Putting the Dissemination and Implementation in Infectious Diseases

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Dissemination and implementation science seeks generalizable knowledge about closing the gap between clinical discovery and actual use in routine practice and public health. The field of infectious diseases enjoys an abundance of highly efficacious interventions (eg, antimicrobial agents, human immunodeficiency virus treatment) which are not adequately used in routine care, thereby missing critical opportunities to improve population health. In this article, we summarize salient features of dissemination and implementation science, reviewing definitions and methodologies for infectious diseases clinicians and researchers. We give examples of the limited use of dissemination and implementation science in infectious diseases thus far, suggest opportunities for application, and provide resources for interested readers to use and apply to their own research and practice.

Keywords: dissemination and implementation; knowledge transfer; knowledge exchange; implementation science.

Research in infectious diseases (ID) has yielded remarkable scientific discoveries and interventions that have improved life across the globe. Infections which formerly decimated populations (eg, smallpox and polio) have been eradicated (or nearly so) by vaccinations. However, many infections linger, while others have changed or emerged. Although effective interventions are available for various infections, they are often slow to reach clinical practice and public awareness. Furthermore, effective interventions can be complicated and nuanced, making their use in real-world settings, as opposed to clinical trials, challenging. Dissemination and implementation (D&I) science is a relatively new field that seeks to maximize the benefits of scientific discovery to improve population health, achieving our full return on investment [1]. Toward this end, D&I research is the scientific study of methods to promote the systematic uptake and long-term maintenance of research findings and other evidence-based practices into routine practice and, hence, to improve the quality and effectiveness of health services [2]. In short, D&I science gets the evidence where it is needed by closing the gap between evidence and practice.

The field of ID would benefit from enhanced use of D&I science, given its impact on clinical outcomes demonstrated in other disciplines [3–6]. ID is fortunate to have numerous, highly efficacious clinical interventions. Antibiotics, when delivered appropriately for bacterial infections, save lives rapidly and inexpensively. Vaccines, when widely used, drastically reduce morbidity and mortality. Direct-acting antivirals cure hepatitis C in nearly 100% of persons who complete therapy. Yet today, we fail to deliver timely antibiotics to septic patients who could benefit and, at the same time, vastly overuse antibiotics in those without indications (thus compromising future effectiveness through resistance). News headlines report a rising tide of anti-vaccine sentiments, as well as large outbreaks of dangerous viruses once considered controlled (ie, measles). Hepatitis C remains highly prevalent and direct-acting antivirals use is inequitable. Each of these examples illustrate why ID needs D&I science. Despite gaps in implementation across the field, as of the writing of this article, only 0.3% of active National Institute of Allergy and Infectious Diseases R01 projects are funded through D&I-specific funding announcements [7, 8]. Notably, although problems translating discovery into practice are found throughout medicine, we focus here on ID.

WHAT IS DISSEMINATION AND IMPLEMENTATION SCIENCE?

D&I science is often considered in the context of translational research. Unlike earlier phases of translational research (T1–T2), which establish the efficacy of an intervention, D&I falls into T3–T4 research, where clinical (ie, real-world) testing of the innovation occurs. A tenet of D&I science is that an intervention, practice, or policy should have a strong evidence base before it is implemented; that is, it should be an evidence-based intervention (EBI). D&I science primarily focuses on how to get clinicians/health systems to adopt and use EBIs. However,

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the goal of D&I science is not simply for clinicians to "do more," but rather for systems to make using EBIs the default or the easiest choice and, at the same time, to remove/replace inefficient or ineffective practices. This may be accomplished at multiple levels through multiple stakeholders, involving policy, economic, and organizational factors, among others.

Here, we limit subdivisions of D&I science into (1) dissemination and (2) implementation. Dissemination is "an active approach of spreading evidence-based interventions to the target audience via determined channels using planned strategies" [9–11]. Implementation is the "scientific study of the use of strategies to adopt and integrate evidence-based health interventions into clinical and community settings in order to improve patient outcomes and benefit population health" [7]. D&I science is variably known as knowledge translation, knowledge integration, knowledge transfer, knowledge exchange, population health intervention research, or diffusion. For simplicity, we will use only the terms dissemination and implementation.

