Topical Review: Translating Translational Research in Behavioral Science

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Abstract

Objective To present a model of translational research for behavioral science that communicates the role of behavioral research at each phase of translation. Methods A task force identified gaps in knowledge regarding behavioral translational research processes and made recommendations regarding advancement of knowledge. Results A comprehensive model of translational behavioral research was developed. This model represents T1, T2, and T3 research activities, as well as Phase 1, 2, 3, and 4 clinical trials. Clinical illustrations of translational processes are also offered as support for the model. Conclusions Behavioral science has struggled with defining a translational research model that effectively articulates each stage of translation and complements biomedical research. Our model defines key activities at each phase of translation from basic discovery to dissemination/implementation. This should be a starting point for communicating the role of behavioral science in translational research and a catalyst for better integration of biomedical and behavioral research.

Key words: behavioral; behavioral research model; biopsychosocial; translational.

Discussions and debates about the application of translational research have traditionally focused on the translation of basic biomedical research findings into clinical trials and practice. Although models of translational research have been proposed in response to the National Institutes of Health (NIH) roadmap initiative (Dougherty & Conway, 2008; Westfall, Mold, & Fagnan, 2007), they do not accurately represent the role of behavioral science in translational research, despite evidence that behavior has significant ramifications for morbidity and mortality. For over 35 years, we have known that 40%–50% of premature death in the United States is attributable to behavior and lifestyle (e.g., smoking, obesity, alcohol use; Schroeder, 2007; U.S. Department of Health Education and Welfare, 1979). While there has been progress in prevention and treatment of behavioral factors that promote disease, much work remains, and new and additional challenges exist, including nonadherence to treatment, health care seeking, complementary and alternative medicine use, etc. This is particularly true in pediatrics, as patients in this segment of the health care population are developing behaviors and lifestyle habits that will protect or place them at risk for health problems throughout their lives.

With exorbitant health care costs, reaching $2 trillion or $6,000 per capita in 2005 (Congressional Budget Office, 2007), and current worldwide economic trends, it is imperative that the pace of translational research be accelerated to maximize the impact on patient care in the most cost-effective manner. Better understanding of the role of behavior in disease onset and progression and integration of behavioral science into biomedical research has the potential to advance and accelerate translational research.
Moreover, applications in pediatric behavioral science have the potential to have widespread and long-standing impact, as advances in science would have implications across the lifespan. However, a considerable misperception and lack of consensus regarding how and where behavioral science fits into existing translational research models remain as critical barriers to communication and collaboration between behavioral and biomedical science. To address these issues, a task force composed of clinical and research psychologists was formed to review the existing models of translational research in the empirical literature, identify gaps of knowledge with respect to behavioral translational research processes, and make recommendations regarding advancement of knowledge in the general scientific community. In this article, we propose a comprehensive model of translational research for behavioral science to communicate the role of behavioral research at each phase of translation and advance translational research collaboration between behavioral and biomedical science.

**Overview of Existing Translational Research Models**

Though definitions of translational research vary, it has been historically described as the process of taking knowledge gleaned from basic science research and applying it to human clinical trials and ultimately patient care. This gradual translation occurs over the course of multiple observational studies, phases of clinical trials, and dissemination/implementation of evidence-based practice. Although a detailed historical discussion of translational research is not within the scope of this article, the interested reader is referred to more detailed articles on the topic (Dougherty & Conway, 2008; Westfall et al., 2007; Woolf, 2008) as well as the Institute of Medicine (www.iom.edu), the Agency for Healthcare Research and Quality (www.ahrq.gov), and the NIH (www.nih.gov).

