

Expanding the Concept of Translational Research: Making a Place for Environmental Health Sciences

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SUMMARY: The National Institute of Environmental Health Sciences (NIEHS) introduces a new translational research framework that builds upon previous biomedical models to create a more comprehensive and integrated environmental health paradigm. The framework was developed as a graphical construct that illustrates the complexity of designing, implementing, and tracking translational research in environmental health. We conceptualize translational research as a series of concentric rings and nodes, defining “translation” as movement either from one ring to another or between nodes on a ring. A “Fundamental Questions” ring expands upon the research described in other frameworks as “basic” to include three interrelated concepts critical to basic science research: research questions, experimental settings, and organisms. This feature enables us to capture more granularity and thus facilitates an approach for categorizing translational research and its growth over time. We anticipate that the framework will help researchers develop compelling long-term translational research stories and accelerate public health impacts by clearly mapping out opportunities for collaborations. By using this paradigm, researchers everywhere will be better positioned to design research programs, identify research partners based on cross-disciplinary research needs, identify stakeholders who are likely to use the research for environmental decision-making and intervention, and track progress toward common goals. <https://doi.org/10.1289/EHP3657>

Background and Objective

Embedded in the mission of the National Institute of Environmental Health Sciences (NIEHS) is the goal of encouraging the translation of research from basic biomedical and environmental health findings to concrete strategies that protect and improve human health. A clear concept of translational research is needed to understand, assess, and categorize environmental health research so that we can track new ideas and knowledge from their origins across the translational research spectrum. A more comprehensive framework that integrates previous concepts, while making a place for environmental health science research, will enable researchers everywhere, as well as NIEHS staff, to identify and facilitate opportunities for translational “bridging” or moving a research idea from one translational area to another (Drolet and Lorenzi 2011). Our goal is to codify the distinct categories of the translational research process as applied to environmental health and describe the types of environmental health science activities that might occur in each one, while continuing to provide a space for clinical research. By expanding the concept of translational research to incorporate environmental health science, we hope to provide our researchers with ideas about potential paths their research might take through the translational process.

The concept of translational research is generally understood to be the evolution of a research idea through a series of scientific categories that typically include basic research, applied research, pre-clinical, clinical, and standard practice (Dougherty and Conway 2008; Khoury et al. 2007; Sung et al. 2003; Trochim et al. 2011;

Westfall et al. 2007). We used these models as the foundation for an expanded framework that provides an opportunity to capture and integrate research that is directed at understanding the complex relationships between the environment and human health. This framework enables us to recognize the translational nature of more environmental health research and to consider nonclinical impacts as translational.

Discussion

The Framework

First, we visualize the framework as a series of concentric rings as depicted in Figure 1. We believe that this depiction reinforces the understanding that research moves between translational research areas in a nonlinear way, and it allows for mapping the complex paths research may follow as it moves through the translational research process.

The framework includes nodes along the rings that describe the types of activities that might occur within an individual translational research category. This level of detail allows researchers to tailor the model to tell a specific translational research story. The nodes reflect potential translational research activities related to environmental health science research. The description below starts from the center and works outward. However, we stress that any specific translational research story may start in any translational category, may skip categories, and will likely follow a complex path from start to finish.

Fundamental Questions. The Fundamental Questions ring enhances the characterization of what other frameworks describe as basic research (Figure 2). In assessing examples of NIEHS-supported translational research, we found that the basic research questions typically fall into three major categories:

- Identification: What is it?
- Observation: What is it doing?
- Understanding: How does it do that and what else is going on?

