Measures of Translational Impact:

"Beyond Business Concepts of Technology Transfer" **or** "Diversifying Beyond Traditional Commercialization Metrics"

Final title TBC.

Draft Perspective for Science Translational Medicine on Translate! 2021 Discussion

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Abstract: *As measures of translational impact represent a key issue for supporting translation and fostering translational careers, a team of academic entrepreneurs describe here the challenges, infrastructure, incentives, evaluation and monitoring criteria, outcome measures, educational benefits, and societal obligations to* ***"do something meaningful"*** *to convert research discoveries into products that impact human health. Real-world experiences contrast the traditional metrics for assessing translational impact.*

Why do we even need measures?

The consensus that measures of success currently used at academic centers (e.g., impact factors, citation index, h-index, etc.) are of limited value in motivating (young) scientists to engage in translational research. Overcoming the risks of a commitment to translational research for the career path of (young) scientists requires a new mindset and meaningful incentivizations based on transparent, comprehensible, reasonable and feasible measures.

Measures and metrics and their meaning depend, however, on context and are not readily generalized. One set of incentives and metrics may be appropriate for academic faculty advancement and recognition; a second set of metrics may be more appropriate in the business environment for return on investment and scalable production; a third set of metrics may help the global development of delivery of life-saving medicines and treatments that enhance wellness for individuals and for the global society. In this Perspective we propose a framework to select principal axes of parameters to optimize for a given context of translation, and we invite readers to examine and research how to optimize metrics for impact for a given context.

Societal and Scientifc Impact of Translation

Often, especially in academic tech transfer offices, the success of translation is measured by the number of patents, licenses and revenues (break even). There is a more comprehensive and holistic need for measures and incentives to support and promote the mindset of translation, which in turn feeds back not only into a scientist's career but also futher impacts beyond academia, in the "real world" or broader "society" (definition of society/societies).

From our point of view, the most important success parameter is the impact that translation has on patients and society – in other words, to give something back to the society that finances our academic research. Return on public investment (ROI) from the research enterprise might be assessed along a spectrum of different possible contributions.

Benefits for Society and Economy:

- Improving and ensuring global accessibility to modern life-saving technologies
- improved survival and quality-of-life for patients, particularly of those with existing or at risk of chronic diseases
- decreasing financial burden on society by current approaches to costly and chronic diseases
- innovative product pipeline for medtech/biotech/pharma industry and new players
  - revenues, jobs generated
- generation and retention of highly specialized workforces and expertise
- setting ethical and quality standards for new therapies

This overarching rubric, which can be defined as key performance parameters, is applicable for the evaluation of academic translational centers, but is less suitable for evaluation and incentivization of individual projects, research teams, or even individual scientists.

A framework of measures should include the entire translation pipeline from project proposal, project selection, project monitoring, to assessments of the outcome, in order to properly incentivize in a targeted manner. This might be categorized in:

- ***inputs/incentives:*** e.g. 3 types of incentives: personal, institutional, societal; going beyond to emotional satisfaction, adding a 4th pillar to the academic promotional/advancement decision;
- ***process/efficiencies***: e.g. project monitoring by risk assessment and risk mitigation strategies
- ***outputs/benefits:*** e.g. progress in added value line (technology readiness levels), impact for patients and society
- ***communication/expansion:*** e.g. creating empathetic engagement– communicating science to the public through striving for public good; societal obligations – land grant universities are non-profits; moral obligation to pay back the taxpayers and donors with benefits
- ***eliminating disparities between social groups, cultures, countries, and populations:*** removing barriers for technology dissemination, costs, adoption, and flattening the global technology landscape to produce parity/equity and comprehensive benefit.

