

# TRANSLATIONAL RESEARCH

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A university distinguishes itself as a fountain of knowledge and is entrusted with the responsibility of creation, dissemination and preservation of knowledge<sup>1</sup>. Research nurtures knowledge and vice versa. In the last few decades research has expanded exponentially and has acquired multiple disciplines. Currently, more emphasis is being placed on translational research, which may mean different things to different schools of thought<sup>2</sup>.

Basic science research has been defined as basic science that involves laboratory studies which provide the foundation for clinical research<sup>3</sup>. Putting it differently, basic science research entails gathering knowledge that is essential for applying discoveries to patient care<sup>4</sup>. In 1945, the director of the US Office of Scientific Development and Research made the following distinction between basic research and applied research: Basic research is performed without thought of practical ends. It results in general knowledge and an understanding of nature and its laws. This general knowledge provides the means of answering a large number of important practical problems, though it may not give a complete specific answer to any one of them. The function of applied research is to provide such complete answers<sup>5</sup>. The NSF definition thus identifies the main objective of basic research being the acquisition of knowledge without the obligation to apply it to practical ends.

What is clinical research? In 1997, the NIH Director's Panel on Clinical Research issued the following 3-part definition of clinical research: 1. Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes:

(a) mechanisms of human disease, (b) therapeutic

interventions, (c) clinical trials, or (d) development of new technologies. 2. Epidemiologic and behavioral studies and 3. Outcomes research and health services research<sup>6</sup>. Translational research has become the buzz word and has become the topic of discussion and action on both sides of Atlantic. Some refer it to the "bench-to bedside" entailing employing knowledge of basic sciences to invent new products, devices or treatment options for patients. This is the interface between basic science and clinical medicine and the end point is to develop a new concept or treatment that can be utilized in treatment or can be commercialized ("brought to market"). This important step is and has been characterized as follows: "effective translation of the new knowledge, mechanisms, and techniques generated by advances in basic science research into new approaches for prevention, diagnosis, and treatment of disease is essential for improving health<sup>7,8</sup>."

Health services researchers and public health investigators focus on health care and consider health as the primary outcome, to them translational research refers to translating research into practice. They try to ensure that new pharmaceutical agents and research developments are used for deserving patients and populations for whom they are intended. Development of a new drug, which is an end point for bench-to bedside translational research, is only the starting point for this second area of research<sup>8,9</sup>. Even in the developed world, such as US, most patients receive only half of recommended services<sup>10</sup>. The second area of translational research pursues to close that gap and improves quality by enhancing access, reorganizing and coordinating systems of care, helping clinicians and patients to change behaviors and make more informed choices by providing reminders and point-of-care decision support tools. More importantly, it strengthens the patient clinician relationship<sup>2</sup>.

The distinction between these two definitions of

translational research was articulated by the Institute of Medicine's Clinical Research Roundtable, which described two translational blocks in the clinical re-search and which some now label as T1 and T2. The first roadblock (T1) was described by the roundtable as the transfer of new understandings of disease mech-anisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans<sup>9</sup>. The roundtable de-scribed the second roadblock (T2) as the translation of results from clinical studies into everyday clinical practice and health decision making<sup>11</sup>.

Using the same name as 'translational research' for both T1 and T2 has become a source of confusion<sup>12</sup>. The two domains are alike only in name. Their objectives, settings, study designs, and even the investigators differ. T1 research necessitates molecular biology, ge-netics, and other basic sciences and requires suitably trained clinical scientists working with cutting-edge technology. As against that, for T2 research commu-nity and ambulatory care setting is the laboratory and population based interventions and practice-based re-search networks bring the results of T1 research to the public<sup>13</sup>. T2 involves different research skills such as implementation science of fielding and evaluating interventions in real world and disciplines like clinical epidemiology and evidence synthesis, communication theory, behavioral science, public policy, financing, organizational theory and system research<sup>14</sup>.

T1 and T2 face different challenges. T1 faces challenges with biological and technological mysteries, tri-al recruitment, and regulatory concerns. T2 has more to do with human behavior and organizational iner-tia, infrastructure and resource constraints, and the messiness of proving the effectiveness of moving tar-gets under conditions that investigators cannot fully control<sup>15,16</sup>. T2 research needs more specific definition and clarity in scope. Names like Translating Research into Practice (TRIP), T2 or even translational research do not truly represent it and even newer names like dissemination, health services, knowledge transla-tion/transfer, implementation or quality improvement research do not do justice with the concept<sup>2</sup>. A third step T3 practice-based research has been identified, which is necessary before systematic reviews and guidelines can be implemented in practice. Even this expanded model seems incomplete. There is a long list of people who are involved in applying this evi-dence that include patients, public health administra-tors, employers, school officials, regulators, product designers, food industry and other consumers of evi-dence. Trials that test the implementation of evidence in these settings can be just as vital as similar T2 work in clinical settings<sup>17-19</sup>.

Many researchers are realizing that for many dis-eases translating research T2 can perhaps save more lives than T1. The bench-to-bedside T1 enterprise achieves breakthroughs that may improve the progno-sis for a disease, but most new drugs and interventions produced by T1 only marginally improve efficacy. The incremental advances are surely required but patients may benefit even more and further more patients may benefit if the health care system performed better in delivering existing treatments than in producing new ones. Many experts fear widening "chasm" in access, quality, and disparities, interventions to close these gaps, which falls into the realms of T2, may do more to decrease morbidity and mortality than a new imaging device or class of drugs<sup>2</sup>.

The journey of research begins with basic sciences, the outcomes mature with clinical research and the desirable results are then presented to the society as a product of translational research. Translational re-search is not an end in its own right, rather it is a long process where basic research provides the platform to conduct clinical research - from bench to bedside - but the necessity of widespread application and maxi-mal utilization for the target population with minimal side effect profile in an efficient and cost effective remains the elusive goal to be achieved. All our ef-forts, regardless of being basic or clinical researchers, are geared towards alleviation of disease and promo-tion of health - the benefit of which should eventually reach the whole mankind.

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