We place those three types of questions at the center of the model and connect these questions with an associated experimental setting (*in vivo*, *in vitro*, *in situ*, *in silico*, or in a population at large) and an organism (e.g., human, animal, plant, bacteria, yeast, worm, fish, other model organisms). These three elements are intrinsically

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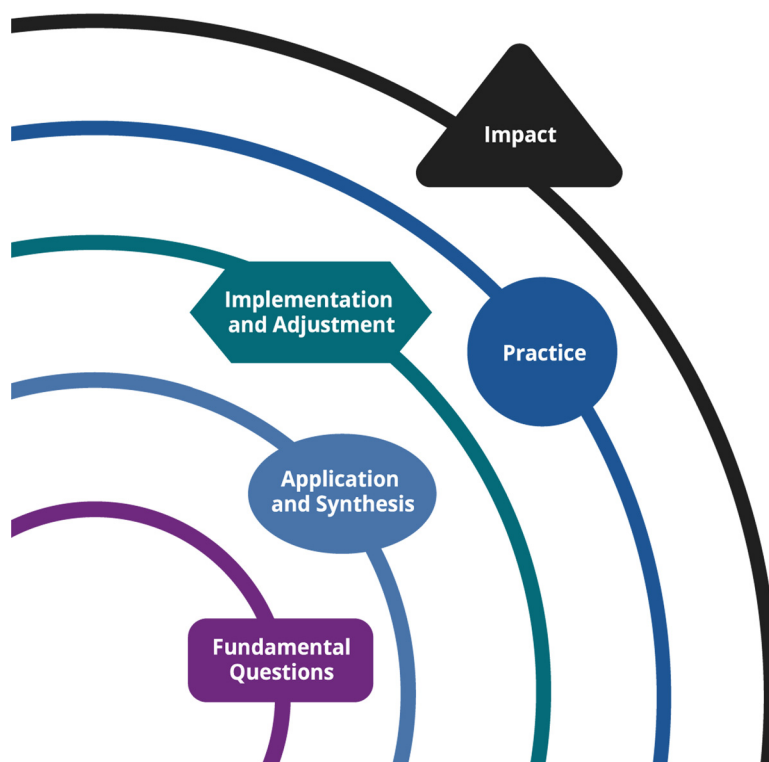


Figure 1. Overview of NIEHS translational research framework. A series of concentric circles represent the categories of translational research. As the rings move from the center ring to the outside ring, the research activities have human impacts.

linked, and we posit that moving from one combination to another represents a clear translational bridge.

For example, a translational research story may start with an observation from an epidemiological cohort study (observation/population/human) that finds a relationship between an environmental exposure and a human health outcome. This study may be used as the basis for a lab-based study designed to confirm that association and to explore potential mechanisms experimentally. This would constitute a translational bridge in the framework (Figure 3), and a further step toward providing evidence to support a public health intervention or application.

Here we recognize that the initial questions, tools, and research methods may differ between the observational and experimental

studies and that the relationship or bridge between the findings of each also requires translational bridging between disciplines. Research conducted to answer fundamental questions uses modern tools (e.g., epigenomic analysis) and concepts (e.g., exposomics) that, in themselves, may require “translation” to investigators in other disciplines and stakeholders who might want to apply the findings in the “real world.” Likewise, methods and approaches for economic analyses, community-based participatory research and community engaged research, qualitative approaches, and geospatial analyses may be unfamiliar to basic scientists and require interdisciplinary translation to help the basic scientists design their research in anticipation of its future utility. Relevant methods,

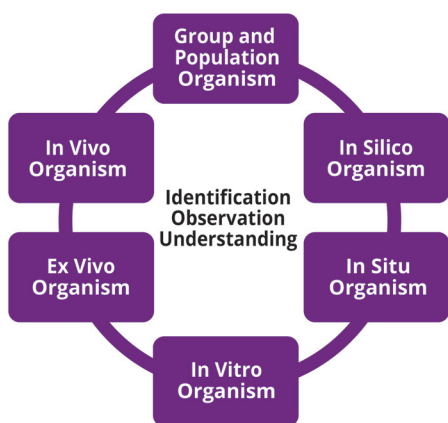


Figure 2. Fundamental Questions ring. In the NIEHS translational research framework, this category of translational research includes three intrinsically related concepts critical to basic science research: research drivers or questions, experimental settings, and organisms.

