Values in Translation: How Asking the Right Questions Can Move Translational Science Toward Greater Health Impact

Maureen Kelley, Ph.D.[1,2], Kelly Edwards, Ph.D.[3,4], Helene Starks, Ph.D.[3,4], Stephanie M. Fullerton, D.Phil.[3,4], Rosalina James, Ph.D.[3,4], Sara Goering, Ph.D.[4,5], Suzanne Holland, Ph.D.[4,6], Mary L. Disis, M.D.[7], and Wylie Burke, M.D., Ph.D.[3,4]

Abstract

The speed and effectiveness of current approaches to research translation are widely viewed as disappointing given small gains in real population health outcomes despite huge investments in basic and translational science. We identify critical value questions—ethical, social, economic, and cultural—that arise at moments throughout the research pathway. By making these questions visible, and promoting discussion of them with diverse stakeholders, we can facilitate handoffs along the translational pathway and increase uptake of effective interventions. Who is involved with those discussions will determine which research projects, populations, and methods get prioritized. We argue that some upfront investment in community and interdisciplinary engagement, shaped by familiar questions in ethics, social justice, and cultural knowledge, can save time and resources in the long run because interventions and strategies will be aimed in the right direction, that is, toward health improvements for all. Clin Trans Sci 2012; Volume 5: 445–451

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Introduction

The push for improvement in translational science and the numerous calls for a return on the public's investment in research reflect the desire to move scientific discoveries more quickly and efficiently toward high impact interventions that will improve patient and population health outcomes.[1,2] The strategic goals of the Clinical Translational Science Award (CTSA) Initiative include the explicit target of "Improving the Health of our Communities and the Nation."[3] While it is clear that accelerating discoveries toward product development is a measure of translational progress, the ultimate goal is better health outcomes for the population.[4] A number of commentators have suggested strategies to improve translation, including increasing funding for implementation and health outcomes research, and greater investment in health technology assessment.[5–8] Further, as advocates of team science have argued, we can be more creative about our approach to problem solving when we have a multitude of perspectives involved upfront in assessing potential research directions; this helps assure that key handoffs do not get missed.[9,10]

For these strategies to succeed, we also need a practical consideration of how critical value judgments—ethical, social, cultural, and economic—at every stage of research determine the quality and direction of translation. Decisions about which diseases to target, which research programs to fund, which populations to prioritize and engage, and how quickly to move to delivery of interventions, all require important but often invisible value judgments. These values questions—and who asks (and answers) them—matter, because they can change the direction of research investments and the ability to move a research finding forward along the translational pathway.[11] Shapiro and Layde have proposed a framework for identifying and addressing bioethics issues across the translational pathway, from preclinical, to human studies, to adoption of best practices in the community.[12] Our work builds upon and expands their framework to highlight the kinds of contributions that could be made by integrating critical perspectives—beyond bioethics—at every phase.

A recent review of models of translational science appropriately names the "conceptual cacophony" that has been created by a debate over "T-phases" of research.[13] These models are useful in helping us step back from the day-to-day practice of science to reflect on that practice in a more deliberative way, with an eye to identifying choke-points, barriers, and also unseen opportunities for improvement and greater health impact.[14,15] But disputes about nomenclature, or where one research phase ends and another starts, can defeat this more practical purpose of guiding better translational research practice.[16] Recognizing the value of these prior contributions, we offer a normative model of the translational process that illustrates the cyclical nature and activities of translational science, the overlap between phases, and the need to recognize the critical role of assessment and priority setting throughout the translational cycle (*Figure* 1). Our aim is to offer a conceptual, visual model that makes the value judgments in science more explicit because we believe doing so is likely to result in better science and better health benefits. Using this model as a guide, we review recent studies and research programs as examples of how researchers and funders can make choices that promote handoffs and accelerate translation towards improved population-level health impact.

Reenvisioning the Translational Cycle: Stopping to Assess Problems and Set Priorities

For simplicity, we adopt common language used in health research—discovery, development, and delivery—to capture the primary focus of different stages in the movement of new knowledge to clinical use, and close the loop with a stage that focuses on outcomes (*Figure* 1).

