PRECISION MEDICINE RESEARCH: How Advanced Data Analytics Support The Journey From Clinic to Bedside

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During an expert panel convened by Parexel and Pharma Intelligence in Santa Clara, industry leaders discussed the use and optimization of precision medicine trial strategies.

MODERATOR

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Executive Director, Editorial
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ROUNDTABLE PARTICIPANTS

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recision medicine offers huge promise to patients and health systems. It can also substantially increase the efficiency of drug development by enabling more focused, data-rich clinical trials. A recent study by The Economist Intelligence Unit (EIU), commissioned by Parexel, found that precision medicines were 10% more likely to reach the market than conventional therapies, and were adopted more rapidly onto payer formularies. The report also found that the number of publication references and abstracts on precision medicine trials captured by the search engine PubMed has increased sharply since 2013, suggesting that adoption of such trials is still in a relatively early phase. On average, precision medicine studies accounted for nearly 14% of the examined 20,000 completed Phase II and III trials between 2012 and 2017, according to Informa’s Trialtrove.

Rapid progress in genomic sequencing, biomarker identification, data capture and data analytics has helped accelerate the adoption of precision medicine. This goes beyond linking a therapy to a diagnostic. Precision medicine is a holistic approach that takes into account multiple aspects of patients’ lives and health, drawing on electronic health records (EHRs), clinical records, wearables and lifestyle personal data – from genomics tests, clinical trials. But very few of them are actually producing direct patient benefit,” said Minnie Sarwal, MD, PhD, Co-Founder and Chief Medical Officer for KIT Bio and Professor of Surgery at University of California, San Francisco.

“Data infrastructure and standards
Data quality, consistency and transparency are key to the successful implementation of precision medicine. Yet much health data, including electronic health records (EHRs), remain fragmented, incomplete and highly variable, often with poor system interoperability. Standards are required to ensure that appropriate tools and methods are used for handling, integrating and interpreting new data types. For instance, determining what kinds of datasets can be shared or linked, under what circumstances, or whether historical data may be used as control arms in some situations, to avoid the burden of recruiting control groups. Building and attracting appropriately trained workforces
Precision medicine involves new skills, and new ways of working. As these

FROM CLINIC TO BEDSIDE

There is incredible research [into precision medicine] and a lot of really interesting hypotheses, biomarkers and clinical trials. But very few of them are actually producing direct patient benefit,” said Minnie Sarwal, MD, PhD, Co-Founder and Chief medical officer for KIT Bio and professor of surgery at University of California, San Francisco.
New trial designs and funding structures

New clinical trial designs – including adaptive trials - are required to develop and employ precision medicine most fully. Such designs may involve identifying, validating and using multiple endpoints within a single study, to maximize the chances of finding meaningful data. Standards must be agreed upon around such trials, as well as around biomarkers, often used as endpoints. These novel trials will require more flexible funding structures. Government grants often involve fixed costs and timelines, which can make it difficult to evolve adaptive trial designs as results emerge. Pharmaceutical firms may also face unpredictable trial costs as a result of developing new kinds of data. Whole genome sequencing, for example, may require providing patients with genetic counselors, which could have long-term implications. Drug firms, interactions with patients are tightly regulated, both within and outside of trial settings, so the relationship beyond a clinical trial is challenging in today’s environment.

“Today’s privacy laws and guidelines can make it difficult to return results to patients outside of the clinical trial setting. It can be done, with the varying experts and a little innovation we can find a solution that enables the sharing of this sensitive information without compromising privacy and the regulations that govern it,” said Anita Nelsen, Vice President of Translational Medicine at Parexel.

Data ownership and privacy

As well as challenging – and changing - the traditional pharmacopoeia, precision medicine urgently requires a clarification of data ownership, access and privacy laws. That means working with ethics committees and engaging in a broader public debate to encourage data sharing where it is to everyone’s benefit. Meanwhile, organizations would require robust guidelines to protect sensitive data and minimize patient risk. “It’s really important for us to get ahead in this privacy issue. If we don’t, it is going to hurt biomedical research. We need to explain the advantages of sharing certain kinds of data, like LIMS data, where it is to everyone’s benefit. This will be especially helpful if through appropriate awareness and education campaigns, will empower individuals to help drive this move forward. Pharma and other stakeholders must continue to encourage more patients to engage in clinical trials and to remain engaged over the course of their treatment and beyond.

SOLUTIONS

Precision medicine’s promise is already driving efforts to overcome these challenges and help improve the efficiency and sustainability of drug research and development. Bringing together stakeholders from government, industry, academia and patient organizations the success these issues and work out how to leverage innovation in clinical trial design may help bridge the gap from bench to bedside. These efforts can then be expanded, and lessons from them shared more widely, to accelerate precision medicine and ensure that all stakeholders benefit.

Growing data infrastructure

Examples of national data-collection programs include the US Department of Veterans Affairs (VA)’s Million Veteran Program, the NIH’s All of Us Program, the UK’s 100,000 Genome Project and France’s National Cancer Institute’s network of diagnostic testing centers. These programs are creating the data infrastructure required for precision medicine, and highlighting implementation requirements and barriers. The VA has shown us what is needed to better understand the barriers, and who is needed to facilitate the use of precision medicine for patients and caregivers,” noted Sam Hanna, Associate Dean of Graduate Programs at American University.

