Not Your Average CRO

NERI was founded in 1986 with a unique mission: “No Research without Therapeutic or Policy Benefit.” This enduring vision has driven more than three decades of research on rare, orphan, and underserved diseases, as well as many studies in special populations of patients such as pediatrics, the elderly, and minorities.

NERI has translated its core mission into tangible results for patients and clients alike by being nimble, flexible, and uncompromising in its scientific rigor. Three recent projects illustrate these corporate traits, which set NERI apart from other contract research organizations (CROs).

Nimble is Better
NERI’s relatively small size and flat organizational structure endows it with an ability to quickly and efficiently adapt to the changing needs of its clients. For example, NERI was providing full CRO services for a client engaged in a large multi-center, randomized trial.

Continued on next page...
of a coronary stent (a device to help open the blood vessels of the heart). During the course of the trial, the client decided to expand the trial internationally. NERI’s long experience with international trials, and its extensive contacts in many countries, allowed our team to quickly partner with on-the-ground local experts for regulatory submissions and site monitoring. When needed, we engaged local CROs as sub-contractors who had country-specific expertise in coronary implantable devices, regulatory pathways, and monitoring. NERI’s smooth facilitation of the greatly-expanded trial contributed to the success of the research and to practice-changing results that are still being talked about.

**Flexibility in Action**

NERI’s 30-year experience in the field of sickle cell disease attracted a client looking to execute a Phase III randomized trial of a drug for pediatric patients with this disease. After the trial was underway, the client’s scope of work increased dramatically with a tight timeline for deliverables. NERI was flexible enough to scale-up personnel and other resources in order accommodate the increased scope of work and timelines, allowing the client to meet its deadlines and deliver results that promise to be transformative for these young patients.

**Rigorous Science**

One key to NERI’s longevity and success is the dedication and passion of our scientists. Our people are our greatest assets and the wellspring of the scientific integrity that permeates our corporate culture.

This well-known attention to scientific rigor drew a top medical device company to NERI for regulatory strategy and design of a Phase III trial for an endovascular graft to treat abdominal aortic aneurysms. After our initial consulting agreement on regulatory strategy, endpoint determination, and protocol design, the client was impressed enough to award us the data management, statistical, regulatory consulting, medical writing, and safety management aspects of the project. Because the client was so satisfied with NERI’s work on the Phase III project, they decided to shift the statistical analysis and medical writing tasks on an existing First-in-Man (Phase I) trial from an existing vendor to NERI. This work then led the client to award NERI a third contract for post-market surveillance that involved project management, site management and monitoring, safety management, data management, statistical analysis, and medical writing. This string of projects demonstrates the outstanding scientific excellence, organizational skills, and efficient implementation of the NERI team.

To order additional copies, or obtain further information on NERI projects and scientists, please contact media@neriscience.com

The content of this newsletter is solely the responsibility of the authors and does not necessarily represent the official views of any funding source or sponsor.
Transinstitutional Research: 
NERI is a Research Hub

For health care educators and researchers, Boston is an unrivalled location. With its plethora of world-class universities, medical centers, private health care-related companies, and community organizations Boston offers an extremely diverse range of opportunities for collaborative, cutting edge research and interventions involving teams with nationally and internationally respected experts working to address major public health challenges.

NERI has long capitalized on its Boston-based location to creatively integrate clinical and scientific talent from the many health care-related organizations in the area. We term our unique approach “transinstitutional.” Our work often cuts across traditional institutional boundaries and we can effectively draw upon international expertise available at different (and sometimes competing) universities and medical centers.

It is not unusual for our projects to involve close collaborations with clinicians and scientists from, for example, Boston University Medical Center, Massachusetts General Hospital, Children’s Hospital Medical Center, the Beth Israel and Brigham and Women’s Hospitals, the Massachusetts Institute of Technology, Brandeis University, the University of Massachusetts and numerous local community agencies and companies.