In our conceptual model, we add Assessment and Priority Setting at the center to signify the important work of evaluating questions, problems, and opportunities as the groundwork for pursuing specific research activities. The implications of making this activity explicit are highly practical: at every phase of work,

[1]Treuman Katz Center for Pediatric Bioethics, Seattle Children's Hospital, Seattle, Washington, USA; [2]Department of Pediatrics, University of Washington, Seattle, Washington, USA; [3]Department of Bioethics and Humanities, University of Washington, Seattle, Washington, USA; [4]Center for Genomics and Healthcare Equality, University of Washington, Seattle, Washington, USA; [5]Department of Philosophy, University of Washington, Seattle, Washington, USA; [6]Department of Religion, University of Puget Sound, Tacoma, Washington, USA; [7]Department of Medicine, Division of Oncology, Tumor Vaccine Group, Center for Translational Medicine in Women's Health, University of Washington, Seattle, Washington, USA
Correspondence: Maureen Kelley, PhD (mckelley@u.washington.edu)

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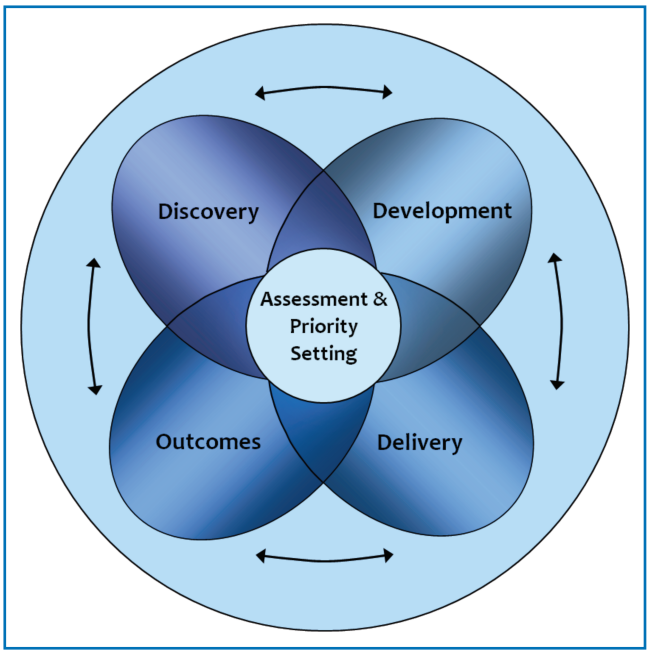

Figure 1. Translational science as a cycle with intersecting phases. This figure was originally published by the authors in Burke W, Edwards K, Goering S, Holland S, Trinidad S. (eds) *Achieving Justice in Genomic Translation: Rethinking the Pathway to Benefit* (New York: Oxford University Press, 2007), p. 7, and has been reproduced by permission of Oxford University Press.

certain evaluative and normative questions must be asked, and made explicit, such as: what is the fundamental question to be addressed? How can different research methods address it? Which populations will be included, and how will research affect them? Were they asked what their research priorities are? Who will collaborate on the project? What benefits are likely to flow from the research, and who will bear the burdens? What will success look like, and, for whom?

How a research team answers these questions depends upon who is at the table. For example, an interdisciplinary conversation focusing on next steps in diabetes prevention could define the problem as genetic, biochemical, nutritional, behavioral, or socioeconomic, with an accompanying range of questions and potential solutions that may include predictive testing, drug targets, health education strategies, or food policy interventions. If representatives of an affected community are included in the discussion, they might point out that no amount of medication or health education will make a difference when their community is disproportionately without healthcare or access to healthy food options. In such a circumstance, the most pertinent approach might follow the example of the recent Centers for Disease Control and Prevention funded efforts to address food deserts in urban counties.[17] Conversely, clinicians may bring new ideas about partnering with patients in management of diabetes to the discussion, offering the opportunity to assess innovative and potentially more effective approaches to specific therapies and case management for individuals with diabetes. This argument for an interdisciplinary approach to problem assessment and priority setting should not be seen as a battle between public health interventions and biomedical models of disease, since ultimately the two are mutually dependent, but rather, as a critical exploration of the available opportunities and how they can be coordinated and prioritized. For example, prevention efforts focus on upstream interventions to reduce overall prevalence rates while new drug targets are identified to improve individual treatment for those with poorly controlled blood sugar levels. Our point in promoting interdisciplinary conversations is to provide opportunities to coordinate and integrate approaches to present a full-court press in tackling these complex conditions that are affecting population health in significant ways. This is both an ethical and scientific requirement.