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tion and is helping build and maintain data quality and consistency. Other technologies gaining popularity, like blockchain, can facilitate data ownership, access and portability, while helping address privacy and security concerns. Technologies such as Apple and Google are working on tools that will enable individuals to securely hold and access their personal data aggregated from across multiple real-world sources. Distributive computing algorithms allow data to be aggregated in a blinded fashion, maintaining anonymity for individual data components, yet generating powerful statistics. Such tools may mean we can “by concerns around data leakage and data privacy,” said Ying Lu, PhD, Co-Director of the Stanford Center for Innovative Study Design (CISD) and the Biostatistics Core of the Stanford Cancer Institute.

Motivated patients
Patients are increasingly involved in their health care, and in advocating for faster, more efficient drug development and approval. The more they understand about precision medicine and its potential benefits, the more likely they are to engage in trials and help build the required datasets, experience and, ultimately, treatments. Rare disease patient groups, such as the Multiple Myeloma Research Foundation, are particularly highly motivated, well-organized communities creating useful, high-quality data. Studies like the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD)-funded Precision Medicine Project put patients front and center, encouraging adherence and interest through shared data and extensive communications.

Integrating patient preferences into endpoint selection is another emerging goal. It may also address the risks of diagnostic development more than anything,” said Gary Gustavsen, Partner, Personalized Medicine, Health Advances.

Progressive regulators
Precision medicine requires a progressive, flexible regulatory landscape. The US Food and Drug Administration (FDA) in 2018 approved a record 25 precision medicines (42% of the total), according to the Personalized Medicine Coalition, including the second drug based on a biomarker, rather than a tumor of tissue type. Companion diagnostic approvals have grown alongside them, and in 2018, the first FDA-approved direct-to-consumer genetic test for determining cancer risk arrived. Regulators also play a key role in defining and helping validate better endpoints to facilitate precision medicine trials, through initiatives such as precisionFDA – a platform to evaluate genomic sequencing assays and explore new ways to regulate them. Patient-centric trial designs are gaining traction among pharma firms, buoyed by government-funded initiatives such as the US Patient-Centered Outcomes Research Institute (PCORI) and the European Medicines Agency (EMA)’s proposals to better integrate patient data into benefits-risk assessments of new drugs. (These form part of EMA’s draft “EMA Regulatory Science 2025 Strategic Reflection,” currently out for public consultation.) More convenient, efficient diagnostic tests are being developed, including multiplex genomic tests that measure several markers at once. Multi-stakeholder collaborations to advance precision medicine are multiplying. One recent example is a project to harmonize the Personalized Medicine Coalition and conducted by Health Advances to understand how precision medicine is being used in patients across US health care systems, setting benchmarks to measure progress, highlighting lessons learned and outstanding integration challenges. Better-adequate and educational opportunities are also emerging, including ways for health care professionals to become more fluent in data science, so they can fully understand and clearly translate test results for their patients. The panelists identified various efforts already underway to promote skills exchange:

• Data scientists and bioinformatics or physics post-docs are embedded among scientists at Sarwal’s lab at UCSF, leading to some interesting learnings.
• Hana highlighted efforts at Ameri
can University’s SPEXs that infuse use of critical analytical tools into medical graduates’ learnings, including data programming languages like R and Python. This means “all our students are better prepared once they get into the real world and actually work in these fields,” he said.
• Lu’s team at Stanford has col-
laborated with the University of Chicago and begun holding “Sta-
t4Onc” meetings, bringing together oncologists and statisticians, and organizing several other annual events bringing together patient advocates, statisticians and industry across the globe. “Accademia can serve as a liaison to bring people together to talk about topics of interest, avoiding conflict of interest,” suggested Lu.

FURTHER ACTIONS FOR ADDRESSING BARRIERS
The panel identified further actions needed to promote the development and implementation of precision medicine. These include:

• Fostering coordinated, multi-stake-
holder (pharma) research teams, including patients, across geog-
raphies to discuss new study designs that will inform patient enrollment and retention, while leveraging endpoints that align with patients’ experience with a disease and their responses to treatment.
• Designating “neutral” institutions, such as academic establishments, that can serve as liaisons for pharma, physicians, statisticians, pa-
tients and regulators to introduce ideas and facilitate consensus and acceptance on both sides. “I think the onus lies upon us in academia to really get pharma engaged,” said UCSF’s Sarwal.
• Producing a master “cheat sheet” for physicians faced with multiple diagnostic tests and drugs to help inform them about which test should be administered first to enhance patient outcomes faster and at lower costs.
• Communicating precision medi-
cine’s value to physicians and pay-
ers. Specifically, physicians must understand how precision medi-
cine can change their interactions with patients. Payers must be will-
ing to reimburse their systems to capture the long-term benefits of precision therapies – including by prescribing them right away in certain cases, instead of after multiple rounds of standard treat-
ment. “Payers are in the driver’s seat, and they are going to get into the game. If they don’t want to pay for it, it [PM] is not going to happen,” warned Abrahams.
• Increasing pharma’s efforts to break down internal silos among research and development and commercialization teams, and ensuring “wiring in” from early phases of scientific research.
• Aligning incentives for diagnostics and drugs, including by reducing the risks of diagnostic develop-
ment, creating incentives for diagnostic reimbursement and developing new kinds of pharma-
diagnostic alliances.
• Identifying and building relevant research programs for graduate students to prepare the future work-
force for precision medicine needs.

Endnotes
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“If there are ways, through precision medicine, to entice patients to get more involved, that will likely move the needle toward more efficient development more than anything,” said Gary Gustavsen, Partner, Personalized Medicine, Health Advances.

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