

Summary Conference Proceedings: Translating Clinical Trials Outcomes to Your Practice

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Abstract

Background: The use of scientific evidence is crucial to the development and success of dentistry, particularly when it comes to assessing and improving patient outcomes. A full understanding of the research process, including the systems in place to protect data integrity, independence and lack of bias, is an important part of translating research into clinical practice. Improved precision, quality and clarity of methods, can result in a more robust and informative dataset which can be better translated into precise, improved patient outcomes.

Objective: To assist practitioners and researchers in understanding clinical research and how it can be translated to patient care, the Council on Scientific Affairs from the American Dental Association (ADA), in collaboration with the Task Force on Design and Analysis in Oral Health Research, worked together to develop a research conference at the ADA Headquarters in Chicago at the end of 2016. The overarching goal of the conference was to highlight existing checkpoints that researchers have to go through - from preclinical validation to the development, execution and publication of clinical trials - and to help clinicians develop their decision-making skills relative to evidence acceptance or rejection.

Overview: Presentations were made by nine leaders in clinical research (both public and private sector), regulatory processes, and dental education, who discussed a wide range of topics involving transparency in research, dissemination channels, educational outreach, data collection tools, and the role of industry-sponsored research. This report provides the proceedings of the conference on the relationship between funding sources, investigators and publishing policies; and the potential for bias.

Implications: It is essential that clinicians have an understanding of the research process, including the checks and balances that provide transparency and improve the quality of clinical research. This understanding can improve decision-making skills relative to clinical research and ultimately result in improved patient outcomes.

Introduction

In view of periodic concerns by a variety of groups (Schwendicke et al. 2016) about the generalizability and potential for bias of industry-sponsored research, there is a need to discuss in detail and clarify the nature of the relationship between funding sources, investigators and publishing policies to determine whether such concerns are warranted. Dental researchers and clinicians are often not aware of the various safeguards that are in place to help assure the validity of new drug and device testing, as well as clinical trial outcomes. Once research outcomes are available, the oral health research community often faces barriers on how to effectively share these outcomes in ways that lead to their use in improving patient care. One barrier that must be overcome is identifying which methods and strategies for disseminating research outcomes result in dentists becoming not only informed but confident consumers of the scientific literature, leading to an understanding that the scientific literature is a valid method to inform clinical practice. Once that confidence is established, the remaining challenge is to develop effective implementation strategies that address the barriers found in clinical settings that prevent dentists from readily adopting new, high quality scientific evidence that can lead to improved patient outcomes.

The Council on Scientific Affairs from the American Dental Association (ADA), in collaboration with the Task Force on Design and Analysis in Oral Health Research, worked together to develop a research conference at the ADA Headquarters in Chicago at the end of 2016. The overarching goal of the conference was to highlight and reinforce existing checkpoints that academic and industry researchers go through during the development, execution, publication and dissemination of clinical research. In addition, the speakers were asked to explore strategies that would improve the likelihood that dentists adopt and routinely employ the best evidence in support of clinical decision making. For dentists to do this, it is required that they not only understand the research process, but trust that it is delivering valid, patient-care relevant results. That trust is built in large part on dentists having the skill to assess research quality such that they understand when evidence is valid and when it should be rejected due to excessive bias or lack of relevance to their patients. When armed with that understanding, they can become effective consumers of the scientific literature and apply it with confidence in patient care. The proceedings of this conference are designed to support such an understanding and assist clinicians in decision-making relative to evidence acceptance or rejection.

Translating Research into Effective Care

The ultimate goal of clinical research is to improve patient and population health outcomes. (Tunis et al. 2003) To do this generally requires that we transform the very nature of clinical practice. Prior to the 19th century, science lacked an objective, reality-based method for assessing the validity of previously-held beliefs, superstitions, or magical thinking. However, the shift away from this mental model happened in what Dr. James Bader characterized as the four ages of dentistry (Bader 2009) (Table 1). The first age is the age of expert, where personal experience drives knowledge, and most specialized dental knowledge was disseminated informally from person to person, most frequently through a master-apprentice system. Towards the end of this era, an appreciation for evidence began to develop. While most continued to ignore the importance of "evidence," it ushered in the next era: the age of the professional. The third age – the age of science - saw the advent of data and a focus on methodology.