Behavioral science has neglected to define itself well with respect to translational research and, importantly, communicate its role in translational research to the broad scientific community. The published literature predominately focuses on translating randomized controlled trial (RCT) research into clinical practice, which is only one piece of translational research. Discussions of translational research have poorly articulated the role and placement of behavioral science in extant models. Woolf (2008) highlighted the role that behavioral science has in translating knowledge of new treatments and prevention methods into practice, but also described behavioral science as a “basic science,” which conveys a limited scope of contributions behavioral science makes. Westfall and colleagues (2007) and Dougherty and Conway (2008) provided excellent models of translational research in alignment with the NIH roadmap and describe activities traditionally associated with behavioral science, such as observational and survey research. Dougherty and Conway also emphasize the role of behavioral science in quality improvement research. However, there is no discussion in these models regarding the multiple ways in which behavioral science can be integrated into biomedical research at each phase of translation or the benefits of such an approach. Thus, the existing models, emphasizing biomedical research translation, are less useful to behavioral science because they are misleading and/or do not capture the types of behavioral science activities that occur at each phase, which consequently de-emphasizes the role of behavioral science across the translational spectrum. Further, these models suggest a fragmented approach to science in which behavioral and biomedical processes operate independently, which is inaccurate and, hence, less helpful to biomedical translational research efforts. Thoughtful integration of behavioral and biomedical translational research is imperative given the large role patient behavior plays in health outcomes. Relevant examples of such integration are evident in the body of research that has led to biobehavioral treatment for pediatric headache, which incorporates the use of cognitive-behavioral pain management techniques, including biofeedback, as well as pharmacotherapy (Powers, Gilman, & Hershey, 2006), and treatment for depression, for which it has been demonstrated through a large number of clinical trials that the most effective treatment is a combination of medication and cognitive-behavioral therapy (CBT; March et al., 2007). Better communication in the general science community of the value behavioral science can bring to health care research will result in better research methodology, more comprehensive analysis of health care problems, and expanded articulation of mechanisms of action, particularly at later stages of translation.

Bender and colleagues (Bender, Aloia, Rankin, & Wamboldt, 2011) recently presented a model of translational behavioral research that articulates the process of translation within clinical research in a stepwise manner, from observational health behavior research to clinical effectiveness evaluation. However, this model is limited in scope and neglects to address the contributions and role of basic behavioral science or the role of behavioral research in dissemination, implementation, or quality improvement research. In our proposed model, we describe each phase of translational behavioral research and the types of research activities that occur at each phase, consistent with the Dougherty and Conway (2008) model. We also provide definitions for Phase 1, 2, 3, and 4 behavioral clinical trials that parallel U.S. Food and Drug Administration clinical trial phases.
The Behavioral Science Translational Research Model (see Figure 1) illustrates the types of research, including specific examples, that occur at each stage of translation, with basic behavioral science (e.g., behavioral theory testing), clinical efficacy knowledge, and clinical effectiveness knowledge representing the milestones along the translational research continuum. The translation to applied science (T1) bridges basic science and clinical efficacy and may involve epidemiologic observational studies, case studies, or Phase 1 trials. Translation to patients (T2) represents the bridge between clinical efficacy and effectiveness and may involve meta-analyses, Phase 3 trials, or health services research. Finally, translation to practice (T3) bridges the gap between clinical effectiveness research and improved quality of health care and population health and may involve implementation or quality improvement research.

In behavioral clinical trials, the objective of each trial phase obviously differs from pharmaceutical trial phases, though the ultimate goal is the same. In Phase 1 behavioral trials, the primary objective is to establish feasibility and acceptability of the treatment protocol. These trials are conducted with small sample sizes that may involve patients or healthy individuals. Phase 2 trials are controlled trials in which preliminary data on efficacy, dosage (i.e., number of treatment sessions), and side effects (e.g., toxicity resulting from successful treatment targeting medication adherence) are obtained using a patient sample that is larger than those in Phase 1 trials. These trials can be blinded or unblinded. Phase 3 trials are blinded RCTs involving larger patient samples with the goal of evaluating efficacy or effectiveness. Phase 4 trials are large multisite trials that are focused on long-term health outcomes and cost analysis.