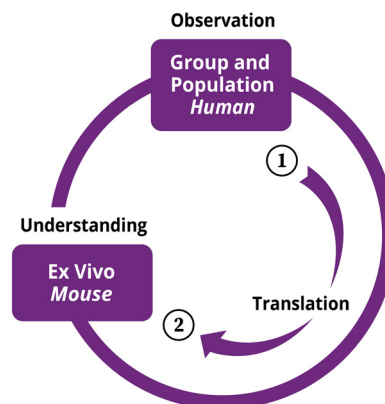


Figure 3. Movement around a translational ring. Although epidemiological observations and rodent research in the lab are both considered within the Fundamental Questions category, the tools, background, questions, and methods used are vastly different and thus we propose that movement from one area to another represents a translational bridge.

tools, and strategies can be mapped using the nodes that we highlight along the Fundamental Questions ring.

This framework reflects the view of fundamental research put forward in the NIEHS Strategic Plan by recognizing that fundamental research “addresses all levels of biological organization—molecular, biochemical pathway, cellular, tissue, organ, model organism, human, and population” (NIEHS 2012, p. 3). It is also consistent with the rationale of the National Center for Advancing Translational Science’s (NCATS) Clinical and Translational Science Awards program in considering certain types of human research as part of the Fundamental Questions category (Surkis et al. 2016).

Application and Synthesis. The remaining rings have close parallels to the categories included in the NCATS translational model (NCATS 2017). Within the Application and Synthesis ring, researchers conduct experiments in a structured and predictable setting to gain a deeper understanding of a process or effect. Such activities could include pilot tests of interventions, methods/approaches, new tools (e.g., exposure sensors), or other highly controlled settings. Also in this category is the formal synthesis or integration of evidence from previous research to inform future research, risk assessment, and other decision-making.

Implementation and Adjustment. The next ring includes research that tests hypotheses in real-world settings and adjusts the product (e.g., the intervention, tool, method, treatment) to account for differences in different settings and populations. Examples include biomarker, screen, or assay validation; clinical testing; tool validation and use; and effectiveness testing. Current work in dissemination and implementation science would fit within this category (e.g., Davis et al. 2007; Glasgow et al. 2012; Huberman 1994; Landry et al. 2001; Majdzadeh et al. 2008; Tabak et al. 2012; Wandersman et al. 2008).

Practice. The next ring focuses on moving established ideas into common practice. This includes using evidence to inform new guidelines for: preventing, diagnosing, or treating exposures, illness, and disease; formalizing new public health interventions; institutionalizing local, regional, state, national, or international policy practices; informing standard risk management protocols; or motivating behavior change at individual, family, group, or population levels.

Health Impact. The final ring includes research that assesses the broader environmental, clinical, or public health impact of a practice, guideline, or policy on human health. For example, if a state implemented a policy to reduce air pollution, researchers might want to continue their research to assess the impact of the policy on air quality and related human health outcomes such as lung function or asthma rates.

Applying the Framework

Overall, the framework provides a novel, more comprehensive conceptualization and definition of translational research (Figure 4). Specifically, any research that either bridges nodes within a ring or that crosses rings is considered translational. The framework provides the ability to track and describe research as it moves through the translational research process and to give recognition to research that bridges nodes in the Fundamental Questions ring. We also expect that there will be degrees of translation, so that more complex or long-term translational stories will include more bridges.

The full framework is designed to enable the depiction of research as moving in any direction, including with the ability to bridge from any ring to another, as well as between any nodes of a ring. The proximity of the rings or categories to the center does not connote any intrinsic value, but rather demonstrates the various categories of research activity that occur, placing activities that have more direct impact on human health in the outer rings.

Moreover, it recognizes that community partners and stakeholders involved in research play a valuable role in the translational research process. They might be involved in such research activities as identifying research questions, conducting and testing interventions, or communicating findings from the research to policy makers and other decision makers. The framework itself focuses on identifying the specific research activities conducted as part of the translational research process. We envision that contextual information about who participated in these activities, the time frame of these activities, and the factors that facilitated translation from one point to another would be described in translational research narratives.