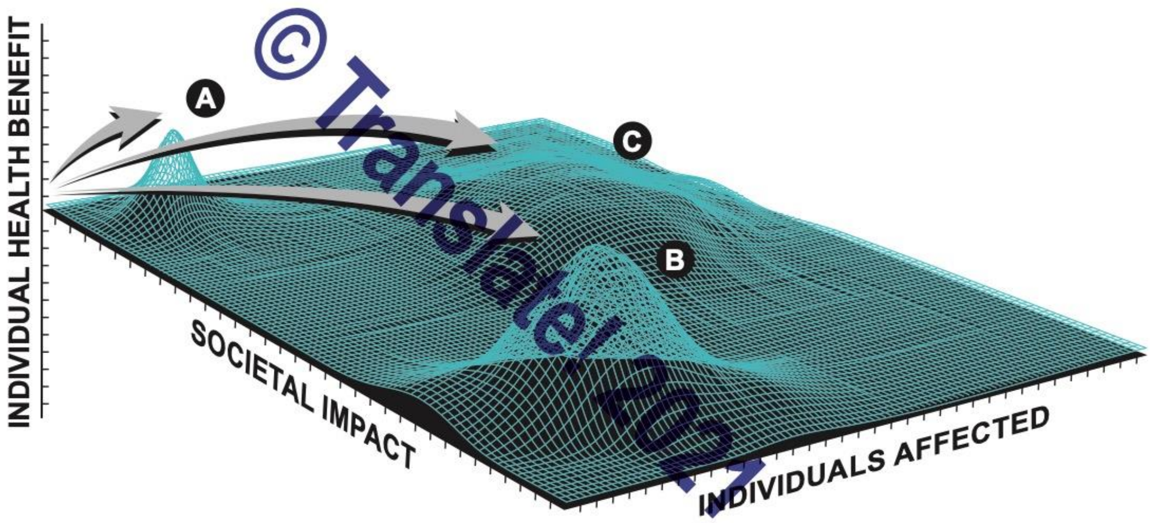

Figure 1. Impact is a Multifactorial Landscape. *Selecting metrics for measuring translational impact is complex. Illustrated here is a landscape of a three-dimensional landscape relating number of individuals affected (x axis), magnitude of individual health benefit (y axis) and societal impact (z axis). The vectors illustrate examples of a life-saving drug for a rare disease (a), a treatment for a chronic disease affecting millions (b), and a mitigating treatment for headaches used by billions of people worldwide (c). Other potential measures generating different or more complex landscapes could include: return on investment (ROI), scalability, disability-adjusted life years (DALY), among others.*

How can the value of translational activities be measured?

Measures and Metrics – pro´s and con´s

There is a common saying in organizational change management that what gets measured gets done. Of course, it is not quite that simple in practice. Simply measuring something is not sufficient to ensure an outcome will happen. Moreover, in the case of promoting the translation of laboratory research into impact, what gets measured and how it is used clearly is important. While measurements (e.g. number of patents) provide a data point in time, metrics define data in context to some baseline (e.g. percent increase in patents) and can therefore be used to promote continual improvement over time. It is also useful to distinguish outcome metrics, which measure work that is completed, compared to performance metrics, which provide measures of activities that are known to lead to a desired outcome metric.

Setting well defined metrics that link to desired outcomes can help track and incentivize progress. However, including all possible metrics can be confusing and incentivize conflicting behaviors. So which to choose? The number of startup companies spun off from an academic institution is one possible metric, but to have a long-term impact, the goal should not just be to form companies but successful companies. Another possible metric is startup company revenue generation. This is a good north star metric which could include several sub metrics. However, emphasizing revenue generation might incentivize supporting only more mature ventures and ignoring early stage technologies with longer-term commercialization potential.

List of metrics, advantages and disadvantages – potentially in table format

Individual vs institutional metrics

Measures/Metrics	Pros	Cons
Invention disclosures		

Patents Licenses Startup companies Publications Consulting Industry contract research Industry affiliates Jobs created Economic impact Patent and paper citations Presentations Acquisitions Revenue generation Societal impact		

Conclusion that some metrics are better than others (intend to stimulate conversation, not dictate an answer); invite people to prove or disprove the conclusions drawn.

Technology Readiness Levels

Useful but lessons learned from EU projects (to be discussed 3rd session on Day 1) - need for adoption of TRL´s for different pipelines and subtaks to get measurable progress in short term (1-2 years)

Further discussion points:

- **Consideration of ethics and the interference with impact.**
- **Consideration of the position/role of open source in translation**
- **Consideration of interdependencies/tradeoffs between impacts (e.g., industrialization vs CO2 emissions; drug pricing vs innovation) and approaches (e.g., open versus proprietary; start-ups versus industry partnerships)**
- **Consideration of the need for commercialisation – whether or not this is for profit or non-profit i.e., at some point a product has to be manufactured, at which point it has become commercialised? Can impact be measured without a straight line to commercialization, e.g. shared resources, network effects? Examples?**

Voices from the real world: series of "interview boxes" on translational impact – from different perspectives

Maurizio Vecchione, Chief Innovation Officer, Terasaki Institute, Los Angeles, USA

View from non-profit, non-academic, non-technology-driven orientation
Maurizio Vecchione serves as the Chief Innovation Officer of the Terasaki Institute for Biomedical Innovation. He is moved by a vision that access to effective and quality healthcare is a human right and critical to equity and progress around the world.

