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Transdisciplinary Approaches Enhance the Production of Translational Knowledge

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Abstract

The primary goal of translational research is to generate and apply knowledge that can improve human health. Although research conducted within the confines of a single discipline has helped

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TC proposed the idea of writing an article providing tangible examples of innovative methods in epidemiology. The general format of the piece was determined in a conference call with all authors. TC drafted the manuscript and all authors provided key feedback and input (RH, MA, CM, SW). SW is the senior author and provided substantial editorial input.

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us to achieve this goal in many settings, this uni-disciplinary approach may not be optimal when disease causation is complex and health decisions are pressing. To address these issues, we suggest that transdisciplinary approaches can facilitate the progress of translational research, and we review publications that demonstrate what these approaches can look like. These examples serve to 1) demonstrate why transdisciplinary research is useful, and 2) stimulate a conversation about how it can be further promoted. While we note that open-minded communication is a prerequisite for germinating any transdisciplinary work and that epidemiologists can play a key role in promoting it, we do not propose a rigid protocol for conducting transdisciplinary research, as one really does not exist. These achievements were developed in settings where typical disciplinary and institutional barriers were surmountable, but they were not accomplished with a single predetermined plan. The benefits of cross-disciplinary communication are hard to predict *a priori* and a detailed research protocol or process may impede the realization of novel and important insights. Overall, these examples demonstrate that enhanced cross-disciplinary information exchange can serve as a starting point that helps researchers frame better questions, integrate more relevant evidence, and advance translational knowledge more effectively. Specifically we discuss examples where transdisciplinary approaches are helping us to better explore, assess, and intervene to improve human health.

Keywords

Decision making; Epidemiology; Epidemiological methods; Methodology; Research methods

INTRODUCTION

The primary goal of translational biomedical research is to elucidate the determinants of disease and apply this knowledge to improve clinical or population health practices. Epidemiologists have been successful in advancing this goal, particularly in the context of conditions with causal factors that have consistently detectable marginal associations. However, in the context of etiologically heterogeneous complex disease, causal factors may not have reproducibly detectable marginal associations because these diseases have multiple interacting determinants. As a result progress in this area has been much slower. Here we take the perspective of epidemiologists and hope to generate further discussion by exploring a general approach for increasing our ability to address multifactorial health problems. Specifically, we advocate that epidemiologists take a transdisciplinary approach, and propose that enhancing the opportunity for cross-disciplinary information exchange can help by making relevant perspectives from multiple distinct fields available for scientific reasoning at each stage of the research process, but perhaps most importantly at the outset of defining a problem and designing a research strategy. This increases our chances of realizing information synergies, thereby allowing us to frame better questions, gather more comprehensive data, and better exploit existing information to guide health decisions.

This general approach addresses the key issues identified in two sets of recent commentaries concerning the future of epidemiologic research. The first group of commentaries proposes that innovative thinking will be central to progress in epidemiology and translational research (particularly in the current age of big data)¹⁻³, and the second group posits that

integrated approaches can streamline the development of effective interventions.⁴⁻⁷ Here we extend this discussion by exploring specific theoretical issues and examples that illustrate how cross-disciplinary information exchange has provided novel insights into disease processes, led to more complete knowledge of causation, and thereby spurred the development of more effective interventions. Thus, the overall purpose of this paper is to reveal the underappreciated utility of transdisciplinary research and fuel discussion about how it can be fostered.

The examples provided here clarify how enhanced communication between fields can cultivate creative approaches that make translational research both more effective and efficient. They also emphasize the often underappreciated advantages of teamwork.⁸ These examples do not argue for the development of a single pipeline for the conduct of transdisciplinary research or even that it is possible to know *a priori* how to design ensemble research strategies for all contexts. We also recognize that transdisciplinary research often involves difficult challenges⁹, and it cannot be forced. However, we propose that we can spur the development of productive transdisciplinary approaches if we create research and training environments that encourage cross-disciplinary information exchange. By extension, failing to take measures to increase our cross-disciplinary fluency will likely impede, or even prevent, the development of solutions to many human health problems. Stated differently, traditional silo-based research can only address a limited number of incomplete questions.

