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Situating dissemination and implementation sciences within and across the translational research spectrum

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Abstract
The efficient and effective movement of research into practice is acknowledged as crucial to improving population health and assuring return on investment in healthcare research. The National Center for Advancing Translational Science which sponsors Clinical and Translational Science Awards (CTSA) recognizes that dissemination and implementation (D&I) sciences have matured over the last 15 years and are central to its goals to shift academic health institutions to better align with this reality. In 2016, the CTSA Collaboration and Engagement Domain Task Force chartered a D&I Science Workgroup to explore the role of D&I sciences across the translational research spectrum. This special communication discusses the conceptual distinctions and purposes of dissemination, implementation, and translational sciences. We propose an integrated framework and provide real-world examples for articulating the role of D&I sciences within and across all of the translational research spectrum. The framework’s major proposition is that it situates D&I sciences as targeted “sub-sciences” of translational science to be used by CTSAs, and others, to identify and investigate coherent strategies for more routinely and proactively accelerating research translation. The framework highlights the importance of D&I thought leaders in extending D&I principles to all research stages.

Introduction
The National Center for Advancing Translational Science (NCATS) was established in 2012 with the goal of hastening the scientific process required to develop and deliver treatments that improve people’s lives. Its purpose is to advance understanding and routine use of translational science; that is, the science concerned with the process of “translation.” Translation has been defined as the problem-oriented practical process of “turning observations in the laboratory, clinic, and community into interventions that improve the health of individuals and the public” [1]. Whereas traditional conceptualizations of science are primarily concerned with the creation of new knowledge, translational science is ultimately concerned with the process of solving – through application of research knowledge – health-related problems. Thus, translational science seeks to understand the “scientific and operational principles” underlying each step of the translational process [1].

To operationalize the advancement of translational science, the Centers for Translational Science Awards (CTSA) Program has funded – since 2006 – the activities of a consortium of more than 60 academic medical centers, referred to as CTSA, or “hubs” [2,3]. Within and
across these CTSA hubs, investigators and clinicians at all stages of the translational research spectrum work together to develop, demonstrate, and disseminate strategies for overcoming common barriers to efficient and effective translation.

Ultimately, the aim of translational science is to identify guiding principles for improving the efficiency and effectiveness of research translation. One can imagine several ways in which insights gained from the sciences of dissemination and implementation (D&I) could be adapted to support this aim and enhance translation [4]. For this reason, in 2016, the CTSA consortium’s Collaboration and Engagement Domain Task Force chartered a dissemination, implementation, and knowledge translation workgroup. This special communication is a product of that workgroup.

Objective

Specifically, the objectives of our workgroup were to (1) communicate the ways in which the sciences of dissemination, implementation, and translation relate and (2) explore the role of CTSAs in supporting and advancing these interrelated sciences. In pursuing these objectives, we determined that a new framework would be helpful in promoting synergy among the sciences and ensuring that the strengths of each are used to advance the work of CTSAs. As such, we also introduce the Integrative Framework of Dissemination, Implementation and Translation (IFDIT) (Fig. 1) as a guide CTSA hubs can use to support their individual and collective efforts to advance translation and improve population health.

The Three Sciences: Dissemination, Implementation, and Translational

The National Institutes of Health (NIH) defines dissemination as the active and targeted distribution of information and intervention materials to a specific public health or clinical practice audience [4]. Dissemination research is defined as the scientific study of this phenomenon, and its goal is to expand our understanding of how best to spread the knowledge required to adopt and deploy evidence-based interventions [5]. Contemporary investigators conducting dissemination research aim to identify approaches to packaging and conveying information to improve clinical care, community, and public health services [6,7].

NIH defines implementation as the adoption and integration of evidence-based health interventions into clinical and community settings for the purposes of improving care delivery and efficiency, patient outcomes, and individual and population health [5]. Implementation research is the scientific study of this process, and its goal is to develop a knowledge base about “how” interventions become normalized and embedded within real-world practice settings and patient populations [5].
D&I research is informed and guided by underlying sciences [8,9] that share a common origin. These sciences trace their roots back to at least the early 1900s and to work from European and American sociologists that described the process of social change as a diffusion of ideas and innovations among individual adopters [10]. More recently, it has become clear that dissemination and implementation are separate but related processes that often co-occur (implementation following dissemination). Some argue that the D&I sciences are in fact different perspectives of the same science, for example, observations in practice and community settings are also used to facilitate the adoption, spread, and sustainment of improved diagnostics, therapeutic, and service delivery interventions, strategies must be developed, used, and continually improved through scientific inquiry. This compels accompanying lines of inquiry.

