How to Bridge the “Valley of Death” Between a Research Discovery and Clinical Application?
Tien Yin Wong, 1,2,3 MBBS (Singapore), FRCS (Edin), PhD (Johns Hopkins)

The Valley of Death

As physicians, one of the key questions we often ask is, “How do we bring new understanding of disease mechanisms and better treatments to our patients?” Is there a process whereby scientific discoveries are identified, assessed and adopted by physicians, healthcare providers and policy makers to ensure our patients benefit from these innovations?

In fact, this “process” of scientific discovery to actual clinical application is long, tortuous and difficult, and many bench discoveries do not actually get to the bedside. As an example, in 2008, more than 800,000 medical research papers were published, but by 2011 only 21 new drugs had been approved by the US Food and Drug Administration (FDA)1—barely 0.003% of the “discoveries”. Of the numerous research publications, observations, clinical trials and discoveries worldwide that the public sometimes are made aware of in the lay media, how many can boast that they have actually made a real impact to improving patients’ lives and have been used by physicians in clinical practice? The answer: very, very few!

The chasm between a laboratory observation and the application of this observation to clinical care outcomes have been dubbed the “valley of death”, where basic biomedical discoveries initially generate exciting new results, are published in high profile journals and lauded as “breakthroughs” by the scientific community and the lay media, but many years later, they subsequently languish, failing to translate to actual improvements for clinical medicine and healthcare.

So how do we ensure that research endeavours, which often consume significant costs to public budgets, reach and make a tangible difference to patients?

What is Translational Medicine?

Translational medicine is the “bridge” to this valley.2 Applying knowledge gained from basic biomedical research to clinical practice; it involves bridging new research findings, scientific discoveries and new techniques to approaches in the prevention, diagnosis or treatment of diseases. This can be in the form of drugs, devices, biomarkers or treatment methods. Translational medicine involves the pursuit of the patient’s health as the ultimate outcome. It involves paradigm shifts such that scientific discoveries should not just be celebrated only in basic laboratories and research institutes or published (and archived) in prestigious medical journals—they also need to make their way to hospitals, clinics and into patients’ lives to be real successes. Translational medicine involves a longer term strategy for research that is beyond the immediate outcomes of a research project.

Translational medicine takes time. An example is the discovery of the treatment of age-related macular degeneration (AMD), one of the major causes of blindness.3 The observation that eyes with AMD have a higher level of a “growth factor” occurred in the early 1970s, leading to the identification of vascular endothelial growth factor (VEGF). Subsequently, this led to the design of antibodies to VEGF, testing of anti-VEGF agents in animal models and then in early phase clinical trials. The results of major phase 3 clinical trials in 2006 led to the clinical adoption of anti-VEGF treatment and for AMD as a gold standard treatment. It is now one of the major treatments for eye diseases in Singapore.4 In 2013, almost 4 decades later, the rate of AMD blindness has started to decline in some countries as a result of anti-VEGF treatment. So the process of translational medicine from bench to the bedside to the population took 40 years!

In the US, the National Institutes of Health (NIH) has recognised the importance of translational medicine and has made it a priority. Since 2006, the NIH has formed centres of translational research at its institutes with a budget that has reached US$500 million a year;2 and it has launched translational science awards for researchers.
Similarly, Singapore’s national biomedical sciences agenda has now shifted towards translational medicine as a priority for the future, and has refocused emphasis on such research that creates greater health and economic impact.5

**An Example of Translational Medicine in Singapore: The Myopia Story**

Because Singapore’s effort in biomedical research is relatively new, there have been few successful cases to date. Nevertheless, there are encouraging signs.

An example close to home is the management of Singapore’s unique problem of myopia. Myopia is a common condition and is almost a “national” problem affecting 28% of children as young as 7 years of age, with the rate hitting 83% at 18 years of age.6,7 Myopia may result in blindness due to myopic macular degeneration and slowing the rate of myopia progression is one way to prevent this problem.7

For 15 years, researchers and subsequently, clinicians at the Singapore Eye Research Institute (SERI) and the Singapore National Eye Centre (SNEC) have been trying to tackle this problem. The work over the 15 years was done with an end goal in mind—to decrease the rising incidence of myopia, and to slow down the condition in its tracks.

The SERI and SNEC research team discovered that eye drops with low-dose atropine slow down the progression of myopia in children with minimal side effects.8 After years of tests and clinical trials, the clinicians and researchers have transformed their findings into a solution. SNEC today now offers new eye drops with a 0.01 atropine dosage—the most effective atropine level proven to combat myopia—for children with severe myopia in a dedicated myopia clinic, and is furthering their research to meet regulatory demands. Concomitantly, community-based clinical trials efforts are underway to tackle the lack of physical and outdoor activities, which are now thought to be a major cause of myopia.9

With translational medicine, this major nationwide problem may become curable in the foreseeable future.10

**What are the Ingredients for Successful Translational Medicine?**

First, driving translational medicine requires a new model of working together. Multidisciplinary collaboration across specialties, disciplines and industries is the key to driving translational research to success. This requires teams of clinician, clinician scientists, scientists, nursing and allied health professionals.

For instance, an observation in the clinic by a doctor may give rise to a hypothesis that a scientist in the lab can work on. A scientist’s discovery may translate into a biomarker that acts as clinical tool for the clinician, or a drug target for drug development by a pharmaceutical company. A physiotherapist’s inspiration may result in the invention of a rehabilitation device that could not be made possible without collaborating with an engineering or a medical technology institution. Translational medicine is not an individual event; it is a team sport that has different roles and skills for each team member. With a critical mass of research teams and sustained collaboration, drugs, treatments and care, outcomes can be brought out of the “valley of death”.

Second, a strong ecosystem and culture that sustains and rewards translational medicine is critical. It involves forging a close partnership between a hospital cluster and a university, similar to the concept of the SingHealth Duke-NUS Academic Medical Centre or National University Health System.11 The partnership must align the traditional divergent missions of healthcare and education, and the cultural differences between academic researchers and practising doctors. These are challenging issues that must be dealt with upfront.12

Third, translational medicine requires a group of people who understand both science and medicine—clinician-scientists.13,14 The clinician-scientist can effectively act as a connector between scientists and doctors, and must speak both “languages”. To translate research, young clinician-scientists must be identified, trained, mentored and supported. Alongside a nurturing environment, supervision, guidance and advice from a sympathetic and wise mentor are essential. In the US and other countries, clinician-scientists face significant challenges in funding and career development.

The final piece of translational medicine is policy implementation. Once new discoveries and clinical evidence have been established, government agencies and healthcare systems should have a clear framework to implement healthcare policy and public health policy accordingly. The importance of policy implementation as the “final step” in the “valley of death” cannot be underestimated.15,16

With these pieces in place, the “valley of death” can be bridged and research discoveries will find their way to the clinic and to our patients.
REFERENCES