Collaborating colleagues at these centers often contribute to NERI’s ongoing Brown Bag lunch time seminars. NERI’s Senior Vice President, Dr. John McKinlay, remarks, “When I was a professor undertaking research at a major local university, I was quite reasonably expected to engage only with others at my university, even though greater local expertise may have been readily available elsewhere. At NERI, we have the freedom to assemble the very best team for any job without the usual organizational constraints.”

The combination of NERI’s ideal geographical location, its transinstitutional relationships, and experienced staff means we can follow the sports dictum, “play the team you need, not the team you have.”

“At NERI, we have the freedom to assemble the very best team for any job without the usual organizational constraints.”

JOHN MCKINLAY 
NERI SENIOR VICE PRESIDENT
What Gets Diabetes?

Some years ago a research colleague asked a beguilingly simple question: “What gets cancer?” This odd-sounding question reflected his astute awareness that the causes of any disease can be viewed at a number of different levels, which, in turn, can be explored by scientists with different perspectives and research methods.

Our colleague, for example, noted that his question could be answered many ways: you could say that a gene “gets” cancer, or a specific organ or organ system “gets” cancer. You could also say a person “gets” cancer, or a group of people, a neighborhood, or even an entire region. All are legitimate answers and subjects for research and intervention—much depends on what explanatory level one is interested in.

The same type of multi-level question can be asked about type 2 diabetes, which has been a long-standing research topic at NERI. Diabetes researchers, with unique disciplinary interests and methods, focus on the influences of particular contributors to diabetes: genomic, physiologic, behavioral, and environmental for example. Each of these levels require a different level of analysis and intervention: genetic engineering, pharmacology, primary and secondary prevention, or changes to healthcare systems and public policy. Unfortunately, researchers with distinct interests and perspectives can become isolated from each other, leading to missed opportunities for learning, communication, and progress. Lacking a broader context, disciplinary-specific findings can resemble the flash of a Roman candle, briefly distracting attention only to quickly burn out and be dismissed. This has sometimes been the case with diabetes research when there is initial enthusiasm surrounding the discovery of some promising new influence at a particular level (a new gene or a sociological influence at the neighborhood level) which temporarily diverts attention from contributions at other levels and which is eventually eclipsed by some new “breakthrough.”

Avoiding Isolation

At NERI, we make a conscious effort to avoid disciplinary isolation and flash-in-the-pan research. Our multi-disciplinary research team, for example, recognizes many different contributors to diabetes and works collaboratively with researchers at other institutions to creatively integrate findings from divergent fields. For many years we have been exploring the worrisome public health question of the racial and ethnic disparities in diabetes. Genetics may play a key role in such disparities, although influences at many other levels are clearly important as well (e.g., lifestyle factors such as diet or lack of exercise, or socioeconomic barriers to adequate health care).

Examining Disparities

Our federally-funded study, conducted with colleagues at the Massachusetts General Hospital and the Broad Institute of MIT and Harvard, set out to examine the question of diabetes disparities.

The results of this comprehensive data-gathering suggest that the high rates of diabetes observed among racial and ethnic minorities are primarily driven by socioeconomic factors such as income and education levels. Our results also demonstrated that while lifestyle factors such as diet, physical activity, and obesity were associated with diabetes, these factors could not explain the excess diabetes among African American and Hispanic individuals. Lifestyle factors appeared to be heavily influenced by socioeconomic factors rather than by race/ethnicity. In other words, having limited economic means likely limits opportunities to practice healthy lifestyle habits, which, in turn, can affect diabetes risk.

This study not only illustrates how diseases such as diabetes and cancer have multiple, overlapping causal factors, but also that a multi-disciplinary and multi-perspective approach to research can generate the most robust and valuable knowledge, which, in turn, may help individuals and society take steps to reduce disease.


This project was funded under grant #DK080786.
NERI Offers Expert Statistical Guidance

We live in the age of “Big Data”: extremely large sets of information that must be analyzed computationally in order to reveal patterns, trends, and associations.

In no field are the challenges and opportunities of Big Data more acute than in health care. Health-related organizations of all types must manage and interpret high-volume, high-velocity data in order to glean the knowledge needed to improve health care delivery and health-related decision making.

