

The Impact of C-Path's Quantitative Medicine Program: Generating Cutting-edge Solutions to Accelerate Drug Development

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As a global leader in regulatory science, the generation of actionable quantitative solutions to accelerate drug development lies at the heart of the Critical Path Institute's (C-Path) core competencies, led by the Institute's Quantitative Medicine (QuantMed) Program.

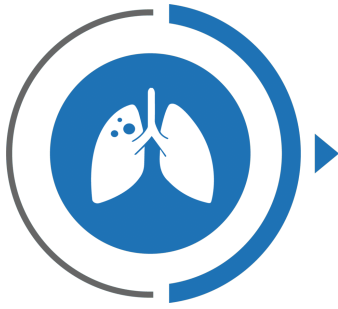
In the context of medical product development, quantitative models are mathematical tools that describe the complex relationships between relevant aspects of product development (exposure/response, disease progression, trial design, etc.).

These tools provide the basis for Model-Informed Drug Development (MIDD), or the application of a wide range of quantitative models to aid in decision-making and reduce uncertainty in medical product development. MIDD facilitates an optimized, more efficient approach to bringing novel products to patients, by reducing costs, time and risks. The U.S. Food and Drug Administration (FDA) formally recognized MIDD as an important component of the Prescription Drug User Fee Act (PDUFA) VI reauthorization, committing to advance many key FDA activities through increased MIDD efforts. However, to provide well-built quantitative models capable of achieving the many goals of PDUFA VI and of product developers, collaborative knowledge sharing efforts must take place.

Due to their complex nature, robust regulatory-ready quantitative models require significant methodological expertise, intimate knowledge of the product development ecosystem, and expertise in the intended area of application for given models.

With the rising regulatory focus on MIDD globally, C-Path formed its Quantitative Medicine (QuantMed) Program to lead the field in the generation of such MIDD solutions. QuantMed's goal is to leverage resources from a network of experts in industry, academia, nonprofit and regulatory sciences to develop solutions that incorporate quantitative methodologies in pharmacometrics, statistics, systems pharmacology, artificial intelligence and digital data analytics. Since its inception, QuantMed has led the generation of 10 novel tools, in close collaboration with C-Path's consortia and Data Collaboration Center. These tools are available to sponsors and regulators through various mechanisms, and six have been successfully reviewed and endorsed for use by FDA or the European Medicines Agency (EMA).

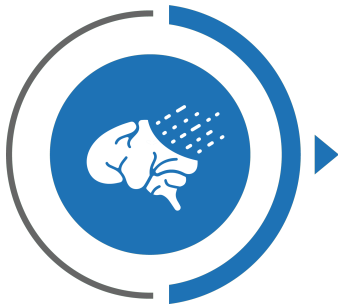
Through the generation of these solutions, C-Path's QuantMed Program has made a significant impact across a variety of chronic illnesses:



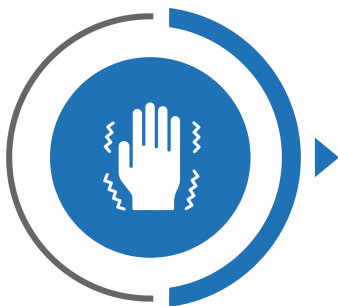
Tuberculosis: C-Path contributed to the approval of the first new drugs and drug-regimens against tuberculosis in over 50 years; the quantitative translational and clinical solutions now support a well-established and solid pipeline of new drugs and drug-regimens under development.



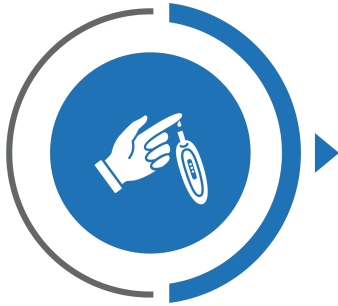
Polycystic Kidney Disease: C-Path paved the way for the approval of the first drug indicated to slow progression of polycystic kidney disease through the use of an imaging-based reasonably likely surrogate endpoint. The availability of a reasonably likely surrogate endpoint in this orphan indication has resulted in a healthy pipeline of new products under development.