The following case study from the University of Cincinnati and Michigan State University illustrates how the framework can be used to highlight a few key translational research milestones from a project funded by the Breast Cancer and the Environment Research Program (BCERP) (Figure 5). In this example, key translational milestones are mapped using the translational research rings. We then highlight the specific activity conducted using nodes within that ring. Contextual information including the partners who participated in the activity, the time frame, and any publications that can be added to the graphic and referenced for additional information to provide a more complete translational research narrative and expanded over time as more research is completed.

Translational Milestone 1. The University of Cincinnati BCERP project added polyfluoroalkyl chemicals (PFCs) to the list of chemicals being screened in their cohort of young girls. This was based on findings from the Centers for Disease Control and Prevention’s National Health and Nutrition Examination Survey that showed elevated levels of PFCs in some populations (Calafat et al. 2007; Hiatt et al. 2009).

Translational Milestone 2. Among the girls screened in the next year, about half had PFC serum concentrations above the 95th percentile (Pinney et al. 2014).

Translational Milestone 3. University of Cincinnati researchers presented these findings at a BCERP grantee meeting. Grantees from a BCERP lab at Michigan State University offered to test the effects of PFC in an animal model. They found a stunting of mammary development and delayed onset of puberty in female mice exposed to PFCs (Zhao et al. 2010).

Translational Milestone 4. Researchers had committed to a community-based participatory research process that valued the input, knowledge, and skills of their community partners. Community partners, including breast cancer prevention advocates, convinced the researchers to share the results with the families, even though they were unable to provide information about the source or potential effects of the exposures. Upon learning of the exposures, families communicated ideas about the suspected source of the contamination to the researchers. The exposure was ultimately confirmed as a pollutant in the public water supply (S. Pinney, written communication, August 2017).

Translational Milestone 5. University of Cincinnati researchers partnered with Cincinnati and Northern Kentucky water treatment departments between 2007 and 2012 to reduce exposure through water filtering (S. Pinney, written communication, August 2017).

We encourage readers and those using the framework to keep the following caveats in mind. Not all research is, or will be, translational; research would be considered translational only when it bridges to another node or different translational category. For example, using our case study, an investigation of PFC serum concentrations in a cohort is not by itself translational, nor is examining PFC serum concentrations in a rodent model. However, the research becomes translational when the epidemiology study is