Organizing, navigating, and interpreting large, complex data sets is the job of statisticians—and this is an area in which NERI excels. NERI's Statistical Consulting Services group provides timely, expert data analyses to address the urgent questions of our clients.

Areas of particular expertise:

- Cardiovascular disease
- Urology
- Endocrinology
- Chronic pain
- Post-traumatic Stress Disorder (PTSD)
- Pediatric cardiomyopathy
- Other pediatric cardiovascular conditions
- Diabetes
- Hemoglobinopathies

Not only does NERI have top-flight statisticians with experience across a wide range of health-related areas, it also has unique access to many valuable datasets because of its long-standing work with federal agencies such as the National Institutes of Health. These registries, trials, and epidemiological studies are immediately available for analyses, and may provide clients with an extremely cost-effective resource for generating new insights or for corroborating or extending existing research.

NERI's immediately available datasets include:

- **BACH (Boston Area Community Health)**, a population-based epidemiological cohort study of diabetes and urological symptoms involving 5,502 men and women aged 30 to 79 years in three racial/ethnic groups from the city of Boston.
  Funded under grant #DK056842

- **The Fontan Study**, conducted by the Pediatric Heart Network (PHN), which enrolled 546 children ages 6 to 18 years old, to examine associations between functional health status and ventricular state and performance.
  Funded under grant #4U10HL068270-15

- **The Single Ventricle Reconstruction (SVR) Trial**, conducted by the PHN, which randomized 555 newborns with heart defects to receive one of two different shunts. One year transplant-free survival was compared with measurements before and after the procedure and at 14 months.
  Funded under grant #4U10HL068270-15

- **The Pediatric Cardiomyopathy Registry (PCMR)**, which has followed 3,500 children with cardiomyopathy until death or transplant, with various sub-studies, to investigate etiologies, clinical courses, and outcomes.

- **Valor**, a registry of combat-exposed men and women, 1,200 with PTSD and 400 without, who were followed for 4 years, in order to describe and predict a range of outcomes.
  Funded under contract #W81XWH-08-2-0102

- **PTSD Exchange**, a unique registry of 600 clinicians providing psychosocial treatment to veterans and active duty personnel with post-deployment stress-related problems.
  Funded under contract #W81XWH-14-2-0139
NERI’s Expertise in Rare and Orphan Disease Research

A rare disease, also called an “orphan” disease, is any condition affecting a small percentage of the population. While there is no single cutoff for what is considered a “small percentage,” the World Health Organization has suggested a condition affecting less than 1 in every 1,000 people, whereas the U.S. Rare Diseases Act of 2002 uses a stricter cutoff of 1 in every 1,500 people.

Recruiting patients with rare/orphan diseases can be challenging, but NERI has developed successful outreach strategies in both adult and pediatric populations. We work closely with clinical sites, patient advocacy groups, and non-profit disease foundations to meet specific study goals. NERI has successfully conducted studies of such rare/orphan conditions as thalassemia, sickle cell anemia, hemophilia, Marfan Syndrome, and sudden infant death syndrome (SIDS).

NERI has worked collaboratively in complex studies of rare/orphan diseases with multi-specialty teams and multiple stakeholders, e.g., industry sponsors, government agencies, professional societies, and foundations. NERI’s offerings to such clients include customized clinical trials, epidemiology, health and policy research, and patient registry services in areas as diverse as implantable pediatric medical devices and periventricular leukomalacia (a brain injury in premature infants). Here are four additional reasons that NERI’s team stands out as a choice for studies or research in rare/orphan disease states:

1. Even with small pools of potential trial subjects we can identify, recruit, and maintain subject involvement in order to meet enrollment and other project deadlines.

2. Through our long expertise in atypical trials we have developed the scientific flexibility and adaptability that will benefit new studies.

3. NERI combines the science, expertise, and focus of an academic center with the technical, regulatory, and statistical expertise of a large CRO.

4. We have in-house regulatory and statistical consulting expertise to ensure sound regulatory strategy and trial design and innovative strategies for statistical methodologies.