Change happens proactively

To facilitate the adoption, spread, and sustainment of improved interventions, and audit and feedback reports are strategies that might be used to support the late-stage adoption of a clinical decision support tool, but the tool itself was first made adoptable (in early-stage research) by developing an understanding of the clinical workflow and the needs of busy clinicians. In short, the sciences of dissemination, implementation, and translation are each consistent with the ideals and function of a learning health care system – they are tools that are used to efficiently collect and apply insight to improve health.

The bidirectional exchange of information and perspectives between stages and disciplines improves the likelihood that research products will bridge translational gaps. This is true even in early stages of research.

<table>
<thead>
<tr>
<th>Principles from D&amp;I sciences</th>
<th>Implications for late-stage research</th>
<th>Rationale for role in early-stage research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Context matters and is multi-level</td>
<td>Successful dissemination of research knowledge and implementation of scientific discoveries are profoundly affected by healthcare policy, organizational and community culture and climate, and attitudes and behaviors of key stakeholders</td>
<td>All research, including basic and pre-clinical, is conducted and translated within a complex multi-level context</td>
</tr>
<tr>
<td>It is not sufficient that evidence exists and/or a practice works</td>
<td>We must be equally concerned with whether evidence can be disseminated to reach key stakeholders and whether practices can be taken up and delivered in real-world settings. This compels accompanying lines of inquiry</td>
<td>Intervention design and development benefits from appreciation of the factors that influence later-stage adoption and implementation, such as usability, desirability, feasibility, and cost</td>
</tr>
<tr>
<td>Both implementation practice and implementation science are team endeavors</td>
<td>Implementation practice requires iterative engagement and involvement of a range of stakeholders, including patients, clinicians, administrators, researchers, and policymakers. Similarly, implementation science is inherently transdisciplinary, involving treatment developers and researchers, health services researchers, and experts from closely related fields such as industrial psychology and communications research</td>
<td>The bidirectional exchange of information and perspectives between stages and disciplines improves the likelihood that research products will bridge translational gaps. This is true even in early stages of research</td>
</tr>
</tbody>
</table>

D&I, dissemination and implementation.
Finally, all three sciences are consistent with CTSA objectives to create generalizable knowledge and to identify broadly useful practices and principles. The rationale for generating products of this type is that their application has pragmatic value. Yet, differences exist among the sciences in this regard. Specifically, only translational science has communicated an explicit role in basic and pre-clinical research as well. Tables 2 and 3 provide examples.

**Table 2. Example strategies and uses of D&I to improve the translational process of research conduct within each research stage**

<table>
<thead>
<tr>
<th>IFDIT stage objective</th>
<th>Research method and output</th>
<th>Potential use of translational science</th>
<th>Potential use of dissemination science</th>
<th>Potential use of implementation science</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic research</strong></td>
<td>To determine whether targets, markers, or pathways exist</td>
<td>Basic and pre-clinical studies that generate knowledge about new targets, markers, or pathways</td>
<td>Develop lab registries and open science models that share insights and avoid unnecessary duplication of efforts</td>
<td>Seek to understand social pressures among basic scientists that inform the research questions they pursue</td>
</tr>
<tr>
<td><strong>Pre-clinical research</strong></td>
<td>To determine whether target, marker, or pathway can be influenced in humans</td>
<td>Phase 1 trials that generate knowledge about whether interventions work in humans</td>
<td>Advance novel study designs that improve the efficiency of phase 1 trials</td>
<td>Apply marketing principles to inform participant recruitment strategies to trials</td>
</tr>
<tr>
<td><strong>Clinical research</strong></td>
<td>To determine whether interventions are effective in patients</td>
<td>Phase 2 and 3 trials that generate knowledge about whether interventions help patients</td>
<td>Develop multi-site IRBs and other infrastructures to increase study efficiency</td>
<td>Utilize key opinions leaders to optimize communication among study teams at multiple sites</td>
</tr>
<tr>
<td><strong>Clinical implementation</strong></td>
<td>To determine whether interventions can be effectively delivered in practice</td>
<td>Phase 4 and pragmatic trials that generate knowledge about whether interventions help patients in practice and how to implement them in these settings</td>
<td>Develop clinical and practice-based research networks that can respond quickly to conduct T3 research</td>
<td>Conduct studies to ascertain optimal strategy for disseminating evidence to improve intervention adoption and reach</td>
</tr>
<tr>
<td><strong>Public health</strong></td>
<td>To determine whether interventions can be effectively delivered to improve population health</td>
<td>Observational, outcome-based studies and implementation research that generate knowledge about whether and how interventions improve population health</td>
<td>Develop informatics approaches and big data practices to efficiently monitor effects of wide-spread intervention roll-out</td>
<td>Conduct comparative studies of different dissemination strategies to determine most cost-effective method of reaching target settings and audiences</td>
</tr>
</tbody>
</table>

D&I, dissemination and implementation; IFDIT, Integrative Framework of Dissemination, Implementation, and Translation.

