Challenges and Drivers of Translational Research

Translational research is aimed at deploying knowledge collected from trials and clinical observations to improve clinical benefits and enhance product attributes.

Translational research is also referred to interchangeably as translational medical or translation science. This research also works on effective optimum migration of knowledge from one system to another or from one level of discovery to another level of discovery. This covers the full translation of animal to human data, and backward for bringing new solutions for different diseases, identifying current and future unmet needs and possible solutions to overcome these.

A final goal of translational medicine is to help patients with the more rapid development of new diagnostics, medicinal products, and new medical knowledge for treating diseases, giving access to care for people at reasonable costs. Insights on where a novel therapy might have the highest impact on diseases and what research needs to be done before clinical testing.

It is a circular concept encompassing so-called bench-to-bedside-to-community factors, which aim to increase the efficiency by which new therapeutic strategies developed through basic research are tested clinically, and bedside-to-bench factors, which provide feedback about the applications of new treatments and how they can be improved. It also facilitates the depiction of disease processes and the generation of connected novel hypotheses based on direct human observation.

Some of the examples could be patient and physician-reported outcomes, community knowledge, and incorporating the clinical observations and questions into scientific hypotheses in the laboratory.

Translation research takes place at every level of the product value chain, and it involves multiple stakeholders.

Translational research is evidence-based research, or disease-targeted
research is a collaboration between clinics, research hospitals, governments, academic institutes, and small to large scale industries where different diseases (infectious, acquired, or genetic) are identified, and discoveries are tested in cell culture, animal models, and clinical trials to determine the relevance of novel discoveries in the biological sciences for human health and longevity.

Different stakeholders in the healthcare value chain such as patients, healthcare providers, and practitioners use the term for the need to accelerate the incorporation of benefits of research into clinical medicine and to close the gap between “what we know” and “what we practice.”

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The most current translation model in the literature is the 4 T’s model:

- **T1**: Basic scientific discovery (basic knowledge) to potential clinical application (theoretical knowledge) to
- **T2**: Evidence-based guidelines (efficacy knowledge) to
- **T3**: Clinical care or intervention (applied knowledge) to
- **T4**: The health of a community or population (public health knowledge)
Need of Translational research - Translational research describes a continuum of research in which basic science discoveries are utilized to prevent or treat human disease. It is an iterative process wherein scientific discoveries are integrated into clinical applications and, conversely, clinical observations are used to generate research foci for basic science: the “bench to bedside and back to bench” approach. *Translational medicine generates a model of continuous evolution:*

Due to the introduction of translational research, the knowledge generated since the inception of the concept is far more than actual implementation in clinical practice. Hence translational research is needed to fill this gap. In history, medicine took more than 15 years to reach the patient since its discovery. Most of the portion of this time was consumed by clinical trials and the correction of erroneous methods.

Translational research creates a developmental playground where scientists can design experimental approaches while maintaining the view of the implications their work may have in the discovery of new therapies. Translational research creates a defined path that allows researchers from different disciplines to walk together in harmony, transcending the barriers left behind by medicine’s historical legacy.

The search for new drugs is at a historic moment of crisis considering the pressures across society as well as scientific limitations. Despite enormous technological advances, the new drug development process is becoming unsustainable. The technological explosion has not been accompanied by reinforcement of quality in experimental designs.
which are radically different from the traditional models, especially in the discovery phases. The high level of failure at a clinical trial in Phase II swallows up economic resources generates exhaustion among researchers and clinicians and more seriously for patients.

**Valleys of Death:** Between basic scientific research and clinical research is what’s known as translational research often referred to as “the Valley of Death,” where promising discoveries meet their demise. To cross the “Valley of Death, several key requirements must be in place to move these discoveries into new treatments, diagnostics, and preventions.

- The translation research has evolved over the years and it is further poised to evolve exponentially due to digitalization, big data, data sharing between competitors, open innovation, formation of indication-based consortiums, patient centricity, and changing disease landscape.

**Drivers and Challenges**

There are several unmet needs at different levels of the value chain such as clinical, commercial, R&D, regulatory, and social levels. The
industry is trying to find solutions to these unmet needs and which are resulting in the drivers. Traditionally translational research is considered as an important bridge joining basic research to clinical research. Following are a few specific drivers.

**Ensure the success of R&D, increase R&D productivity and shorten the R&D lifecycle** - On the one hand, the product prices have eroded due to social pressure and competition, and on the other hand, R&D expenses have increased over the years. The drop in R&D productivity has pushed the industry to improve the success rate of R&D programs, improve R&D productivity by optimally utilizing existing knowledge, collaboration with other industry players, and taking novel approaches.

**Repurposing and life Cycle Management** - Efforts to resolve medical unmet needs through the existing and proven science/material/methods

**Increasing life expectancy and evolving disease pattern** - Aging population and rapidly growing life expectancy in most world populations have resulted in an increased prevalence of the chronic disease. Also, the changing disease pattern, emerging new diseases, and re-emerging infectious diseases have pushed the industry to bring new solutions to address clinical needs.

**Promise and expectations of growth in healthcare** - The continued rise in prevalence have resulted in the projected growth of health care spending. Despite the pricing pressure, treatments are getting costly due to the prolonged use of medicines and hospital stays.

