How real-world data is powering rare disease research

Part 3. RWD advances in China

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As real-world data (RWD) transforms the drug development landscape, its power to advance research is becoming tangible in the most challenging therapeutic arena—rare diseases. In this series, Parexel experts discuss current initiatives in North America, Europe and China that are accelerating the use of RWD in rare disease research.

Rare Disease Research in China: Rapid Advances, Strong Government Drivers

The view from China is one of dramatic change as the nation of 1.4 billion takes up the challenge of improving care for millions affected by rare diseases. In less than a decade, China has laid the groundwork for a cohesive, national approach to assess rare disease impacts, to advance and coordinate research, and to speed development and access to therapies.

"RWD and real-world evidence (RWE) are integral to China's rare disease infrastructure," says Lin Zhang, head of Parexel's real-world data strategy in the Asia Pacific region. "National rare disease registries are growing. Electronic health records are becoming an important data source. And an innovative regulatory pathway—the Pilot Zone in Hainan—is a laboratory for RWD-based regulatory submissions."

Defining the problem. According to the U.S. definition, a rare disease is a condition that affects fewer than 200,000 people. The EU defines a rare disease as one that affects fewer than 1 in 2,000. In China, a disease must meet one of three criteria to be considered "rare": an incidence among newborns of less than 1 in 10,000; a prevalence of less than 1 in 10,000, or an affected population of less than 140,000.[1] It is generally acknowledged that rare disease prevalence is underestimated. According to a recent analysis based on Orphanet's estimated population prevalence of 3.5% to 5.9%, China's rare disease population may be as large as 82 million.[2]

"This is a huge unmet medical need, and also a serious economic issue," Lin says. "China is strongly committed to solving the rare disease problems of high costs and poor access to therapies." Results of a 2019 registry survey found that among 5,810 rare disease patients, 80% of their income was spent on disease management.[3] A study of orphan drug access from 2017 to 2022 found that, on average, rare disease drug approvals granted by China's National Medical Products Administration (NMPA) lagged six years behind approvals in the U.S.[4]

Building the infrastructure. China's efforts to confront this multi-dimensional public health issue coalesced in 2018 with the publication of the Compendium of China's First List of Rare Diseases. This pioneering catalogue of 121 rare diseases—followed in 2023 by the Second List of 86 diseases—serves as a core tool in China's initiatives to shape policy that advances drug research and patient access to therapy.[5]

In 2018, a national coalition was established to share data and bridge rare disease initiatives across government, medical and patient communities. The China Alliance for Rare Diseases (CHARD) platform shares diagnosis and treatment data among members including the Peking Union Medical College Hospital and national research and hospital associations.[6] In 2019, China established the National Rare Disease Sample Base (NRDSB), a network of 324 hospitals deploying a three-level approach to rare disease prevention and control.[6]

"Collection and sharing of RWD and RWE are central to these collaborations," Lin says. China's rare disease infrastructure is supported by two national registries: the National Rare Disease Direct Reporting System comprised of 540,000 cases; and the National Rare Disease Registry System with 68,000 cases.[6] Patient advocacy plays a major role as well. The Chinese Organization for Rare Disorders (CORD), for example, has been the catalyst for the establishment of more than 100 patient organizations representing more than 60,000 families.[7]

RWD powers faster approvals: the Hainan pathway. China's traditional regulatory pathway, which requires randomized clinical trials and other bridging studies, typically takes from three to 10 years for approval. To accelerate drug access, China created the Bo'ao Lecheng International Medical Tourism Pilot Zone on the island of Hainan. The Hainan pathway provides both a fast track for rare drug approval and a proving ground for RWD-based clinical evaluation.