5. We have a strong digital strategies team which collaborates on clinical trial recruitment and retention efforts.
CASE STUDY: Pediatric Neuromuscular Diseases

Details:
› Phase III non-interventional study
› Orphan indication
› 120 pediatric subjects (diseased and healthy cohorts)
› 18 clinical study sites
› 2 countries (U.S., Canada)

Key Highlights:
› Study capitalized on NERI's strength in biomarker identification for surrogate endpoints
› Conducted extensive site training in how to present the study opportunity to parents
› Created and trained sites in an outreach strategy for enrolling healthy volunteers via friends, siblings, and families of enrolled subjects
› Created and trained sites in community and physician outreach strategies to enroll healthy volunteers
› Conducted study coordinator training in the accurate use of a motor function scale to ensure inter-rater reliability
› Enrolled 100% of subjects in 19 weeks

Mixed methods research—study designs which entail collecting, analyzing, and mixing both quantitative and qualitative data in a single study—is central to NERI’s mission. By integrating the two, mixed methods research provides strengths that offset the potential limitations of both quantitative and qualitative methods and helps to answer research questions that cannot be answered by either approach alone.

In many cases, the combination of quantitative and qualitative approaches provides a better and more comprehensive understanding of the research problem than either approach independently. For example, in an experiment in which quantitative measures (e.g., red blood cell counts or incidence of heart attacks) assess the impact of a treatment, qualitative research can be conducted before the experiment to help design the treatment or, alternatively, to better recruit appropriate participants for the trial.

Another example: in a study using a quantitative survey instrument (e.g., a numerical rating scale), we may follow up by conducting open-ended interviews with a subsample of individuals who participated in the survey to learn more detail about their experiences and better understand their responses. The process can work in either direction: quantitative first, then qualitative, as just described, or flipped, for example exploring how individuals describe a topic by conducting qualitative interviews or focus groups and then using an analysis of this information to develop survey instruments, interventions, or patient-reported outcomes.

NERI employs a wide array of rigorous mixed methods study designs across a broad spectrum of projects, offering clients unrivaled expertise in both qualitative and quantitative approaches, allowing our scientists to choose the best methods for achieving project goals rapidly and effectively. 📈
As a world-class research organization, NERI generates dozens of scientific articles every year on a wide range of topics in health and medicine. But NERI is also frequently called upon to serve a different, although equally important, role: organizing and facilitating large meetings of experts with the goal of reviewing the literature in an entire field of medicine and reaching a consensus on how that literature should guide clinical practice.

Consensus building is both an art and a science. The science takes the form of rigorously following the rules and protocols for reviewing evidence in order to answer important questions about specific treatments or techniques. For example, does evidence show that robot-assisted surgical techniques are superior to traditional techniques for the removal of cancerous prostates? The systematic reviews of evidence required to answer such questions require a high degree of expertise in evaluating the methodologies and statistical analyses of research papers, as well as of the systematic review itself.

The art of consensus building involves bringing together groups of highly skilled medical experts—with often varying points of view—from around the world and facilitating such groups to discover where agreements can be reached. An equally important task is articulating, in writing, what is agreed upon in the meeting in the form of a publishable journal article. This may require numerous rounds of writing and revisions to incorporate the edits and suggestions from many contributors, with very tight time constraints.

That NERI excels in organizing and leading scientific consensus meetings is evidenced by the numerous papers that have been published in leading medical journals as outcomes of those meetings. Here is a sample:

- Best Practices in Robot-Assisted Radical Cystectomy (*European Urology*)
- Nocturia Advisory Conference on Outcomes of Therapy (*BJU International*)
- Best Practices in Robot-Assisted Radical Prostatectomy (*European Urology*)
- Systematic Review and Meta-analysis of Oncologic Outcomes after RARP (*European Urology*)
- Systematic Review and Meta-analysis of Perioperative Outcomes after RARP (*European Urology*)
- Consensus Statement on the Evaluation and Treatment of Nocturia (*BJU International*)

To learn more about NERI’s expertise in organizing consensus conferences, conducting systematic reviews, and medical writing and editing, please contact Lisa Marceau at media@neriscience.com.
Less well known is the fact that sudden unexplained death persists past infancy into childhood. Sudden unexplained death in childhood (SUDC) is the term that describes such deaths in children older than one year of age. Although much less common than SIDS (1.3/100,000 for children ages 1 to 4, compared to 38.7/100,000 for ages under 1), SUDC is just as devastating to parents.

