Expanding the Role of Bioethics in Translational Science

Currents in Contemporary Bioethics

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Abstract: Translational science attempts to accelerate and increase the significance of research progressing from bench to bedside. Support from the NIH through its institutional grant program has increased the prominence and importance of translational science. The inclusion of a broadly based bioethics component to translational science presents an opportunity for bioethics scholars to address fundamental social issues, including the effects of translational science on public health, health equity, and human flourishing. Large-scale bioethical inquiries could examine research priorities, unintended consequences of research, and access to and uptake of research discoveries.

Translational science studies the processes used to accelerate and increase the significance of research progressing from bench to bedside. Among the innovative aspects of translational science are employing cross-disciplinary team science, utilizing big data and artificial intelligence, and adopting bold new approaches to biomedical research. Several multi-step models have been proposed to characterize and illustrate the stages of translational science.[1] However, the simplest way of describing the goal of translational science is that it seeks to translate basic science into human studies and to translate human studies into clinical practice.

Although the term "translational" has been used in the medical literature since the 1970s, the concept grew in importance in 2006 when the National Institutes of Health (NIH) started funding sixty medical institutions under its Clinical and Translational Science Award (CTSA) Program.[2] In 2012, the NIH further demonstrated its support for translational science by establishing the National Center for Advancing Translational Sciences (NCATS) to expand and coordinate translational science activities conducted or funded by the NIH.[3]

Ethical components are often a part of translational science programs, regardless of the funding source, but they are rarely given prominence. They also tend to focus on "human subjects" issues, such as community engagement, recruitment strategies, informed consent, and institutional review board (IRB) submissions. Although these issues are important, if translational science is designed to foster "disruptive translational innovation,"[4] then the ethical component should be similarly ground-breaking, and on a scale comparable to the scientific elements. Translational science presents an important opportunity for bioethics assessments to address fundamental societal issues, including the effects of translational science on public health, health equity, and human flourishing.[5]

Illustrations of an Expanded Role of Bioethics

Research Priorities

Bioethical implications of health research often arise long before human participants become involved.

About This Column

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According to a report by the National Research Council, the choice of the topic for investigation may have profound implications.

> One myth about scientific research is that science is value neutral — that new scientific understandings await discovery, that these discoveries have no independent moral significance, and that they take on moral significance only when individuals and groups of individuals assign weight to scientific findings. One flaw in this argument is that there are seemingly limitless areas for scientific inquiry, yet there are finite numbers of scientists and limited resources to pursue research. Therefore, scientists and society must set priorities for research, and those priorities are a function of societal values. Even though scientists often make adventitious discoveries, they generally discover what they are looking for, and what they look for are the things that science and society value discovering.[6]

"Translational science is often referred to as 'disease agnostic,' which is true but limited. It is more properly described as 'disease universal' because it addresses the scientific and operational bottlenecks that are common to translational research for most all diseases."[7] With such a broad scientific remit, it is essential to establish priorities for scientific inquiry. Both the process and substance of selecting topics involve expressed or unstated values and priorities.[8]

Bioethical perspectives can be extremely valuable at this stage. For example, bioethical inquiries regarding a potential topic might ask what population is likely to benefit from the research, whether the research is related to past or likely future research, whether ethical or societal problems have arisen from similar research or methodologies, and whether there is an opportunity cost in pursuing this topic rather than another one or funding research instead of clinical care (prevention, diagnosis, and treatment) using existing drugs, devices, or technologies.[9] Too often, bioethics issues are considered in a reactive rather than a proactive context — and long after essential priorities have been established.

Unintended Consequences

Some unintended consequences of biomedical research are reasonably foreseeable, and a sound bioethical analysis of a proposed or ongoing translational science activity should consider whether foreseeable, negative consequences of the undertaking can be identified and avoided or minimized. For example, neuroscientists are researching whether implantable brain chips and other emerging technologies can be used to ameliorate or reverse the devastating effects of dementia and similar neurological disorders.[10] If cognition can be enhanced for these patients it would be a scientific triumph of great importance to patients, their families, and society.

Nevertheless, there are foreseeable, unintended consequences of implantable brain chips. If the risks, benefits, invasiveness, cost, and other factors are deemed acceptable, it can be expected that some parents would seek to enhance the cognition of their children to boost their academic performance and earn a coveted spot at an elite college. Should this be permitted? Could it be prohibited? Would it cause academic achievement and educational opportunities to be further skewed by wealth? Would it matter if scarce materials and personnel diverted to lucrative enhancement limited the ability to treat patients with Alzheimer's disease? These questions, mostly involving distributive justice, do not even consider the seemingly imponderable questions of future integration of humans and computers.[11]

In *The Great Secret*, Jennet Conant tells the story of the German air attack in 1943 that caused the explosion of 2,000 mustard gas bombs secretly stored on an American ship docked in Bari, Italy.[12] Stewart Alexander, a young medical officer attached to General Eisenhower's staff, observed the toxic effects of the mustard gas on the white blood cells of the victims. This clinical finding supported the theory that tiny and calibrated doses of nitrogen mustard could be valuable in treating certain types of cancer. Within ten years, researchers were able to develop the initial chemotherapy treatment for childhood leukemia and later other cancers involving the proliferation of white blood cells. This was a wonderful result from a tragedy that killed over 1,000 American and British service members.