While the Translation research is getting traction across the industrial corridors, there are still large and small level challenges that need to be undertaken before applying at the institutional level. The questions could the know-how of the translational process, detailed risk-benefit analysis, and strategic intent bearing in mind the consequentialist approach. A few of the challenges faced during the Translational research could be-

1. Lack of **coordination** and connectivity between research and clinical teams
2. Available **funds** for projects and ideas at critical stages in the research process
3. Lack of **novel ideas** to design clinical trials
4. **Cross therapy** area applicability of MoAs and targets, and repurposing
5. **Culture** of translation and shared goals of fundamental research for humanities
6. **Availability** of data related to success rates and real-time examples of implementation
7. Financial **conflicts of interest**
8. **Ethical issues** with respect to resource allocation basis the nature of the research, chances of success, and impact

Additionally, some of the challenges are Interdisciplinary training, Translational research as a recognized discipline, Evolution from departments to interdisciplinary research centers, and widely shared resources across the structural setup of organizations and eco-systems.

**Overcoming the Challenges**

Across the developed countries, almost all major public group health institutions and drug companies have addressed the issue of translational medicine in one way. In collaboration with the academics and research community, the NIH launched the Clinical and Translational Science Awards (CTSA) Consortium in 2006 with the plan of linking approximately 60 institutions to energize the discipline of clinical and translational sciences. The primary goal of the CTSA Programs is to assist institutions to forge an integrative academic home for Clinical and Translational Science. American universities addressed the challenge by establishing centers for translational medicine, e.g. at Duke or Pennsylvania University.

In Europe, the National Translational Cancer Research Network was set up by the British government to facilitate and enhance translational research in the United Kingdom. Depending on the structure and focus, institutional structures range from independent departments of translational or discovery medicine to completely dependent department which works cross-functionally with drug discovery/development teams without central facilities.

From the funding point, the US being the largest healthcare market, it had invested the most (NIH has announced to spend a total of up to 10 billion USD) and are at the forefront of translational institutionalization, while Europe lagging behind at very different distances knowing the geographical challenges.
In general, the US had been at the forefront where innovation to commercialization process could be speeded up through adequate re-modeling of institutional structures and translational medicine has a lot to do with expertise accrued during commercialization processes.

When following a structured approach the translatability potential of a given drug, device, or diagnostic test project is assessed by multiple variables such as Lab results, associated markers and ligands, disease models, wet-med results, genetic and omics data, and other dimensions.

However, to develop a strategy for identifying the gaps in the existing process such as the environment of competing projects for a Go-No go decision or a program such as a biomarker development, it is imperative to develop a long-range approach that impacts stakeholders across the value chain such commercials, funding authorities, regulatory agencies, academia. The potential novel approaches could be new mechanisms to rate funding application with regards to translation potential, reasonable balances of associates risks, high potential exploitation, expert opinions to drive evaluation processes, and connecting investments with translational evidence-based analysis. While academic institutes should consider completely or partially re-shape research approached as a route to out-licensing success.

With this increased focus on the ability to influence traditional research and commercialization paradigm, there are hopes for promotion of multi- and inter-disciplinary clinical and translational research and new knowledge and techniques which would become more readily available to patient care.

Illustrative Examples and Conclusion

While Translational Research is still evolving, there are some specific examples and the way it has helped to shape discoveries made in basic research, into clinical treatments:

1. Professor Fölling’s research in partnership with the Egeland family began the long journey to discover what we know about phenylketonuria (PKU) today. PKU is a metabolic disorder that can lead to intellectual disability, seizures, and other serious medical problems. This amazing story, which took place before the concept of translational medicine was even known, led
doctors, biochemists and geneticists to discover more congenital metabolic diseases, which can also cause neurological damage.  

2. Children with **Marfan syndrome** were treated by Harry Dietz and his colleagues at Johns Hopkins University. This resulted in findings that medicine already approved in the United States as a treatment for high blood pressure can also prevent the aortic aneurisms found in mice with Marfan syndrome. This syndrome affects the body’s connective tissue and the complications are normally defects of the heart valves and aorta, which often lead to early death. The medicine has now been tested as a therapy in a group of children with this syndrome and was found to inhibit the development of the potentially deadly abnormalities in the aorta.

3. In patients with early-stage prostate tumors, Anant Madabhushi and colleagues at Rutgers University used sophisticated image processing algorithms to analyze the texture of medical images made with high-resolution **magnetic resonance imaging** (MRI), to detect and locate tumors at an early stage. This led to a more sensitive and reliable technique for clinical application than other existing approaches.

4. James Tunnell’s group at the University of Texas in the USA developed **gold nanoparticles** that can be targeted at cancer cells, allowing detection by fluorescence spectroscopy even when the tumors are quite small. These same particles can then be activated with strong light to potentially destroy the tumor. This approach combines optical imaging, spectroscopy, and nanotechnology for early cancer diagnosis and treatment.

5. To delay the onset of blindness, many patients with glaucoma must administer eye drops multiple times during the day, a demanding routine that can prevent effective control of the disease. The work of Erin Lavik at Case Western Reserve University led to an improvement in the way that glaucoma patients receive their medication, and to more consistent levels of the medicine being applied, and thus to better outcomes for the patient. Prof. Lavik developed **microspheres** containing a glaucoma medicine, which can be injected into one spot in the eye, where the microspheres secrete controlled amounts of the medicine for over a month.

Strategic and cross-functional collaborations between academic institutions and bio-industries have been gaining momentum over the last decade due to the mutually beneficial and synergistic values each
The broader goals of Translation Research are not limited to a specific topic or condition but the impact that it should have on overall populations and society at large. For example, if a state implements a policy to reduce the psychological disease burden in kids, it will not only promote the research related to it but also, various other stakeholders such as movies, advertisements, or children related touchpoints where any examples of violence, drug use or other such activities might be taking place. Translational medicine seeks to coordinate the use of new knowledge in clinical practice and to incorporate clinical observations and questions into scientific hypotheses.