As the examples here demonstrate, open-minded cross-disciplinary communication can yield useful but unpredictable results. Before researchers begin talking to people from other fields (or at least start reading their papers), it will often not be clear how different disciplines may help each other address a given problem. Additionally, it will usually not be clear beforehand if the help will come in framing questions (the beginning), analytic methods (the middle), or information integration and intervention (the end). This communication could result in the cross-disciplinary transfer of a single critical piece of information or it could generate a long-term symbiotic relationship between researchers. The nature of this communication and character of its benefits are inherently unpredictable. Therefore, we will not unnecessarily constrain this process by proposing the use of rigid constructs or specific protocols.

Unfortunately, the utility of cross-disciplinary communication is frequently overlooked even though it has already produced significant advances. For example, how long would it have taken to reduce cholera transmission if John Snow had not: 1) thought beyond some existing concepts in his discipline (miasma), 2) looked for patterns in new ways (his maps) and 3) worked with relevant people from outside his immediate field (Rev. Henry Whitehead)?¹⁰ Essentially, the utilization of information from multiple disciplines throughout the research process creates a transdisciplinary approach^{11, 12} that can extend knowledge beyond the limitations of the contributing disciplines. Transdisciplinary research does not refer to the combination of fully formed ideas from distinct fields (multidisciplinary research), or the integration of ideas from distinct fields (interdisciplinary research), rather it refers to the generation and utilization of research frameworks and ideas that could not come from, or fit into, any one field.^{11, 13} This emergent property of transdisciplinary translational research

can enable us to: 1) explore widely, 2) assess diversely, and 3) intervene effectively in our efforts to promote human health. These three areas provide the framework for our discussion below.

TRANSDISCIPLINARY PERSPECTIVES CAN HELP US GENERATE BETTER HYPOTHESES

A key to getting better answers is asking better questions, and transdisciplinary perspectives can generate hypotheses that uni-disciplinary perspectives might otherwise miss. If we utilize a fuller set of scientific perspectives, and tools from more than one discipline, we can frame critical questions that are not apparent from the data and tools of a single discipline. On the other hand, if we exclusively use canonical exploratory methods, we will define relatively simple questions that will likely fail to identify many of the complex phenomena that lead to health problems.

Example: Exploratory research in a single discipline often fails in the context of complex disease

“ . . . the problem of identifying and quantifying multiple component causes of disease is one of the most basic limitations in modern epidemiology”

-Paolo Vineis and David Kriebel¹⁴

In population health and medicine we often employ simple descriptive epidemiology techniques to generate hypotheses about the causes of illness and disease¹⁵ (e.g. univariate analyses from surveillance data, frequency tables, and histograms). Analytic epidemiology techniques can then be used to test these hypotheses, correcting for potential biases.¹⁵ This two-step process is foundational to epidemiology, but its effectiveness can be limited when the first step is insufficiently informative. Stated differently, if the relevant causal factors do not have detectable marginal associations then standard descriptive epidemiology techniques may not effectively direct our subsequent efforts.

Most epidemiology training focuses on analytic epidemiology and encourages the evaluation of effect modification (interaction) only if it is suspected *a priori*. This rule of thumb makes sense in the context of standard statistical models, because with these methods, screening for all possible interactions is at best problematic and at worst impossible. Therefore, if a critical cofactor is not suspected to be an effect modifier, it is not usually addressed in standard epidemiologic investigations. The ability of a cofactor to have important effects, however, is not contingent on our ability to suspect its role *a priori*. Therefore, we need to develop exploratory methods to identify putative component causes¹⁶ whose etiologic role is not evident from marginal associations. A variety of potentially useful new methods can be found in fields where techniques for analogous problems have already been developed (e.g. genetics, computer science, economics, and ecology). Such methods can advance complex disease research by expanding descriptive epidemiology beyond histograms and correlations, to include methods capable of generating novel multifactorial hypotheses.