To illustrate the translational research continuum using this model, we provide a general example from treatment adherence promotion research. A basic behavioral science study might examine the behavioral/emotional factors and processes within families that predict treatment adherence in children with asthma. T1 translation of this study could be a Phase 1 trial examining feasibility and acceptability of a brief family-based intervention to improve adherence by targeting behavioral functioning with four or five families of children with asthma. A Phase 2 trial might be a small controlled clinical trial of this behavioral intervention compared with treatment as usual to establish preliminary clinical efficacy in a sample of children with asthma and their parents. T2 translation would
then establish clinical efficacy using a Phase 3 multisite RCT with children with asthma and their parents. This study could also compare the family-based intervention with an educational intervention used as a control group. Clinical effectiveness would be established via a Phase 4 trial of the intervention using a large clinical sample representative of those seen in regular practice within the clinic-based setting and examining long-term health outcomes (e.g., pulmonary functioning, number of asthma episodes). T3 translation might then use quality improvement methodology and large-scale dissemination tactics to implement the intervention in general clinical practice and examine the impact at a health care systems level (e.g., emergency room visits, hospitalizations) and costs. Table I provides an additional illustration.

**Benefits of Translational Behavioral Research Model**

There are clear advantages to using a translational behavioral research model. It provides a coherent conceptual basis for researchers and clinicians regarding the role and impact of behavioral science on health outcomes. In addition, it can facilitate understanding of how to integrate behavioral and biomedical sciences in a complementary manner by providing parallel processes at each translational stage that can be compared with biomedical models for synergistic opportunities. It can also provide a model for a continuum of translational research: A blueprint with specific steps and key activities at each step for behavioral scientists to follow in order to accelerate adoption of research findings into practice and directly impact patient outcomes. Scientists sometimes operate in silos of translation (i.e., conducting only observational research, only Phase 3 trials, etc.) and do not actively pursue the next phase of translation toward patient care, resulting in slowed application of important research findings in clinical practice. There have been numerous examples over the past several years illustrating the slow process of adopting research findings into practice. These include the 25-year span between demonstration of efficacy to implementation of β-blockers for standard treatment of myocardial infarction (Dougherty & Conway, 2008) as well as evidence-based behavioral treatments for obsessive-compulsive disorder (OCD), encopresis, enuresis, and feeding disorders, among others, which are still not uniformly delivered as standard care.

**Table I. Example of Research Progression Through Translational Stages**

<table>
<thead>
<tr>
<th>Basic behavioral science</th>
<th>T1: Translation to applied science</th>
<th>Clinical efficacy knowledge</th>
<th>T2: Translation to patients</th>
<th>Clinical effectiveness knowledge</th>
<th>T3: Translation to practice</th>
</tr>
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<tbody>
<tr>
<td>Examination of patterns of medication nonadherence and resulting drug efficacy and tolerance in animal models.</td>
<td>Observational study of medication adherence in clinical population. Phase 1 feasibility trial of behavioral intervention targeting nonadherence.</td>
<td>Phase 2 clinical trial examining dosing and preliminary efficacy of behavioral intervention for nonadherence in clinical population.</td>
<td>Phase 3 comparative effectiveness trial examining effect of behavioral intervention vs. chronic condition support group intervention on health outcomes of interest.</td>
<td>Dismantling study to examine most effective components of behavioral intervention. Phase 4 clinical trial examining long-term outcomes and cost-effectiveness of behavioral intervention.</td>
<td>Implementation of behavioral intervention for nonadherence across a large number of sites/practices. Use of quality improvement methods to determine optimal approach to implementation and adherence to treatment guidelines across health care system.</td>
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</table>

**Translational Behavioral Research Examples**

In an effort to address the issue of adopting research findings into practice, our team has successfully navigated the translational research spectrum in targeted conditions to improve care delivery. The first example involves behavioral treatment for regimen adherence in cystic fibrosis (CF). CF is a life-threatening autosomal recessive disorder, which results in thick mucus in the respiratory and digestive tracks. As such, lung functioning and nutrition are critical elements to the care of these patients. CF requires a highly demanding medical regimen, which includes dietary changes, medication, and enzyme use, as well as daily airway clearance. A large body of research exists in the medical literature that has demonstrated the importance of weight gain/nutrition on lung functioning (Konstan et al., 2003), needed caloric intake and enzyme use for sufficient weight gain (Borowitz, Baker, & Stallings, 2002; Ramsey, Farrell, & Pencharz, 1992), and even which types of air way clearance are most efficacious (McIlwaine, 2007). Similarly, there is a strong literature within behavioral medicine/pediatric psychology evaluating how to best meet these medical needs for children with CF and assisting families in reaching
these goals. This line of research includes a number of T1 studies, which are observational or small case series that assess patient-specific and family systems factors, which impact meeting dietary intake goals (Powers et al., 2002) or identifying barriers to various aspects of the treatment regimen (Modi & Quittner, 2006). For example, Powers et al. (2002) identified that mealtime duration, family mealtime interactions, and problematic mealtime behaviors all impacted adherence to intake recommendations, while Modi and Quittner (2006) identified barriers to airway clearance (92% of the sample) and nutrition (69% of the sample), including child oppositional behaviors, forgetting, and poor time management.