Of note, scientific methodology continued to improve (thus limiting the impact of human bias), and there was a general standardization in how we identified acceptable levels of evidence. During this age we also moved from case studies to randomized controlled trials (RCTs), and began to use the latter in assessing treatment efficacy. Lastly, the introduction of technology like MEDLINE improved the way that we maintained our knowledge base.

The final age – that of evidence – has emerged over the last thirty years. The result, now termed evidence-based medicine, was developed in large part by Drs. Gordon Guyatt and David Sackett, at McMaster's University, in the early 1990s. Their model was in response to the growing need among busy clinicians for improved accessibility to patient relevant information that could be easily retrieved from the rapidly expanding evidence base of clinical research. With rapid increases in available therapies and technologies, the availability and prevalence of biomedical literature increased quickly, and to such a scale that busy clinicians were often overwhelmed with evidence, which impeded their professional obligation to stay current in an ever-changing world.

Table 1: Four Ages of Dentistry (Bader 2009)

1. Age of Expert	Personal experience drives knowledge; most specialized dental knowledge disseminated informally from person to person, most frequently through a master-apprentice system.
2. Age of the Professional	Dental knowledge disseminated through scientific literature; professional knowledge gained through formal dental programs in university.
3. Age of Science	Advent of data gathering and collection; dental knowledge focused on methodology and efficacy; focus of research moves from case studies to more formal studies, such as random controlled trials (RCTs).
4. Age of Evidence	Increased focus on scientific literature as the basis for making informed decisions; widespread dissemination of scientific literature and a professional obligation to remain current in dental knowledge.

Modern research continues to evolve in all aspects, including a solid scientific methodology for creating relevant evidence, a strong infrastructure for funding and conducting research, effective regulation keeping ineffective treatments at bay, and methods to better synthesize and disseminate information. What lies ahead for dentistry involves the implementation of research, including the routine deployment of new evidence into care. Implementation is heavily dependent on setting or context, and it remains unclear whether implementation strategies that work in nursing homes or mental health facilities will work in dental clinical settings. Ultimately, patients cannot benefit from interventions they do not receive, and developing effective implementation strategies for dental clinical settings should be a major goal of our research agenda. There is no general solution to implementation; strategies will need to be developed on a case-by-case basis. Despite this challenge, the ADA is working to move this goal forward by developing and implementing high quality evidence through its evidence-based efforts and programs,

and making it more readily accessible and better understood throughout the profession (American Dental Association, Center for Evidence-Based Dentistry, 2017).

The Use of Guidelines to Improve Pre-Clinical and Clinical Studies

Scientific studies are incredibly valuable, but much of that value can be lost if the information gleaned from these efforts do not find their way into clinical use. Editorial rigor establishes a level of quality that, when layered with clarity, builds credibility and a preponderance of proof. These all work together to create a crucial level of public trust, which is the most important trait of any successful journal. The landscape of scholarly publications has become more challenging under an expanding number of regulatory bodies, including groups from the government and from research foundations. Publications engage the peer-review process and require meeting the scientific rigors through multiple evaluators and iterative revisions until finally being acceptable by consensus. These editorial requirements and guidelines can help reduce bias within the system and improve the quality of reporting, resulting in a study that the public is more likely to trust and implement. These goals speak to a broader aim: to better facilitate a path from regulatory approval to patient care and outcomes.

The need for disclosure of conflicts of interest or potential perception of conflicts of interest establish a high bar for avoiding bias. The transparency of methodology prior to implementation and of results prior to publication is an important step when seeking to translate clinical research to patient care. Establishing transparency and consistency can be done through various channels, many of which are now commonly-used tools. One method, to ensure transparency, growing in popularity is the use of open access study registries, such as ClinicalTrials.gov, which is provided by the United States National Institutes of Health (NIH). Registries like this allow researchers, clinicians, and even patients to access study information and results that can help to better inform their future decision making. Publishing a project's findings is one of the most important ways of disseminating results, but trials can be hard to find, and more than one third of NIH-supported clinical trials never end up in publication, often due to negative results. Requiring registration of clinical trials can help communicate the existence of research, and encouraging the publication of findings, regardless of outcome. To meet this challenge the ADA is committed to providing readily-available, practitioner-accessible summaries of important and contemporary information on clinically-relevant topics.