NERI researcher Felicia Trachtenberg and colleagues, working collaboratively with other groups, including Children's Hospital in Boston, have been exploring SIDS and SUDC for more than two decades, accumulating an unprecedented depth of expertise in this area. Trachtenberg collaborated with colleagues to publish two significant papers in the past year on different aspects of such sudden unexplained deaths.

Looking Beyond Sleep Position
The National Institute of Child Health and Human Development (NICHD) has long sponsored the Back to Sleep and Safe to Sleep Campaigns advising parents to put their infants to sleep on their backs, in their own sleep area, and on a firm sleep surface. The simple strategy of placing babies on their backs to sleep is credited with an impressive 50% decline in SIDS. New research shows that, aside from this one-time dramatic progress, the decline in SIDS deaths generally follows decreases in infant deaths from other known causes, suggesting that broad trends in the health of pregnant women and babies influence infant mortality across the board.¹

This study raises the question of other factors being critical in declining SIDS rates (e.g., improvements in prenatal and neonatal care and breastfeeding rates; decreases in maternal smoking rates), in addition to sleep environment and points to the need for more research to better understand the full spectrum of biologic vulnerabilities of infants.

Exploiting Risk Factors for and Potential Causes of SUDC
Like SIDS, SUDC almost always occurs during sleep and is often associated with prone (tummy) sleeping and fever or illness. In the second major report involving Trachtenberg, it was found that in about half of the SUDC cases studied, a personal or family history of fever-related (febrile) seizures was present, and half had malformations in a key part of the brain called the hippocampus (in some cases both of these issues were present).²³ Such hippocampal malformations appear to be similar to those reported in cases of sudden unexpected death in epilepsy (SUDEP). The studies hypothesize that some sudden deaths in children may be related to an unwitnessed seizure during sleep that originates in the malformed hippocampus. Potential triggering events are sleep itself, fever, unwitnessed febrile seizure, and/or prone sleep, the latter raising the possibility of hypoxemia decreasing the seizure threshold. The mechanism of death associated with seizures is unknown, as in SUDEP. Trachtenberg notes that parents should be reassured that although febrile seizures are common in children, death associated with such seizures is extremely rare.

The Opioid Epidemic
What Can We Learn From Other Countries?

The abuse or misuse of prescription opioids (POs)—what the Centers for Disease Control and Prevention has called an “opioid epidemic”—is a major public health challenge for the US.

While Americans comprise just 4.6% of the world’s population, we consume 80% of the global opioid supply, 99% of the global hydrocodone supply, and two-thirds of the world’s illegal drugs. Some 259 million opioid prescriptions are written annually in the US by primary care and Emergency Department (ED) providers (enough to supply every household their own bottle of pills), mainly for common chronic pain conditions (e.g., arthritis and back pain).

The origins, magnitude, costs, and consequences of the nonmedical use of POs are now well known: a majority of POs are obtained from a relative or friend, of whom 80% received them from a single physician during a regular office or ED visit. Non-medical use of POs in the US is estimated to cost $55 billion annually.

More Prescriptions, More Deaths
Pain relief is a major reason for nonmedical use of POs (by 40% of patients), but half of non-medical users report other motives, such as to get high or to relax. The correlation between increased opioid prescriptions and fatalities has been firmly established; since 2000 in the US there has been a 200% increase in the rate of overdose deaths (poisoning) involving opioids.

The focus of research on the “opioid epidemic” in the US has shifted as the problem has worsened. First, large national surveys identified the demographic characteristics of heavy opioid users (age, race/ethnicity, gender, geographic location, etc.). Unfortunately, these characteristics are mostly non-modifiable and continuing such research is unlikely to yield major advances.

