Rare Disease Healthcare and Research in China: Advancement and Prospects

Peking Union Medical College Hospital (PUMCH)

November 2024

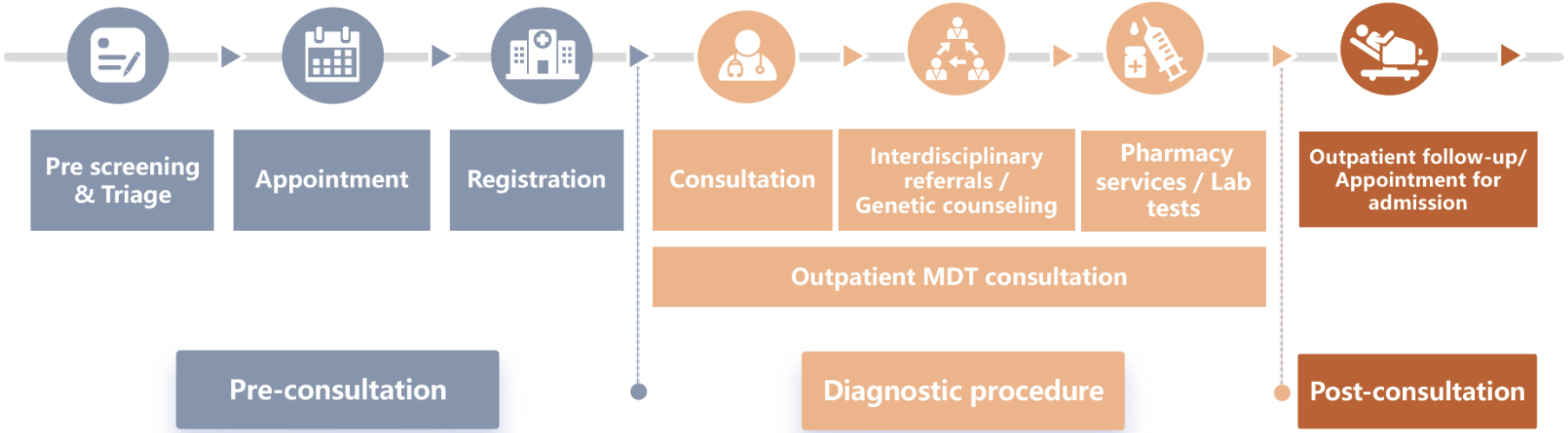
Peking Union Medical College Hospital (PUMCH): a national tertiary referral center

- The National Center for Diagnosis and Treatment of Complex and Severe Diseases designated by the National Health Commission of China
- Patients with complex conditions are referred to PUMCH from local institutions across the country
- Leading the country in the diagnosis and management of RDs and undiagnosed conditions
- Multidisciplinary team (MDT) consultation and collaboration

PUMCH PRACTICE:

Exploring the "Chinese Solution" to Rare Disease Healthcare and Research

The Multidisciplinary Outpatient Clinic for RDs



- ❑ **Over 50 clinicians from 18 specialties provide services here.**
- ❑ **Patients have the opportunities to meet with multi specialists with one-time only registration.**

The first specialized inpatient ward for RDs in China

Medical team

- ❑ Multidisciplinary medical team
- ❑ MDT rounds:
  - ✓ Multi specialists
  - ✓ Clinical geneticist
  - ✓ Pharmacist

Patient population

- ❑ Patients with confirmed RDs requiring MDT management
- ❑ Patients with undiagnosed conditions
- ❑ Participants in clinical studies






The MDT Consultation Center for RDs: one-stop service

Metrics:

- ❑ 300+ consultations
- ❑ 40+ specialties
- ❑ 400+ specialists
- ❑ 160+ RDs / undiagnosed conditions
- ❑ Each consultation meeting
  - ✓ 20+ specialties involved as needed

Significantly streamline the complex diagnostic and therapeutic strategies

4yr → 4wk

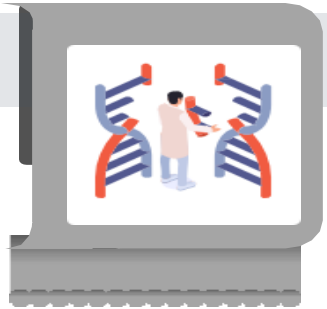
Substantial reduction in the cost of multiple rounds of visits and referrals