In addition to transparency, consistency can allow for more informed analyses. The use of checklists such as CONSORT (Consolidated Standards of Reporting Trials) (Moher et al. 2012) or STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) (Sanderson et al. 2007) for human studies and ARRIVE (Animal Research Reporting In Vivo Experiments) for animal studies (Kilkenny et al. 2010) can ensure that research is being done in accord with basic best practices with regard to authorship, funding, and conflicts. They can also provide clarity on recruitment and assessment of patients within a study and refine the quality and focus of clinical research. While these checklists can be an additional layer to the publication in many journals, much of them are generally in harmony with existing university guidelines.

The interaction between the publication, academic, industry, and regulatory domains is an important one. While the use and volume of regulation and checklists required by journals has increased over time, the ultimate goal of these efforts is to improve the quality of clinical and preclinical studies, and to provide more transparency in the process.

NIDCR: Overview of Clinical Trials Portfolio

One of the main drivers in dentistry's forward movement comes from governmental sponsorship and facilitation of clinical research. In the United States, that governmental body is the National Institute of Dental and Craniofacial Research (NIDCR) within the National Institutes of Health (NIH). NIDCR was founded in 1948 and supports the majority of dental research funding and nearly all dental research training at NIH. At NIDCR, clinical research is generally funded in two ways: intramural (internally) and extramural (externally).

In 2016, clinical research comprised a little more than one third of NIDCR's portfolio, of which approximately 13% were clinical trials. One method of diversifying NIDCR's research portfolio is through its collaborations and partnerships with external groups. A current collaboration with the National Academies of Sciences led to the Regenerative Medicine Forum, whose goal is to address the gap between research funding and patient application (Sciences engineering medicine, health and medicine division 2017). Another valuable channel is the National Dental Practice-Based Research Network (NDPBRN) that encourages practitioners to generate a database of evidence. More than 6,000 practitioners - enrolled across all 50 states - are involved in a variety of studies, including those on predicting pain outcomes of root canal therapy, HPV screening for oral cancer risk, and opioid prescribing practices in dental offices (The national dental practice-based research network, 2017).

Several important factors for translating and ultimately adopting the findings of clinical research are rigor, reproducibility and transparency, and implementing policies to address and improve these factors is paramount for translating clinical research. The NIH is currently working to improve all of those factors across all of their clinical research projects. These policies target key points along the lifespan of a clinical research project. Despite the fact that more than half of research participants are women, most animal studies had been conducted in male animals. In order to prioritize and address this research gap, the NIH implemented a policy requiring scientists to account for the possible role of sex as a biological variable in vertebrate animals and human studies.

The NIH, while not a regulatory agency, can help researchers navigate their relevant regulatory requirements, and provide a pathway to successful clinical trials. Continuing to analyze the various factors involved in research gaps can assist organizations like NIH/NIDCR in improving the rigor, reproducibility and transparency of their clinical research and reducing the time and barriers to translating research into improved patient outcomes.

How Dentists Gain Information About Evidence-Based Practices: Should Clinicians Consider Industry Funded Studies As Biased?

Bias is defined by Cochrane as “a systematic error, or deviation from the truth, in results or inferences.”(Assessing risk of bias in included studies, 2017) When bias exists the truth or evidence is often distorted by personal perception, experience, or other motivation. Bias can be found throughout the entire study process, from funding source to randomization, intervention delivery, patient retention, outcome assessment, and reporting. Current practice does not consider funding sources as a risk of bias, but the potential risk of bias related to financial incentives is more nuanced. A recent study from Cochrane explored both sides of this issue, and specifically “whether industry sponsored drug and device studies have more favorable outcomes and differ in risk of bias, compared with studies having other sources of sponsorship.”(Lundh et al. 2017) The study found mixed results, which further opens the discussion of bias, its sources, and how it may impact the scientific community in different ways.