In 2018, the Hainan provincial government was granted approval authority for urgently needed imported drugs and medical devices. This allowed use of medical innovations marketed overseas but not yet registered domestically. Under Hainan's "Fast Act, Fast Use" policy, a drug or medical device can be used to treat Chinese patients before NMPA approval ***if***: it is approved in the U.S., EU, or Japan; it meets an urgent, unmet medical need in China; it is innovative.[8]

RWD and RWE generated in Hainan can be used to apply for NMPA market approval. Rare disease research is conducted through Hainan's Bo'ao Lecheng Rare Disease Clinical Medical Center, established in 2020. The center has introduced more than 40 internationally licensed drugs. Average time to approval is four to12 months.[9] Lecheng introduced a total of 317 urgently needed clinical drugs and devices by May 2023.[10]

One limitation of China's fast-act, fast-use portal is the island's small population; it can be difficult to collect sufficient data for regulatory applications. Registry data, the backbone of Hainan's RWD system, also poses challenges for sharing and interoperability. In 2020, the Hainan Real-World Data Research Institute was established to develop standards for the use of RWD in place of bridging studies in regulatory applications.[11]

Success story: Ravicti approved via Hainan. The first rare disease therapy to reach patients through the Hainan pathway—the oral medication glycerol phenylbutyrate (Ravicty/Reviang)—was approved by NMPA in 2023 for the long-term treatment of urea cycle disorders (UCDs).[12] UCDs, which occur in from 1-in-22,000 to 1-in-53,000 births, are rare inherited metabolic conditions that lead to brain damage, coma and death.[13] Ravicti was approved in the U.S. in 2013 and in the EU in 2015.[14, 15]

"Hainan is a doorway for existing rare disease drugs to enter China safely and quickly based on real-world data studies rather than long, costly clinical trials," Lin says. "It offers a research environment to advance decentralized trials, new RWD applications and experimental designs. However, there is also work to do in developing RWD approaches."

Work ahead: ensuring high-quality data. Preparing for wide adoption of RWD, China's regulators have addressed RWD barriers—such as inconsistent terminology and lack of transparency and traceability—in a group of guidances aimed at defining high-quality RWD and its use in regulatory submissions.

In 2020 and 2021, Chinese regulators published four RWD guidances.[16] *The Guidance on Real-world Evidence Supporting Drug Development (Pilot)* defined and clarified RWD sources and their uses to support regulatory review in market authorization of traditional Chinese medicines. The Center for Drug Evaluation issued a technical guidance on RWD use in development and review of pediatric medicines. Another NMPA guideline addressed RWD use in clinical evaluation of medical devices. These were followed in 2021 by *Guiding Principles for Real-World Data Use to Generate Real-World Evidence*.

EHRs on the horizon: Parexel adds AI to REDCap. "China is making huge strides in the availability and use of electronic health records (EHRs)," Zhang says. "The challenge here is the variability of RWD from multiple health centers. Collecting and applying the unstructured data of EHRs can be a long, complicated process."

To reduce EHR-driven time and cost, Parexel is harnessing artificial intelligence (AI) to automate data collection processes. Working with a data standardization task force led by the Third Affiliated Hospital of Sun Yat-sen University, Parexel is helping to develop an AI-powered tool to collect and standardize real-world data across multiple hospitals and health centers. Building on the compliance standards of REDCap, the clinical research system developed by Vanderbilt University,[17] the REDCap-founded EDC tool—CHB-EDC—uses natural language processing and optical character recognition technologies to collect and standardize data, then load anonymized data into the REDCap software databased. CHB-EDC's efficient workflow reduces the average data collection time from 63.64 mins to 3.57 mins for one patient.[18]