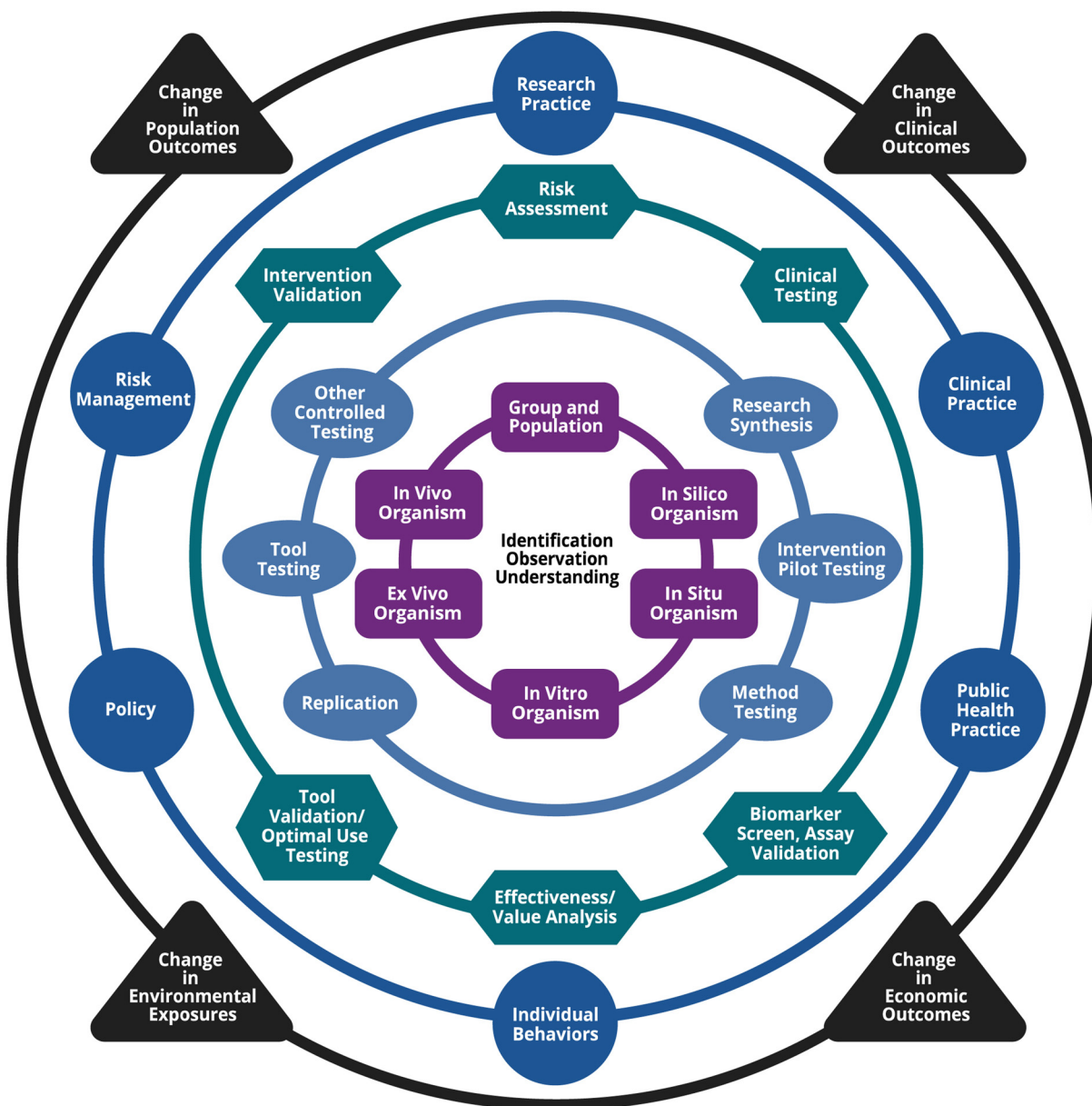


Figure 4. The full translational research framework represents five categories of translational research in concentric rings: Fundamental Questions (rectangles), Application and Synthesis (ovals), Implementation and Adjustment (hexagons), Practice (circles), and Public Health Impacts (triangles). Within each ring, nodes describe the types of activities that might occur.

used to motivate or inform the animal study, and it is more likely to become so when designed with the need for public health impact from the start. Thus, the link between the two research products becomes a translational bridge. We hope this framework can help provide a common vocabulary and structure for telling translational research stories.

As others have noted ([Waldman and Terzic 2010](#)), translational research is not a linear process. A translational research idea can start at any point in the framework, move in any direction, and potentially skip entire rings. New findings lead to new questions that can start the whole translational research process over again. Many translational research stories are told in retrospect. We hope that use of this framework will help collaborating groups map research plans and strategies to be translational by design.

NIEHS supports several programs that advance “research translation,” an approach for interpreting scientific information and creating messages and materials that can be readily used by a specific

audience (such as lay community, educators, or healthcare professionals). Although research translation is not a specific node in our framework, we view it as an activity that can take place at any point in the translational research process, much like community outreach and engagement.

Coordination of research within this framework, especially if undertaken with the goal of achieving research translation to meet a specific need, will likely include multiple investigators, laboratories, and institutions. A variety of skills, training, and perspectives are needed to move a research idea through the various categories of the complex translational research process. Our hope is that by providing this framework, investigators will be able to see a path for their research to have an impact on preventing environmental exposures, reducing disease, and improving human health and will be able to see the types of partners they might need to bring into their circle to help facilitate the bridging of research within and across translational rings.