He is also the co-founder and co-General partner of AdAstral, and is also jointly serving as the president and CEO of Washington Global Health Alliance, a non-profit organization that plays a pivotal role in fostering collaboration among leading global health institutions

Maurizio has spent the last 30 years at the forefront of biomedicine in global and public health, focusing on innovation to improve the lives of the world's most vulnerable people. From 2014 until 2020, he was previously the executive vice president for Global Good and Research at Intellectual Ventures (IV) where he oversaw collaboration with Bill Gates to invent and deploy technology to address some of humanity's most daunting challenges. He simultaneously managed the Global Good Fund, the research programs of the Intellectual Ventures Laboratory and the Institute for Disease Modeling.

Maurizio has built global alliances for breakthrough programs in women's health, infectious disease prevention and elimination, primary care, and chronic disease management as well as cancer. He has been a pioneer of the use of Artificial Intelligence in medical applications, including being involved in breakthroughs in cervical cancer screening through machine learning as well as automatic interpretation of ultrasound images via AI. He serves on the Leadership Board of the University of Washington Department of Global Health and the Advisory Board of the UCLA Ronald Reagan Medical Center; he is on the governing board of the Italian Scientists and Scholars in North America Foundation; on the Advisory Board of the Performance Theater; the editorial Board of IEEE Spectrum; an Advisor to Bill Gates' private office Gates Ventures; an executive partner in Ethos Capital. He also has been from time to time an advisor to the US Government, the EU and multilateral organizations such as WHO and UNICEF in matters of innovation and population health.

Throughout his career, Maurizio has blended scientific research and innovation with impact investing delivering a double bottom lines of investor return and social impact.

Tejal Desai, Ernest L. Prien Professor and Chair of the Department of Bioengineering and Therapeutic Sciences at University of California, San Francisco, Director of Health Innovation Via Engineering Initiative (HIVE), and head of the UCSF Therapeutic Micro and Nanotechnology Laboratory, San Francisco, USA

Impact from academic innovation. Tejal Desai's research merges advanced micro and nanotechnologies, fundamental insight into cellular behavior in engineered environments, and novel pharmacologic delivery approaches to address disease treatment and clinical translation, with some of her medical technologies now in translation. Prof. Desai describes translational success a bit differently to some of her academic peers, seeking to change the paradigm for translational success by solving select aspects of technologies that might produce that unexpected, yet significant, gains in manufacture, scale-up, cost-of-goods, or some functional challenge - stimulating new thinking about addressing old problems with a more focused, rather than holistic strategy.

Scott Gochnour, VP, R&D, Civica Inc., Salt Lake City, USA (civicarx.org)

Impact from non-profit innovation. Today, often over 200 drugs reside on the FDA's "drug shortage list", termed "shortage medicines": generic but essential medications with no more manufacturing incentive so they simply are not made or marketed. Hospitals cancel procedures and treatments, and patients suffer without key medicines, that are no longer available. Civica, a uniquely structured non-profit generic drug company, was created to reduce and prevent drug shortages and associated price spikes that can accompany them. Scott claims that Civica is a disruptive model for a pharma company – they are not interested in protecting intellectual property nor in producing a profit. They are motivated to solve a single problem: shortage medicines. They have successfully innovated a new business model to counter market forces driving drug availability, including their status as the first not-for-profit pharma company, formally declared a "social welfare organization" in the US.

Emmanuelle Charpentier, Max Planck Unit for the Science of Pathogens, Berlin, Germany

A greater understanding of the fundamental mechanisms of regulation in pathogens (bacteria and viruses) is critical to generate new findings in basic science and possibly translate them into novel and transformative biotechnological and biomedical applications (e.g. genome editing tools, anti-infective strategies). A successful example of the application of our basic research in biotechnology and medicine is our recent discovery of an RNA-guided DNA cleavage mechanism that has been harnessed as an RNA programmable genome engineering technology and that stems from our research on the CRISPR-Cas9 adaptive immune system against bacteriophages (viruses of bacteria) in bacterial pathogens, especially *Streptococcus pyogenes*. Such discoveries are revolutionizing life sciences research and are opening whole new opportunities for biomedical gene therapies among other opportunities that are impacting society and humanity. The field of CRISPR-Cas applications continues to develop at dazzling speed, with exciting new developments emerging almost weekly.