White paper

Real-world evidence

Leveraging implementation science to enhance the value proposition for medicinal products and devices

Seven ways to improve asset lifecycle management

Authors:

Meredith Y. Smith, PhD, MPA, FISPE, senior director and lead, implementation science group
PPD clinical research business of Thermo Fisher Scientific

Rachel Davis, PhD, research scientist, implementation science group
PPD clinical research business of Thermo Fisher Scientific

Klaudia Kornalska, MSc, research associate III
PPD clinical research business of Thermo Fisher Scientific

Addressing research-to-practice challenges through implementation science

Understanding how best to accelerate the translation of clinical research into practice (from "bench to bedside") is one of the biggest challenges that sponsors of new medicinal products face today.

Implementation science aims to address these research-to-practice gaps so that potential challenges in uptake, integration and sustained adoption of new medicinal products and/or supportive practices, tools and technology into clinical care can be overcome.

Using scientifically informed frameworks, strategies and outcomes, implementation science examines how best to achieve effective implementation and uptake of proven innovations and practices into routine use so they can reach their expected health benefits. As a result, patients, providers, policymakers, payers, regulators and sponsors benefit.

Sponsors can improve implementation effectiveness, efficiencies and systems with implementation science research

There are many ways in which implementation science can help sponsors of investigational or marketed medicinal products (and/or supportive practices, tools and technology) in clinical care.

Improving operational efficiencies across a clinical trial, increasing medication adoption and uptake, tackling nonadherence and improving systems for monitoring adverse drug events are a few examples. Similarly, as sponsors seek to differentiate their products by going "beyond the molecule" to provide a suite of supportive services and tools that offer a comprehensive care experience for patients, these new ancillary tools and practices can benefit from implementation science research approaches as well.

Implementation science research can improve the development and lifecycle management of medicinal products in multiple areas (Figure 1). For example, for a newly licensed drug, implementation science research can aid in understanding ways to improve the implementation of new support tools to facilitate prescribing and dispensing. In contrast, for a newly approved therapy that requires daily patient visits to a clinic, implementation science research can help identify how to improve the patient experience (e.g., via streamlining the care-delivery process).

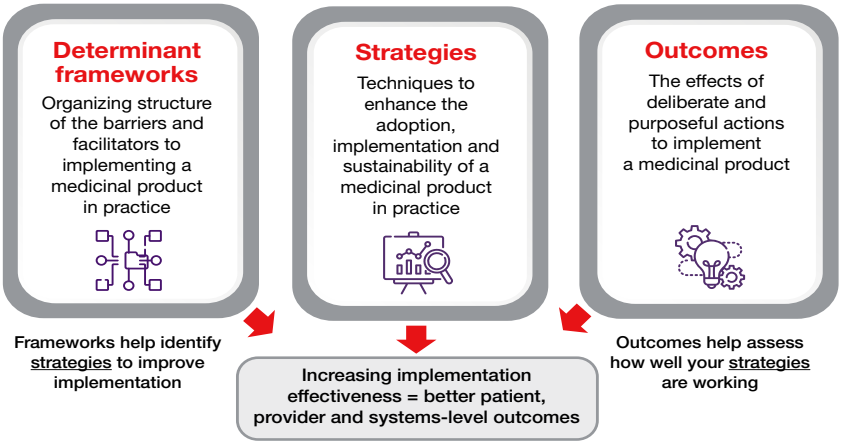
How implementation science research could have helped: The Pfizer-BioNTech COVID-19 vaccine case study

Despite the proven efficacy of Pfizer-BioNTech's COVID-19 vaccine, its uptake (among both providers and patients) was lower than expected, given past experience with prior vaccine rollouts.

Concerns about long-term side effects, inefficient distribution channels, the requirement for ultra-cold storage and the lack of accessibility to vaccine clinics were just some of the implementation challenges.

If implementation science research had been initiated earlier in the vaccine development phase, these barriers could have been anticipated and policy makers would have been able to plan and implement specific strategies to address barriers during vaccine rollout.[2]

Figure 1. How implementation determinant frameworks, strategies and outcomes work together to improve outcomes for medicinal products.



