NCATS Advisory Council Working Group on the IOM Report: The CTSA Program at NIH

A Working Group of the NCATS Advisory Council to the Director

DRAFT REPORT

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This report draws on the experiences and insights of many, and we owe them our thanks for sharing their ideas, particularly the National Center for Advancing Translational Sciences (NCATS) leadership and staff, and members of the translational science community.

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Ron Bartek, Nora Disis, Scott Weir
Co-Chairs, NCATS Advisory Council Working Group on the IOM Report

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INTRODUCTION

In the 21st century, scientists are poised to transform our understanding of the factors that contribute to exceptional health — or its decline — by turning discoveries made in the laboratory, the patient's bedside and the community into effective health interventions through a process known as translation. Translational science is the field of investigation focused on understanding and addressing the scientific and organizational challenges underlying each step of the translational process. Basic scientists have made breathtaking advances in our understanding of the human body's biology and physiology. Along the long and complex road from promise to impact, translational science works to improve the health of individuals and the public — from therapeutics to medical technologies to medical procedures to behavioral changes.

A top priority for the National Center for Advancing Translational Sciences (NCATS) is to accelerate the process of transforming discovery to application and to increase the rate of adoption. NCATS' Clinical and Translational Science Awards (CTSA) program is key to achieving that goal. This program supports a national consortium of medical research institutions that work together to improve how clinical and translational science is conducted nationwide. The institutions that participate in this program study the translational science process in great detail to iteratively develop and test methods that enhance bench-to-bedside and bedside-to-practice research. Each institutional CTSA functions as a living laboratory for the study of the translational science process. The CTSA program members create new knowledge, technologies, methods and policies to benefit the conduct of translational science across the nation. By redesigning and accelerating the process of translational science, as well as addressing present and potential future gaps in the translational continuum [Institute of Medicine (IOM) Report, page 20], new discoveries will reach patients and communities faster. Moreover, improving the quality of the translational science process will result in tangible health benefits for our nation and beyond.

NCATS is continuing to develop the CTSA program to meet the needs of clinical and translational investigators and the communities they serve. In June 2013, IOM issued a report of its findings following an in-depth review of the CTSA program. Its recommendations included formalizing and standardizing the evaluation processes for individual CTSA institutions and the program as a whole, advancing innovation in education and training programs, and ensuring community engagement in all phases of translation.

In November 2013, NCATS assembled a Working Group of council and non-council stakeholders who have extensive expertise in the subject areas addressed in the IOM Report, to provide guidance on programmatic changes needed to implement the report's recommendations. The Advisory Council Working Group on the IOM Report on the CTSA program was **charged to develop meaningful, measurable goals and outcomes for the CTSA program that speak to critical issues and opportunities across the full spectrum of clinical and translational sciences.** [See operational phases of translational research (T1-T4) IOM Report, page 20] The Working Group deliberations took place from November 2013 to May 2014. The group met four times, including two face-to-face meetings in Bethesda. Their findings and conclusions comprise the content of this report.

To achieve the goals stated in this document, it clearly will be necessary to "strengthen NCATS' leadership of the CTSA program," as recommended in the IOM Report. [IOM Report, page 6] This strengthened leadership will be essential to the Center's ability to evolve the CTSA program further into a fully collaborative, integrated network so as to catalyze the next generation of genuinely innovative technologies and methods. To succeed, NCATS will need flexibility in executing the vision for the CTSA program as well as enhanced collaboration within NIH and with translational science stakeholders outside the institutes.

This report serves as a reference for developing strategies to strengthen the CTSA program and as a guide for measuring and reporting progress. Further, the report sets forth a framework within which translational science stakeholders can address some of the most perplexing challenges and emerging opportunities that hinder the translation of basic science discoveries into interventions that improve human health.

Overview of Process

The IOM committee was asked to assess the CTSA program and its mission and strategic goals and to provide input on implementation of the program by NCATS to improve the efficiency and effectiveness of the CTSA program. [IOM Report, page 17] The committee's report, released in June 2013, identified seven recommendations, of which the Working Group was charged to consider the following four:

- Formalize and standardize evaluation processes.
- Advance innovation in education and training programs.
- Ensure community engagement in all phases of research.
- Strengthen clinical and translational science relevant to child health.

The remaining three IOM committee recommendations — strengthen leadership of the CTSA program, reconfigure and streamline the CTSA consortium, and build on the strengths of the individual CTSAs across the spectrum of research — are being addressed internally by NCATS staff.

Figure 1. Process for implementing IOM recommendations. Shown in the blue squares is the Working Group (WG) process. Purple boxes represent the future work of NCATS in considering the recommendations and the way forward.

Figure 1 outlines the approach NCATS took in considering the IOM recommendations. The following discussion topics were addressed at the first Working Group face-to-face meeting:

- Training and education
- Collaboration and partnerships
- Community engagement of all stakeholders
- Academic environment for translational sciences
- Translational sciences across the lifespan and unique populations
- Resources
- Pilot projects

The Working Group decided that the last two topics, resources and pilot projects, were program-level concerns and should be addressed by NCATS. However, both the Working Group and NCATS leadership acknowledged that much of the work done by the Working Group will influence subsequent development in these topic areas.

The five topic areas of focus for the Working Group were further refined into four Strategic Goals that broadly capture the selected IOM Report recommendations. These Strategic Goals were considered in detail by the Working Group.

Workforce Development

Goal: The translational science workforce has the skills and knowledge necessary to advance translation of discoveries.
This goal focuses on:

- Building an environment that supports and values translational science as "the place to go" for those who want to pursue high-impact careers in health sciences.
- Training and educating a world-leading, continuously learning workforce.
- Developing a translational science workforce that can meet the needs of today and tomorrow.