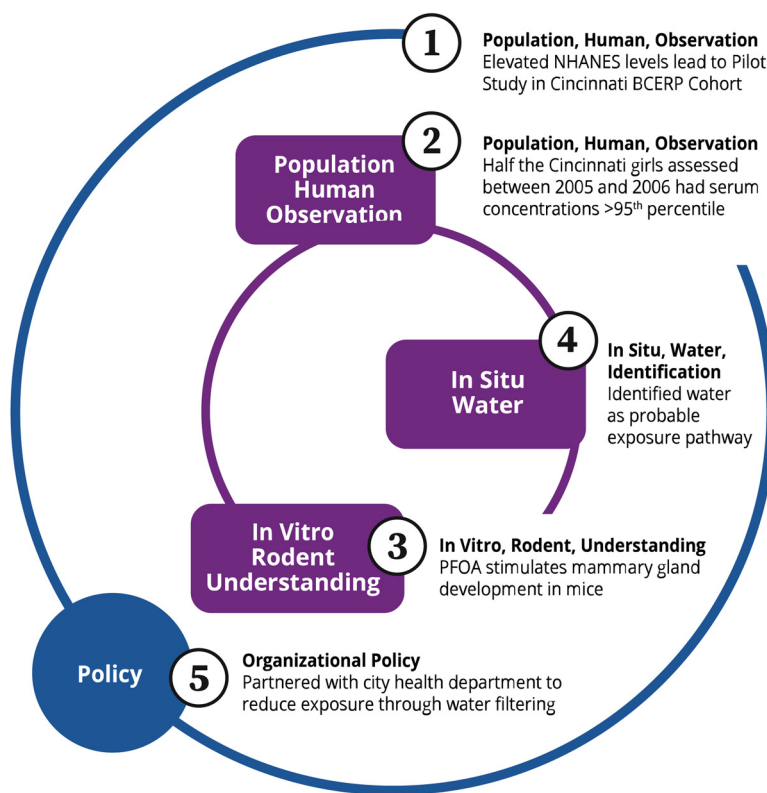


Figure 5. Mapping a case study using the NIEHS translational research framework. Five research milestones are mapped onto the translational research framework. The research moves through several nodes within the Fundamental Questions category (rectangle) and ultimately bridges to the Practice category (circle) when the researchers begin working with the health department to implement water filtering procedures to reduce the levels of PFOAs in the city water.

The path to using fundamental research for the benefit of humankind, whether in medicine, environmental health or both, is long and complex. Most research is documented incrementally, in grant progress reports and publications, which by their very nature focus on the findings of individual studies. These snapshots of research do not fully capture the dynamic and often lengthy process of designing, conducting, and reporting research that can then be integrated and translated into action. We argue that new efforts and formats are needed to collect, categorize, and evaluate translational research narratives so that we capture the full spectrum of research activities that contribute to the translational story, including the role of community partners, stakeholders, and other research collaborators. Richer translational narratives might also include descriptions of the connections or hand-offs from one research area to another, including highlights of any facilitators or challenges in the process.

Anticipated Benefits of This Translational Research Framework

This comprehensive concept of translational research, which incorporates all elements of environmental health research, from basic to applied science to finding real-world solutions, helps support the NIEHS strategic plan and mission. It fosters a culture in which environmental health researchers, program staff, and institute leadership work in concert toward common ends. Its storytelling structure should enable researchers to clearly articulate progress in the complex, multiyear process of translational research.

Although we have focused this framework on addressing the needs of the environmental health science research community, we believe it is applicable to any agency or organization attempting to move research from a fundamental or basic research question to

application in the real world and would be adaptable for use by other NIH institutes, as well as by researchers and planners in other fields, including education and social services. The nodes on each ring enable us to identify key translational research areas applicable to the field of environmental health, but they are broadly defined and can be applied to many fields.

The framework will also help NIEHS to better assess where a given research project falls along the translational research spectrum, provide a mechanism to categorize and understand the status of the Institute's research portfolio, and enable us to track movement of research through the translational spectrum. As an evaluation tool, the framework will enable us to code research projects using these modified categories and give more recognition to research that moves through several iterations in the fundamental research area.