Alzheimer's Disease: C-Path helped transform paradigms in clinical trials involving Alzheimer's through quantitative clinical solutions. These solutions are being implemented by developers to support the design of many clinical trials and are expected to contribute to successful new drug approvals.



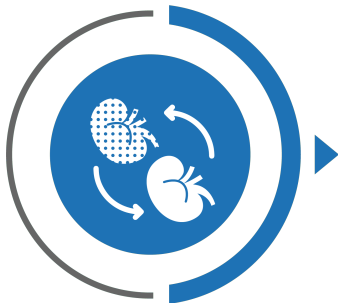
Parkinson's Disease: C-Path helped improve trial efficiency by generating the evidence to support a model-based imaging biomarker tool for patient selection deemed acceptable by regulators for use in Parkinson's disease clinical trials.



Type 1 Diabetes: C-Path further optimized patient selection for T1D prevention clinical trials by developing quantitative models that predict disease progression according to patient features and autoantibody status.

QuantMed's work to generate new tools that further its impact in these therapeutic areas continues.

Existing efforts by QuantMed in other disease areas are also ongoing:



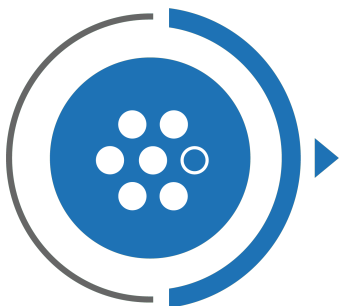
Kidney Transplantation: C-Path is generating a series of quantitative solutions to optimize the implementation of novel metrics to evaluate the efficacy and safety of novel medical products to extend the useful lifespan of kidney transplant grafts for patients in need.



Duchenne Muscular Dystrophy (DMD): C-Path recently completed a clinical trial simulation platform, comprised of quantitative solutions for multiple clinically relevant measures of DMD progression, transforming drug development paradigms for this rare condition.



Neonatal Drug Development: C-Path is transforming real-world data into actionable real-world evidence in neonates, to help optimize drug development for bronchopulmonary dysplasia, as well as to improve the understanding of actionable laboratory values for future clinical trials in neonates.



Rare Diseases: C-Path's work is helping accelerate drug development in rare diseases, by generating actionable quantitative insights across multiple conditions, which can inform the design of clinical trials in diseases with very limited sample sizes.



“The MIDD post-doctoral fellowship at C-Path has transformed my knowledge and experience in MIDD. I have been able to work closely with experts in the field of quantitative modeling and continue to receive guidance, direction and training to better hone my modeling skills and become involved in other important projects that I wouldn’t have otherwise had the chance to be a part of. Having been included in a project involving cutting-edge computer medical image analysis with increasing size and demand is an opportunity I might not have received anywhere, but C-Path. This post-doctoral fellowship has advanced my knowledge and skillset in a multitude of areas and has boosted my self-esteem and confidence with projects, especially in therapeutic areas I had previously had little exposure to. The Quantitative Medicine Program at C-Path will have a lasting impact on my career well

beyond the conclusion of my fellowship.”

-Maedeh Beheshti, PhD, Post-doctoral Fellow

With the growing importance of MIDD, C-Path’s QuantMed Program has now begun to train the next generation of quantitative scientists that will transform paradigms in medical product development. QuantMed leads a postdoctoral fellowship program in MIDD and is currently overseeing training of a postdoctoral fellow. QuantMed has developed a strong presence within the modeling and simulation community, teaching and presenting their work at several high-caliber conferences each year, including American Conference of Pharmacometrics and American Society for Clinical Pharmacology and Therapeutics. Additionally, QuantMed has led an effort with members of the MIDD stakeholder community to develop a training course and provide broader penetration of the MIDD concepts and techniques to scientists from the academic, industrial and regulatory communities. This training is being launched in a common training platform with support from an extensive network of experienced MIDD practitioners to expand the pool of trained scientists in each environment and, ultimately, ensure robust adoption and uptake of MIDD principles.

Collectively, C-Path’s QuantMed Program has made an immense impact on the medical product development community. With over 10 tools currently being utilized by product developers across diverse therapeutic areas and many more under development, alongside a broad and robust training and education portfolio, QuantMed will continue to impact the field into the future.

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