An example of one such tool is Multifactor Dimensionality Reduction (MDR), a machine learning method that explores all possible combinations of categorical variables to identify

combinations that best associate with the phenotype of interest.^{17, 18} This method was developed by geneticists to detect gene-gene and gene-environment interactions that are associated with a phenotype, and it has demonstrated great utility in this role.^{17–26} Thus, this method, perhaps in combination with other machine learning techniques^{27, 28}, can be used as a tool to identify multifactor patterns associated with disease. For example, researchers have used MDR to identify putative gene-environment interactions in the development of lung cancer (predictive single-nucleotide-polymorphisms [SNPs] differ by smoking status)²⁹, and childhood asthma (several SNPs interact with indoor dampness)³⁰. Additional strategies for detecting multifactor patterns associated with disease continue to be developed in genetics^{31–33}, and techniques such as these can extend our capacity to identify combinations of factors that are linked to disease risk.

Another promising set of approaches from computational biology leverages visual data representations to help translate complex patterns into specific etiologic questions.^{34, 35} Visual methods may be of particular relevance in the development of transdisciplinary discovery epidemiology because they reduce jargon-based barriers to cross-disciplinary communication (Figure 1), by replacing field specific terminology with broadly-accessible visual aids. Additional non-standard computational tools, such as agent based models and other complex systems models, may be useful for learning about multifactor causes and system properties when disease risk is modulated by multiple non-linear interactions that vary temporally.^{36–38} Furthermore, establishing transdisciplinary teams can promote communication between diverse subject matter experts to advance the development of new complex systems models.³⁹ These models can allow researchers to think about the relationships between putative causal factors from multiple fields in novel ways. Such methods create a unique opportunity to develop the multilevel hypotheses that are needed to address complex health problems.

Of course, thoughtful trials and discussion are required to better clarify the strengths and weaknesses of these non-traditional approaches. This process is already underway for MDR^{23–28} and agent based models.^{40–43} Because non-traditional discovery epidemiology methods (e.g. MDR) are prone to bias, as are all descriptive epidemiology methods (e.g. unadjusted associations), validation with traditional analytic epidemiology models is important. Furthermore, even analytic epidemiology approaches that properly account for known confounding and biases are limited in their ability to infer causality. Therefore, experimental, biological, and implementation research strategies will continue to be crucial for validating and characterizing the causal relationships suggested by any observed statistical associations.

We note that it is not surprising that transdisciplinary approaches can generate advances in descriptive epidemiology because in recent years techniques from other fields have enhanced the practice of analytic epidemiology. In particular, Directed Acyclic Graphs (DAGs) from computer science have advanced our ability to communicate causal structures and identify bias, thus allowing us to build better analytic epidemiology models (Table 1).⁴⁴ Here we simply note that methods from other fields might help us advance descriptive epidemiology as well. Importantly, if we fail to utilize new pattern finding algorithms for

discovery epidemiology, we will likely miss opportunities to identify modifiable component causes of disease.

TRANSDISCIPLINARY PERSPECTIVES CAN HELP US BETTER ASSESS AND INTERPRET EVIDENCE

Transdisciplinary perspectives can help us to gather and utilize more relevant and comprehensive evidence for vetting putative etiologic factors. This allows us to better address our concerns about potentially misleading findings.⁴⁵ By including diverse types of data and encouraging multiple modes of assessment, transdisciplinary perspectives can rigorously evaluate the strength of evidence supporting a given hypothesis. The process of including more and diverse approaches that are encompassed by a transdisciplinary paradigm can result in a detailed understanding of the current uncertainties and thus clarify for decision makers which courses of action (or inaction) are most reasonable in light of the existing knowledge. It can also clarify for researchers what additional evidence is most needed to advance our understanding of disease etiology and potential interventions. In short, transdisciplinary approaches can improve our decision making by enhancing our ability to reason with imperfect and incomplete evidence from many sources.

Example: Transdisciplinary information allows for diverse convergent validation of findings