Collaboration/Engagement

Goal: Stakeholders are engaged in collaborations to advance translation.
This goal focuses on:

- Engaging stakeholder communities so they contribute meaningfully across the translational sciences spectrum.
- Enabling team science to become a major academic model.
- Ensuring that all translational science is performed in the context of collaborative team science and that shared leadership roles are the norm throughout the entire translational science process.

Integration

Goal: Translational science is integrated across its multiple phases and disciplines within complex populations and across the individual lifespan.
This goal focuses on:

- Integrating translational science across the entire lifespan to attain improvements in health for all.
- Launching efforts to study special population differences in the progress and treatment of disease processes.
- Developing a seamless integrated approach to translational science across all phases of research.

Methods/Processes

Goal: The scientific study of the process of conducting translational science itself enables significant advances in translation.
This goal focuses on:

- Enabling CTSA programs to function individually and together as a research engine transforming the way translational science is conducted across the nation to make tangible improvements in the health of individuals and the population.
- Rapidly translating CTSA-generated new knowledge and technologies into health interventions in real world settings.
- Developing technologies, methods, data, analytics and resources that change the way translational scientists approach their work.
- Generating and curating comprehensive data sets or other resources that catalyze science.

These overarching and overlapping Strategic Goals provided the foundation for deliberation at the second face-to-face meeting. Using the Results-Based Accountability process (see Appendix A for a description of this process), the Working Group determined the factors that impede or advance progress toward achieving each Strategic Goal. Based on these factors, the Working Group identified measurable objectives that could be undertaken by NCATS.

STRATEGIC GOAL

Workforce Development: The translational science workforce has the skills and knowledge necessary to advance translation of discoveries.

Introduction

The IOM Report notes: "The health needs of the nation call for a generation of scientists trained in 'interdisciplinary, transformative translational research' and in the leadership and team skills to engage in effective collaborative partnerships." [IOM Report, page 105]

There have already been great strides in translational science workforce development. The field of translational science is growing worldwide and the demand for trained professionals who specialize in translational science is high, not only in industry, but also in academia, government and disease philanthropy organizations. Seasoned and newly educated professionals are seeking translational science educational opportunities, and there is growing recognition of translational sciences as a legitimate, highly valued career path.

The development of components of training and education, such as core competencies and standards, needs to be balanced with flexibility for individual needs and a focus on innovative learning approaches. The traditional benchmarks for academic promotion and advancement — publications, peer-reviewed research funding and teaching — need to be revised and harmonized with new benchmarks that value team-based efforts and collaborative approaches to translational science. Success in translational science will require multidisciplinary and, in many cases, multiorganizational teams. Industry recognized this importance decades ago. Educational opportunities must be provided to all members of the team to advance translational science goals. Thus, in addition to sustaining and building on graduate and postdoctoral education, further work is needed to expand training and continuing education opportunities for faculty, professional staff and community partners.

Where We Are Now (Positive/Negative Factors)

Workforce Development	
Positive Factors	**Negative Factors**
A significant number of interested young people want to engage in translational science (TS).	There is no clear funding strategy for TS workforce development.
The worldwide demand is increasing for TS professionals with many career opportunities in academia, government, industry, non-profits, etc.	There is no collective strategy for developing a TS workforce.
Potential partners and collaborators are ready, willing and able to be engaged in TS projects.	There is a fear of putting one's career at risk; that is, that one would not grow as an academician in a TS career pathway.
Industry has demonstrated the value of multidisciplinary teams in driving TS within their organizations. This knowledge can be utilized.	TS workforce team members other than the principal investigator (PI) or M.D. (e.g., nurses, community members) do not feel their role or value is considered as legitimate as that of the PI or M.D.

New disciplines are forming such as “regulatory science” or “team science,” which offer novel career pathways.	TS is an early science with many moving parts; curriculum is still too general, which makes it harder to be a legitimate discipline.
The diversity of career pathways in TS is appealing and offers unique opportunities for cutting edge research.	Career pathways are not as clear as with other more established disciplines.
There is an increasing demand among researchers for building skills/competencies in TS.	Skills and competency models are not defined.
There has been a great deal of progress in CTSAs to develop TS training programs and career paths.	Creation and implementation of TS workforce development strategies do not usually involve key stakeholders outside of academia (e.g., community health workers).
Technology can enable global networks of educational resources.	Traditional methods of learning, such as classroom didactics, may not fit all educational needs of TS.
The time is right and demand is high for novel curriculum development for TS.	Academic institutions lack the necessary leadership to establish the importance of TS.

Where We Need To Be — What Does Success Look Like?

If a successful translational science workforce is developed, we will have demonstrable evidence of numerous discoveries being translated to patients and the community. Worldwide, translational science will be viewed as “the place to go” by those who want to pursue high-impact careers in health sciences. The U.S. and global community will value translational science and provide a supportive environment for its conduct. A well-qualified translational science workforce will meet the recognized needs of today and the emerging needs of tomorrow, and will shape the vision for the future. Achieving success will require that:

- The translational science “workforce” is broadly defined and includes researchers, clinicians, practitioners, patients, patient advocacy organizations, industry and community members.
- Curriculum is developed to train a world-leading, globally connected, continually learning workforce with the skills needed to excel in translational science.
- Translational science training draws from sources outside the academic arena (e.g., from industry and non-profit sectors).
- The subdisciplines within translational science are well defined.
- The steps to advancement within each translational science subdiscipline are well defined.
- Resources are available for the research and development of needed educational competency models in each translational science subdiscipline, as well as the tools and methods needed to develop those competencies so that education constantly evolves.
- The needs of the translational science workforce are identified and forecast.