Finally, the framework will enable NIEHS staff, as science managers, to talk more clearly about how our funded research projects connect across areas of the translational research framework. The framework will also enable staff to actively engage in bridging science between nodes of the framework. Similarly, the framework can provide researchers with a map of potential paths that their research might take through the translational research cycle. A known barrier to translational research is the difficulty of finding the right "next step" for planning new research. Not every scientist has the perspective or the interest in shepherding research through all the phases of translation. As Chris Austin, the director of the National Center for Advancing Translational Science, has said, "the translational process is so multifaceted that no one person, no matter how committed or talented, can succeed alone" (NCATS 2013). We hope that the framework will be used prospectively by researchers and NIEHS program staff to identify opportunities for collaborations and for determining when and to whom to "hand

off” their research, thereby accelerating translational bridges and achieving greater public health impact.

Next Steps

Our next step is to develop a concrete, objective checklist that can be used to categorize existing research into the nodes and rings. Future research efforts will include an evaluation of NIEHS translational research narratives. The evaluation will compare the categorization of these narratives using the NCATS translational research spectrum and the NIEHS translational research framework, which should enable us to describe and quantify the differences between the two frameworks. We may also attempt to prepare case studies that demonstrate the utility of the framework to diverse types of environmental health science research, including tool and sensor development, environmental remediation, and clinical research. Finally, we will continue to engage NIEHS stakeholders in assessing the utility of this framework in planning, conducting, and evaluating translational research.