Genome Wide Association Studies (GWAS) are expensive endeavors and researchers would like to increase the usable knowledge gained from these studies to learn more about disease etiology and intervention options. It is becoming recognized that, when utilized in isolation, GWAS analyses have a variety of weaknesses that can hinder the discovery of genetic risk factors.^{46–52} Essentially GWAS, like all epidemiologic analyses, are prone to both type-1 and type-2 error, as well as the influence of unrecognized biases. However, if GWAS data is systematically evaluated in the context of relevant evidence from diverse areas, it can be part of a larger process that more effectively discovers and vets genetic risk factors for disease. For example, DiCE (Diverse Convergent Evidence) is an evidence integration process that combines information from observational association studies, bioinformatics, and laboratory experiments to yield a metric that reflects the likelihood that a given genetic factor is involved in the disease pathophysiology.⁵² As a proof of principle, this metric identified the role of Hemoglobin S in severe malaria resistance^{52–54} and the role of PPAR-gamma in type 2 diabetes^{52, 55–57} when standard GWAS validation criteria alone failed to detect these etiologically relevant factors. DiCE can also highlight potential false positive findings in GWAS analyses, including those that reach canonical thresholds for statistical significance, and suggest future research to address the ambiguous evidence. Overall, DiCE allows more diverse evidence to enter the process of determining what leads to follow and how to follow them. This promotes well informed decisions and faster knowledge acquisition.

Example: Transdisciplinary approaches allow us to work with disparate inconclusive evidence

How can we even begin to ameliorate a problem with as many potential causes as the obesity epidemic? Again, a broad perspective and systematic information integration can be useful.

In 2010 the Institute of Medicine developed a framework to promote this type of translational approach for combatting obesity: the IOM L.E.A.D. framework.⁵⁸ And recently Chatterji *et al* discussed the application of this type of approach in New York City's policy decisions regarding fat and calorie information for restaurant food.⁵⁹ In this framework researchers: A) Locate Evidence, B) Evaluate It, C) Assemble It, and D) Inform Decisions. The structure for this translation process reflects our need to make policy decisions when there are many disparate pieces of relevant but inconclusive evidence. Imperfect evidence may only provide decipherable guidance in our research and intervention decisions, if it is considered in its totality. Narrow assessments of the evidence from one field could prove misleading or just plain false. Thus, the structure and purpose of L.E.A.D. is analogous to DiCE, although it is more directly focused on implementation.

Example: Transdisciplinary teams can facilitate information synthesis and decision making

Physicians need to quickly learn what the research evidence suggests should be done for their patients. If that voluminous information is not comprehensively and cogently distilled in an ethical manner, then physicians cannot effectively use it to guide patient care decisions. For over 20 years the non-profit Cochrane Collaboration has been using a network of diverse working groups to synthesize medical research information and increase its utility in decision making.⁶⁰ By promoting input from a broad array of sources, the available evidence and its quality have been considered and organized to address the types of questions that physicians and patients ask. For example this approach has translated the complex literature on vitamin C and the common cold into actionable information (Table 2).

Example: Transdisciplinary approaches can clarify research and intervention priorities

How can we properly allocate limited research, remediation, and policy efforts to the environmental chemicals that pose the greatest risk to human health? This situation represents another instance where there is incomplete and non-definitive information and a need to advance knowledge quickly to minimize human health problems. One effective strategy can be found in the IARC monographs.⁶¹ In this approach multidisciplinary IARC working groups are assembled to discuss four aspects of a given exposure: 1) the potential for human exposure, 2) the evidence for association with cancer in humans, 3) the evidence for causation of cancer in animals, and 4) relevant mechanistic/toxicokinetic evidence. This broad scope of information is then converted by a cross-disciplinary consensus building process into a carcinogenicity assessment (e.g. probably not carcinogenic, not classifiable, possibly carcinogenic, probably carcinogenic, and carcinogenic). Recently, the National Toxicology Program (NTP) developed a similar general strategy for integrating human, animal, and in-vitro evidence in chemical assessments.⁶² The NTP also makes relevant evidence available for alternative integration analyses by compiling it into publically accessible databases (e.g. CEBS, DrugMatrix, and ToxFX).⁶³ Overall, these transdisciplinary approaches can highlight the largest potential problems based on the available evidence and simply convey this information to both researchers and decision makers.

These examples indicate that more comprehensive and integrated information can allow for improved validation of potential risk factors and enhanced characterization of health problems. The long-standing transdisciplinary approaches (e.g. IARC monographs and Cochrane Collaboration) provide evidence that these strategies are very useful and the newer techniques (e.g. DiCE, LEAD, ToxFX) demonstrate that these approaches can be further optimized for efficiency.