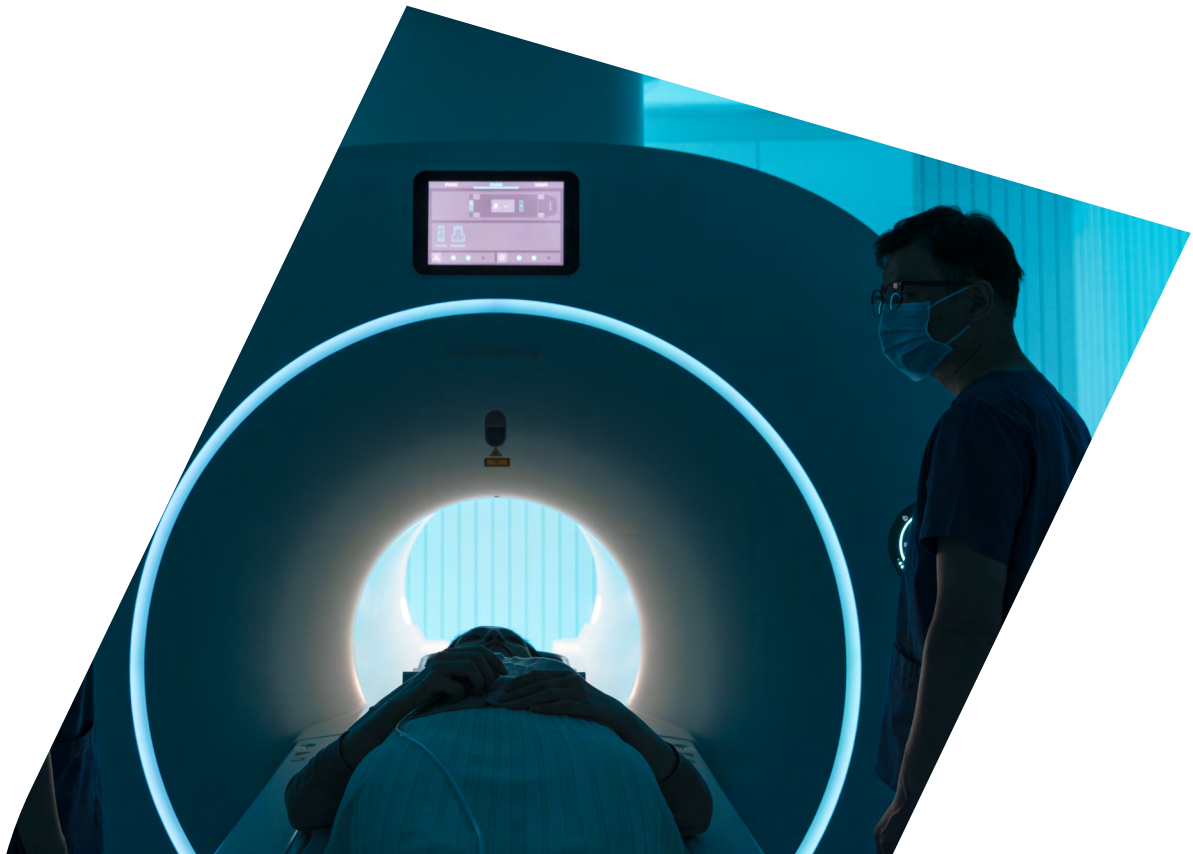
China is conducting a nationwide study to test the CHB-EDC model, aiming to standardize data collection and application for chronic hepatitis B patients.

So far, the model has demonstrated benefits in efficiency, safety, and data traceability compared to traditional collection methods. As the next step, the project team aims to establish RWD collection standards for patients with chronic HBV infection.

Future view. NMPA approved 19 rare disease drugs in 2023; eight were innovative.[12] China continues to strengthen its rare disease research capabilities. "In 2023, China released more than a dozen policies in efforts to improve rare disease prevention and treatment and to advance rare disease drug development, approval and access," Zhang notes. China's evolving RWD infrastructure offers a model for RWD adoption in rare disease research worldwide.

A glimpse of that future can be seen in the ICH Reflection Paper proposing standards to harmonize the use of RWE in drug research across North America and Europe. An international coalition of regulatory authorities is working to develop standardized terminology and general principles that will foster RWD use in international research collaborations and regulatory decision-making.[19]

Progress toward international harmonization promises to connect RWD across North America, Europe and China, evolving a shared, operable platform to advance rare disease research worldwide.



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