But science can work in both directions, and it is conceivable that insights from cancer or other scientific research could be used to develop chemical or biological weapons. What, if anything, should researchers do if they recognize the possibility that their work could be adapted for destructive or inhumane purposes? Should this concern be applied to less tangible consequences, including the possibility that scientific research can be misreported or misperceived in ways that undermine essential societal values?[13]

Bench scientists often develop a laser-like focus on the narrow, technical challenges of their research. Integrating bioethics into translational science can help to identify key implications and to initiate a more broad-based assessment of the risks and benefits, including mitigation strategies.

Access to and Uptake of Scientific Discoveries

Some new products of biomedical research, such as pharmacogenomics-based drugs, are extraordinarily expensive.[14] A substantial literature considers a range of questions related to equitable access to pharmaceuticals,[15] including whether it is appropriate for government-funded research to help develop medicines that benefit only very wealthy individuals, whether public or private health plans should pay for these treatments, whether intellectual property laws should be reformed to increase access,[16] and whether other

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incentives can support research without resulting in high consumer prices.[17] The economic and bioethics issues related to equitable access to established and emerging health discoveries, especially in low- and middle-income countries,[18] should be given a high priority by researchers and policy makers.

Research and development of marvelous, life-saving interventions will be of little value if the public is unwilling to accept them. One lesson of the pandemic is that research on new public health measures should be accompanied by research on ways to increase trust in scientists and public health officials, as well as to persuade our diverse population to take advantage of safe and effective measures to prevent and treat disease. Studies of the population's willingness to embrace new discoveries should be done concurrently with scientific research and not as an afterthought or marketing measure during the roll-out of the new intervention.

One important bioethics issue exposed during the current pandemic was the reluctance of millions of Americans to become vaccinated despite the fact that newly developed vaccines are extremely safe and effective, they were provided at no cost, and it was crucial to achieve a vaccination rate sufficient to establish herd immunity.[19] In retrospect, widespread vaccine hesitancy or reluctance in contravention of public health should not have come as a surprise. For decades there has been a growing movement in some parts of the United States and other countries for parents to refuse to vaccinate their children, including because of the erroneous and discredited belief that vaccines cause autism.[20]

These attitudes were on display in 2009, when many individuals declined to become vaccinated against the H1N1 influenza virus, which public health officials regarded as a substantial epidemic threat. Millions of doses had to be destroyed because people refused to be vaccinated, and political party affiliation was the leading factor in individuals accepting or refusing the vaccine.[21] Even before the pandemic in 2020, there was a high level of distrust in government[22] and a growing hostility to scientific "elites."[23] This hostility to public health measures was exploited for political advantage in our polarized country,[24] resulting in the needless deaths of an estimated hundreds of thousands of unvaccinated people.[25]

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ELSI for Translational Science

A broadly focused bioethics research program as part of translational science would be analogous to the Ethical, Legal, and Social Implications (ELSI) Research Program of the National Human Genome Research Institute at the NIH. Establishing the program in 1990 was one of the first acts of James D. Watson when he was appointed to direct the NIH's genome research program.[27] Since 1990, the ELSI Research Program has funded "hundreds of research projects, conferences, and other activities through grants and contracts [resulting in] many peer-reviewed journal articles, books, newsletters, websites, television and radio programs and educational materials."[28]

Christopher P. Austin, former NCATS director, has written that "translational projects fail for both 'hard' science (e.g., biology, chemistry, pharmacology, and toxicology) and social science (e.g., incentive structures, credit allocation, economics, and intellectual property) reasons, so translational science need[s] to innovate in both areas."[29] To date, innovative social science has not been sufficiently incorporated into translational science, but there are several ways in which bioethics innovation can be achieved.

An expanded bioethics component of translational science could involve increased ethics research requirements for CTSA awards, independent investigator-initiated research funded by new NCATS initiatives, research funded internally by CTSA awardees or other institutions, or collaborations by CTSA awardees. Collaborative arrangements are especially appealing. There is a "need for innovation in collaborative structures to support the broad and frequent partnerships that characterize translation."[30] The collaborative model also has the advantage of leveraging technical capacity within institutions with essential expertise in bioethics, law, social sciences, and other disciplines uniquely available at certain collaborating institutions. Some excellent bioethics research along these lines already has been published, but increased levels of "trans-

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lational bioethics" should be encouraged, supported, funded, and valued.

Conclusion

The purpose of expanding the role of bioethics in translational science is not to discourage, delay, or impede research. It is to advance the traditional research ethics principle of beneficence by minimizing risks and maximizing benefits. Of great significance, the expanded role for bioethics proposed here would concentrate on risks and benefits on a societal level. By anticipating possible consequences and, where necessary, alerting researchers, policy makers, and the public through consultation and scholarship, bioethics researchers will advance the goals of translational science by helping to ensure that research does not include unacceptable risks and that beneficial discoveries are promptly and seamlessly integrated into clinical practice.

One of the unique strengths of bioethics is its multidisciplinary nature. Broad bioethics collaboration could involve psychology, sociology, anthropology, political science, law, economics, philosophy, theology, and other disciplines. It will be challenging to develop productive, collegial, and focused multi-disciplinary and multi-institutional collaborations, but the payoff will be worth it — successfully integrated and broadly supported translational science breakthroughs.

Notes

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