→ 90%

The Clinical Genetic Analysis Platform

Genetic testing

Data analysis & interpretation

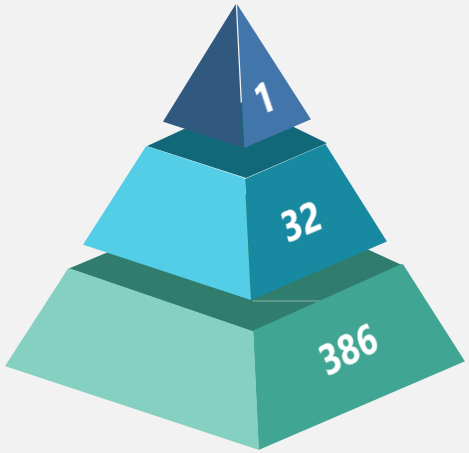


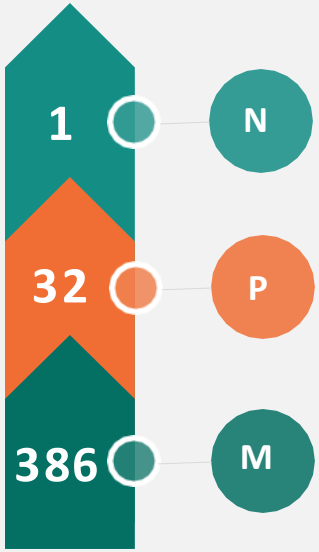
Genetic counseling

Research & training

The National Collaborative Network for RD Diagnosis and Treatment

419 hospitals across the country





National-level leading hospital – Peking Union Medical College Hospital MDT consultation and telemedicine support

Provincial-level leading hospitals

Accepting regional referrals; implementing diagnosis and management plans

Member hospitals

Initial patient assessment; summarizing and reporting medical conditions

Patient follow-up

Genetic counseling

Patient referral

Telemedicine support

Reduce diagnosis delay & improve outcomes and safety for patients

The Public Welfare Project for Rare Disease Service Improvement (UPWARDS)

Support for free genetic testing and counseling, MDT consultations for patients with RDs

Genetic testing for patients and their families

- ❑ Genetic testing for RD patients and their families (≥40,000 cases)
- ❑ Guidance for genetic testing and counseling (≥1 set)
- ❑ Quality improvement of healthcare and satisfaction of patients (satisfaction evaluation)

Multidisciplinary healthcare for patients

- ❑ MDT collaborative management of RD patients (≥9000 cases)
- ❑ Building the capacity of hospitals to provide MDT collaborative services (≥100 hospitals)
- ❑ Production of training resources of MDT collaborative healthcare for RDs

Doctor training program on RDs

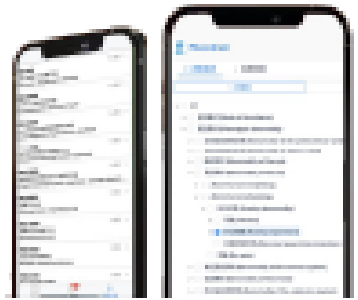
- ❑ Training of doctors in diagnosis and treatment of RDs (≥825 sessions)
- ❑ Improving the capacity of local and young doctors in the healthcare of RDs (satisfaction evaluation)

Supported 20,155 free genetic tests submitted by 1809 doctors at 309 hospitals (as of 2023)

Artificial intelligence tool for the diagnosis of RDs

PhenoBrain for RDs

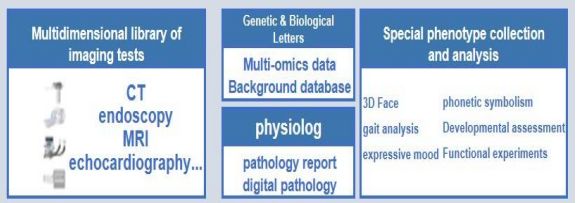
- Phenotype extraction through aChinese medical text processing algorithm
- Phenotype-based clinical diagnosis of 9000+ RDs
- Improve initial clinical diagnosis of RDs by 20%-30%



Patent Certificate

PUMCH · Taichu Rare Disease Model V1.0 Features

Database for clinical phenotype collection

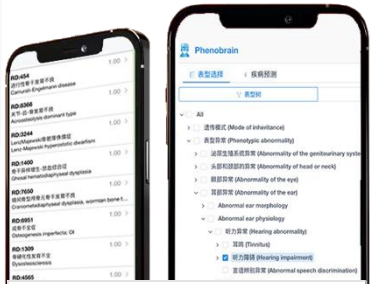


- Medical record and lab testing dataset
- Radiology, pathology, ultrasound, nuclear medicine, and electrophysiology dataset
- Facial features, speech, semantics, developmental abnormalities, gait, and other phenotypes