On one end of the argument, the study found that industry-sponsored studies more often had favorable efficacy results, harms results, and conclusions compared with non-industry sponsored studies.(Lundh et al. 2017) It also found that industry-sponsored drug and device studies led to more favorable results and conclusions than sponsorship by other sources.(Lundh et al. 2017) While industry studies were found to show more favorable results, the review also found that industry-funded studies have a lower potential for bias related to blinding, likely due to the regulatory approval standards related to study design.(Lundh et al. 2017) These results provide conflicting views of industry-led bias. However, there is a publication bias in that negative findings are not often perceived as worthy of publication. The study also identified additional areas of potential bias that could be found in industry-funded studies, including the use of an inferior or unfair comparator, data analysis, selective outcome reporting, and publication bias. What is important to note is that both academic and industry-funded research have conflicts of interest in relation to study results. While the industry's financial conflicts may be easier to see and measure, the intellectual conflict of interest found in academia is a key piece that can be just as harmful. Because studies with favorable results can have an immediate and direct impact on a company's ability to market a product, there is an underlying assumption that industry may choose not to publish studies with less-than-favorable results. In fact, the opposite has been shown to be true. A higher percentage of registered, industry-led studies saw publication compared to those led by academic or government institutions. (Lundh et al. 2017) It should be emphasized that industry-sponsored research can lead to the final release of products to improve oral health and no company is served by releasing products which are potentially harmful or ineffective.

With these factors in mind, there is little evidence that trial methods are more likely to be flawed, or evidence fraudulent when generated by industry, and it is important to remember that industry-led studies utilize highly-skilled professionals (often academic researchers funded by federal grants in state-supported, university laboratories) whose research is constrained by highly regulated and standardized procedures. It should also be noted that many journals now require authors to list financial conflicts of interest as a requirement of publication. There remains conflicting opinions on funding as a source of bias, as explored above. While some may argue that bias should not be ignored, and that funding source should be examined, even where it is not necessarily fully understood, others argue that doing so may unfairly communicate a bias to industry studies and divert attention from needed improvements to

industry trials. I would ask readers to explore their thoughts on these factors, and the full spectrum of bias, including financial and intellectual conflicts of interest, present in both academic and industry-led studies.

Facilitating the Pathway from Innovation to Patient Care

The development of a clinical product may take several years, and there are some critical steps along the process that should be followed to ensure the safety and efficacy. Translational Science teams welcoming a multidisciplinary team will offer the required expertise to provide direction along the multiple phases of the development. A major component is the transition from academia to industry, when the idea/product will change hands. The collaboration between academia and industry is essential, and finding the right partner, at the right time, will increase the chances to get to the finish line. In exploring the role of industry in research, it's important to also explore the industry-academia partnership model. This model, while perhaps more common outside of the US, is growing in popularity domestically for its ability to infuse a more holistic view of the research and development process into dental education. This kind of model can help to propel translational research forward, aligning research with resources, and creating channels for both academia and industry to thrive. Dental students who are educated in translational research learn about the end result and the efforts required to bring a product to market. The knowledge transfer required to push translational research forward is a key component, and can be much more difficult than the technology transfer. Educating students on the full spectrum of research and the ways those results translate to working products can result in practicing dentists with a better understanding and appreciation for new technologies and their clinical implications, and helps create an openness to new developments and innovations that pushes the industry forward at the clinical level.

This model of dental education is also a valuable way to diversify funding for academic research. Through partnerships and established relationships across academia, government, foundations and industry, funding can increase and stabilize. These relationships, in conjunction with academic patent policies, can expand patent portfolios and create an internal, self-sustaining funding source. This diversification becomes increasingly important as Federal funding becomes harder to find. Programs with established industry relationships can attract visiting scientists from industry and academia, industry partners may find value in encouraging their employees to pursue advanced degrees at universities with industry relationships, and students, with the holistic education that these programs provide, can bring incredible value to industry research teams. As students continue to graduate from programs with a focus on translational research, the roles they continue to play in both industry and academia help to create a long-lasting, sustainable, and valuable partnership model that can assist in the knowledge transfer necessary to bring innovation and research to the patient.

Use of Oral Health Records in Dental Research

Disease prediction & prognosis is imprecise and often subjective, which creates a challenge for practitioners seeking to implement more personalized and effective evidence-based patient care.

Currently, periodontal disease classifications are based upon history, clinical signs and symptoms as well as treatment needs. In reality, diseases such as chronic periodontitis or gingivitis can actually be multiple conditions with similar and overlapping clinical presentations with differing etiologies and cofactors, and responses to therapy vary widely from patient to patient. In order to better arm clinicians with the information necessary to effectively treat the individual, new tools for precision diagnosis and measurements of treatment outcomes are required. These tools and metrics can lead to new diagnostic and therapeutic strategies that emphasize underlying factors and more clearly identify causality. This process can help to create a more precise level of patient care and better understanding of health outcomes.