The National Institutes of Health (NIH) support for 10 Centers for Population Health and Health Disparities represents an effort to launch such an integrated multidisciplinary approach. The centers address a strategic priority—health disparities in cancer and heart disease—and are required to pursue a multidisciplinary research agenda incorporating both social sciences and genetics.[18] However, the inclusion of genetics in this research agenda may take different forms depending on how the problem of health disparities is framed. If disparities are conceptualized primarily as population differences, genetic investigations are likely to focus on associations between disparities and genetic variation.[19] Conversely, if disparities are seen as strongly influenced by social determinants of health, genetic investigation might more productively focus on differences in gene expression and their correlation with differences in social and environmental exposures.[20,21] The methods of genome science can support either approach, but value-driven assumptions, questions, and judgments about the research problem will inform how the translational research cycle is launched, and ultimately, which outcomes are likely to be achieved.[22] This is where ethics meets science.

We argue that making explicit the values behind our research will lead to better science with more just outcomes for all stakeholders.[23] An assessment process can also identify barriers to translation, such as the regulatory and market difficulties that researchers and others face in their attempts to move promising discoveries across the so-called "valley of death" to product development.[24–26] Assessment and priority setting activities serve as a bridge, connecting stakeholders within and across the stages of translational research to ensure efficient handoffs and facilitate the larger goal of delivering on the promise of scientific discovery. With common understanding of the problem and goals, interdisciplinary teams can be more effective in making successful handoffs to assure discoveries reach development, delivery, and outcomes.

Cautionary tales

The recent setback experienced by the biotechnology company Dendreon, whose focus is on novel cancer therapeutics, illustrates how better communication might have facilitated more uptake or revisions in the delivery process.[27] In this case, a prostate cancer drug went to market at a price point of 90,000 dollars per year while providing an average life extension of 3–4 months. Providers have been reluctant to prescribe the medication, having not yet received an endorsement from insurers regarding reimbursement. The company's stock fell dramatically when it became clear that the promise offered by the drug discovery was not paying off in delivery or outcome phases. These limited outcomes were predicted in the development phase but an opportunity was missed in negotiating a realistic delivery plan with insurers, providers, and patients.

In the global health context, nongovernmental organizations (NGOs) and other health agencies have learned that moving

efficiently from bench to bedside requires early consideration of cultural, religious, and other social values held by key stakeholders in the affected communities.[28] For example, the Gates Foundation's campaign to eradicate polio met with significant setbacks that reinforce the importance of a broad understanding of delivery outcomes in the planning process. These included a range of issues, from inadequate supply chains and distribution networks, to combating rumors from local imams that polio vaccinations cause adverse effects such as "sterilization in Muslim girls." Polio remains a significant worldwide health problem because "(technological solutions) can be hampered by political, religious and societal obstacles."[29] In the case of polio, the Gates Foundation and other lead organizations are embracing a renewed strategy that involves engaging key stakeholders in religious and political circles as well as health and technology sectors in designing a response. This approach not only continues vaccination programs and quick responses to local outbreaks, but also incorporates social and cultural elements, such as expanding efforts to train healthcare workers and improve community sanitation.

The cautionary tale in these and other examples of stalled or failed translation is that successful translation often requires pausing to distinguish technical obstacles from failures to acknowledge social realities, beliefs, and implicit differences over the appropriate priorities along the research pathway.

Closing the circle

Current translational incentives that focus on intellectual property rights and commercial opportunities, such as the Bayh-Dole Act in the United States, encourage the development of marketable drugs, devices, and tests. These incentives emphasize the role of industry and venture capital in determining which basic insights go on to development as health applications. This incentive structure works effectively to produce new drugs and devices but fails to assure that these inventions will necessarily affect important population health outcomes.