Measurable Objectives

1. Core competencies for a translational science workforce and the methods for evaluating those competencies are defined.
    - Skills and competency models are created.
    - Information on skills and competencies are broadly and readily available.
    - Effective practices are shared and adopted in a continuously learning environment.
    - Core competencies are developed for, and with the involvement of, all stakeholders.

2. Translational science is a fully developed, highly valued and rewarding discipline with formal career pathways.
    - Translational science organizational units are established at academic health centers. These translational science organizational units hold the same stature as traditional biomedical research departments (e.g., anatomy) yet engage all disciplines in team science.
    - There is a national strategy for developing a translational science workforce that has been developed collaboratively with the involvement of all stakeholders.
    - There is a defined educational pathway for translational science specialties that enables focused preparation to begin at the undergraduate level.
    - The workforce is broadly trained across the full spectrum of translational science, regardless of the specific specialization of an individual translational scientist.
    - The systems for staff development and faculty promotion at academic health centers recognize and reward the collaborative nature of translational science.
    - Mentoring programs are established, evaluated and made widely available.
3. Translational science is conducted by interdisciplinary teams for optimal impact.
    - There are means to define, recognize and reward the contributions of all team members regardless of role or degree.
    - Sustainable partnerships are the norm.
    - Reward systems are built around team science metrics.
    - Individual team members are valued and have clear career paths.
    - The translational workforce is trained in the core competencies of collaboration/engagement.
4. Core competencies are available to all members of the workforce through vehicles for learning that are readily accessible and flexible.
    - Degree programs in translational science are widely available.
    - Certificate programs in subdisciplines of translational science are widely available.
    - Ongoing continuing translational science educational programs exist at sites where translational science is performed.
    - Criteria for translational science competence have been defined and evaluation of that competence can be documented.
    - Quality programs for translational science are operating at all institutions involved in the discipline.
5. Training curricula on effective teams, high-performing organizations and productive collaborations are developed, made broadly available and viewed as a core element of success. For example, training is available on how to create effective and streamlined collaborative processes.

STRATEGIC GOAL

Collaboration/Engagement: Stakeholders are engaged in collaborations to advance translation.

Introduction

Translational science is complex and multifaceted. Discovering the means to accelerate it will require a collaborative approach to projects and the ability to build effective teams. The benefits of collaboration and engagement are numerous and can lead to a more robust translational science enterprise, stronger community support and funding, and the attraction of young people to careers in translational research. [IOM Report, page 117] In addition, diverse collaborations can lead to greater innovation. Finding solutions and demonstrating the ability to adopt those solutions widely requires multidisciplinary teams representing multiple partners. Further, the extent and strength of the partnerships and collaborations that are formed will determine the speed with which benefits to the nation's health can be realized.

Within the CTSA program, collaborative partnerships are often limited to academic and industry collaborators with select interactions from the community. This is not sufficient. There is a need for extensive integration with collaborators outside academic institutions. There are a host of individuals, teams and networks of volunteers (citizen scientists) who are eager to help. These stakeholders provide unique and valuable viewpoints — regardless of whether those individuals are patients or members of foundations, community programs, governmental agencies, community health practices, non-profit organizations or other entities. These invaluable community participants must be thoughtfully included in key partnerships to accelerate health discovery.

Despite the recognized need and strong support for collaboration as a concept, effective collaborations and partnerships are often hard to come by. The resources and infrastructure to support them are frequently lacking. There is a great need for scientific approaches to the definition and maintenance of successful collaborations.

Translational science is a team-based endeavor. To accelerate the field, we must know how to build effective teams, form effective partnerships and overcome barriers. We need to address issues related to trust and respect, and clearly define the benefits and value of collaborative partners and meaningful roles. We must overcome the challenges to collaboration that exist within academic cultures, and provide clear expectations for protocols of engagements, training and education for partners and collaborators, and assessment measures. Successful collaboration models need to be actively disseminated. The creation of new knowledge often does not on its own lead to widespread implementation or impacts on health. Collaboration and partnerships with key stakeholders are essential to transforming research findings into changes in health care practice and policy.

Where We Are Now (Positive/Negative Factors)

Collaboration/Engagement	
Positive Factors	**Negative Factors**
There has already been progress in collaborations with industry, other CTSAs, non-CTSAs, and the community. The "glass is half full." TS scientists have a common end goal: to cure human disease, enhance health, lengthen life and reduce illness and disability.	Many ideas and research interests are tangential rather than central to the health and research interests of the community.
Scientists already are forming interdisciplinary research teams and collaborations with community, industry and other partners as strategies for more efficient and effective research.	The current system (structure, hierarchy) is not built for the "science of engagement." Rather, engagement is viewed as a service to the community instead of a part of the research activity.
Collaboration combines and leverages the resources that each partner brings to the table, including funds, ideas and talent. There are examples of academic institutions developing criteria to reward collaboration.	The current structure facilitates grant-initiated research; the grant recipient calls the shots and little is generated by the community.
Some successful models for collaborative TS exist, including practice-based research networks and community-based participatory research partnerships.	In general, the rewards system is not aligned with TS, whether it is money, promotion, tenure, a sense of belonging, or a sense of respect.
There are excellent examples of different scientific approaches to the study of collaboration in industry, academia and transformative scientific endeavors (e.g., space missions).	TS capacity building and infrastructure support is needed to enable patient advocates and community members to participate fully as partners.
The CTSA program has attempted in a systemic way to engage the public in the process of translational sciences.	We do not teach collaboration as well as we could, and many collaborations fail.
Diversity of skills, experiences and backgrounds enhances performance of teams and organizations.	We encourage competition rather than collaboration, from science fairs to graduate school; it is part of the culture.
High performing teams are based on trust, diversity and collaboration.	There is a lack of understanding about what each party can bring to the table.
Diverse teams are often the most innovative.	Collaborations take a lot of time and must begin with creating a trusting partnership.
There is a growing group of patient advocates and community members who are eager to participate as partners in TS. Many people embrace the concept of "citizen scientist."	The practice of community engagement in TS is often limited to community outreach for recruitment of study participants, particularly minority populations.
	There are many roadblocks to collaboration across sectors and across the entire TS spectrum.

