REVIEW ARTICLE

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Enduring and Emerging Challenges of Informed Consent

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INFORMED CONSENT IS A WIDELY ACCEPTED LEGAL, ETHICAL, AND REGULATORY requirement for most research and health care transactions. Nonetheless, the practice of informed consent varies by context, and the reality often falls short of the theoretical ideal. Contemporary developments in health care and clinical research call for renewed efforts to address the enduring and emerging challenges of informed consent, such as what information should be disclosed, how it should be disclosed, how much the persons providing consent should understand, and how explicit consent should be.

The moral force of consent is not unique to health care or research. Integral to many interpersonal interactions and well entrenched in societal values and jurisprudence, consent can render actions morally permissible that would otherwise be wrong. For example, with consent it is fine to borrow a person's car or draw blood, but these actions without consent are considered theft or battery.[1] Recent research conducted by Facebook and OkCupid, which made use of user information and generated arguments about whether the general consent given when joining a social network suffices as consent for such research or whether express consent is required,[2,3] illustrates both how deeply rooted the idea of consent is in society and the changing landscape in which it may apply.

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ETHICAL AND LEGAL FOUNDATIONS

Consent is a long-standing practice in some areas of medicine, yet only in the last century has informed consent been accepted as a legal and ethical concept integral to medical practice and research.[4] Informed consent, in principle, is authorization of an activity based on an understanding of what that activity entails and in the absence of control by others.[5] Laws and regulations dictate the current informed-consent requirements, but the underlying values are deeply culturally embedded — specifically, the value of respect for persons' autonomy and their right to define their own goals and make choices designed to achieve those goals.[5] This right applies to all types of health-related interventions, including life-sustaining interventions. An early President's Commission report noted, "Informed consent is rooted in the fundamental recognition . . . that adults are entitled to accept or reject health care interventions on the basis of their own personal values and in furtherance of their own personal goals."[6]

Although informed consent is widely accepted in the United States and in many other countries, this understanding — and, indeed, the focus on an individual right to self-determination — varies according to culture. Cultural differences manifest in both the practice of informed consent — that is, what is told to whom and who makes decisions — as well as in an understanding of the normative underpinnings of informed consent as respect for individual autonomy. Persons in

many cultures, both in the United States and around the world, rely on their families and sometimes on their communities for important decisions, and this may be the norm in cultures that stress the relationship of individuals to others and the embeddedness of individuals within society. Commentators and empirical evidence have shown that culture influences moral values and that other key values such as loyalty, compassion, and solidarity may be more dominant than autonomy in some cultures.[7] Respecting persons includes respecting their cultural values and may require adapting the specifics of information disclosure or obtaining authorization for treatment or research accordingly. Yet respecting cultural values does not negate the need to respect the persons for whom care or research is being considered or the need to implement respectful and appropriate procedures. As Gostin points out, "Vast personal, cultural, and social differences will perennially pose challenges to meaningful dialogue among physician, patient, and family; it is the regard, consideration, and deference shown the patient that remains the hallmark of respect for persons."[8] The World Medical Association Declaration of Lisbon on the Rights of the Patient emphasizes that patients everywhere have a right to information and to self-determination.[9] The Declaration of Helsinki and other international codes of research ethics similarly emphasize the centrality of informed consent in the context of research globally.[10]

GAPS BETWEEN THEORY AND PRACTICE

Informed consent is a process of communication between the health care provider or investigator and the patient or research participant that ultimately culminates in the authorization or refusal of a specific intervention or research study. According to the American Medical Association, "Informed consent is a basic policy in both ethics and law that physicians must honor . . . ."[11] The process involves multiple elements, including disclosure, comprehension, voluntary choice, and authorization. In theory, physicians and investigators disclose understandable information to patients and research participants to facilitate informed choice.[4] These persons use this information to deliberate and decide whether the intervention offered is compatible with their interests and whether to authorize or refuse it. Persons should have the capacity to understand the information and should be in a position to make and to authorize a choice about how to proceed. Neither medical nor research interventions should commence until valid consent has been obtained, except under limited circumstances (e.g., emergencies). When a patient or research participant is a child or an adult who is not capable of providing informed consent, permission for medical care or research is often sought from a substitute decision maker, such as a parent or legally authorized proxy.