Implementation science draws upon a set of scientific methods and approaches. The defining hallmarks of implementation science research include the following:

1. Determinant implementation frameworks (i.e., "things" that tell you what factors may affect successful implementation)
2. Implementation strategies (i.e., "things" that tell you what you can do to address these factors)
3. Implementation outcomes (i.e., "things" that tell you how well your implementation strategies have been working)

Implementation science research provides key insights in the drug and device development process

Identifying barriers in preclinical and clinical development

There are many ways that the general principles and methods of implementation science research can be applied to provide critical insights in early phases of the product research and development process (Figure 2). For example, implementation science research studies can disentangle the reasons for low patient uptake and/or retention across Phases I–III in clinical trials. Based on the barriers identified, implementation strategies can be selected and implemented to minimize attrition rates at later stages in the trial trajectory.

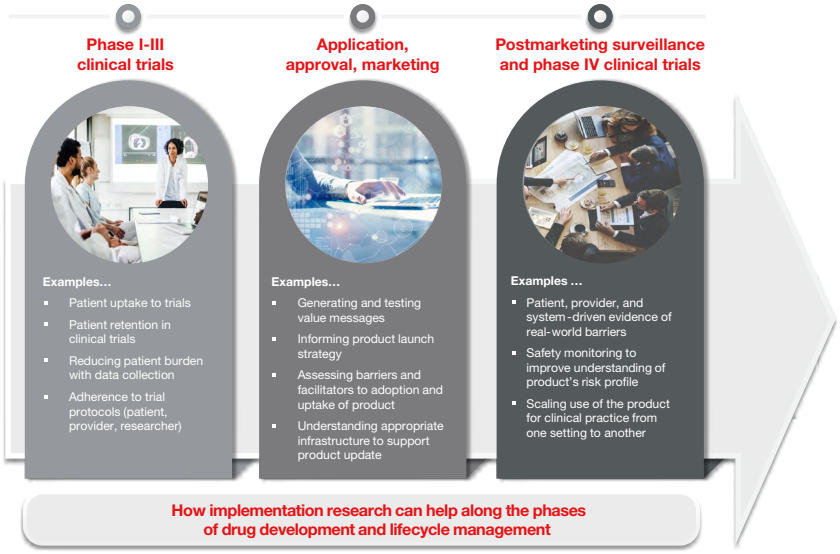
Implementation science studies can also be conducted to examine the early causes of patient nonadherence or to understand patient barriers (and facilitators) to initial drug use (initiation), to taking the drug as prescribed (implementation), to continuing to use it (persistence) or to understanding providers' nonadherence to trial protocol procedures.

The benefit to sponsors of conducting implementation research concurrently with clinical trials is that problems can be mitigated as early in the development process as possible through multilevel solutions that target different implementation issues. For the sponsor, this means fewer delays in achieving trial completion, a greater likelihood of obtaining a representative sample (because of higher trial retention rates) and improved clinical outcomes (because of increased adherence). These factors, in turn, can generate greater trust in the product among patients and providers, thereby potentially accelerating product uptake once on the market.

Did you know implementation science can help your product development and lifecycle management in all these areas?

- Self-management
- Market access
- Pharmacovigilance
- Patient involvement
- Medication ancillary tools
- Marketing
- Manufacturing and distribution
- Adherence
- Patient and provider satisfaction
- Data collection
- Licensing
- Health care system partnership
- Trial operational efficiencies
- Medication reconciliation
- Scale-up and rollout
- Patient experience
- Resource saving
- Product uptake

Figure 2. Implementation science research along the medicinal products and device management life cycle.