Where We Need To Be — What Does Success Look Like?

If collaborative team science becomes the norm rather than the exception, we will see diverse stakeholders engaged as full partners in translational science and involved in shared leadership roles throughout the entire research process. Team science rather than the "single principal investigator" will become the major academic model. Translational science will serve as the model for research collaboration and engagement. Community engagement will be acknowledged as an essential ingredient of translational science. With stable, functioning, diverse teams in place, the CTSA programs could study the impact of collaboration models on the acceleration of translational research. Achieving success will require that:

- Translational scientists are aligned toward a common goal: to cure human disease, enhance health, lengthen life and reduce illness and disability.
- The role and function of the CTSA program is clear to all potential collaborators.
- Communities involved in all aspects of the translational science spectrum contribute to the development of all aspects of translational sciences.
- Translational science is governed by collaborations and partnerships that reward all stakeholders, including researchers, patients and the community.
- Government funding agencies, such as NIH, routinely collaborate in translational science initiatives and effectively engage other federal agencies, industry, academia and philanthropic organizations as partners.
- The value of collaboration is enhanced while the cost and difficulties of collaboration are reduced by methodologies and approaches emanating from CTSA programs.
- Collaboration to accelerate translational science extends beyond U.S. borders.
- Patient advocates, community members and citizen scientists have the capacity and infrastructure in place to participate fully as partners in all phases of translational science.
- All stakeholders are respected, valued and rewarded for their time and expertise.
- We can measure the impact of the collaborative culture change on translational science.

Measureable Objectives

1. Methods, processes and systems are developed and utilized to identify and effectively engage relevant and diverse stakeholders across the translation spectrum.
    - Developed methods are adopted broadly.
    - Approaches studied rigorously add valuable insights and information, regardless of whether they succeed or fail.
    - Both positive and negative results are widely disseminated through suitable means of communication.
2. Methods, processes and systems for collaborating are innovative and evolve to meet the needs of the translational science field.
    - Novel methodologies, study design and technologies are developed and tested.
    - The existing barriers to effective collaborations are reduced.
3. Each partner within a diverse translational science team has the capacity and infrastructure support to be both a collaborator and to lead collaborations as complex translational science projects evolve.
    - Project roles are clearly defined.
    - Leadership values diverse expertise.
    - Institutions demonstrate their support for establishing, maintaining and expanding collaborations and partnerships.

4. Translational science collaborations involve individuals, organizations and disciplines that are appropriate to the study aims.
    - Rationale for choice of stakeholder engagement is clear and meaningful.
5. There are established measures for assessing and improving collaborations.
    - Methods have been developed for evaluating the value and productivity of collaboration.
    - Methods have been developed collaboratively by translational science stakeholders for assessing the quality and impact of community engagement and collaboration in translational science.
6. Diverse stakeholders and community members play key roles throughout the infrastructure of the CTSA program both locally and nationally.
    - There is full and effective integration of all stakeholders at all levels of governance.
7. The translational science workforce is competent in community engagement and collaboration.
    - Robust training programs are developed and outcomes assessed.
    - The science of successful collaboration becomes part of the translational science portfolio.

STRATEGIC GOAL

Integration: Translational science is integrated across its multiple phases and disciplines within complex populations and across the individual lifespan.

Introduction

Focusing on “science that works” will refine our understanding of the interplay of biological processes, lifestyle changes, environmental exposures, disease prevention, and behavior modifications so that the greatest health impact can be achieved with the greatest efficiency. Translational science will be needed to directly impact the integration of evidence-based interventions into practice settings. A systems approach will capture critical interrelationships that fragmented or narrower approaches miss.

Ensuring that breakthroughs in science become breakthroughs for people depends on our ability to explore and adapt to the changing landscape — both inside and outside the lab. In the 21st century, health will be determined by societal trends as it never has before. People are living longer, providing unprecedented opportunities to study interventions across the lifespan from many angles. For example, the number of adult survivors of childhood illness will rise dramatically, underscoring the need for research that specifically assesses the impact on adults with chronic health conditions that originated in childhood. We need proactive identification of better strategies during childhood for prevention of the disease or the complications of disease treatments. Consider sickle cell disease. Thirty or 40 years ago, the majority of patients died during childhood. Now, thanks to advances in care, patients with sickle cell disease live long enough to reach older adulthood. Although researchers and doctors have come a long way in understanding the disease and providing screening and treatment for children, adults with the condition still face many challenges, including misperceptions and a lack of access to proper care. In another example, acute lymphocytic leukemia (ALL) now has a 5-year survival rate of more than 90 percent. As pediatric ALL patients become adults, they experience new health issues in adulthood that are tied to cancer treatment. A good model of the iterative cycles of the improvement that can result from lifespan research is the collection of these emerging health issues in adulthood, coupled with development of effective new therapies in childhood that are less debilitating in the long term.