The Integrative Framework of Dissemination, Implementation, and Translation

Finally, we present the IFDIT in Fig. 1. The IFDIT seeks to integrate and expand current understanding and practice related to the dissemination, implementation, and translational sciences in order to optimize their contributions into a cohesive framework for translational activities and research. It uses as its basis an NCATS conceptualization which represents the translational research spectrum as a set of five interconnected and non-linear circular stages connecting basic research, pre-clinical research, clinical research, clinical implementation, and public health [22] (some rights reserved: https://creativecommons.org/licenses/by/2.0/). Each stage builds upon and informs each of the others via bidirectional relationships and all the stages center on and are assumed to benefit from a commitment to broad stakeholder engagement. Upon this foundation, the IFDIT adds a conceptualization of translation as a pair of processes that occur both within and between translational stages. The process that occurs within each of the five stages is termed research conduct, and it consists of the practical matters of carrying out a research study and generating new knowledge (e.g., formulating a research question, collecting and analyzing data, drawing conclusions). The process that occurs between the stages (via the 10 connecting lines) is termed research application, and it consists of the practical matters of using this new knowledge to guide the development of interventions, conduct other research, and ultimately improve health. Conceptualizing translation in this way – as a pair of processes – is intended both to (1) support targeted efforts to overcoming specific barriers within and between particular stages (e.g. by focusing on the unique goals of that stage or gap) and to (2) clarify opportunities for advancing a generalizable science of translation (e.g. by focusing on the larger conceptual issues of the underlying process, either research conduct or application).
The framework reinforces the prevailing paradigm that health interventions are first developed and evaluated (e.g. in basic, pre-clinical, and clinical stages) and then implemented (e.g. in clinical implementation and public health stages), but it includes additional guidance on the role of the D&I sciences in both activities. Specifically, the framework’s outer ring proposes that, in early-stage research, questions of intervention viability and efficacy should be prioritized, but that D&I principles should still be applied in considering the intervention’s design, usability, desirability, and potential for dissemination – a concept referred to as “designing for D&I [14,23].” Conversely, in late-stage research, questions concerning how best to disseminate and implement interventions should be prioritized and issues related to effectiveness should only be explored pragmatically and as they relate to the new circumstances in which the intervention finds itself. The framework’s outer ring transitions from one focus to the other (e.g. from intervention development and evaluation to D&I) at the mid-point of the clinical research stage. This represents the potential for hybrid effectiveness-implementation studies that occur within this stage and simultaneously consider both topics [24].

Finally, the IFDIT positions D&I sciences as “sub-sciences” of translational science that are used, when appropriate, to contribute to the larger goal of translation. To that end, the framework shows how understanding from and principles commonly associated with D&I sciences can be used to optimize processes both within and between all stages. This is best depicted in tables. Table 2 provides examples of how D&I sciences and principles can inform the conduct of research within a translational stage. Table 3 provides examples of how D&I sciences and principles help to move research from one stage to the next. Clearly, the most important and obvious role for D&I sciences is in supporting the uptake of research knowledge from one stage to another (research application) and in the later stages of research conduct. However, as shown in the tables, D&I sciences can help improve the efficiency and quality of research conduct within any stage.

### Three Examples

To further highlight the ways in which D&I sciences can and do support translation, we provide three diverse and illustrative examples. In the first example, no actual D&I research was conducted, but rather translation was advanced through an understanding of D&I processes and an application of D&I principles. In the second example, implementation research was conducted to understand barriers to adoption and to evaluate the effectiveness of implementation strategies. In the third example, D&I principles were used to integrate parallel lines of inquiry to generate new evidence, and stakeholder engagement was used to troubleshoot late-stage translational barriers. In each example, we refer to key stages and processes from the IFDIT framework.