TRANSDISCIPLINARY PERSPECTIVES CAN HELP US DEVELOP AND COORDINATE INTERVENTIONS

Discipline-specific strategies can limit our ability to develop policies and interventions that improve human health. For example, imagine our goal was to fill a barrel with water and keep it filled. If the barrel has a hole in it, how would we best coordinate the efforts of a cooper with that of a person getting water from a well? No matter how hard each individual works, their efforts will be inefficient or even ineffective unless they are applied in the right order. The development of effective interventions can suffer from similar issues.

Example: Interventions can be more effective when etiologic characterization is transdisciplinary

Chemical exposures, social exposures (neighborhood and family interaction styles), genetics, educational strategies, and nutrients can individually be evaluated for their association with neurodevelopmental outcomes. These variables may be studied separately by environmental epidemiologists, social epidemiologists, geneticists, developmental pediatricians, neuropsychologists, and nutritional epidemiologists, but if they work in isolation, information about how to most effectively intervene is likely to be obscured. How can you characterize the relationship between lead exposure and adverse neurodevelopmental outcomes without considering how psychosocial factors may generate potential confounding and other biases?⁶⁴ Also, what good is an educational intervention if the child is still exposed to lead because the home is not properly remediated or the source of exposure remains unidentified? Educational, social, medical, and environmental interventions can fail or they can be synergistic. Understanding the relationships between component causes from a variety of traditionally separate fields can clarify the overall public health problem and intervention possibilities, and this principle has become a driving factor behind the emerging concept of “exposome” research.^{65, 66}

Example: Moving from genes or environment, past genes and environment, to genes with environment

Studying genetic and environmental factors together can help us to avoid missing causal factors.⁶⁷ The effect of each may depend on the context defined by the other, and thus some causal factors may not be detected by looking only at their marginal associations (note that here we are referring to environmental factors in the broadest sense: xenobiotic exposures, social/psychosocial factors, nutrition, etc.). Even when a marginal association is detectable, broader consideration of genetic and environmental variables taken together can illuminate the mechanisms that create this marginal association, and provide information about etiologic subtypes that may benefit from distinct interventions.^{68, 69} Furthermore, finding an

isolated genetic cause of disease may not suggest obvious interventions but if a genetic factor is found to interact with a modifiable environmental factor, then knowledge of the environmental factor can create a prevention or treatment opportunity. For example: children with genetic disruptions of phenylalanine hydroxylase function (phenylketonuria) can avoid many adverse health consequences by eating phenylalanine-limited diets that would not be optimal for other children.⁷⁰⁻⁷²

Example: Diverse perspectives allow us to handle etiologies that change in response to intervention

How can we design interventions that promote stable positive changes in complex dynamic systems when the effect of the same action may vary temporally? RCTs and experiments are ideal for learning about single factors in systems that you can randomize and control, but are less useful when multiple dynamic non-linear interactions are modulating disease risk. Some of the computational tools mentioned above (e.g. agent based modeling) may be useful for learning about how complex systems react to interventions, and thus they may also be useful for developing strategies that have consistently positive impacts.^{36, 37} These methods can allow us to ask important novel questions. Would a combination of interventions work well? Do certain policies only have a high probability of success in specific contexts? Can multifactorial interventions or contingency algorithms generate better outcomes in these settings? Along these lines the *Cancer Intervention and Surveillance Modeling Network* (CISNET)⁷³ has developed a simulation process that leverages clear modeling assumptions and comparison of results from multiple simulations to acquire convergent evidence that highlights putative causal factors. Importantly, whatever is learned from complex intervention simulations and the careful observation of new interventions, can be fed back into an evolving knowledge base for guiding future research and interventions.^{74, 75} Overall, broad transdisciplinary approaches are essential to better coordinate both our knowledge and efforts (Figure 2).

EPIDEMIOLOGISTS CAN PLAY A KEY ROLE IN ADVANCING TRANSDISCIPLINARY APPROACHES

Epidemiologists are well positioned to facilitate transdisciplinary translational research^{74, 76} because good epidemiology training provides a familiarity with a broad range of causal factors, and makes practitioners aware of the “big picture”. In fact, many epidemiologists are already at the forefront when it comes to advancing transdisciplinary research, and a variety of transdisciplines that depend on study design and analytic principles from epidemiology have already emerged. For example, epidemiologists are working with social scientists to understand the social determinants of health (social epidemiology)⁷⁷, and epidemiologists are cooperating with toxicologists to identify chemical etiologic factors (environmental epidemiology).⁷⁸ These fields have even been further combined to allow transdisciplinary insights to flow from the consideration of social, ecological, and biological factors in infectious disease epidemiology.^{79, 80} These are just a few examples but we emphasize that epidemiology continues to spur synergy in new ways. Among the newest epidemiology-based transdisciplines are epigenetic epidemiology⁸¹⁻⁸³ and molecular pathological epidemiology^{84, 85}. These transdisciplines are demonstrating that when molecular biologists,