A second line of research has focused on provider characteristics and prescribing behavior; again unfortunately, much of this resembles victim blaming (primary care physicians are poorly trained in pain management, fail to adhere to clinical guidelines, are overworked with limited time, and too easily succumb to patient requests). Some 60% of deaths from opioid misuse occur in patients given prescriptions based on prescribing guidelines.

A third approach is to identify variations within and between practices in the use of opioids and to highlight system-level contributions to the opioid epidemic. For example, to reduce escalating costs in the US, hospitals are enforcing shorter stays with patients being sent home earlier with POs for ongoing self-management of acute pain, and complex surgery is increasingly performed on a day-stay or 23-hour stay basis with patients discharged much earlier than in the past. This increases over-prescription of discharge opioids and, with a significant amount not consumed, produces a large pool of unused POs available for use by others.

A study of opioid storage and disposal patterns among ED patients found 36% stored opioids in plain sight, 53% kept them hidden but unlocked, and only 15% locked their opioids; 78% were unaware of proper opioid disposal methods, 6% believed they were prescribed more medication than required, and 67% had unused POs at home at the time of the survey.

What Do Other Countries Do?
Increasing awareness of practice variations and system contributions has caused NERI researchers to focus on a fourth approach and ask: how are other countries, with very different health care systems, coping with the opioid epidemic? Is the opioid epidemic
a worldwide problem or a uniquely American phenomenon? International comparisons indicate that some countries at comparable stages of economic development and with similar prevalences of pain and increased use of POs, are not, in fact, experiencing its dire consequences in terms of ED visits and fatalities. A large survey of 15 European countries found that rates of PO abuse varies from 0.7 to 13.7 per 10,000 adults. Another study reported no signs of an opioid epidemic in Germany. A comparison of PO misuse in the US and the UK found that while a similar trend of increasing opioid consumption is occurring in the UK (albeit at lower levels) this has not produced increases in opioid misuse or deaths. The authors suggest the reason for this may be found in structural elements of the UK’s National Health Service.

Why these between-country differences exist is presently anyone’s guess. Perhaps they are due to onerous regulations and legislative barriers, the relative speed of drug approval, authorization and marketing, the for-profit incentive driving US health care, cultural differences and barriers limiting access to primary care, wider use of alternative and complementary therapies for chronic pain, wider use of substitute treatments (methadone), and differences in professional education and variations in guideline adherence.

Since accumulating evidence points to the importance of organizational and health care system-level contributions to the opioid epidemic there is an urgent need to study how other countries are able to reduce the untoward consequences of increased use of POs. Rather than continuing the ethnocentric US focus on patients and providers, which has produced generally disappointing results, perhaps we can learn from the successful experience of other countries. Cross-national comparative analyses may prove instructive.
Women veterans experience additional obstacles to readjustment, and mental health challenges for spouses and families are as high as for service members. The Veteran’s Administration (VA) is a primary resource for counselors who support these individuals by providing a range of services and training programs. NERI has been a proud partner of the VA and the Department of Defense (DoD) on an ongoing project to build and test a registry that will support clinicians who treat veterans and active duty military personnel with PTSD. A key responsibility for NERI was to develop the PTSD Clinicians Exchange website, currently being evaluated in a randomized controlled trial.

As with all its media projects, NERI’s experienced team of producers and writers incorporated scientific methods into the development and dissemination of this digital tool. Employing the ADDIE Model of Instructional Design (Analyze, Design, Develop, Implement, Evaluate), we conducted semi-structured interviews with a sample of mental health providers to better understand the practical and conceptual training needs of clinicians for treating active duty military and veterans with PTSD. Our qualitative interview process ensured that the final web-based resource had the appropriate level and depth of information related to evidence-based practices for PTSD, self-care resources for counselors, and tools they can both use and share. The interviews also informed the format of the web-based exchange and helped us understand barriers to participating in a research study to evaluate it.

Clinicians were asked to share their experiences and insights on predetermined topics corresponding to the project objectives. They were also queried about professional development and training needs, feasibility of registry participation, clinical practices and perceptions, clinician well-being, and effective methods for disseminating information about the website.