In order to improve the precision of patient care, we must first increase the strength of our data. To do so, two key areas must be examined: identification of underlying factors and treatment options, and a coding system to capture and track those nuances within patient datasets. Diagnosis of chronic periodontitis is often based on clinical phenotype, but should be based upon a biological phenotype. There is a lot of biology underpinning clinical presentations – everything from common environmental exposures, genomic determinants and biological phenotypes – but outside of common biological markers like sex or age, these underlying factors are rarely examined. This underlying variety can pose a problem when diagnosing at the genetic level, as effective genetic analysis requires a homogenous population of disease. Looking at genetic variants can provide insight into mechanisms of pathogenesis and can help researchers define different molecular/microbial pathways associated with disease; however, many of these methods produce information on populations, not individuals. The ultimate goal is to separate out the heterogeneity within the population to create stratified groups of patients (or “buckets of similar patients”) for which more tailored responses can be developed. In order to improve patient-level responses, populations must be divided into subgroups using clustering techniques like latent class analysis (LCA), which works to identify traits that might otherwise be non-observable. LCA involves a disease-agnostic stratification using both patient and tooth classifications. (Morelli et al. 2017) While diagnostic tools like LCA are valuable for precision treatment, they can only be successful when paired with more robust data collection tools. One potential method of data collection and standardization includes a more robust coding system that can capture a patient's score by establishing profiles that incorporate parameters such as tooth loss as well as clinical periodontal status. For complex systems, standardization is both novel and critically important. There is a gap in our profession when it comes to measuring treatment outcomes. Diagnoses like severe periodontitis or diabetes often remain attached to the patient forever. By capturing and collecting better outcome data in this way, clinicians and researchers can improve the quality of longitudinal cohort studies and case-control interventions, which generally determine who is at risk, who should be treated, and how.

Improving phenotype precision is an important enabling tool for moving into precision, patient-centered care. Working to improve the quality of the data and its collection can assist in better determining the need and effectiveness of treatments on the individual patient. The advantages of considering various biological and genomic profiles and patterns, in addition to traditional clinical signs, are clear when applied to a variety of diseases, and provide an improved avenue for individualized care.

The Relevance of Industry-Sponsored Research

Industry-sponsored research (often in the form of clinical studies) are a crucial component of industry development, public safety and product improvement. The U.S. Food and Drug Administration (FDA) regulates a wide variety of dental products, including drugs, devices, biologics, cosmetics, and foods. Each of these categorical classifications are subject to their own regulations. For all regulated products, the FDA's goal is to ensure its safety and efficacy prior to public consumption. As part of this regulatory process, the FDA requires a lengthy and rigorous clinical testing process for all prescription drugs, and some OTC drugs. As practitioners are increasingly looking towards incorporating evidence-based decision-making in the clinical environment, it is important to understand how these trials are conducted within the regulatory environment, and how the FDA acts as a neutral buffer between corporate interest and public safety. Because industry research is often done as part of the FDA approval process (Tunis et al. 2003), they utilize stringent and consistent guidelines, methodologies and measures, which can provide a useful and effective framework for analyzing findings and comparing products.

Similarly, safety requirements and standards, as developed by groups such as American National Standards Institute (ANSI)/ADA and International Organization for Standardization (ISO), play an important role in industry-sponsored research. (International Organization for Standardization 2011) In addition to a product's safety, clinical studies also establish efficacy requirements. These studies are developed and performed in accordance with good clinical practice (GCP) guidelines set forth by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and FDA guidance. (Use 2016)

Clinical research can be brought to the public in a meaningful way through channels like the ADA Seal of Acceptance program (Seal), which analyzes product safety and efficacy. Requiring safety and efficacy studies, and ensuring that data is generated using current and relevant methodologies, helps to maintain the scientific integrity of the research. While the mechanisms for establishing a product's safety and efficacy through clinical trials are important, getting that information to the public is equally important. Part of the FDA's approval process involves the approval of product labeling included as a package insert. Product inserts help the patients to have informed conversations with their healthcare providers, who decide the most beneficial course of treatment for each case. Product labeling can also be used by the clinicians to educate their patients on potential side effects or risks related to the treatment.

The innovation funded by industry can be tapped by independent researchers in academia who can contribute to innovation by developing protocols, techniques or methodologies from bench to chair. In addition, collaboration fosters an improvement and enhancement of communication between independent researchers and industry.