The next series of studies aimed to develop interventions to address behavioral concerns of children with CF with the goal of improving both child behaviors and pulmonary functioning and nutritional outcomes (“Clinical Efficacy Knowledge” in proposed model). For example, Powers and colleagues (2005) developed an efficacious behavioral intervention that provided guidelines on reducing meal length, modeled and taught behavior management, and used goal setting to improve toddler adherence to nutritional guidelines and height/weight growth. Similarly, researchers have developed interventions that improve adherence to the CF regimen through contingency management (Bernard & Cohen, 2004; Stark et al., 1996).

The next important step in translational research was to take these findings and apply them to a medical inpatient unit (“T3” in proposed model), which cares for children and adolescents with CF at Cincinnati Children’s Hospital Medical Center (Ernst et al., 2010). In 2001, increased national focus was placed on the discrepancy between recommended (evidence-based) treatment and actual care delivered (Institute of Medicine, 2001). Quality improvement/health care systems research is an excellent tool for applying evidence-based care within the complicated real-world setting, where each system has unique barriers regarding implementation. Within our CF center, during an admission for a pulmonary exacerbation, airway clearance is prescribed four times a day. Baseline data indicated that only 41% of patients were receiving airway clearance four times a day and the quality of the airway clearance was poor, with only 21% of treatments meeting best practice guidelines. Ernst and colleagues (2010) conducted education workshops with respiratory therapists (RTs) and implemented a multidisciplinary intervention (pulmonologists, RTs, psychologists) targeting patient behaviors (“T3” in proposed model). The intervention included contracting with the patient airway clearance expectations, schedule of treatments, and type of treatment patient will do during the admission; behavior monitoring of best practice airway clearance behaviors and techniques; and contingent positive reinforcement in the form of a token economy.

The multidisciplinary unit-wide approach to the project was novel. Although a pediatric psychologist was integrally involved in the whole quality improvement process, the RTs were responsible for ongoing management and implementation of the strategies that were taught. This T3 project demonstrated considerable improvements with quality (from 21% to 73%) and quantity (from 41% to 64%) of airway clearance adherence. Following the implementation of this project, the consistency of conducting quality airway clearance routinely has been maintained on the unit.

A second example demonstrates another T3 level project, which served to improve the delivery of evidence-based care in the outpatient setting. OCD is a condition for which there is a well-established empirically based treatment, CBT with particular emphasis on exposure and response prevention (March & Mulle, 1998). Before the implementation of this T3 project, psychologists varied greatly in their adherence to this evidence-based protocol, and thus patient outcomes varied. The overarching goal of this long-term project was to assure that any patient presenting to the Division of Behavioral Medicine and Clinical Psychology at Cincinnati Children’s Hospital Medical Center for treatment of OCD would receive the prescribed evidence-based treatment, effectively and efficiently, regardless of the clinician treating the patient. While most psychologists in the division had received training in CBT, including Exposure and Response Prevention, mastery of these skills varied and the first step to this project involved a day-long seminar in the treatment of children and adolescents with OCD. The improvement team then developed a manual (“T2” in proposed model) that included guidance on the components of treatment and relevant resources (e.g., exposure hierarchy forms, fear thermometers, symptom severity measures). To further build on the information provided in the initial training and the treatment manual, the team provided periodic 1-hr continuing education presentations. These trainings aimed to increase mastery of skills by addressing, for example, means of conducting exposures with challenging OCD symptoms. Ongoing case presentations with group discussion further facilitated consistent use of evidence-based strategies, as well as the implementation (“T3” in proposed model) of relevant tools that were tried and proved to be useful through the “small tests of change.”