This project illustrates the NERI approach: scientific, thoughtful, and thorough. This process ensures that we not only develop high-quality programs, tools and products, but that we create them in ways that the end-users find informative, helpful, and accessible.

This project is funded under contract #W81XWH-14-2-0139
Moving Research to Reality:

NERI as an Innovation Incubator

Technology is becoming ever more integrated in the way we live, work, and interface with our personal health care.

Artificial intelligence, virtual reality, wearable technology, and mobile applications are becoming ubiquitous and are changing the ways in which we interact with the health care system. This evolution relies on—and is informed by—technologies that have been developed through innovation incubators, often supported by venture capital. The National Institutes of Health Small Business Innovative Research (SBIR) program exists in this space to encourage the development of ‘the next great health-based invention’ that is grounded in strong scientific evidence. Over the past three decades, NERI has been committed to this mission, having received over 130 successful SBIR grants.

Science bookends our SBIR product development process by incorporating multiple stages of research. We start by creating opportunities to move scientific knowledge into a marketable product. NERI’s SBIR grants evolve from research by generating products based on the expertise of our investigators and from research programs being conducted at NERI. Our collaborative environment encourages the incubation of ideas that go beyond the aims defined in a traditional research grant. Because NERI collaborates with so many other for-profit and non-profit institutions, we are constantly in contact with external investigators seeking digital strategies to move their scientific concepts to tangible products.

Freedom to Explore

NERI investigators have the freedom to explore innovative ideas in collaboration with our digital strategies team. Here, ideas evolve into interventions or products which have broad potential including, for example, impacting clinical guidelines, improving the in-clinic encounter, personalizing health care, and addressing preventive health measures.

Each SBIR concept is evaluated for its applicability to the target audience and undergoes rigorous qualitative research to identify the audience needs, likes, and dislikes before a product is developed. After developing a prototype, we assess feasibility to identify gaps or missed opportunities. As part of the second phase of development, the complete program is evaluated in a randomized controlled trial to make sure the product meets the user’s needs and fills an un-met need in the current field of knowledge. This process results in successful, high quality, evidence-based products supported by peer reviewed publications and presentations and strategic dissemination plans.

The rapid pace of technological development will continue to drive global change in health care as well as the meaning of personalized, precision medicine. NERI, under the direction of Lisa Marceau, VP of Digital Strategy, is uniquely positioned to be a leader in this dynamic evolution with our depth of scientific expertise, breadth of knowledge in digital strategies, and decades of commitment to dissemination and implementation approaches.

Case Example: Type 1 Teamwork

Research being conducted in the area of diabetes has led to the development of a mobile application that helps parents and their teen-age children communicate about the transition to diabetes self-management. The mobile app builds on evidence-based research, collaborative expertise in diabetes and pediatric research, proficiency in digital strategies, and a history of successful implementation and dissemination.

This project is funded under grant #DK098857
Research—and researchers—often operate in subject-specific, or discipline-specific “silos” that impede a free flow of ideas. For example, clinical, behavioral, and social sciences can often feel like different worlds, with little overlap.

Such distinctions, and the barriers that can result, are eliminated in an inclusive, comprehensive online anthology created by a multidisciplinary team at NERI and available via the Office of Behavioral & Social Sciences Research (OBSSR) at www.esourceresearch.org. Dubbed “eSource” this digital resource offers 20 in-depth chapters about research methods that are applicable across a wide spectrum of disciplines and content areas.

The focus on behavioral and social science research is important because this field lies at the crossroads of persistent public health needs and emerging data from clinical and epidemiological science. In creating the eSource anthology, NERI’s research teams brought together biomedical, behavioral, and social science researchers to address complex questions impacting how we investigate current health challenges. Our ability to assemble internationally recognized interdisciplinary teams of scientists to address specific questions across a range of research methods is evidenced in this online resource. eSource is a one-of-a-kind open-access digital anthology funded by OBSSR. It is the largest and most authoritative open-access electronic source in its category for researchers, professors, and students.

Since its launch in December 2009, the anthology has grown in popularity. It is currently viewed by nearly a quarter million visitors each year. Mobile use has increased in recent years consistent with the way in which users prefer to access information. The program is international in its reach, with 42% of visitors from the U.S. (with every state represented) and the remaining 58% spanning 216 different countries.