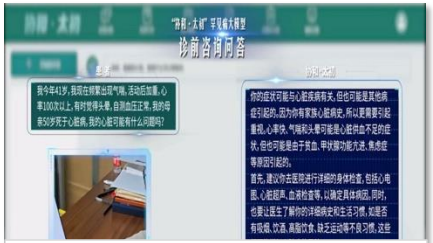
Clinical database

Pre-, in-clinic and post-consultation

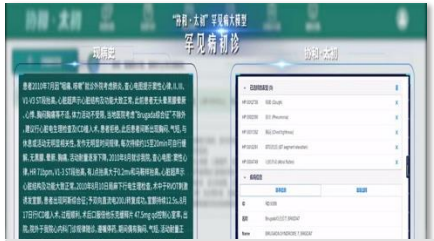
Phenobrain



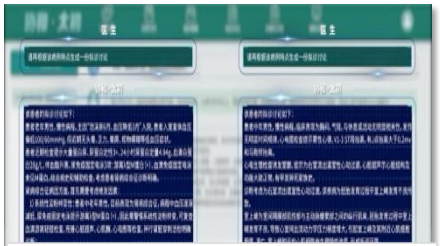
AI-powered diagnostic tool access



Pre-consultation screening



Medical records summarization & preliminary diagnosis

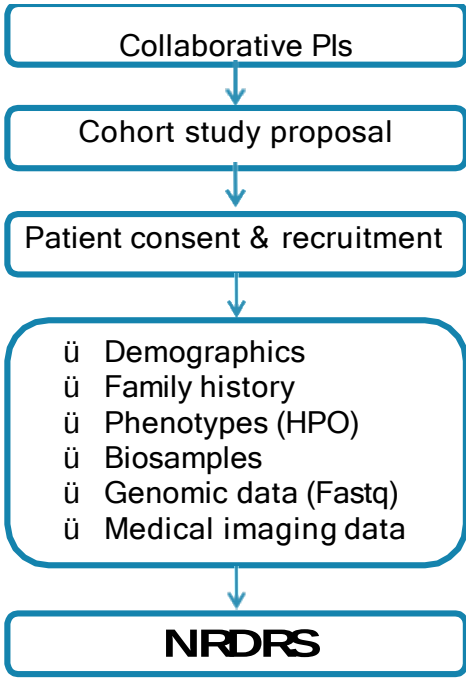


Follow-up management & Q&A

The National Rare Diseases Registry System of China (NRDRS)

www.nrdrs.org.cn

- **107 institutions across the country**
- **248 cohorts**
- **88,142 cases**
- **105 clinical trials**
- **456 publications**



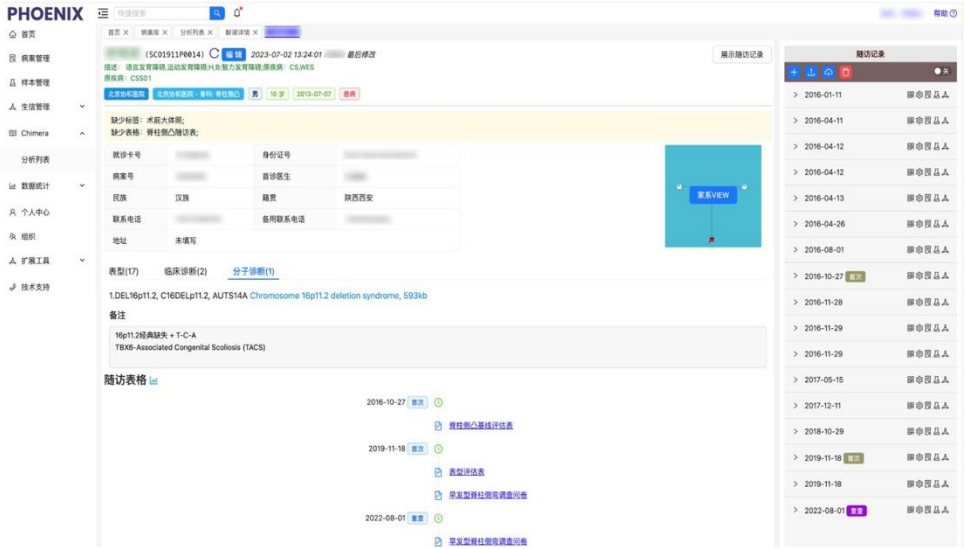
NRDRS: the most important database for RD research in China