Perhaps the most useful improvement resulting from this project was the development of a session-by-session outcome measure (“T1” in proposed model) that greatly enhanced the value of services and patient experience. The project initially used an outcome measure that was too cumbersome for routine
practice, so the team developed a simple measure that ascertained the child’s control of symptoms, distress associated with the experience of OCD, and functional impairment, which are all goals of treatment. This measure was found to be highly reliable ($r = .89$ with gold standard) and more efficient. The team used quality improvement methodology (“T3” in proposed model) to “spread” the use of this measure so that clinicians were using it consistently and regularly. Two years following the end of the project, this measure is used in 95% of treatment sessions. Its use provides immediate feedback about progress on goals and patterns of symptom severity, prompting discussion and problem-solving to move treatment along at a more efficient and effective rate. The resulting briefer course of treatment yields benefit to patients and their families by bringing about quicker relief from symptoms and value in the form of reduced health care costs.

These projects are two exemplars for the bench to bedside translation in behavioral health; yet, there are numerous other areas in which behavioral research has yielded significant improvements for patients across the proposed translational model. However, there are several areas in which efficacious treatments are not implemented at the bedside. Further, despite the potential impact on population health, T3 translational work is uncommon across the health care system, particularly in behavioral science. One recent biomedical example of T3 translation in pediatric inflammatory bowel disease has demonstrated improvement in remission rates within a large multicenter collaborative in which standardization of care is heavily emphasized (Crandall et al., 2011). With new health care system policies increasing the focus on integrated care at lower cost, combined with a growing demand for complex and chronic care, it is increasingly important for behavioral and biomedical scientists and clinicians to streamline and expedite the translational process.

Remaining Challenges

There are several barriers that exist to widespread adoption and application of this model in research and practice. The perceived need to fit behavioral translational research into a traditional biomedical translational model has resulted in significant difficulty in behavioral science’s ability to coherently define its role in the translational process. The proposed model, however, provides a complementary approach that indicates an integration of biomedical and behavioral research. Indeed, the lack of thoughtfully integrated biobehavioral research in many medical and behavioral conditions has slowed the translational process. Collaboration between biomedical and behavioral researchers in the early stages of theoretical and applied research will help facilitate a comprehensive understanding of these conditions and facilitate application at the bedside. In addition, the scientific community’s traditional categorization of research (i.e., biomedical vs. behavioral, basic vs. clinical) may not encourage investigators who are seeking funding/publication to examine both the biological and behavioral underpinnings of conditions or to work on various projects along the translational spectrum. Unfortunately, this approach results in restricted collaboration and creativity, both of which are needed to successfully integrate biomedical and behavioral science.

Our field’s ability to bridge the collaborative gaps between behavioral and biomedical science has substantial implications for research, practice, and public health policy. A broad understanding of disease etiology and sequela, both medical and behavioral, will inform development of better therapies that can be tested and implemented in practice. This approach would allow for better understanding of the impact of disease on medical outcomes as well as behavioral outcomes including quality of life, psychosocial dysfunc-
tion, and functional disability. Moreover, a comprehensive translational approach would allow us to better account for health care costs for treatment of various conditions, which would significantly inform health care policy and standards of practice.

Conclusions

Behavioral science has struggled with defining a translational research model that effectively articulates activities at each stage of translation and complements biomedical translational research processes. Our model defines key activities at each phase along the translational process from basic discovery to dissemination and implementation of evidence-based treatments. There have been recent exemplars for translating behavioral trial research to the bedside, though many other conditions could be effectively treated with better implementation of behavioral treatments into practice. Thoughtful integration of biomedical and behavioral science early in the translational spectrum is necessary to realize the full potential benefit of comprehensive multidisciplinary health care from treatment outcome and cost savings perspectives. This model should serve as a starting point for communicating the role of behavioral science in translational research and as a catalyst for integrating biomedical and behavioral research more thoroughly.

Conflicts of interest: None declared.
References