Most accept that in practice, particular aspects of informed consent vary by context, and both scholars and practitioners continue to debate these aspects — such as the scope and level of detail provided and the methods of disclosure,[12,13] whether and how to assess comprehension, what constitutes necessary and sufficient understanding for valid consent,[14] approaches to assessing persons' capacity to consent and steps taken when they lack that capacity,[15] how to know when choices are sufficiently voluntary,[16] and issues concerning the documentation of consent.[17] Consent for an elective surgical procedure differs from that for a simple routine blood test or from a complicated research study, for example. Cultural, socioeconomic, and educational factors can also influence the process and practice of informed consent, as can different decision-making practices and norms related to the role of individual autonomy.[18]

Furthermore, in practice, emphasis is often given to the written documentation of consent, despite wide agreement that consent requires more than a signature on a form. Faden and Beauchamp acknowledge that there are two common and starkly different meanings of informed consent: autonomous authorization by a patient or research participant and institutionally or legally effective authorization, determined by a complex web of prevailing rules, policies, and social practices.[5] The latter meaning, which is not necessarily accompanied by autonomous decisions, may overemphasize written documentation and risk communication, and it serves to help protect providers and institutions from liability.

A substantial body of literature corroborates a considerable gap between the practice of informed consent and its theoretical construct or intended goals and indicates many unresolved

conceptual and practical questions.[19-22] Empirical evidence shows variation in the type and level of detail of information disclosed, in patient or research-participant understanding of the information, and in how their decisions are influenced.[23] Physicians receive little training regarding the practice of informed consent, are pressed for time and by competing demands, and often misinterpret the requirements and legal standards. Patients often have meager comprehension of the risks and alternatives of offered surgical or medical treatments,[24] and their decisions are driven more by trust in their doctor or by deference to authority than by the information provided.[25,26] Informed consent for research is more tightly regulated and detailed,[27] yet research consent forms continue to increase in length, complexity, and incorporation of legal language, making them less likely to be read or understood.[28,29] Studies also show that research participants have deficits in their understanding of study information, particularly of research methods such as randomization.[30] Research participants, who are often patients with illnesses, frequently misunderstand the way in which research is distinct from individualized clinical care, and some worry that this "therapeutic misconception" can invalidate informed consent.[31] The federal regulations require most research informed-consent documents to include a standard set of informational elements and to be approved by an institutional review board before use.[27] However, recent controversy over a study of neonates, the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) study, illustrates that even when these requirements are adhered to, reasonable people disagree about the adequacy of the information presented on the consent forms.[32,33]

Various strategies to improve patient understanding in informed consent have been evaluated. Studies show that patients understand risk better when physicians are taught communication strategies.[34,35] Decision aids and decision-making tools[36] and a focus on shared decision making also enhance patients' understanding and satisfaction.[37,38] When time is spent explaining information about the study, the participants' understanding of research seems to improve.[39] Practical strategies, such as synthesizing and simplifying information and using technological tools and nonphysician providers to explain the research, have been suggested as ways to help achieve the ethical goals of consent.[40] More provocatively, some suggest a need to revisit the concepts and the contours of acceptable consent, noting that current notions of informed consent may be outdated[41] or that we may be expecting too much of consent.[42] Clearly, there is a need for continued consideration of the normative and practical aspects of informed consent in an attempt to reconcile practice with the theoretical ideal. Several contemporary trends in health care and research accentuate this need, as described in Table 1.

CHANGING MODELS OF HEALTH CARE AND RESEARCH

Informed consent is one among several important challenges that have arisen as health care institutions and practitioners adopt robust learning models that hybridize patient care with research and evidence generation to efficiently integrate improved prevention, treatment, and care-delivery methods. The models include the Institute of Medicine Learning Health Systems, continuous quality improvement, comparative effectiveness trials, pragmatic clinical trials, and practice-based research, among others.[43,44] Accompanying the adoption of these models are debates about how specific the disclosed information should be, about when express prospective consent is necessary or when routine disclosure or notification might suffice, and about how closely consent for these activities should resemble a research model of informed consent.[45,46] Conventionally, information disclosure differs between clinical and research informed consent in detail, formality, and level of prior review; these differences are often justified by differentiating the primary goal of clinical care — helping the patient — from the primary goal of clinical research — generating useful knowledge.[47,48] With more recently embraced learning paradigms, these goals are converging, or at least the boundaries are shifting.[49] Some argue that in the context of learning activities, "research-like" written informed consent may be ethically unnecessary, overly burdensome, and likely to thwart improvement efforts.[50,51] Disagreement remains, however, about the right consent model for these clinical and research learning activities, and high-profile cases have spurred controversy.[52,53] One argument against research-like consent presumes that many learning activities — for example, evaluating the importance

Table 1. Current Trends in the Health Care and Research Landscape That Have an Effect on Enduring and Emerging Challenges in Informed Consent.

