



Implementation science: accelerating the pharma pipeline to its full potential

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In a recent letter to the editor, Olson *et al.* [1] discussed obstacles – often called ‘valleys of death’ – to the translation of healthcare innovations from clinical trials to routine real-world use [2]. They focused on implementation science’s capacity to speed the flow of innovations through the pharmaceutical/biotech research pipeline, allowing fast and successful translation of innovative products, pills and programs into standard clinical practice.

Defined as “*the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice and, hence, to improve the quality and effectiveness of health services and care,*” [3] implementation science has the potential to shorten innovations’ time-to-market by supporting organization- and clinician-level adoption while enhancing reach to diverse patients and populations. Surprisingly, while these implementation outcomes largely determine the success of pharmaceutical/biotech innovations, implementation science has received little attention from those sectors [1,4]. Indeed, considering implementation science’s explosion across clinical fields over the past decade and the results that have fueled that growth [5], such conservative adoption rates among industrial players defy understanding.

Implementation science: a missing link in improving uptake of pharma innovations

In a 2021 *Science* article, Proctor *et al.* [6] called implementation science a ‘missing link’ that would allow research infrastructures to span valleys of death by identifying barriers to uptake, then providing strategies to overcome them. For example, they cite the COVID-19 vaccines: even with an urgent clinical need and proven effectiveness vaccine uptake was a limiting factor, also among healthcare workers [7], in battling the pandemic. They also recall the case of low-dose beta-blocker treatment after myocardial infarction. Despite evidence from randomized controlled trials dating back to 1982, adoption spread at a snail’s pace: 15 years after registration, only 34% of patients discharged after MIs received beta blockers. This treatment took 25 years to achieve universal adoption [6].

In fact, there is no guarantee that even iron-clad evidence from randomized controlled trials or pragmatic trials will yield speedy clinical adoption for new treatments. As Olson *et al.*’s [1] commentary reminds us, even after the PARADIGM-HF trial results indicated that sacubitril/valsartan treatment brought clear improvements in heart failure patients, slow clinical uptake was observed.

Based on these and similar cases, we are certain that every pharmaceutical/biotech company has encountered unexpected post registration barriers to their products’ clinical adoption. Failure to proactively identify and address such barriers can lead to longer time-to-market, suboptimal adoption by healthcare systems and prescribers and decreased reach of target patients.

Even when early successes, for example, adoption by healthcare systems and providers accompany extended reach, innovations’ sustainability is far from guaranteed. Implementation issues are also associated with poorer



clinical outcomes and higher healthcare costs. Especially in pharma, methodologically sound, proactively planned implementations that anticipated such issues would lead to faster and larger returns on investment.

Likely multilevel barriers to real-world translation in pharma

Multilevel barriers that can hinder pharma or biotech innovations' translation to daily clinical practice include new routes of administration (e.g., needle fear [8]), incongruencies between follow-up timing and/or facilities and those of usual clinical care, inadequate time, personnel or other resources to implement innovations and reimbursement issues, to name a few. While pharma/biotech firms have integrated market research and real-world data analysis into their research pipelines, these typically focus on product registrations and launches, not on anticipating barriers identified early based on early in the development phases. After a product's launch, then, pharma firms have no adequate strategies to overcome such barriers when they arise. Results would include slowed or even stalled implementation.

Methodological building blocks

Asking implementation science research questions can enhance pharma innovations' uptake and sustainability, maximizing opportunities for real-world success. To address these questions, implementation science offers six building blocks: contextual analysis, (patient and public) stakeholder involvement, the use of theories and frameworks, implementation strategies, focus on both effectiveness and implementation outcomes (e.g., hybrid designs) and a transdisciplinary approach [9].

No 'one size fits all' approach will work for implementation: each successful implementation is tailored to the context and setting for which it is planned. Very early in the process, a thorough contextual analysis will identify relevant multilevel barriers to an innovation's development, refining and testing [10,11]. Theoretical framework(s) guide researchers through project phases and ensure that relevant elements (e.g., contextual factors) are identified and addressed. Defining a patient and public involvement strategy to inform all project phases guarantees that the relevant stakeholders' voices are heard. For instance, stakeholder input helps anticipate and overcome barriers via contextually adapted implementation strategies, in other words, methods or techniques to enhance a program or practice's adoption, implementation, sustainment and scale-up [12].

In addition to effectiveness outcomes, implementation science methods explicitly illuminate implementation processes via implementation outcomes – intermediate outcomes that indicate chosen implementation strategies level of success. This dual focus on effectiveness and implementation outcomes is achieved through hybrid study designs. Finally, implementation science requires expertise from multiple fields: a transdisciplinary approach is essential.

Some of these methodological considerations are not exclusive to implementation science. It is their combination that increases an innovation's chances of successful adoption, reach and sustainability in real-world settings and that enhances clinical and economic benefits.

Early consideration of implementation questions

While attention to multiple methodological principles is a complex undertaking, a scientifically rigorous approach to translating innovations to real-world settings – and doing so early in the pharma/biotech R&D process – will most likely enhance a product's chances of success [4]. Managing translational efforts without drafting an implementation blueprint is analogous to piloting a jet without devising a flight plan, inspecting the runway for hazards or even checking the fuel levels (i.e., conducting a barriers and needs assessment) and without making contingency plans to minimize potential issues' effects (i.e., implementation strategies to overcome identified barriers).

Additionally, there is often not a planned consideration of what implementation success looks like. Until the product's launch, then, little thought is devoted to how to encourage and measure adoption by clinicians, reach to patients or other critical implementation outcomes that occur before traditional clinical outcomes (e.g., symptom improvement, morbidity and mortality, etc.) can be achieved.

The details of how to integrate implementation science into the pharma/biotech pipeline will require close collaboration between all involved actors. That pipeline's well-defined processes from phase I–IV will not be equally enriched by implementation science; still, early consideration of context will certainly help alleviate challenges that generally appear in phases III or IV. After registration has been achieved, implementation science methods can be intensified.

Triple win also in collaboration with the academic world

No definitive business case is yet available for applying implementation science methods to the pharma/biotech pipeline; still, numerous clinical examples illustrate how complex interventions can be sustainably implemented in real-world settings [5,13,14].

Olson *et al.* [1] posit that implementation efforts should involve all players along the pharma research pipeline in interaction with each target healthcare system and its decision makers. With implementation science developing rapidly, close collaboration with academic teams specialized in its methodologies offers synergies to realize what Olson *et al.* [1] called a ‘triple win’: partners from healthcare systems, pharma/biotech and the academic world will strengthen implementation science as part of the tool box to decrease time to market and increase patient reach.

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