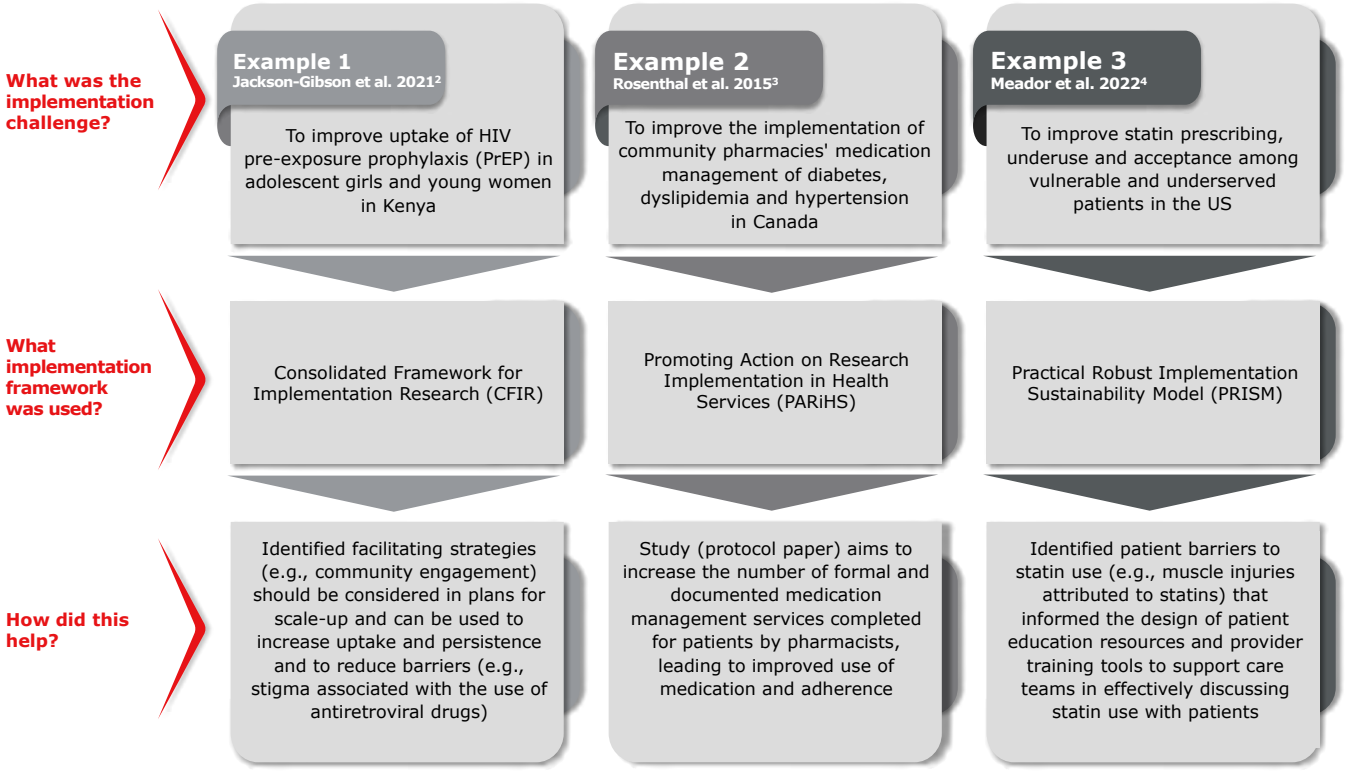
Evidence-based practices to increase uptake and adoption

At times, it can take years for providers to prescribe or adopt a newly approved medicinal product or for patient uptake to occur.

The reasons for the delays are complex and result from incomplete data on clinical effectiveness and long-term side effects of the drug, as well as a range of other factors including manufacturing issues, distribution complexities, providers' unfamiliarity with the new product, lack of clinical staff adequately trained to administer the drug or other health care system constraints.

Implementation science methods can help increase uptake and adoption by guiding how best to position a drug at launch as well as determining what infrastructure, policies and procedures need to be in place to adequately support its use in real-world health care delivery. (Figure 3)

Figure 3. How implementation science frameworks can support appropriate uptake and medication use.



Strategizing scale-up and dissemination

Although a wealth of clinical effectiveness evidence may exist for a drug in one setting with one patient population, it does not mean that attempts to implement it in other contexts will be successful. Factors relating to the clinical setting or infrastructure, patient (or provider) education, inappropriate use of diagnostic tools and cost pressures are just some of the challenges that can contribute. Increasing uptake or improving the rollout of a drug from high-resource to low-resource contexts can be particularly vexing. Implementation science research can be used as a means for sponsors to work within the health care systems where the drug is being implemented so that they can understand and anticipate potential bottlenecks. With this approach, appropriate strategies can then be developed to ensure that the medicinal product (i.e., drug or device) is reaching as many eligible patient populations that can benefit.