Furthermore, within the next 5 years, the number of adults aged 65 and older will outnumber children under the age of 5. By 2050, these older adults will outnumber all children under the age of 14. By the same year, the number of adults aged 80 and older will quadruple. [World Health Organization] This longer lifespan has implications for the progression of chronic diseases. Translational studies will be needed to uncover the interrelationships of disease with environmental exposures, health-related behaviors, and social factors across the lifespan. Heightened attention is needed for preventive strategies during pregnancy, childhood and early adulthood to improve health in older adults.

In addition to differences for individuals across the lifespan, huge differences among populations also can affect health outcomes. These special populations (e.g., racial, ethnic, and gender-specific) are poised to benefit most from translational science, yet are rarely ever a focus of study. The role of translational science is critical to understanding the causes of these disparities; how they relate to social, economic and health system factors; and how evidenced-based interventions can be implemented.

Finally, translational science itself is not a one-step process. This multistep, multiphase, multidiscipline scientific process needs greater integration, not only within the translational science spectrum (from early translation to practice and back), but also within complex populations and across the individual lifespan.

Where We Are Now (Positive/Negative Factors)

Integration	
Positive Factors	**Negative Factors**
CTSAs are poised to understand diseases in the transition from childhood to adulthood and from adulthood into old age.	There are barriers to lifespan research; for example, age restrictions for studying drug interventions in pediatric and geriatric (80+ years) populations.
CTSAs are uniquely positioned to play a coordinating/convening role for bringing together scientists from the disparate fields needed to study disease longitudinally.	There is tension about the relative value of translation from basic science to human studies, versus translation of new data into the clinic and health decision making.
Analytical and computational tools are becoming available to release new information and subsequent insights by integrating increasingly large and diverse sets of data.	Scientists who are focused on a specific field (either life-stage or type of intervention) do not routinely interact with colleagues in other fields.
Integration of scientific information across periods of time leads to knowledge formation, including longitudinal disease-specific databases.	There is a lack of a knowledge base for all types of interventions at the extremes of age as well as within special populations.
There is a growing body of knowledge about the non-clinical determinants of health (e.g., a robust network of community-based public health practitioners, urban planning).	Patients are not engaged as collaborative partners in the clinical care and clinical research process.
Patient advocate groups are eager to help partner in research.	There is a research gap in the transition phases of aging.
Academics and NIH attempt to create awareness on the study of minorities and special populations.	There are many barriers to working with the pediatric population if one is not formally trained as a pediatrician.
There are some medical subspecialties that have a track record of following disease across age ranges (i.e., cystic fibrosis, sickle cell).	Support is lacking for maintenance of long-term databases and biorepositories.
Academic health centers are interested in defining and providing best practices, and this increases interest in defining quality care at the extremes of the lifespan.	Many ethical issues exist for dealing with special populations, but there is limited access to ethics expertise.
Disease prevention is a field of study of high interest to the CTSA program.	More robust training programs are needed for investigators studying lifespan transitions.
Strong progress has been made in computing power to integrate and display vast amounts of disparate information.	There is no single clear solution for which data analytics system to use.

Where We Need To Be — What Does Success Look Like?

If successful, translational science always will include integration across the entire lifespan; the highest level of health for all people, regardless of age, will be attainable. If translational science always includes efforts to study special populations, differences in the progress and treatments of disease processes will be identified. We will have a seamless, integrated approach to translational science across all phases of research. Success is achieved when:

- Translational science efforts lead to quantifiable improvements to the health, health care outcomes and quality of life for people living with chronic disease and for racial, ethnic and underserved populations.
- Laboratory and clinical advances are translated rapidly into lifesaving and life-prolonging interventions in both the young and elderly, without unnecessary delay.
- Expertise, scientific data and technologies are shared to broaden the impact and enhance productivity of translational science across the lifespan.
- New models (including regulatory, ethical or policy considerations) exist that include all patients in biomedical research.
- Opportunities to prevent, postpone the onset or otherwise alter the natural history of acute and chronic conditions through interventions early in the life course are examined by translational scientists.
- Data across the full lifespan are integrated, analyzed, displayed and exploited as relating to translational science.
- Translational research on health conditions that are specific to different life stages (childhood, adolescence, early adulthood, reproductive ages, pregnancy, and older adulthood) are emphasized.
- Mechanisms are in place to ensure that interventions reach the patients who need them the most.

Measureable Objectives

1. Translational science addresses special populations (e.g., children, the elderly, Latinos, African-Americans) and all transitions across the lifespan.
    - Interventions and devices are developed for population-specific needs.
    - Participant risk in translational sciences is managed appropriately for all populations (e.g., pediatrics, geriatrics).
    - All populations are welcome to participate in translational science.
2. Translational science addresses all types of interventions (e.g., devices, medical procedures, behavioral changes, non-clinical determinants of health) in all populations.
3. Translational science is integrated from basic research to clinical to care implementation and to populations across the spectrum of the lifespan.
    - Clinical research objectives are aligned with clinical care.
    - Academic medical centers embrace translational research as a critical part of their clinical care mission.
    - Translational science enhances patient outcomes by understanding and improving medical care compliance and adherence to treatment plans.
4. Translational scientists integrate the entire translational science spectrum into how they conceptualize and implement their research for patients throughout the lifespan.
5. The methods that influence the integration of evidence-based interventions into practice settings (i.e., implementation science) become fully realized across the lifespan and for all populations, especially those experiencing health disparities.

STRATEGIC GOAL

Methods/Processes: The scientific study of the process of conducting translational science itself enables significant advances in translation.

Introduction

The rapid pace of breakthrough discoveries is transforming our world — from developing new tools for genome surgery, to making organs from stem cells and designing electronic sensors to work inside the body. Technological advances and unprecedented scientific opportunities that exist *right now* are prompting a cascade of new insights that will change not only the way we do translation but also the way we think about it.