Alternatives to Communicate and Disseminate Research Outcomes

Despite many of the efforts to communicate results, the impact on practice behavior has not been high. One way to measure this impact is to look to recent areas of study that have widespread application and clear clinical results, such as sealants. For example, the extensive research focus and industry

communication that sealants are an extremely effective cavity prevention tool had little impact on actual implementation; more than half of children in the U.S. do not have them (regardless of income level). (Griffin et al. 2016) This type of gap is common, as the traditional path from basic discovery to clinical research, adoption and global application is long. However, support from various funding groups, such as NIDCR has increased recently with regards to reducing the time between discovery and adoption, and “de-implementing” the use of interventions that are no longer supported by current evidence.

Implementation science addresses many of the common barriers to adoption, which are often at the root of implementation gaps. One way of addressing these implementation gaps is through educational outreach. While practitioners may be more familiar with the industry form of this (an office visit from an industry representative), this method can also be used by research groups to improve practices through the identification of potential implementation barriers. In-person interviews can identify baseline knowledge and motivations for current clinical patterns, and can be used to create clear education or behavioral objectives focused at specific categories of clinicians. This face-to-face outreach can also help to establish research credibility through the presentation of unbiased, balanced information on controversial issues, as well as the use of graphic educational materials, key messaging, and positive reinforcement. Two examples of studies that utilize forms of educational outreach can be found in the United States and Europe: these innovative approaches to improving implementation involve analysis of current clinical practices as a means of improving patient outcomes.(An innovative approach to disseminate dental research, 2017), (Advocate consortium, European Union's Horizon 2020 Research and Innovation Programme, 2017) In one current NIDCR study using simulated patients, treatment planning patterns are analyzed after exposure to evidence-based simulations and feedback support(An innovative approach to disseminate dental research 2017). This study expects to show that future treatment planning will begin to reflect successful, evidence-based decisions following simulation exposure. In another study, the ADVOCATE program seeks to collect and analyze oral health data across six European countries in public and private insurance schemes. (Advocate consortium, European Union's Horizon 2020 Research and Innovation Programme, 2017) While still in its planning stage, future data will be used to create a feedback platform for dental practices that incentivizes preventive approaches over restorative for better health outcomes. In looking at current trends and patterns in science-based treatments, it becomes clear that publishing, presenting, and distributing research findings is insufficient to alter practitioner behavior. Adoption of the more interactive tools of implementation science can offer a ways to improve clinical practice and patient outcomes.

Conclusion

This conference was intended to discuss existing guidance and mechanisms currently utilized in clinical research, as well as to highlight potential areas where additional steps or practices may be employed to support the translation of clinical data to patient care. It was also designed to provide an understanding of the relationship between funding sources, investigators and publishing policies. The potential for bias and the existing checkpoints were discussed, in addition to the alternatives to disseminate research outcomes.

Key findings:

- With the rapid increase in available therapies and technologies, the availability and prevalence of biomedical literature has increased, as professional obligation requires one to stay current in an ever-changing world.
- Scientific journals are increasingly utilizing submission requirements such as open access registries and checklists to encourage consistency and transparency in the publication of clinical research.
- Conflict of interest statements by authors can be helpful in reducing bias in publications.
- There is little evidence that trial methods are more likely to be flawed, or evidence fraudulent when generated by industry, and it is important to remember that industry-led studies utilize highly-skilled professionals whose research is constrained by highly regulated and standardized procedures.
- Regulatory bodies act as a neutral buffer between corporate interest and public safety in that they can help reduce bias within the system and improve the quality of reporting, resulting in a study that the public is more likely to trust and implement.
- Increasing the strength, quality, and classification of clinical research data can help to improve health outcomes and result in better patient care.
- A crucial element in translating clinical research for public impact is the transition from academia to industry. The collaboration between academia and industry is essential, and finding the right partner, at the right time, will increase the chances to get to the finish line.
- Implementation science addresses many of the common barriers to adoption, which are often at the root of implementation gaps. One way of addressing these implementation gaps is through educational outreach.
- There is no general solution to implementation; strategies will need to be developed on a case-by-case basis.

These proceedings should provide a valuable tool for both researchers and clinicians to apply the outcomes of research to chairside patient care.

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