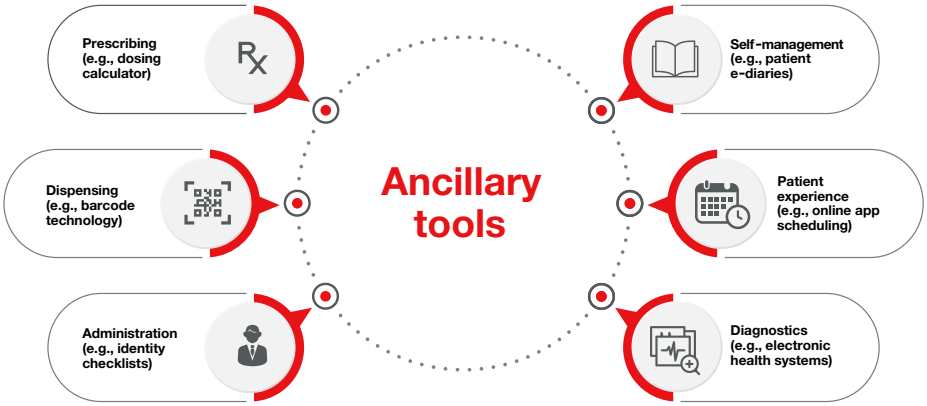
Tackling medication nonadherence

Medication nonadherence is a global endemic issue that transcends every patient population and disease group. Approximately half of prescription drugs are not taken as prescribed, resulting in increased morbidity, premature death and high costsworldwide. Implementation science research offers a novel and innovative way of tackling nonadherence, which, despite concerted efforts, has not improved considerably over the years. By taking a systemic approach that identifies and breaks down the multilayer barriers and facilitators to adherence for different patient populations, tailored strategies can be put in place to encourage successful and sustainable medication use.

Supporting safe and appropriate medication management with ancillary tools

In the past decade, an increasing number of ancillary tools aimed at patients and providers have been developed to support safe and appropriate medication use and improve care processes and efficiencies. As a result, this has enhanced the patient experience through providing a more comprehensive care package. However, like the medicinal products they are intended to serve, these tools can face implementation challenges that may result in suboptimal uptake and use. Through implementation science research, challenges to implementation (and use) of these ancillary tools can be addressed, which can increase the likely uptake, adoption or continued use of the drug. (Figure 4)

Figure 4. Ancillary tools to support safe and appropriate medication use.



Redesigning approaches to pharmacovigilance

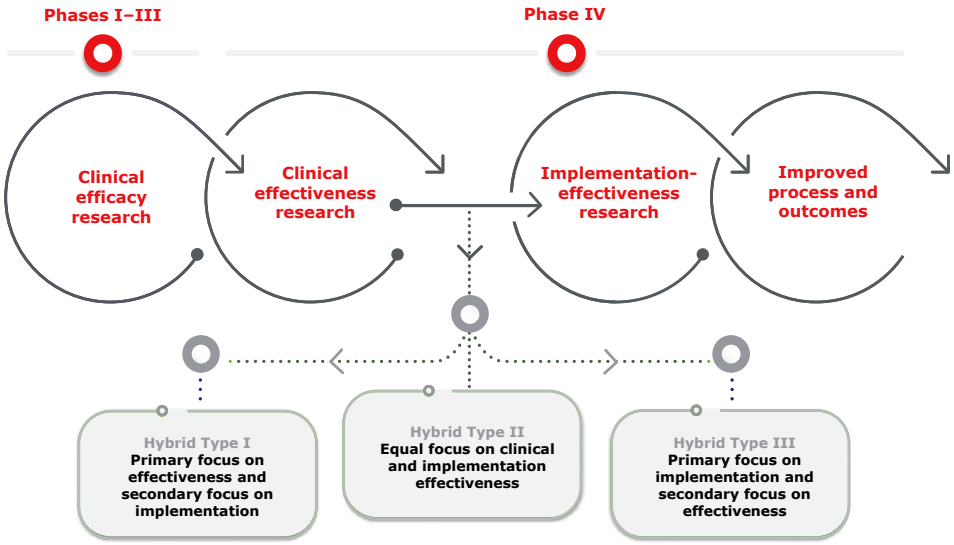
It is vital that providers, patients and caregivers report any adverse effects (AEs) of a medicinal product to the marketing authorization holder in a timely manner so that appropriate actions can be taken. However, various factors can deter individuals from reporting such events to pharmacovigilance systems. Providers or patients who are unfamiliar with reporting guidelines or lack confidence on how to appropriately report a medication-related AEs are just two of many factors that may contribute to this problem. Implementation science research helps uncover the myriad barriers that prevent timely reporting of AEs. Comprehensive information on the range of factors that inhibit AE reporting can help companies redesign their processes and approaches to pharmacovigilance that can robustly support safe and appropriate medicinal use.