Common research questions addressed by D&I researchers are:

1. What is the most effective approach to make practitioners or the public aware of new treatment guidelines so that the guidelines can be used?
2. How can we help practitioners integrate the latest scientific evidence with their clinical expertise to make better treatment decisions for patients?
3. Can we adapt an intervention that is successful in one population to another population?
4. When practitioners are aware of a new intervention, what are the barriers that prevent them from using it and what are the best strategies to overcome identified barriers?

In addition to these kinds of research questions, D&I science recognizes that current evidence can be difficult for clinicians to access [12–15], and their knowledge of evidence gives them no means to integrate it into practice. Passive approaches to disseminating research, such as publishing exclusively in scientific journals, are ineffective for making practitioners aware of new evidence [16, 17]. Furthermore, it can be difficult to use or implement the latest evidence into practice, particularly when studied populations differ in critical ways from the practitioner's patient. Most research interventions take place in controlled settings with a well-defined population that is motivated to participate by incentives. In practice, the environment of the intervention is less rigid and more prone to fluctuations and adaptations. The target population may be more heterogeneous, encompass different demographics, or be less motivated to participate/continue the intervention than the studied sample [18]. Exemplifying real-world heterogeneity, Dolcini et al [19] studied 6 California agencies that received funding by the Centers for Disease Control and Prevention to implement

3 different evidence-based, behavioral interventions for human immunodeficiency virus (HIV) prevention. Of the 6 agencies, 5 had to adapt the intervention they chose to accommodate the needs of their target populations. This included adding/deleting program sessions, translating to another language, integrating the program into other services, and nonsystematic adaptations to the intervention [19]. Even if practitioners are aware of an effective intervention and when to use it, there may be other factors, like cost, that may prohibit access [20]. D&I science can also help focus on modification of larger, structural issues, rather than just more well-recognized, front-line organizational practices (eg, making sure everyone performs hand hygiene). That is, societal and political priorities (eg, public opinion, policy decisions, research priorities) can be understood, addressed, and influenced by approaches and strategies identified through the methodologies of D&I science [21].

Fundamental Concepts in Dissemination and Implementation: Theory, Frameworks, and Methods

Understanding the local context and relationships between stakeholders (eg, leaders, physicians, patients) are important concepts in D&I science. Keys to the success of intervention implementations include understanding the relationship between evidence, the local context of implementation, the intervention's use by clinicians (or lack thereof) to improve service delivery, and subsequent patient outcomes [22, 23]. The field of D&I uses theory and frameworks to guide conceptualization of these relationships. Frameworks emphasize the multilevel contexts that influence the translation of evidence into practice, considering providers, organizations, governmental policy, and society as a whole (see Figure 1) [24]. Multi-level refers to the different levels of stakeholders, which could include those in Figure 1: organizations, leaders, managers, and individuals.

There are many available frameworks for D&I research, which can be tailored and combined to best fit the needs of the study, investigators, and the practice setting. Frameworks are particularly useful for clinical experts with deep knowledge about medicine, but limited experience thinking about the behaviors of health-care workers, patients, communities, and organizations. A full description of D&I frameworks is outside the scope of this viewpoint, but interested readers can seek out an excellent review on the topic [23].