In almost one decade, we have gone from completion of the first human genome sequence to being able to sequence more than 1,000 human genomes for a single study. In the span of a few years, we have developed increasingly faster sequencing techniques to help identify the genes that cause diseases and, in turn, generated discoveries leading to better interventions. Personalized medicine now makes it possible for people to find out, with just a cheek swab, their own genetic risk for disease.

International collaborations are creating the most complete inventory ever assembled of the millions of variations among people's DNA sequences. And just months ago, in a defining moment for science and technology, researchers built a synthetic genome and used it to transform the identity of a bacterium's DNA so that it produced a new set of proteins. In the future, researchers envision synthetic genomes that are custom-built to generate biofuels, pharmaceuticals or other useful chemicals.

Some of the most promising medical advances come from the field of stem cell research. For example, scientists can grow human stem cells into tiny "organoids" — such as pituitary glands, livers and even rudimentary human eyes — in the lab. A research team has grown a brain organoid that develops various discrete, although interdependent, brain regions. These so-called "cerebral organoids" have the tissue and structure that mimic the anatomy of the early developing human brain. They offer researchers an unprecedented view of human brain anatomy that, in turn, could help scientists better understand conditions such as autism and schizophrenia, which have been linked to problems in brain development.

Given these young and relatively uncharted territories, scientists often must develop every step of the process — from testing in animals to manufacturing the cells to meet the required clinical grade standard. They must obtain ethical and regulatory approval and evaluate safety and efficacy. In the drive to rapidly move discoveries such as the genomics and stem cell examples described above to patients and the community, we must reimagine the way we do translational science. This is the role of the CTSA program.

The translational science process is complex, dynamic and frequently non-linear — just like the factors that influence health or its decline. The usual sequential step-by-step style of academic research often is not a good fit. To advance, translational science must evolve from the sequential to the parallel; from linear to bidirectional; from single discipline to multidiscipline; from single institutions to collaborative, integrated networks of institutions; and from investigator-initiated to stakeholder-driven processes. Translational science must adhere to high quality methods and processes, and must use and advocate for models that are clearly reliable, reproducible, and ultimately validated in humans. Translational science must be conducted in structures that are much flatter, more cooperative and more process-oriented, with a focus on teams and collaborations. New technologies, approaches, methods and policies must be developed to speed tangible improvements to human health.

To accomplish this, the CTSA program must focus on redesigning the way translational science is conducted. Such a redesign will require "a more centralized approach to leadership, one in which NCATS plays a much more active role." [IOM Report, page 5] To be effective in the strengthened leadership role recommended in the IOM Report, NCATS will need sufficient flexibility in applying its resources and increased prerogative in identifying and supporting genuinely innovative, transformative translational science projects at CTSA sites. The Center also will need enhanced collaboration and partnership with the translational science programs of the NIH Institutes as well as with stakeholders outside NIH.

Where We Are Now (Positive/Negative Factors)

Methods/Processes	
Positive Factors	**Negative Factors**
Standardization of methods and processes frees investigators to focus on innovation.	There are no established standards in TS for performance measures to gauge, for example, the achievement of research objectives or the efficiency and timeliness of the research process.
Effective processes enhance productivity while minimizing waste.	There is no standardization or harmonization of information among CTSA sites.
Reproducibility and validation of science is enhanced by high-quality methods and processes.	Regulatory science competencies of researchers are not standardized, are inconsistent, or are not strong.
There is recognition of the need to change methodologies to advance TS.	A regulatory pathway for emerging technologies does not exist (e.g., for regenerative medicine).
There are examples of applications of business methodology to address TS.	There is no clear funding strategy for studying method development or process improvement in TS.
There is interest in driving new technologies to the clinic.	TS processes are slow and cumbersome and often were designed without the investigator or the patient in mind.
CTSAs have access to the diverse expertise needed to redesign the TS enterprise.	Historically, CTSAs have not had a strong focus on the "science of translational science." This should be a main goal.
Novel methodologies and processes have come from the CTSA program.	"Out of the box" thinking or solutions often are met with skepticism.
CTSAs now have the flexibility to focus on new areas of science.	Effective methods for dissemination of novel technologies, methods or practices are not readily available.
Academia is often the birthplace of new disciplines, and CTSAs can be involved at the onset in determining what is needed to move emerging fields forward.	Many major improvements to the TS structure will require redesign of resources outside the control of CTSAs (i.e., technology transfer or institutional review board offices).

Where We Need To Be — What Does Success Look Like?

We will have achieved success when the CTSA programs function individually and together as a research engine that transforms the way translational science is conducted across the nation. The programs will routinely establish new scientific fields or paradigms, develop technologies and methods that change the way scientists approach their work, and generate and curate comprehensive data sets or other resources that catalyze science. CTSA-generated new knowledge and technologies will result in the rapid translation of scientific discoveries into health interventions. We will have achieved this goal when:

- Key roadblocks that impede the translation of science into improved impacts on human health have been identified and eliminated.
- New tools, technologies, data sets and models are widely available to enable translation across organizations, accelerate translation of science, and test new approaches that foster innovation in real world settings.
- Translational science uses digital technologies to create scientific information and to communicate, replicate and reuse scientific knowledge and data.
- Data sets are integrated; data sharing and access to secondary data is the norm across the translational spectrum.
- By changing methods and processes, translational science dramatically improves translation of discoveries into tangible effects on health in real world settings.
- Successful translational science practices and effective solutions are adopted across the nation.
- Outcomes from implemented solutions are correlated with expected changes.
- Common processes exist to strengthen clinical study, implementation and impact.