Explicit reflection on initial decisions made at the outset of a project can cause investigators to examine their own assumptions about the benefit of their contributions and reflect on exactly how, and by whom, their contributions will be used in the context of the overall translational purpose for the research endeavor—whether it be to identify cancer treatment, reduce the burden of diabetes, suicide prevention, or to increase access to HIV treatment for an underserved population. In this way, reflection on value-based judgments at this initial assessment phase may make the science better, that is, more likely to actually reach its intended goal of impacting health. In the next section, we give examples of researchers working along the translational pathway and highlight the kinds of value judgments that can catalyze successful and high impact translational science.

Value questions that inspire and direct discovery science

Many have argued passionately that we must leave room for serendipity in discovery science and bristle at the thought that every basic science project must provide a justification for how the line of inquiry will lead to a health impact.[30] We acknowledge the value of unpredictable discoveries, where one line of inquiry driven by scientific insight leads to unanticipated applications in a completely different sector. But serendipitous leaps will be more likely to occur if researchers are in dialogue with one another, particularly with those outside of their fields and area of specialty.[10]

When research groups build in cross-disciplinary exchange, we see new hypotheses emerge and applications become clearer. For example, in the Obstetric-Fetal Pharmacology Research Units Network, clinicians describe the problems they face most directly with patients, and pharmacology researchers develop strategies for gathering preliminary pharmacokinetic data with some opportunistic studies occurring in the clinic.[31] Or a discovery science researcher may redirect her investigation after listening to clinicians describe a problem they face in practice, for example, estimating effective dosing levels for pregnant women requiring the H1N1 vaccine. "Why" questions with a social justice bent often make great discovery questions. For example, one team investigating the causes of premature birth among women in the United States has asked, "Why is the African American and white disparity in infant mortality growing despite reduction efforts, and despite an increasing rate of white low birth weight infants?"[32] These types of studies represent a shift in thinking about what constitutes good science: the criteria of significance and impact can include weighted consideration of novel, rigorous science that also addresses a stubborn and puzzling health disparity.[33–35]

When discovery science is viewed not only as the "starting block" for new, serendipitous ideas but is also responsive to pressing needs, several important ethical questions arise:

(1) Given scarce resources and several pathways for investigation, which areas of investigation seem most likely to lead to significant health impacts, and for whom?
(2) In a particular field, how should resources be allocated to maintain robust discovery science and also ensure scale-up of known, effective interventions?
(3) Where do we need to improve the visibility of disease burden through better epidemiology and health systems infrastructure—are there marginalized or unseen populations affected, whose needs could be more directly served?
(4) How do we address short-term needs when we can only offer downstream applications, and whose responsibility is it to consider interim interventions while investigating questions with uncertain downstream applications?

Value questions driving translation between discovery and development

Once an insight has been made at the discovery phase, there are a series of decisions needed to move the insight into development. For example, a researcher may have identified a potential drug target or have discovered a potential vaccine. The next step is to find out whether these potential findings will bear out when tested in human models and trials; but which of the literally thousands of potential findings get worked up and moved forward along the translational cycle? It is the rare researcher who can bridge discoveries into human trials for further development. Well-funded partners are needed, with an understanding of expected marketability of the product, and the ability to take financial risks. Yet these practical, economic considerations can be tempered by more explicitly ethical concerns. Several funding organizations have married savvy business models with the explicit prioritization of diseases affecting the worst off, often choosing to develop low-cost, highly portable interventions to populations bearing the greatest burden of disease.[36,37]

When we consider translational science not merely as a series of scientific phases, but also give due weight to the hand-offs between the phases, a number of value questions arise that are

pertinent to the transition from discovery to development: Who has the responsibility to be the matchmaker, to find likely insights within laboratories and bring them forward to the attention of funders or applied researchers in a way that is responsive to those bearing the burden of particular diseases? What kind of deal is appropriate to strike between partners (e.g., patent restrictions)?

