consent is more than just a signed form. Informed consent is based on true understanding and clear physician-patient communication and strives to preserve patients’ autonomy and integrity.

CLINICS CARE POINTS

- The most important first step in informed consent is assessing capacity.
- If a patient lacks capacity, identify a surrogate decision-maker.
- When obtaining informed consent, deliver adequate information, assure patient’s comprehension, and assure patient’s voluntariness in providing or withdrawing consent.
- Informed consent is the foundation of ethical conduct of clinical research, and engaging the Institutional Review Board is an essential step toward that goal.
- Consider developing or supporting development of guidelines to mitigate contemporary challenges to informed consent including meeting the complex needs of the aging population and comfortably managing large volumes of stored data from artificial intelligence and biobanks.
DISCLAIMERS

The authors do not have any relevant disclosures.

REFERENCES