D&I researchers use various research designs and analyses, including quantitative, qualitative, and mixed-method approaches [25]. Because it is often unclear *why* practitioners or patients do not use an intervention, qualitative methods, particularly adept at explaining phenomena, help D&I researchers understand the myriad factors that serve as barriers/hinder use of an intervention or serve as facilitators/promote the uptake of an intervention. [27] Like any scientific inquiry, research design is carefully selected based on the research question, constraints of the research setting, available budget, and etc.
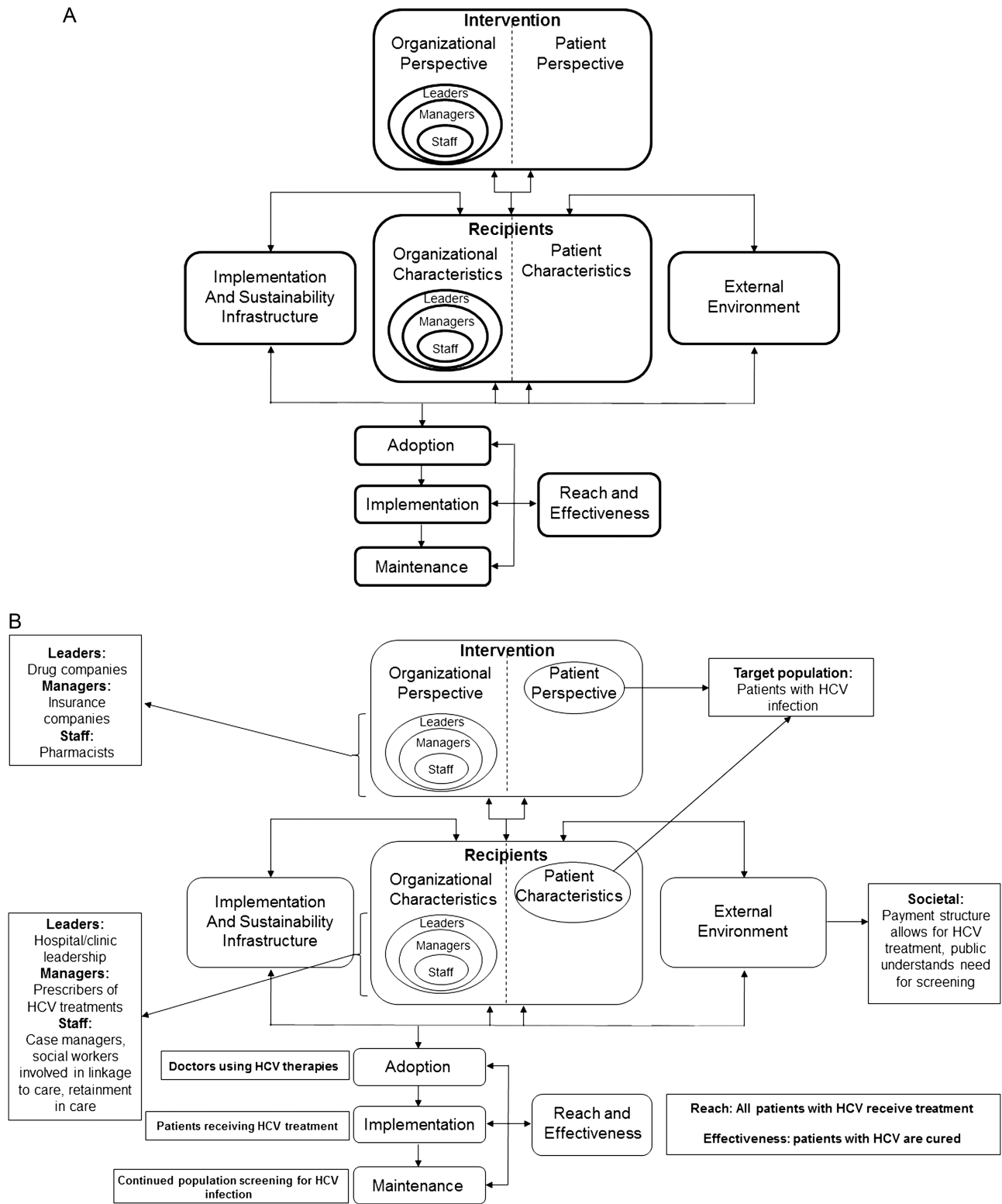
Figure 1 *A*, PRISM, an example of an implementation science framework that considers the multilevel involvement of relevant stakeholders, including recipients, interventionists, leaders, managers, staff, policymakers, and society as a whole. Adapted from Feldstein and Glasgow [24]. *B*, The PRISM framework, imagined for HCV management across the implementation issues currently faced. Abbreviations: HCV, hepatitis C virus; PRISM, practical, robust implementation and sustainability model.

However, D&I researchers must address several special challenges. D&I researchers often must assume there is sufficient evidence that an intervention is beneficial. Operating under this assumption, it would be unethical to withhold treatment or continue to provide standard-of-care treatments, as is commonly done during randomized, controlled trials (RCTs).

D&I research also frequently works with a small number of organizations or a set of practitioners, making it difficult to adequately power RCTs. Lastly, clinical efficacy trials are often well supported by academic institutions and conducted using eligibility criteria that minimize variability and maximize internal validity [27, 28]. D&I research seeks to maximize the benefit of evidence for the maximum number of populations or settings: that is, to maximize external validity.