pathologists, and epidemiologists collaborate, they can evaluate molecular factors in new ways that permit the identification of etiologic subgroups and the physiologic mechanisms of disease.

As a group, epidemiologists can further advance this approach by creating working environments that are more open to (and capable of) cross-disciplinary conversation at all stages of research. This allows for better integration and application of existing relevant information that can lead to more complete and useful knowledge⁸⁶, and also promotes the more efficient acquisition of new relevant information. In Table 3 we list specific feasible strategies that can stimulate transdisciplinary thinking and create opportunities for intellectual crosspollination through better channels of communication.

CONCLUSION

In this paper we cite examples which demonstrate that transdisciplinary approaches can cultivate and vet useful new strategies for dealing with complex health challenges. These ensemble science methods can develop whenever we make tangible efforts to improve cross-disciplinary information exchange, and they allow us to streamline the development of effective health interventions. Transdisciplinary approaches can be as sophisticated as an international team of specialists working together in a coordinated fashion, or they can be as simple as talking more often with people who have distinct training. The examples presented here are not intended to provide a blueprint for conducting transdisciplinary work. Instead they serve to 1) demonstrate what transdisciplinary insights can look like and 2) show that these insights can advance translational research. Overall, we have observed that being open to cross-disciplinary information exchange is the defining feature of transdisciplinary translational research, and it has tripartite utility. It helps us to explore widely, assess diversely, and intervene effectively in complex systems.

This review does not suggest that transdisciplinary collaboration is a panacea for health research challenges. However, it does suggest that transdisciplinary collaboration can help in some situations, and failing to enhance cross-disciplinary communication and subsequent research approaches may slow down our progress. That said, many barriers to the conduct of true transdisciplinary/team science are ingrained in our research infrastructure, including promotion criteria, funding, training strategies, and field specific jargon^{13, 87–91}, and these barriers must be overcome if we are to realize the benefits of transdisciplinary research. Importantly, the limitations of uni-disciplinary research may not always be apparent, but if we utilize transdisciplinary approaches, those shortcomings are clarified and our ability to improve human health is enhanced. We cannot answer questions that we do not ask and we cannot guide our actions with evidence that we do not assess, but in these tasks transdisciplinary perspectives can expand the capabilities of epidemiologists and the translational research community.

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Abbreviations

SNP	Single Nucleotide Polymorphism
MDR	Multifactor Dimensionality Reduction
DAG	Directed Acyclic Graph
GWAS	Genome Wide Association Study
DiCE	Diverse Convergent Evidence
L.E.A.D.	Locate Evidence, Evaluate It, Assemble It, and Inform Decisions
IARC	International Agency for Research on Cancer
NTP	National Toxicology Program
CEBS	Chemical Effects in Biological Systems
IOM	Institute of Medicine
CISNET	Cancer Intervention and Surveillance Modeling Network
CSTA	Clinical and Translational Science Awards program

Glossary

Multidisciplinary

The aggregation of fully formed ideas that come from distinct fields

Interdisciplinary

The integration, adaptation, and harmonization of ideas that come from distinct fields

Transdisciplinary

The generation and utilization of research frameworks and admixed ideas that could not come from, or fit into, any one field

Cross-Disciplinary

A general term referring to the unspecified involvement of more than one discipline

Perspective

Intellectual orientation or viewpoint that can vary in its capacity to assess and adapt to external input

Strategy, Approach, Process, or Method

A general code of conduct or way of proceeding that does not have a rigid, pre-specified, or detailed sequence or parameters

Protocol or Procedure

A specific code of conduct or way of proceeding that has a rigid, pre-specified, and detailed sequence and parameters

Communication

A general term referring to the exchange of information, strategies, protocols, hypotheses, or ideas (through talking, reading, graphical image presentation, etc.)