Drug and device development fall primarily in the realm of private companies and funders. Most academic researchers are not positioned to do the scaling-up and risk-taking required to bring a discovery to the next level. Public–private partnerships represent an implicit contract that we will move insights forward, usually into market, for a return on investment and recognition within peer-reviewed circles. However, a few select funders, partnerships, and proposals exist that put different priorities forward (other than market share). For example, philosopher Thomas Pogge has partnered with economist Aidin Hollis to propose the Health Initiative Fund (HIF) that acknowledges the pharmaceutical companies' need for return on investment while using incentives that foreground human health impact of the innovations.[38] On the HIF scheme, drug companies who create inventions that improve health will be rewarded from the Fund in an amount proportional to their impact, provided they offer the drugs at cost.[39,40]

In other cases, advocacy groups have intervened to shepherd discoveries forward into trials, lobbying FDA and other regulatory bodies to open trials early and make potential life-saving drugs available more quickly (e.g., ACT-UP and some cancer advocacy groups). These advocates have been effective, facilitating hand-offs for ideas that otherwise languish in laboratories for want of the right partner to move them to the next phase of development. As such, they have enacted the values and motivations that drive their goals for research—the need to find innovations that will impact human health. However, critical advocacy gaps remain for less visible communities. We need to ask: Who will advocate for diseases and conditions that impact smaller, more diffuse, or less empowered populations, or that disproportionately affect the underserved, those without health insurance, and those without resources to buy medications or complicated delivery systems once distributed? Who should take on the burden of ensuring handoffs or finding partners when the health and welfare of such populations are at stake? And what happens when we get it wrong?

Finally, improving translation is not necessarily about speed, but rather about the quality and ethical appropriateness of translation on health outcomes. Some insights, however marketable, perhaps should not move forward to delivery and dissemination because they do not yet have sufficient evidence to show health improvements over existing remedies or diagnostics.[41] Occasionally, the promise of a new development does not pay off as hoped when scaled-up and delivered to a broader population (e.g., bone marrow transplant for breast cancer). What checks and balances can we develop in the system to permit more dynamic and nimble trials and reassessments, when needed?

Economic incentive structures in development science are not fixed; many global health research programs have demonstrated that incentives can be harnessed to improve health outcomes for all populations. When stopping to assess and set priorities, the following kinds of value-based questions characterize a more explicit approach to value deliberation at this stage:

(1) What are the potentially harmful consequences of not moving forward with an idea?
(2) What are the opportunity costs in terms of health impact by foregoing development of this idea over another? Who is benefiting, at the expense of whom?
(3) Have communities affected by, or participating in, basic science research via donation to repositories shared what they see as the greatest need, and is the research and development program responsive to their priorities?
(4) Who has responsibility for assuring effective handoffs, and handoffs that ensure ethical development of promising innovations?

Value questions driving translation between delivery and outcomes

When an innovation has been developed, has amassed some or sufficient evidence of safety and efficacy in human studies, the next step is to determine whether the intervention is ready for scaling-up for delivery. As with the earlier hand-offs, different researchers, systems, and funders are involved at the delivery stage, requiring partnerships to move effective innovations out into practice.

Again, many practical considerations affect transitions to delivery. A researcher could have developed a vaccine strategy that is effective in human trials, and yet, is turned down at the delivery stage because the implementation is too costly or cumbersome (e.g., multiple shots per day, refrigeration required, careful follow-up, etc.). Where such circumstances arise and when the intervention is the only one that shows evidence of efficacy and significant health impact, whose responsibility is it to address barriers to delivery and bear the cost of overcoming those barriers? Encouraging more explicit recognition and discussion of the implicit value trade-offs that drive such decisions creates opportunities to find creative solutions for translation of interventions with significant social value.

Sufficient evidence standards are needed to achieve practice guidelines, which may or may not be in place when a new development first breaks into delivery systems. Once a research innovation has cleared development, benefit to human health is by no means assured. The innovation may not perform as anticipated from the initial research, or other priorities may need to be addressed before communities can truly benefit from the innovation. By collecting data on barriers to delivery, the responsible clinical translational researcher working at the intersection of development and delivery can provide valuable feedback to other funders, other delivery researchers, or even basic scientists, to improve relevance, access, and equity in distribution. For example, one of the authors of this paper, at the development phase of a research study, realized she had a vaccine delivery model that was too complex and expensive for all but the most privileged patients. Rather than push into widespread delivery, she went back to discovery and worked to find an alternative approach, using the same target but simplifying her delivery system to a cheaper and more portable version. In this way, much more than efficiency drove the clinician scientist. By talking with her global health colleague down the hall, she recognized the opportunity to have a significant health impact and recognized serious inequities in access. Rather than acquiescing to delivery barriers she took the initiative and bore the direct and opportunity costs of taking the vaccine model back to the bench. Real advancements in translational science are marked not only

by individual investigator-initiative or team-initiative, but in the more systematic cultural shifts in how funding is restructured to support such initiative.