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References

- Calafat AM, Wong LY, Kuklenyik Z, Reidy JA, Needham LL. 2007. Polyfluoroalkyl chemicals in the U.S. population: data from the National Health and Nutrition Examination Survey (NHANES) 2003–2004 and comparisons with NHANES 1999–2000. *Environ Health Perspect* 115(11):1596–1602, PMID: 18007991, <https://doi.org/10.1289/ehp.10598>.
- Davis SM, Peterson JC, Helfrich CD, Cunningham-Sabo L. 2007. Introduction and conceptual model for utilization of prevention research. *Am J Prev Med* 33(1 suppl):S1–S5, PMID: 17584588, <https://doi.org/10.1016/j.amepre.2007.04.004>.
- Dougherty D, Conway PH. 2008. The “3T’s” road map to transform US health care: the “how” of high-quality care. *JAMA* 299(19):2319–2321, PMID: 18492974, <https://doi.org/10.1001/jama.299.19.2319>.
- Drolet BC, Lorenzi NM. 2011. Translational research: understanding the continuum from bench to bedside. *Transl Res* 157(1):1–5, PMID: 21146144, <https://doi.org/10.1016/j.trsl.2010.10.002>.
- Glasgow RE, Vinson C, Chambers D, Khoury MJ, Kaplan RM, Hunter C. 2012. National Institutes of Health approaches to dissemination and implementation science: current and future directions. *Am J Public Health* 102(7):1274–1281, PMID: 22594758, <https://doi.org/10.2105/AJPH.2012.300755>.
- Hiatt RA, Haslam SZ, Osuch J. 2009. The Breast Cancer and the Environment Research Centers: transdisciplinary research on the role of the environment in breast cancer etiology. *Environ Health Perspect* 117(12):1814–1822, PMID: 20049199, <https://doi.org/10.1289/ehp.0800120>.
- Huberman M. 1994. Research utilization: the state of the art. *Knowl Policy* 7(4):13–33, <https://doi.org/10.1007/BF02696290>.
- Khoury MJ, Gwinn M, Yoon PW, Dowling N, Moore CA, Bradley L. 2007. The continuum of translation research in genomic medicine: how can we accelerate the appropriate integration of human genome discoveries into health care and disease prevention? *Genet Med* 9(10):665–674, PMID: 18073579, <https://doi.org/10.1097/GIM.0b013e31815699d0>.
- Landry R, Amara N, Lamari M. 2001. Climbing the ladder of research utilization: evidence from social. *Science research. Sci Commun* 22(4):396–422, <https://doi.org/10.1177/1075547001022004003>.
- Majdzadeh R, Sadighi J, Nejat S, Mahani AS, Gholami J. 2008. Knowledge translation for research utilization: design of a knowledge translation model at Teheran University of Medical Science. *J Contin Educ Health Prof* 28(4):270–277, PMID: 19058259, <https://doi.org/10.1002/chp.193>.
- NCATS (National Center for Advancing Translational Sciences). 2013. “Director’s message, Feb. 26, 2013: translation is a team sport.” <https://ncats.nih.gov/director/message2013/feb2013> [accessed 9 March 2018].
- NCATS. 2017. “Translational science spectrum.” <https://www.ncats.nih.gov/translation/spectrum> [accessed 24 October 2017].
- NIEHS (National Institute of Environmental Health Sciences). 2012. “2012–2017 Strategic plan. Advancing science, improving health: a plan for environmental health research.” https://www.niehs.nih.gov/health/materials/niehs_20122017_strategic_plan_frontiers_in_environmental_health_sciences_booklet_508.pdf [accessed 24 October 2017].
- Pinney SM, Biro FM, Windham GC, Herrick RL, Yaghjian L, Calafat AM, et al. 2014. Serum biomarkers of polyfluoroalkyl compound exposure in young girls in Greater Cincinnati and the San Francisco Bay Area, USA. *Environ Pollut* 184:327–334, PMID: 24095703, <https://doi.org/10.1016/j.envpol.2013.09.008>.
- Sung NS, Crowley WF Jr, Genel M, Salber P, Sandy L, Sherwood LM, et al. 2003. Central challenges facing the national clinical research enterprise. *JAMA* 289(10):1278–1287, PMID: 12633190, <https://doi.org/10.1001/jama.289.10.1278>.
- Surkis A, Hogle JA, DiazGranados D, Hunt JD, Mazmanian PE, Connors E, et al. 2016. Classifying publications from the clinical and translational science award program along the translational research spectrum: a machine learning approach. *J Transl Med* 14(1):235, PMID: 27492440, <https://doi.org/10.1186/s12967-016-0992-8>.
- Tabak RG, Khoong EC, Chambers DA, Brownson RC. 2012. Bridging research and practice: models for dissemination and implementation research. *Am J Prev Med* 43(3):337–350, PMID: 22898128, <https://doi.org/10.1016/j.amepre.2012.05.024>.
- Trochim W, Kane C, Graham MJ, Pincus HA. 2011. Evaluating translational research: a process marker model. *Clin Transl Sci* 4(3):153–162, PMID: 21707944, <https://doi.org/10.1111/j.1752-8062.2011.00291.x>.
- Waldman SA, Terzic A. 2010. Clinical and translational science: from bench-bedside to global village. *Clin Transl Sci* 3(5):254–257, PMID: 20973923, <https://doi.org/10.1111/j.1752-8062.2010.00227.x>.
- Wandersman A, Duffy J, Flaspohler P, Noonan R, Lubell K, Stillman L, et al. 2008. Bridging the gap between prevention research and practice: the interactive systems framework for dissemination and implementation. *Am J Community Psychol* 41(3–4):171–181, PMID: 18302018, <https://doi.org/10.1007/s10464-008-9174-z>.
- Westfall JM, Mold J, Fagnan L. 2007. Practice-based research—“Blue Highways” on the NIH roadmap. *JAMA* 297(4):403–406, PMID: 17244837, <https://doi.org/10.1001/jama.297.4.403>.
- Zhao Y, Tan YS, Haslam SZ, Yang C. 2010. Perfluorooctanoic acid effects on steroid hormone and growth factor levels mediate stimulation of peripubertal mammary gland development in C57Bl/6 mice. *Toxicol Sci* 115(1):214–224, PMID: 20118188, <https://doi.org/10.1093/toxsci/kfq030>.