Selected Current Trends in Health Care	Emerging Questions and Challenges	Enduring Questions and Challenges	Proposed Strategies
Learning health care systems, pragmatic trials, and quality improvement	Should informed consent for these activities be more similar to research informed consent or clinical informed consent? How much information should be given to participants in advance? Under what circumstances (if any) is notification rather than express consent sufficient? When can consent be ethically waived or altered? What information is important to patients and research participants? Is it ethically acceptable for a patient or research participant to provide consent for an unspecified or broad range of activities?	What is the appropriate amount and detail of information for valid consent in various contexts? What is the best way to disclose or present information to be sufficiently comprehensive but not overwhelming? What are the contextual elements that determine the appropriate amount, complexity, and format of disclosure?	Integrated consent, shared decision making; consent to be governed, more evidence about what persons giving consent want to know, alternative strategies
Adoption of complex technologies, such as next-generation genetic sequencing	How should information be presented, and what level of understanding should be sought when obtaining consent for complex technologies (such as genetic sequencing) characterized by voluminous and complex information, substantial uncertainty (e.g., variants of unknown significance), incidental findings, and implications for blood relatives?	Empirical evidence shows that patients and research participants often do not understand the information provided to them. Complex information and interventions may be more difficult to understand, especially in the setting of limited health and science literacy.	Use of technology to present information; broad or dynamic consent; consent to be governed; enhancement of science literacy
Consent for future use of clinical data or biologic specimens	Is it ethically acceptable for a patient or research participant to provide consent for an unspecified or broad range of possible future research or to consent to a program or system of governance?	How specific does the information provided in the consent process need to be regarding future uses of data or specimens? Does the answer differ if the data or specimens are deidentified or if future projects are subject to oversight?	Broad consent; dynamic consent; consent to be governed; deidentification of data and samples
Demographic changes with an aging population and increase in prevalence of dementia	Older age, diminished mental capacity, and dementia per se do not indicate that a person is incapable of consenting, yet the increasing numbers of elderly people and increasing prevalence of dementia and other disorders suggest that professionals in both clinical care and in research should consider a person's capacity to consent and be trained in how to assess capacity. There is a need for respectful and efficient tools and processes for assessing capacity, promoting decision making, appropriately involving families and friends, respecting cultural values, and using substitute decision makers when appropriate.	Capacity is assumed for adults, and the capacity to consent is only occasionally assessed. Capacity may be questioned only when a patient or research participant disagrees with the physician or researcher. The standards for substitute decision makers vary by jurisdiction and are different for clinical and research decisions.	Respectful and effective assessment of capacity and training of health professionals; creative approaches to presenting information; involving trusted friends and family members in consent discussions and decision making; studying new paradigms for substitute decision making

of repeat laboratory tests or how well health care providers use a checklist — add little or no risk for patients already receiving care, involve details of slight interest to patients, and have overall goals that patients support. Some would extend to learning activities a "simple" consent or notification paradigm that is used for certain clinical interventions, usually when the risks are low and patients are not likely to have strong preferences between treatment options or when there is only one logical choice.[54] The SUPPORT study, for example, brought to the forefront the unresolved question of the extent to which research in which participants receive standard medical care or the care that they would routinely receive outside the study poses "research risks" that require review by an institutional review board and comprehensive disclosure of these risks in a research informed-consent process.[55-57] Further research and dialogue will help guide decisions about how much disclosure is necessary in different learning contexts, the extent to which risk to participants matters in these decisions, how we should think about risk presented by research involving standard medical interventions, the role of patient preferences, and which, if any, activities can proceed without explicit prospective consent. Crucially, these efforts should include identifying what patients, research participants, providers, and others care about in various contexts.

CONSENT AND EMERGING TECHNOLOGIES

A second challenge to informed consent emerges from the complexity and uncertainty of the information generated by advanced technologies and expanded research opportunities. For instance, next-generation genomic sequencing technologies, such as whole-genome sequencing, which allow the quick and increasingly inexpensive detection of variation in the human genome, are rapidly being adopted into clinical research and routine clinical practice.[58] Although the routine implementation of genomic sequencing into standard clinical practice may be premature, turning back may be difficult.[59,60] Many recommend a robust informed-consent process for the use of genomic sequencing technologies.[61-63] Yet the complexity, volume, and density of generated health information, the anticipated discovery of variants of uncertain significance and secondary and incidental findings, and the implications for blood relatives present substantial challenges.[64,65] Comprehensively explaining in advance the elements necessary for obtaining informed consent, such as the expected risks, benefits, and likely outcomes of sequencing, can be difficult because of the sheer volume and inherent uncertainty of the information generated. Further, the level and type of details presented in an informed-consent process may appropriately differ between the clinical and research contexts, as well as according to population or setting. For example, the type of information and the way it is disclosed to informed healthy consumers who purchase direct-to-consumer genomic analysis may vary from that for ill patients seeking clinical diagnosis and treatment.[66]