The limited external validity of traditional research has led to the development of alternative study designs, including hybrid trials and the stepped-wedge trial. Hybrid designs measure both implementation outcomes and clinical/patient outcomes to help parse questions about whether intervention implementation or evidence behind an intervention is the problem for lack of effectiveness [29]. The stepped-wedge design (or cluster-randomized trial) allows D&I researchers to conduct RCTs where randomization determines when participants will receive an intervention. In stepped-wedge studies, the unit of randomization is not the patient, as in traditional RCTs, but larger groups: for example, an organization, system, practice, clinic, or provider. This design allows all participants and their patients to benefit from implementation of the latest evidence while simultaneously requiring fewer participants.

Implementation Strategies: Conceptualizing and Specifying

Once issues that help (facilitators) or hinder (barriers) the uptake of evidence are identified, D&I researchers pick from a cache of well-studied implementation strategies, which are designed to expedite or enhance the dissemination and implementation of evidence. There are numerous implementation strategies, but recent taxonomic efforts have defined several broad categories, including evaluative strategies, interactive assistance, innovation tailoring, relationship development with stakeholders, stakeholder education and training, providing supplemental support, engaging consumers, leveraging financial mechanisms, or changing system infrastructure [30]. A researcher may select one or multiple strategies to improve evidence implementation, simultaneously testing the effectiveness of these approaches. For example, if leadership interest or support is a significant barrier to patients' access to a highly effective treatment, stakeholders at levels that might not typically be engaged must be involved for success. These include, but are not limited to, health services researchers, economists, sociologists, community health providers, politicians, "C-suite" executives, patients, and community members.

The reader may be familiar with several implementation strategies without recognizing their ties to implementation science. Audit and feedback, used often and successfully in antimicrobial stewardship efforts, is an example of an implementation strategy. Appeals to social norms and peer performance are implementation strategies that can teach antimicrobial

stewardship, as demonstrated by a recent RCT [31]. Changes to record systems (ie, electronic medical records) is an implementation strategy that has been successful in ID. An example involved changing order sets to have reflex urine testing rather than isolated urine cultures, resulting in reductions in positive urine cultures with negative urinalyses [32]. Train-the-trainer is another implementation strategy that has been successfully used in Ebola preparedness for personal protective equipment donning and doffing [33, 34].

Implementation Outcomes: Concepts and Reporting

D&I researchers assess implementation strategy success by measuring implementation outcomes upstream of patient outcomes that indicate the successful dissemination and implementation of evidence. D&I researchers also distinguish between interventions that are not effective and interventions that are not implemented correctly, thereby appearing ineffective. Common, so-called implementation outcomes include: adoption, or uptake of an intervention among organizations or providers; fidelity, or the extent to which patients or providers maintain adherence to how the intervention is intended to be delivered; and penetration or reach, or the extent to which the population of individuals that would benefit from an intervention are using it. For a more comprehensive list of implementation outcomes and definitions, see Table 1. Implicit in the measurement of implementation outcomes is the assumption that improving the dissemination and implementation of an EBI will subsequently improve patient and population outcomes. Table 2 provides an example of the importance of tracking implementation outcomes, as interventions can fail by implementation rather than effectiveness. From a population at risk for HIV infection, only 9.1% made it to the maintenance and adherence stage of taking pre-exposure prophylaxis (PrEP) [35]. Without the measurement of intermediate implementation outcomes (adherence/adoption), it would appear that ~90% of patients were failing PrEP.

Table 1. Dissemination and Implementation Outcomes

Implementation Outcome	Examples of Synonym(s)/Antonym(s)
Acceptability	Agreeable, acceptable, usability
Adoption	Uptake, utilization, initial implementation, intention to try, de-implementation, de-adoption, de-institutionalization
Appropriateness	Fit, usefulness
Feasibility	Utility
Fidelity	Adherence, integrity, adaptation
Implementation cost	Marginal cost, cost-effectiveness, cost-benefit, incremental cost, cost impact
Penetration	Spread, service access, saturation, reach
Sustainability	Maintenance, continuation, integration, sustained use, abandonment

Adapted from [22, 54].