Information

Data and facts

Knowledge

Understanding of the relevant causal mechanisms that generated the data and facts (note that information and knowledge have similar meanings and are often used to define each other, however here we emphasize that knowledge implies an understanding of why the data or facts are as they are)

Complex Systems

Systems with multiple interacting components and emergent properties that often cannot be accurately characterized with narrow or rigid research frameworks

Marginal Association

The association between one exposure (factor) and one outcome (disease) independent of other variables. If potential biases and other observational data imperfections are properly accounted for, this association is thought to provide evidence for or against the involvement of the exposure with the disease.

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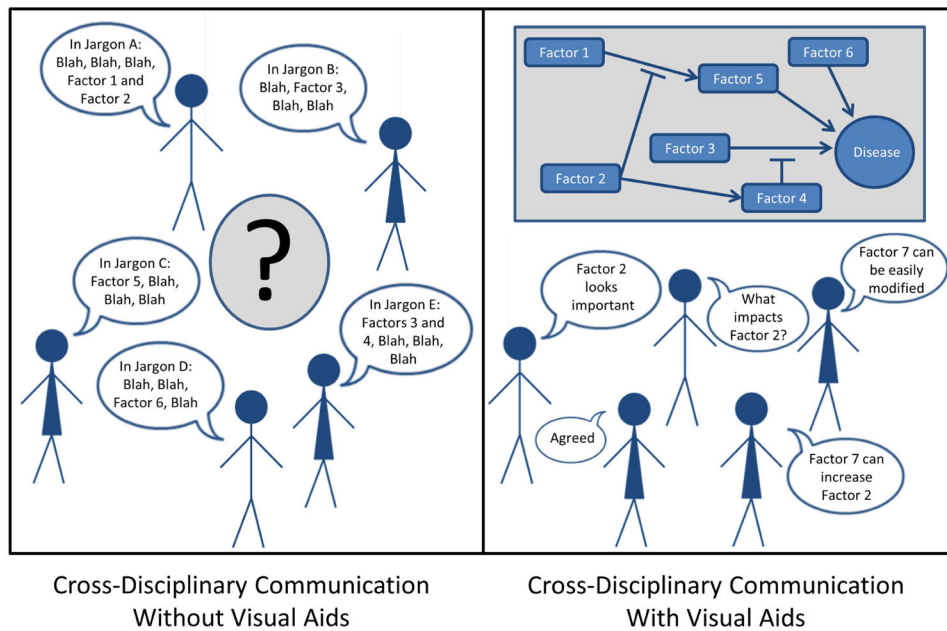


Figure 1. Visualization techniques reduce jargon-based barriers to cross-disciplinary communication

Visual information summaries can stimulate productive conversation in transdisciplinary teams by helping researchers to reason with relevant factors that are beyond their individual disciplinary expertise. In this example the putative causal factors in the etiology of a disease are summarized in a jargon-free visual schematic. Discussing this schematic allows the team to access additional relevant information from the collaborators (i.e. factor 7 may provide an intervention opportunity). In this way the team identified a previously unrecognized key modifiable factor even though no individual had enough information to think of it on their own.