As these examples illustrate, when viewing the translational pathway as cyclical with critical overlaps between development and delivery, a number of important value judgments can provide a catalyst for more just and effective translation:

(1) When is it appropriate or even imperative to accelerate delivery of an intervention, e.g., if it is the only available intervention and only chance to save lives or decrease morbidity?
(2) What is the expected value gained in health/lives saved and expected risk of unknown harms compared to delaying delivery to better determine efficacy?
(3) Are there barriers to delivery (cultural, socioeconomic, practical) and how can we address them?
(4) What harmful or ineffective interventions have become programmatically entrenched and need to be discontinued or sent back to the discovery phase?

How value judgments can help close the loop: from delivery and outcomes back to discovery

Assessing the actual outcomes of a research innovation is the area most neglected by funders and academic researchers, but it is one of the most ethically compelling steps to take. While scientific specialization is a necessary characteristic of focused, rigorous discovery and development research, closing the loop is essential to ensuring effective health impact. This requires following through to evaluate the health impact and other outcomes of a scaled-up program or innovation. Colleagues in health services and other evaluation sciences can assist with this phase, and also have a responsibility to engage with discovery, development, and delivery phases to ensure that assessment data are being communicated to investigators to inform research in development. For example, health outcomes researchers recognized that women experience substantial mortality from heart disease yet most of the available research had been based on men. Recognition that heart disease in women was understudied led to a change in research investment and understanding, potentially contributing to observed reductions in mortality.[42]

In another example, following a string of youth suicides in a small Alaska Native village, State Senator Lisa Murkowski released a call for funding to "determine the specific genes that contribute to major depressive disorders and alcohol abuse leading to targeted treatment options for Alaska Natives."[43] In this case, the assessment of the health problem framed youth suicide in terms of a genetic hypothesis, potentially directing future research in that area. Rather than launch that funding initiative alone, a multiple-stakeholder group was convened first to review evidence and experience.[44] This group recognized that purely genetic research would not serve their purposes well. More than a simple process of consultation, such reflective dialogue is a means for stakeholders to develop new interdisciplinary processes and goals for research that includes benefit for the targeted population.[45]

Public deliberation and partnership are critical features of translational science, informed by a sense of shared responsibility in scientific inquiry aimed at health impact and made possible by the trust of communities and participants. We need observations from multiple perspectives to develop a rich sense of what the outcomes are within the community of interest. When we view clinical translational research as an organic cycle, with numerous points of feedback, the ethical questions that emerge from the outcomes phase include the following:

(1) Among the outcomes we might measure, are we including outcomes that will positively impact the health of underserved communities, or address health inequalities?
(2) Are we capturing what is important to these communities vs. what we may think is important to them?
(3) Are there other perspectives (disciplinary, community, clinical) that would frame the problem or understand these outcomes differently?
(4) Are data on outcomes and priorities of these diverse stakeholders getting back to discovery researchers?
(5) Are there policy or socioeconomic issues that need to be addressed before the research can move forward productively?

Where We Can Go From Here: Using Research Centers to Catalyze Translation

The examples discussed here indicate that opportunities for multistakeholder engagement and exchange can facilitate problem assessment and accelerate translation toward better health outcomes. The CTSA and other NIH initiatives are funded to have an interdisciplinary approach so they can pursue different arms of a problem within a community. Other funders, such as the National Science Foundation, routinely use metrics of societal impact and mandated dissemination plans as part of their evaluation strategies.[46] If we are serious about the translation of basic science discoveries to improved health applications, we will need to keep experimenting with new approaches, new collaborations, and perhaps most importantly, with documenting the outcomes of explicitly attending to the potential for translational opportunities at the discovery phase.