Table 2. From Effective Intervention to Failed Implementation: Human Immunodeficiency Virus Prevention With Pre-Exposure Prophylaxis

Stage	Retention
At-risk population	100%
PrEP contemplation	47.3%
PrEParation	23.9%
PrEP action and initiation	12.9%
PrEP maintenance and adherence	9.1%

Adapted from [35]. Stages correspond to those in the transtheoretical model of change: contemplation (PrEP contemplation), determination (PrEParation), action (PrEP action and initiation), and maintenance (PrEP maintenance and adherence).
Abbreviation: PrEP, pre-exposure prophylaxis.

Infectious Diseases: Examples of Where We Need Dissemination and Implementation

As a field, ID has many areas with robust evidence of clinical efficacy and effectiveness that lack only implementation science to get the evidence to patients. We use 5 examples to illustrate this point. Ignaz Semmelweis became the first proponent of hand hygiene in 1847, yet it remains incompletely implemented, even in intensive care units (ICUs), where sick patients at high risk of hospital-acquired infections reside [36]. Antimicrobial stewardship programs are highly effective [37, 38] and progress is being made, but adherence to the Centers for Disease Control and Prevention's 7 core elements of antimicrobial stewardship programs remains under 50% [39]. This deficiency does not take into account the incomplete implementation of antimicrobial stewardship programs in outpatient settings, long-term care settings, or other countries, all of which could be aided by D&I science [39].

On the virology side of ID, human papillomavirus vaccination is so effective in preventing cervical cancer that Australia estimates they will eliminate cervical cancer by 2028 after a string of policy and practice implementation successes [40]. This success has not been realized worldwide, including in the United States, where human papillomavirus vaccination rates are a dismal 49% [41], resulting in unnecessary morbidity and mortality. The efficacy of PrEP for HIV prevention has been well established [42], but significant barriers to implementation remain, as <10% of eligible patients continue using PrEP [35]. Implementation science gives us tools to address these gaps in the application of effective treatments, such as through assessing barriers and facilitators and through community engagement. Similar issues have arisen in the management of hepatitis C, for which there are well-proven and effective treatments. Only about half of patients with hepatitis C infections are diagnosed and aware of their infection, 16% are prescribed treatment, and 9% achieve a sustained virologic response [43]. Figure 1B maps hepatitis C management to the practical, robust implementation and sustainability model (PRISM) framework through implementation science. Conceptualized through the PRISM framework, the multilevel nature and barriers to implementation of hepatitis C treatment become apparent. What follows is a list of barriers and implementation strategies that could be/could have been used to facilitate universal hepatitis C treatment.

Public awareness: educational campaigns (lay public and physicians).

Affordability: change payment structures (important at multiple levels, including drug and insurance companies, pharmacists, physicians, and patients).

Linkage to care and retention in care: local needs assessments and assessments of barriers and facilitators for patient populations/subgroups.

Patient screening: changing record systems (eg, automated testing based on risk factors such as age, drug use, etc.).

HOW CAN DISSEMINATION AND IMPLEMENTATION AND INFECTIOUS DISEASES HELP EACH OTHER?

D&I science has particularly been used in ID for HIV prevention and treatment, but has been less frequently used in other areas [44, 45]. In one study, investigators used D&I science to guide the implementation of universal decolonization treatment for ICU patients. Key stakeholders employed the Universal ICU Decolonization Toolkit, which provided in-depth implementation protocols and materials. Enterprise coaching calls informally assessed the uptake of the toolkit and substantiated the intervention implementation. The toolkit embodied several key implementation strategies, including training and educating stakeholders (ie, nurses), using evaluative strategies (ie, assessing readiness-and-monitoring process and outcome metrics), and employing interactive assistance (ie, the use of audio podcasts and physician-specific communication resources and evidence tools). In the intervention, patients were treated with chlorhexidine bathing and nasal mupirocin in 136 ICUs from 95 hospitals over 6 months, resulting in a 23.5% decrease in central line–associated bloodstream infections [44]. This massive undertaking with significant clinical benefits was made possible by D&I science. In another study, investigators found that a program to disseminate and implement findings of an acquired immunodeficiency syndrome clinical trial increased rates of early antiretroviral therapy initiation for HIV from 50 to 83% [45].

Examples of ID topical areas that could benefit from D&I science follow.