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**Table 3. Example strategies and uses of D&I to improve the translational process of research application between translational stages**

<table>
<thead>
<tr>
<th>IFDIT inter-stage gap objective</th>
<th>Potential use of translational science</th>
<th>Potential use of dissemination science</th>
<th>Potential use of implementation science</th>
<th>Potential synergizing application of all three sciences</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic research to pre-clinical research</strong></td>
<td>To have knowledge about a potential therapeutic target tried in humans</td>
<td>Develop phased funding mechanisms to pre-emptively pair pre-clinical scientists and phase 1 trialists</td>
<td>Compare strategies for disseminating evidence from basic research to potentially receptive pre-clinical research centers</td>
<td>In designing pre-clinical research intervention for trial, consider barriers to adoption of similar interventions and modify</td>
</tr>
<tr>
<td><strong>Pre-clinical research to clinical research</strong></td>
<td>To have knowledge about an efficacious intervention in humans tried in patients</td>
<td>Develop funding incentives and RFAs targeted to promising pre-clinical results that encourage clinical research uptake</td>
<td>Compare strategies for disseminating evidence from pre-clinical research to potentially receptive clinical research centers, funders, and other stakeholder partners</td>
<td>In designing clinical research intervention for trial, use design methods to iteratively consider barriers to adoption among target patients and organizations and modify</td>
</tr>
<tr>
<td><strong>Clinical research to clinical implementation</strong></td>
<td>To have knowledge about an efficacious intervention in patients evaluated in practice</td>
<td>Provide funding incentives and reduce administrative and human subjects burdens to increase receptivity for clinical implementation research</td>
<td>Identify organizations that could help disseminate the intervention once proven and co-create strategies for disseminating the evidence to optimize enrollment of diverse and representative practices</td>
<td>In designing clinical implementation intervention for trial, engage clinical stakeholders to identify barriers to adoption and modify; identify stakeholders that can lead in adopting the intervention in target organizations</td>
</tr>
<tr>
<td><strong>Clinical implementation to public health</strong></td>
<td>To have knowledge about an effective intervention in practice evaluated in population</td>
<td>Develop partnerships with community stakeholders, policymakers, and the private sector that can facilitate efficient roll-out</td>
<td>Compare strategies for disseminating clinical implementation evidence to optimize adoption by diverse and representative end users</td>
<td>In research design, engage stakeholders in identifying optimal strategies for implementation</td>
</tr>
</tbody>
</table>

D&I, dissemination and implementation; IFDIT, Integrative Framework of Dissemination, Implementation and Translation.
The effectiveness of In SHAPE was established in two randomized mental illness and leaders of mental health provider organizations.

intervention that would be successful in engaging people with multi-level context at this pre-clinical stage and to developing an consisting of program leaders from New Hampshire was designed to evaluate the effectiveness of a intervention (approximately half of the participants experienced clinically significant cardiovascular risk reductions [29]). To determine the most effective and feasible way to scale the intervention more broadly, a national, randomized implementation study is currently underway within 48 health organizations. Half of the organizations are participating in a virtual learning collaborative and the other half are receiving individual technical assistance. By considering the diverse, multi-level contexts in which the intervention is deployed, this research is able to understand whether, why, and to what extent the intervention is adapted, and the resulting effects on uptake and effectiveness.

Example 1: Glycomacropeptide-Based Food for Phenylketonuria

Individuals with phenylketonuria (PKU) cannot metabolize phenylalanine and thus must maintain their nutrition through a synthetic amino acid formula-based diet that smells and tastes bitter and is difficult to adhere to. Basic science research at the University of Wisconsin resulted in the isolation of glycomacropeptide (GMP) in 1999, a by-product of cheese-making with essentially no phenylalanine [25,26]. After isolation – and in an example of bidirectional research application between stages – the research team reached out to the National PKU Alliance to learn about the broader context and potential desire by patients and families for development of GMP-based foods. This activity established the value of proceeding down this line of research by confirming high stakeholder demand for the product. A multi-stakeholder “GMP for PKU Task Force” was formed at the university. This “team science” initiative was intended to shorten the time required to move from pre-clinical research to clinical implementation. A researcher in nutritional science was recruited to lead mouse and human studies of GMP safety and comparative efficacy and, after finding positive results [26], the university’s Dairy Research Center was engaged to develop palatable GMP-based food products, exemplifying understanding of the multi-level context and the need to quickly move from pre-clinical to clinical research. After successfully developing several products, the research team used pre-existing collaborative relationships with PKU patients to facilitate recruitment of participants into clinical trials, thus improving the process of study conduct during the clinical research stage [25]. To support late-stage dissemination, a foundation with ties to the university provided commercialization support and a small foods company started by a family with a child with PKU took ownership of the license in 2010. Currently, this company’s GMP-based foods make up 10% of the world market of medical foods for PKU, improving adherence and quality of life for thousands of patients with PKU.