With the creation of eSource, NERI has contributed to the global expansion of high-quality research methods across disciplines and subject-area silos. For more information, see www.esourceresearch.com
Listening to Patients

NERI Leads in Developing Patient-Reported Outcome Measures

A Patient-Reported Outcome (PRO) is any report of health status that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else.

Historically, a patient’s subjective report of how they feel has not been viewed as a reliable form of evidence when it comes to FDA approval of a drug, device, or medical procedure. Such reports were considered “soft” data, while quantifiable data such as blood cell counts, cholesterol levels, or death itself were considered the kinds of “hard” data on which regulatory approval decisions needed to be based.

In the past decade, however, leading clinicians, scientists, and regulators have embraced the importance of patient-reported outcomes (PROs) in evaluating treatment efficacy and outcomes. Not only are PROs seen as necessary and valuable in evaluating efficacy in drug and device trials, they are recognized as irreplaceable in many clinical research areas because they provide data that cannot be captured any other way. In short, these measures are increasingly indispensable.

Do patients feel any better, for example, after taking treatment X vs. treatment Y, and how closely does the patient’s experience match the objective benefits of treatment? Such questions are especially relevant when objective measures of treatment benefits are lacking or unreliable. For an increasing number of common conditions (for example, vulvovaginal atrophy or erectile dysfunction), it’s the patient’s degree of bother, discomfort, or distress that is the main target of treatment, and this aspect is best assessed via a scientifically constructed and validated PRO.

Another increasingly important use of PROs is for diagnostic screening, where a short questionnaire can be used to identify patients at risk for a condition, or who need further assessment and alternative treatments. Short screeners are used increasingly in the Veteran’s Administration (VA), for example, for screening potential symptoms of post-traumatic stress disorder (PTSD) or...
traumatic brain injury (TBI) in returning veterans. Such instruments are currently being used in the Project VALOR study, a NERI-directed, national registry study of Operation Iraqi Freedom/Operation Enduring Freedom veterans.

A Case Study in PRO Design

Underactive Bladder (UAB) has been identified by an international consensus panel in 2015 as a potentially common urologic syndrome in men and women which can lead to incontinence, leakage and other highly bothersome difficulties with urination. Little is known about the causes or risk factors for UAB, and NERI has recently been awarded a new grant from the National Institutes of Health (NIH) to perform the first epidemiologic study of UAB. An essential first phase for this project will be the design and construction of a new patient-reported diagnostic aid, or symptom screening tool, to be used in the future by physicians to identify patients with symptoms of UAB who may need treatment, or for assessing potential benefits of treatment.

The screener will be based on qualitative interviews with carefully selected patients. Further validation studies will be performed and the screener will be tested in large samples of men and women with clinically diagnosed UAB. A UAB screener tool will then be developed and validated clinically in Phase II. The iterative process of screener development and validation is depicted above.

In addition to the UAB Screener, NERI has developed similar PRO screening instruments for understanding symptoms of hypogonadism in men, and symptoms of vulvovaginal atrophy (or genitourinary syndrome of menopause) in women. The NERI Hypogonadism Screener was developed based on qualitative interviews with male patients with hypogonadism and tested in a psychometric validation study with patients and healthy controls. A brief questionnaire has similarly been developed in collaboration with Dr. Jan Shifren, Director of the Women’s Health Program at MGH, for detecting symptoms of vulvovaginal atrophy, a common condition in women following menopause. Finally, working in collaboration with researchers at MGH (Dr. David Henderson) and Rutgers University (Dr. Steven Silverstein) NERI has developed a novel PRO instrument for assessing subjective aspects of cognitive disturbance in schizophrenia.

In each of these innovative PRO development projects, highly scripted and meticulously analyzed qualitative interviews with patients serve as the cornerstone for identifying and measuring subjective aspects of these common and highly distressing conditions. With its outstanding team of qualitative researchers, NERI is well positioned to create the kind of thorough, validated PRO instruments required by the next generation of researchers.