Measureable Objectives

1. Methods and processes are developed or optimized for carrying out translational sciences within different stakeholder environments.
2. Emerging areas in science proceed more quickly due to CTSA-driven innovations.
3. The business of translational science is managed with accountability and data-driven decision making:
    - There are established performance measures for the conduct of translational sciences (including achievement of research objectives).
    - Using performance measures, management practices are analyzed for effectiveness and efficiency. Strategies are developed and implemented to enhance effectiveness.
    - Processes among and between translational science stakeholders are harmonized (e.g., data elements, medical records, institutional review board approval process, procurement)
4. Methods and processes are optimized for the development of both regulated and non-regulated interventions so requirements are transparent and consistently applied.
5. Analytical and computational tools are developed and deployed to manage the explosion of data and enable optimal utilization of those data to make tangible improvements to human health. For example, new sets of data are visualized, integrated and made broadly available for a diverse range of translational science uses.
6. Tangible improvements are made in the timeliness, quality and ethical standards of research design (e.g., institutional review boards, human subject protections). For example, a multisite clinical proof-of-concept trial is carried out in a timely manner.

APPENDIX A: RESULTS-BASED ACCOUNTABILITY

Results-Based Accountability™ (RBA)[1] is used by organizations to improve the performance of their programs. RBA starts with "ends" and works backward, toward "means." It is a simple, common sense framework that all stakeholders can understand. The NCATS Advisory Council Working Group applied the following RBA principles in its deliberations.

RBA Principle

Distinguish accountability for the well-being of populations from accountability for program performance. RBA distinguishes between (1) results for whole populations (e.g., all children, all seniors, all citizens in a geographic area) and (2) results for the customers or clients of a particular program, agency or service system. The most important reason for this distinction is the difference in *who* is accountable. Performance accountability can be assigned to the managers who run the various programs, agencies or service systems. Population accountability cannot be assigned to any one individual, organization or level of government. The whole community, public and private sectors, must share responsibility for results. To illustrate this point, Dr. Michael Lauer of the National Heart, Lung and Blood Institute, in a commentary on RBA in the journal *Circulation Research,* used the analogy of a job-training program and asked, "Should a job training program be held accountable for a city's employment rate?"[2]

Application to the CTSA program. In its deliberations, the Working Group focused on identifying the appropriate program accountability to assign to the CTSA program. The Working Group distinguished such program accountability from accountability for the health of whole populations (e.g., rates of death and suffering due to diseases), for which the CTSA program should not and cannot be held solely accountable.

RBA Principle

Performance accountability includes asking not just "how much did we do?" and "how well did we do it?" but also, and most importantly, "is anyone better off?" In RBA, the managers of a program ask: What is the desired impact of our services on our customers or clients? The most important performance measures gauge the extent to which the desired impact is being achieved.

Application to the CTSA program. In focusing on the performance accountability of the CTSA program, the Working Group began with the desired impact of the CTSA program on the translational workforce, outlined in terms of the four Strategic Goals:

1. The translational workforce has the skills and knowledge necessary to advance translation of discoveries.
2. Stakeholders are engaged in collaborations to advance translation.
3. Translational science is integrated across its multiple phases and disciplines within complex populations and across the individual lifespan. The scientific study of the process of conducting translational science itself enables significant advances in translation.

RBA Principle

In decision making, work from ends to means: What do we want? How will we recognize it? What will it take to get there? In RBA, whether focusing on the conditions of well-being that we want for populations or the performance of an agency or program, decision making starts with clearly identifying ends, determining how to gauge the achievement of those ends, and then systematically working backwards to determine the best means to achieve those ends.

Application to the CTSA program. For each Strategic Goal, the Working Group developed (1) a description of what the achievement of each Strategic Goal would look like; (2) an analysis identifying the most important factors (positive and negative, internal and external to the CTSA program) impacting the success of the CTSA program in achieving that Strategic Goal; and (3) a set of Measurable Objectives to guide the CTSA program's development and implementation of strategies to improve the achievement of the Strategic Goals.

RBA Principle

Engage stakeholders collaboratively by making the decision-making process transparent. RBA enhances stakeholder engagement and collaboration by making the decision making process systematic and transparent.

Application to the CTSA program. In developing its recommendations for the CTSA program, the Working Group has purposely made transparent its deliberations — the ends to which the CTSA program should be assigned accountability, the Working Group's analysis of the factors impacting the achievement of those ends, and the recommended measurable objectives to inform the development and implementation of strategies to improve performance.

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[1] Results-Based Accountability™ was developed by Mark Friedman, author of *Trying Hard is Not Good Enough: How to Produce Measurable Improvements for Customers and Communities.* Victoria, B.C., Canada: Trafford Press, 2005. Available at: http://resultsaccountability.com and http://raguide.org.

[2] Lauer, M.S. *Thought Exercise on Accountability and Performance Measures at the National Heart, Lung, and Blood Institute: An Invited Commentary for Circulation Research. Circ Res* 108:405-409, 2011. Available at: http://circres.ahajournals.org/cgi/content/full/108/4/405.