Disseminating a novel digital asthma inhaler across different clinical settings

Care Gap: Asthma continues to be sub-optimally managed for many patients in the United States (U.S.) due to limited access to clinical care. A novel digital asthma inhaler was developed to address this challenge.

Implementation science study and results: A mixed methods implementation study was conducted involving interviews with and surveys of asthma specialists in sites across the U.S. who were early adopters in prescribing the digital inhaler. Results revealed that the amount of time spent training and onboarding patients to use the inhaler, and pharmacy, procurement and prior authorization challenges were barriers that limited the uptake and adoption of the digital inhaler. Initial use of the technology, careful selection of appropriate patients, specific training and onboarding strategies and processes to facilitate prior authorization were implementation facilitators that helped increase uptake of the digital inhaler.[1]

Figure 5. The use of hybrid implementation-effectiveness trials to understand medicinal product outcomes across the drug development lifecycle.



There are three main types of hybrid study designs, each of which places a different emphasis on clinical and implementation effectiveness objectives. (Figure 5)

Resource savings

Another important way that implementation science research can help sponsors is through accelerating understanding on the real-world effectiveness of drugs using "hybrid" trials.[6,7] In contrast to traditional randomized controlled drug trials that take a staged approach examining drug efficacy first, then aspects of real-world effectiveness after, hybrid studies assess clinical effectiveness and implementation effectiveness in parallel. By assessing these factors for the same patient populations and settings, sponsors can better determine why a drug's effectiveness may be lower than expected.

Although these types of studies have been applied to different patient populations in the context of medication use, they are still largely underused in the context of pharmaceutical product development. The benefits to sponsors undertaking these studies are considerable and include quicker translational gains, better return on investment and targeted solutions to implementation barriers that are more reflective of real-world issues.

Conclusion

Implementation science research studies offer many benefits to sponsors of new medicinal products and devices. Through application of scientifically informed methods, implementation science research can shed light on barriers to the uptake, adoption, sustained use and scale-up of new health care innovations and identify appropriate and effective strategies to address those barriers. Studies can be conducted at any stage of the medicinal product and development lifecycle, ranging from early-stage clinical trials to large-scale rollout in clinical practice across different geographic settings. By using implementation science research to close important research-to-practice gaps, these new innovations can reach more patients and help achieve better health outcomes.

References

1. Schafer E, Mosnaim G, Bajowala S, et al. Use of theory-based implementation research to evaluate barriers and facilitators to implementation of a novel digital inhaler technology in clinical practice. J Allergy Clin Immunol. 2023;151(2 suppl):AB164. 2023 American Academy of Allergy, Asthma and Immunology Annual Meeting abstract 504. doi:10.1016/j.jaci.2022.12.512
2. Olson MS, Rootkin L. The triple win - implementation science benefits patients, healthcare systems and industry alike. J Comp Eff Res. 2022;11(9):639-642. doi:10.2217/cer-2022-0058
3. Jackson-Gibson M, Ezema AU, Orero W, et al. Facilitators and barriers to HIV pre-exposure prophylaxis (PrEP) uptake through a community-based intervention strategy among adolescent girls and young women in Seme Sub-County, Kisumu, Kenya. BMC Public Health. 2021;21(1):1284. doi:10.1186/s12889-021-11335-1
4. Rosenthal MM, Tsuyuki RT, Houle SK. A cluster-randomized controlled knowledge translation feasibility study in Alberta community pharmacies using the PARiHS framework: study protocol. Pilot Feasibility Stud. 2015;1:2. doi:10.1186/2055-5784-1-2
5. Meador M, Bay RC, Anderson E, Roy D, Allgood JA, Lewis JH. Using the Practical Robust Implementation and Sustainability Model (PRISM) to identify and address provider-perceived barriers to optimal statin prescribing and use in community health centers. Health Promot Pract. 2022:15248399221088592. doi:10.1177/15248399221088592
6. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care. 2012;50(3):217-226. doi:10.1097/ MLR.0b013e3182408812
7. Landes SJ, McBain SA, Curran GM. An introduction to effectiveness-implementation hybrid designs. Psychiatry Res. 2019;280:112513. doi:10.1016/j.psychres.2019.112513

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