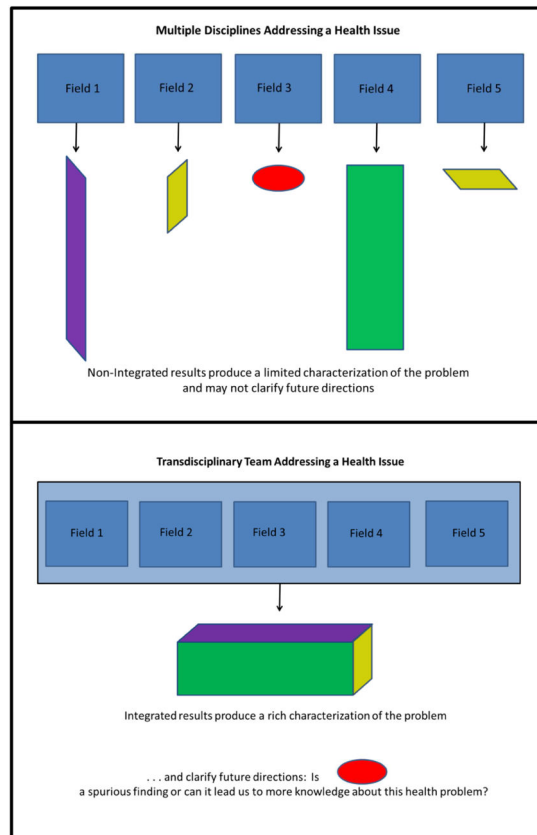


Figure 2. Transdisciplinary approaches coordinate evidence to generate more useful knowledge
 Cross-disciplinary cooperation allows us to see how information from multiple sources can fit together to build our understanding of health issues. *“Science is built up with facts, as a house is with stones. But a collection of facts is no more a science than a heap of stones is a house.”* - Jules Henri Poincare ⁹⁸, p. 127

Table 1

A transdisciplinary advance in analytic epidemiology: Directed Acyclic Graphs

<u>Directed Acyclic Graphs (DAGs) adapted from computer science have:</u>
1. Helped us to better identify adjustments that introduce rather than reduce bias ⁹²
2. Provided a general analytic framework that can explain the “birthweight paradox”, and backs up our common sense notion that trials of prenatal smoking to reduce infant mortality are not a good idea ⁹³

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Table 2

Cochrane Reviews⁹⁴ can convert literature that is unwieldy and inaccessible into evidence that is widely accessible and relevant to decision makers^a

Many doctors and patients may ask: Can vitamin C supplements prevent or treat the common cold (viral respiratory infections)?			
Potential utility	Unclear utility	Feasibility	Safety
Strong evidence suggests that regular vitamin C supplementation can reduce the duration and severity of common colds that occur	The evidence is inconclusive as to whether vitamin C can prevent the common cold or reduce symptoms if it is started after cold onset	Inexpensive	Thought to be without adverse effects.

^aInformation extracted from a scientific abstract and plain language summary that are freely available (in several languages) at the Cochrane website.⁹⁵

Table 3Simple Ways that Epidemiologists Can Promote Transdisciplinary Translational Research^a

A. Incorporate more non-epidemiology concepts and knowledge into epidemiology training	
1	accept students and postdocs who have diverse prior training outside of epidemiology
2	include non-epidemiology experiences in doctoral training (e.g. laboratory, clinical, or policy rotations)
3	encourage epidemiology students to do postdoctoral training in complementary areas (e.g. physiology, demography, public policy, computer science, regulatory agencies, etc.).
B. Diversify traditional epidemiology working environments	
1	present and discuss epidemiologic research at disease specific conferences
2	hire individuals who trained in more than one area, or have a unique background outside of epidemiology (these individuals will share an overlapping vocabulary with people from a separate discipline thus expanding the “fluency” of the epidemiology department)
3	explain and demonstrate the value-added of including epidemiologists in translational team science to the wider scientific community ^{74, 76}
4	invite basic researchers, clinicians, and policy experts to speak in epidemiology departments
5	develop proactive outreach mechanisms for embedding epidemiologists in clinical and basic science departments to promote collaboration.
6	create a multidisciplinary seminar/discussion series to promote information integration and collaboration by focusing on a specific health issue at each meeting and advertising widely
7	offer small pilot funds for projects that access/integrate information from other fields to promote the development of proposals for extramural funding
8	read papers from other disciplines that analyze large complex datasets to better harness diverse perspectives for crucial insights. ⁹⁶

^aIt is possible that structural changes in research institutions and funding sources might further promote transdisciplinary thinking and the success of team science oriented researchers, but the small steps listed here are achievable in the near term and capable of informing potential next steps. Additionally, the epidemiologists that experiment with these small steps could serve as key resources in the development of large-scale transdisciplinary efforts such as the NIH’s Clinical and Translational Science Awards program.⁹⁷ Beyond exploring the specific actions proposed here, the most important thing that we all can do to contribute to the conduct of effective transdisciplinary research is to “hold our knowledge lightly”⁸⁶ and promote a culture of open-mindedness. This receptive yet objective perspective is the oil for transdisciplinary engines. Essentially, it allows for discussions that illuminate crucial information from many disciplines to generate sound and comprehensive reasoning.