APPENDIX B: CONSOLIDATED LIST OF POSITIVE/NEGATIVE FACTORS

Workforce Development	
Positive Factors	**Negative Factors**
A significant number of interested young people want to engage in translational science (TS).	There is no clear funding strategy for TS workforce development.
The worldwide demand is increasing for TS professionals with many career opportunities in academia, government, industry, non-profits, etc.	There is no collective strategy for developing a TS workforce.
Potential partners and collaborators are ready, willing and able to be engaged in TS projects.	There is a fear of putting one's career at risk; that is, that one would not grow as an academician in a TS career pathway.
Industry has demonstrated the value of multidisciplinary teams in driving TS within their organizations. This knowledge can be utilized.	TS workforce team members other than the principal investigator (PI) or M.D. (e.g., nurses, community members) do not feel their role or value is considered as legitimate as that of the PI or M.D.
New disciplines are forming such as "regulatory science" or "team science," which offer novel career pathways.	TS is an early science with many moving parts; curriculum is still too general, which makes it harder to be a legitimate discipline.
The diversity of career pathways in TS is appealing and offers unique opportunities for cutting edge research.	Career pathways are not as clear as with other more established disciplines.
There is an increasing demand among researchers for building skills/competencies in TS.	Skills and competency models are not defined.
There has been a great deal of progress in CTSAs to develop TS training programs and career paths.	Creation and implementation of TS workforce development strategies do not usually involve key stakeholders outside of academia (e.g., community health workers).
Technology can enable global networks of educational resources.	Traditional methods of learning, such as classroom didactics, may not fit all educational needs of TS.
The time is right and demand is high for novel curriculum development for TS.	Academic institutions lack the necessary leadership to establish the importance of TS.
Collaboration/Engagement	
Positive Factors	**Negative Factors**
There has already been progress in collaborations with industry, other CTSAs, non-CTSAs, and the community. The "glass is half full." TS scientists have a common end goal: to cure human disease, enhance health, lengthen life and reduce illness and disability.	Many ideas and research interests are tangential rather than central to the health and research interests of the community.
Scientists already are forming interdisciplinary research teams and collaborations with community, industry and other partners as strategies for more efficient and effective research.	The current system (structure, hierarchy) is not built for the "science of engagement." Rather, engagement is viewed as a service to the community instead of a part of the research activity.
Collaboration combines and leverages the resources that each partner brings to the table, including funds, ideas and talent. There are examples of academic institutions developing criteria to reward collaboration.	The current structure facilitates grant-initiated research; the grant recipient calls the shots and little is generated by the community.

Some successful models for collaborative TS exist, including practice-based research networks and community-based participatory research partnerships.	In general, the rewards system is not aligned with TS, whether it is money, promotion, tenure, a sense of belonging, or a sense of respect.
There are excellent examples of different scientific approaches to the study of collaboration in industry, academia and transformative scientific endeavors (e.g., space missions).	TS capacity building and infrastructure support is needed to enable patient advocates and community members to participate fully as partners.
The CTSA program has attempted in a systemic way to engage the public in the process of translational sciences.	We do not teach collaboration as well as we could, and many collaborations fail.
Diversity of skills, experiences and backgrounds enhances performance of teams and organizations.	We encourage competition rather than collaboration, from science fairs to graduate school; it is part of the culture.
High performing teams are based on trust, diversity and collaboration.	There is a lack of understanding about what each party can bring to the table.
Diverse teams are often the most innovative.	Collaborations take a lot of time and must begin with creating a trusting partnership.
There is a growing group of patient advocates and community members who are eager to participate as partners in TS. Many people embrace the concept of “citizen scientist.”	The practice of community engagement in TS is often limited to community outreach for recruitment of study participants, particularly minority populations.
	There are many roadblocks to collaboration across sectors and across the entire TS spectrum.
Integration	
Positive Factors	**Negative Factors**
CTSAs are poised to understand diseases in the transition from childhood to adulthood and from adulthood into old age.	There are barriers to lifespan research; for example, age restrictions for studying drug interventions in pediatric and geriatric (80+ years) populations.
CTSAs are uniquely positioned to play a coordinating/convening role for bringing together scientists from the disparate fields needed to study disease longitudinally.	There is tension about the relative value of translation from basic science to human studies, versus translation of new data into the clinic and health decision making.
Analytical and computational tools are becoming available to release new information and subsequent insights by integrating increasingly large and diverse sets of data.	Scientists who are focused on a specific field (either life-stage or type of intervention) do not routinely interact with colleagues in other fields.
Integration of scientific information across periods of time leads to knowledge formation, including longitudinal disease-specific databases.	There is a lack of a knowledge base for all types of interventions at the extremes of age as well as within special populations.
There is a growing body of knowledge about the non-clinical determinants of health (e.g., a robust network of community-based public health practitioners, urban planning).	Patients are not engaged as collaborative partners in the clinical care and clinical research process.
Patient advocate groups are eager to help partner in research.	There is a research gap in the transition phases of aging.
Academics and NIH attempt to create awareness on the study of minorities and special populations.	There are many barriers to working with the pediatric population if one is not formally trained as a pediatrician.

There are some medical subspecialties that have a track record of following disease across age ranges (i.e., cystic fibrosis, sickle cell).	Support is lacking for maintenance of long-term databases and biorepositories.
Academic health centers are interested in defining and providing best practices, and this increases interest in defining quality care at the extremes of the lifespan.	Many ethical issues exist for dealing with special populations, but there is limited access to ethics expertise.
Disease prevention is a field of study of high interest to the CTSA program.	More robust training programs are needed for investigators studying lifespan transitions.
Strong progress has been made in computing power to integrate and display vast amounts of disparate information.	There is no single clear solution for which data analytics system to use.
Methods/Processes	
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APPENDIX C: WORKING GROUP TIMELINE

- Initial face-to-face meeting with Working Group — December 6, 2013
- WebEx with Working Group — January 27, 2014
- Second face-to-face meeting with Working Group — February 11, 2014
- Working Group Review of Draft Report Outline — March 13-26, 2014
- Working Group Review of Draft Report — April 16-21, 2014
- Co-Chairs Presentation of Report to NCATS Advisory Council — May 16, 2014