Dialogue between outcomes and discovery research may be particularly important in promoting solutions to the health needs of people in resource-poor environments, but it is relevant for all translational research. The CTSAs are one example of a funding initiative for research centers that can facilitate efforts to promote the necessary cross-disciplinary dialogue including shared space, joint training programs, and institutional or funding incentives. However, to be effective, CTSAs need to go beyond funding distinct disciplinary cores, and provide more models of integration and interdisciplinary team science. In the current form, we risk repeating siloed efforts, for example, by keeping the Community Engagement Key Function Committees distinct from Strategic Planning Committees that are setting basic science research priorities.

We recognize that to advocate for additional time for exchange and reflection may sound counter intuitive to those who wish to shorten the translation timeline. We argue, however, that such a worthy up-front investment will pay off in terms of projects that are appropriately aimed and targeted. As research projects move through the translational phases from inception to discovery to development to delivery and assessment of outcomes, individual investigators, research teams, research institutions, funding institutions, and community stakeholders should be engaged in an ongoing and deeply evaluative process. Explicitly acknowledging and assessing value judgments along the translational pathway, and recognizing that the pathway in its most effective form is a cycle, empowers those engaged in clinical translational science to engage in robust debate about the normative assumptions and judgments that guide and shape their work (*Table* 1). This model enables us to more explicitly specify the value-based questions most relevant to responsible translational research along the pathway and between the phases of the pathway. Posing such questions is a necessary element in responsive science and ethically appropriate translation.

Research phase	Values inform key scientific decisions	Specific value questions
Assessment and priority setting	Which research problems should be undertaken?	Which stakeholders should be involved in the setting of research agendas?
	Which methods or tools or teams?	Does the research question address an important problem from nonscientific stakeholders, for example, potential research communities or marginalized populations?
	What are the likely benefits to flow from the research?	For domestic and international research programs receiving public or private funding, under what conditions is it permissible to privilege particular populations over others?
	Which populations will participate in and/or benefit from the research?	Does the privileging of certain research tools or methods—e.g., the randomized controlled trial—put some populations at a disadvantage, when considering the impact of translational research?
		When considering the potential benefits and risks of translational research, what is the appropriate scope of responsibility for investigators, teams, institutions, review boards, study sections, and funding agencies/foundations?
Development and delivery	How are opportunities to improve health identified and pursued?	What are the potentially harmful consequences of not moving forward with an idea?
	How does the innovation function in a broader population or human study application?	What are the opportunity costs in terms of foregone health impact by foregoing development of this idea over another?
		Have communities affected or participating in basic science research via donation to repositories shared what they see as the greatest need, and is our research and development program responsive to their priorities?
Delivery and outcomes	What are the opportunities and mechanisms to move developments into practice?	When is it ethically appropriate or even imperative to accelerate delivery of an intervention, for example, if it is the only available intervention and only chance to save lives or decrease morbidity?
	What determines the transition from potential to actual health application?	What is the expected value gained in health/lives saved and expected risk of unknown harms compared to delaying delivery to better determine efficacy?
		Are there barriers to delivery (cultural, socioeconomic, pragmatic)?
		What harmful or ineffective interventions have become programmatically entrenched and need to be discontinued or sent back to the discovery phase?
Outcomes to reassessment and priority setting, and back to discovery	What is the impact of the research (on health among other outcomes)?	Among the outcomes we might measure, are we including outcomes that will positively impact the health of underserved communities, or address health inequalities?
		Are we capturing what is important to these communities vs. what we may think is important to them?
		Are there other perspectives (disciplinary, community, clinician) that would frame the problem or understand these outcomes differently?
		Are data on outcomes, and priorities of stakeholders getting back to discovery researchers, to inform the discovery science agenda?

Table 1. Critical value judgments to consider at each transition in the translational cycle.

An expanded view of translational research helps everyone engaged in research along the translational pathway to keep the goal of translational science front and center, aiming for research that facilitates health improvement and impact. It also reveals the shared responsibilities involved in transitioning between research phases when shaping a research question and study design, and when disseminating the results or closing out the study. Making ethical, social, economic, cultural value questions explicit can challenge scientific paradigms and stimulate new ways of thinking and problem solving.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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