Example 2: Reducing Early Cardiovascular Mortality Risk in Mental Health Populations

People with serious mental illness experience one of the nation’s greatest but least well-recognized health disparities: an 11–25-year reduction in life expectancy due to mainly cardiovascular causes. Building on meta-analytic data leveraging “basic” data science and demonstrating this disparity, a community-engaged partnership was formed with researchers at Dartmouth to co-develop and evaluate the “In SHAPE” intervention, a “health mentor” program with weekly coaching sessions and monthly motivational “celebrations.” Stakeholder engagement was critical in understanding the multi-level context at this pre-clinical stage and to developing an intervention that would be successful in engaging people with mental illness and leaders of mental health provider organizations. The effectiveness of In SHAPE was established in two randomized controlled trials (RCTs) demonstrating a clinically significant reduction in cardiovascular risk [27,28]. Broad uptake of the program by the public mental health sector was limited; however, due to the fact that mental health organizations were not organized, trained, staffed, or funded to provide health promotion and prevention interventions targeting cardiovascular risk factors. To address these barriers to uptake, a statewide implementation research study was designed to evaluate the effectiveness of a “learning community” consisting of program leaders from New Hampshire’s 10 mental health centers. The implementation strategy proved effective at increasing the reach while maintaining the effectiveness of the intervention.

Example 3: Bridging Animal and Human Research to Maximize Brain Development

Animal studies in the late 1990s demonstrated a positive effect of maternal nurturance on hippocampal growth and adaptation to stress [30]. Relationships between animal researchers and human researchers in the area of brain development prompted the conduct of observational studies in humans. Insights from these longitudinal neuroimaging studies, combined with insights from additional animal research, suggested the presence of “sensitive periods” in early childhood when the brain would be more powerfully impacted by environmental forces [31]. Independent of this research, a parallel line of clinical investigation had validated and described depression in the preschool period and resulted in the development of parent–child psychotherapies. In an example of bidirectional application of research knowledge between clinical and basic research stages, Luby and colleagues bridged these two lines of investigation by using neuroimaging and measures of brain function to assess the effects of the psychotherapy on brain development and function [32]. This enabled researchers to generate evidence of effectiveness for the treatment and a rationale for broad D&I. Unfortunately, and despite widespread support within the medical center and department of psychiatry, the program met contextual and policy barriers related to reimbursement (the program was designed to be delivered in a cost-effective way by master’s-level therapists, who could not be reimbursed). In an example of stakeholder engagement and the proactive development of an effective implementation strategy, the investigator team adapted the program to be delivered broadly in the school setting and is preparing to evaluate this version of the program in an RCT. Parallel efforts are underway to educate payers and other stakeholders to support policy changes that will facilitate delivery in clinical mental health settings as well.

Discussion

In this Special Communication, we sought to communicate the relationship between translational science and the sciences of D&I and to demonstrate a potential expanded role for D&I sciences within and across the spectrum of translational research. In pursuit of this goal, we developed a framework and provided tables and examples to clearly communicate the ways in which D&I sciences can and do support the translational process. The major proposition of the framework is that it situates D&I sciences as essential “sub-sciences” of translational science that can be used to overcome specific barriers to the translational process. Along these lines, the framework also describes two different and equally necessary translational processes (research conduct and research application). The assumption is that advancements in translational science will need to occur both within and between...
translational research stages, and that these lines of inquiry may need to distinguish themselves from one another. Additionally, the framework provides, to our knowledge, the first clear examples of the ways in which principles from D&I science can be extended to support the earliest phases of translational research. Our tables do not fully communicate the multi-directional nature of processes and instead imply an overly linear journey from basic science to population health benefit. In reality, translational processes can begin with observations at any stage, move in any direction, and skip any stage. Our framework is a representation of our own ideas and experiences and does not represent empirical findings. However, we recommend that CTSA have an opportunity to support its testing and subsequent refinement, confirmation, or refusal. Indeed, the concepts outlined in this paper should be useful to CTSA and NCATS alike in helping to shape a coordinated agenda for the advancement of translational science. Specifically, we recommend NCATS convene a working group to consider the implications of adopting this framework as a guiding model for the activities of Domain Task Forces across the CTSA Consortia.

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**References**