The uptake of treatment and management guidelines. Passive dissemination (current *de facto* practice) is known to be poorly effective in guideline uptake [16]. Dissemination should include active methods to spread information not just to practitioners and staff, but to organizations and politicians, so that institutional, organizational, and governmental policies incorporate research findings to best serve patients. Furthermore, evidence should be presented in a way that is understandable to the target audience [17].

Practice variability [46, 47]. Many factors contribute to practice variability, but deviations from best-care practices can result in patient harm. D&I science can help reduce practice

variability when evidence demonstrates the superiority of one intervention or management strategy.

Problems with loss to follow-up [48], given their association with mortality [49] and the failure to treat sexually transmitted infections (among other important clinical outcomes) [50]. D&I science could help plan and organize the engagement of patients and communities.

Problems with linkage to care, given its association with untreated HIV and hepatitis C [51, 52]. D&I science could inform community engagement, as well as barriers and facilitators of linkage to care.

Train-the-trainer methods, which are applicable to many areas, including the Project Extension for Community Healthcare Outcomes approach for hepatitis C [53], hand hygiene, surgical site infection prevention, and antimicrobial stewardship, among others.

Conversely, because D&I is a relatively new field, there are many opportunities for problems in ID to help understand the cross-cutting issue of how evidence is disseminated and implemented in health. Some potential areas for collaborative problem solving are listed below.

End phases of implementation, sustainability, and de-implementation.

Disparities in evidence-based intervention dissemination and implementation.

Testing of D&I strategies.

CONCLUSIONS AND HOW CAN I LEARN MORE?

While we have provided a high-level review of D&I science and its potential applications in ID, there is much more literature available for interested readers. Table 3 includes a series of relevant resources, articles, and trainings. Alternatively, we would encourage individuals who do not wish to learn an entirely new field to partner with D&I researchers. The Clinical and Translational Science Awards programs, funded through the National Institutes of Health, are dedicated to the translation of research, and commonly have opportunities to collaborate with D&I researchers. The Patient-Centered Outcomes Research Institute also has toolkits and funding available for D&I research. Included in Table 3 are organizations that provide D&I consultation to clinical researchers on how to incorporate D&I into their current research programs.

The goal of D&I research is to narrow the research-to-practice gap and, in the process, to reduce the time elapsed until populations gain maximum benefits from effective interventions. In addition, by getting evidence into practice, D&I science not only reduces health-care disparities, but also improves returns on investments of grant funding/taxpayer dollars. If the methods of D&I science were applied to all ID research, the result would be improvements in research output and quality, as well as patients' clinical outcomes. For every patient, every trial, every study in ID, we should be asking ourselves, "where's the D&I?"

Table 3.   Dissemination and Implementation Science Resources

Resource Type/Title	Description	Link/Reference
Textbook: *Dissemination and Implementation Research in Health: Translating Science to Practice*	Comprehensive introduction to D&I science	https://prcstl.wustl.edu/dissemination-and-implementation-research-in-health-translating-science-to-practice-2nd-edition/
D&I model selection tool	Interactive website to select D&I models that best fit research questions or practice problems	http://www.dissemination-implementation.org/
D&I toolkits	Various toolkits, information, and resources designed to support novice investigators interested in D&I	https://sites.wustl.edu/wudandi/di-toolkits/
Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda	Delineates and describes implementation outcomes	Proctor et al [22]
Evaluating the public health impact of health promotion interventions: the Reach, Effectiveness, Adoption, Implementation, and Maintenance framework	Discusses implementation outcomes, includes RE-AIM framework	Glasgow et al [54]
Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact	Describes different types of hybrid trials	Curran et al [29]
Training courses through University of California San Francisco	Online Certificate in Implementation Science	https://epibiostat.ucsf.edu/online-certificate-implementation-science
NIH grant RFA	R01 for D&I science	https://grants.nih.gov/grants/guide/pa-files/par-16–238.html
AcademyHealth D&I science conference	National conference on D&I science (annual)	https://www.academyhealth.org/events
Society for Implementation Research Collaboration	Society for D&I research collaboration and communication between providers, researchers, and communities	https://societyforimplementationresearchcollaboration.org/

Abbreviations: D&I, dissemination and implementation; NIH, National Institutes of Health; RFA, request for application.

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