In all settings, determining how to present complex scientific information is further complicated by the low prevailing rates of science and health literacy.[67] It has been suggested that in certain circumstances, it may be acceptable to ask people to consent to an oversight mechanism that serves to evaluate specifics (i.e., consent to be governed) rather than to consent to specific details[42]; there may also be a need for ongoing communication processes that allow the incorporation of changing information and changed expectations over time.[43] Engaging patients in the identification of suitable consent mechanisms or in the development of mechanisms of dynamic consent are additional strategies that have been suggested.[68,69] Similar consent strategies have been proposed for research involving biologic specimens and data. Inspired by the story of Henrietta Lacks (whose tumor gave rise to HeLa cells but whose permission to use her tumor cells for research was not sought),[70] scientists and policymakers are investigating and discussing models of consent to identify those that are both ethically and practically suitable for the future use of samples and data.[71,72]

CHANGING DEMOGRAPHICS

A third contemporary challenge to informed consent emerges from expected sociodemographic trends. The U.S. population will become considerably older and more racially and ethnically diverse over the next few decades, with an expected doubling of the number of persons 65 years of age or older and an even more dramatic increase in

the number of the "oldest old" (85 years of age or older).[73,74] Persons older than 65 years of age generally use more health care services, have a higher prevalence of chronic diseases, and more often have declining physical and cognitive function than do those who are younger.[75] The number of people with Alzheimer's dementia is also expected to more than double by 2050 and to increase more dramatically among the oldest old.[76] Preparing for these realities and their effect on health care is critical. For informed consent, they suggest the need for respectful, effective, and efficient methods of both ascertaining whether persons have the capacity to consent for themselves and facilitating decision-making processes for those who do not. Although many elderly persons, including some with dementia, retain the capacity to give informed consent for certain treatment decisions, others do not. Clinicians, who often lack training in assessing capacity, do not always recognize incapacity and may question a patient's capacity only when they face a risky decision or when the patient disagrees with their recommendations.[77] Cultural understandings of health and illness can also sometimes play a role when patients disagree with clinical recommendations. Assessing capacity and identifying appropriate and legally acceptable alternative decision makers or processes take time and resources and often receive short shrift in a busy clinical or research setting. Assessing the reasoning capacities of persons from cultural backgrounds that are not well understood by clinicians can also pose considerable challenges. Clinicians and investigators should be taught to assess capacity and should be provided with validated and useful tools[78] and the resources to help resolve difficult or borderline cases. Joint decision-making approaches that support the existing capacity of each patient but involve friends and family members have been recommended, because even "autonomous" decisions are often made together with trusted loved ones.[79,80] Patients may have the capacity for certain decisions but not for others, and capacity can wax and wane, so patients should remain involved in treatment decisions to the extent that it is possible. Creative and applicable methods of information disclosure are also necessary for persons whose capacity is diminished, as well as for the increasing numbers of patients who are not primarily English speakers.

Despite the enduring and emerging challenges of informed consent in health care and research, consent is recognized as morally transformative authorization, making certain activities permissible that otherwise would be wrong. Assiduous efforts to clarify and fine-tune concepts, expectations, practices, and the critical role of context are necessary to bridge the gap between the realities of informed consent and the ideal. Continued exploration through research, public dialogue, and creative approaches will help address the ethical permissibility and public acceptability of new models of consent, such as allowing consent for a broad set of activities, sometimes with an explicit system of governance over specifics; recognizing the validity of joint approaches to consent and decision making; refining processes to respect those who cannot consent for themselves; and finding creative, practical, and respectful ways of presenting information and supporting decision making tailored to each context. Respecting and promoting the informed choices of patients and research participants or persons acting on their behalf remain of paramount importance, despite the challenges of varied and changing contexts, altered capacity, limited health literacy, complex interventions, and shifting boundaries between health care and learning. Continued persistent and thoughtful efforts to bring the theoretical and practical realities of informed consent closer together are essential.

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