Data drives discovery

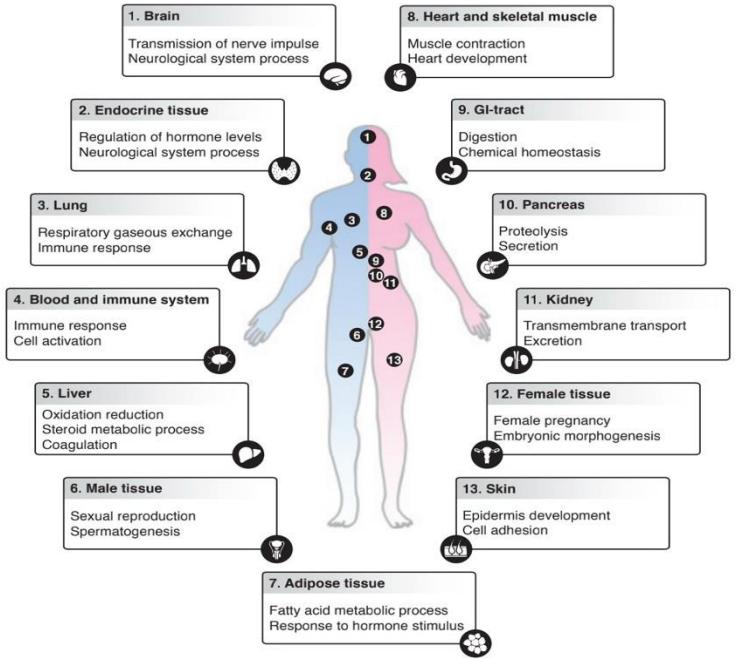
- A platform connecting patients, providers, academia, industry and policymaker
- Natural history studies
- Epidemiologic studies
- Basic research
- Clinical trials

National Genotype-Phenotype Database for RDs

- Genetic RD: **7,000+**
- Genetic variants in Chinese population: **110,000+**
- Research on pathogenesis
- Research and development for genetic screening and diagnostic testing product



The National Rare Disease Biobank



ISO20387 certified

120+ disease, 230,000+ samples

- **Technical standards of biobank**: validation and revision to provide abasis for national standardization
- **Biospecimens**: crucial resources and essential elements in the basic, clinical and translational research
- **Community**: industry–academia collaboration

The National Rare Disease Surveillance System

- Launched in Nov 2019
- **581** institutions covering **31** provincial-level administrative regions in China
- **990,000** confirmed RD cases were reported
- Based on the data of cases reported nationwide, the Rare Disease Surveillance Report of China was released

- China Rare Disease Surveillance Report (2024)

PUMCH designated as the National Center for Healthcare Quality Management in RDs

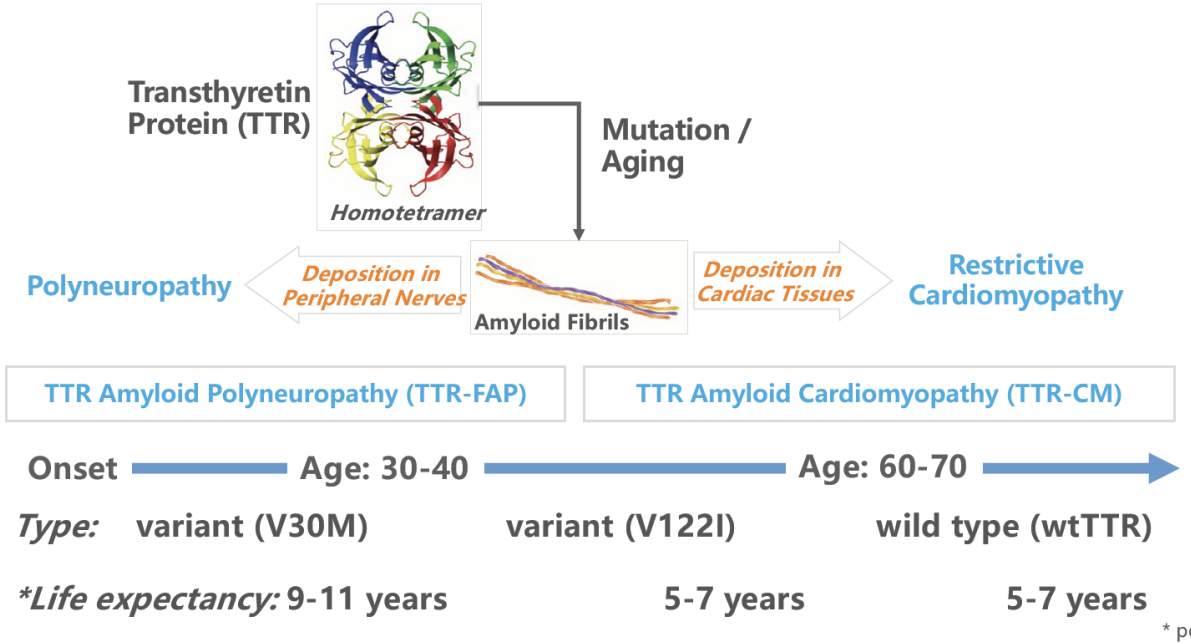
Twenty provincial-level centers have been set up

Quality improvement projects implemented

Educational materials & training program In person & online training courses

Transthyretin Amyloid Cardiomyopathy (ATTR-CM)

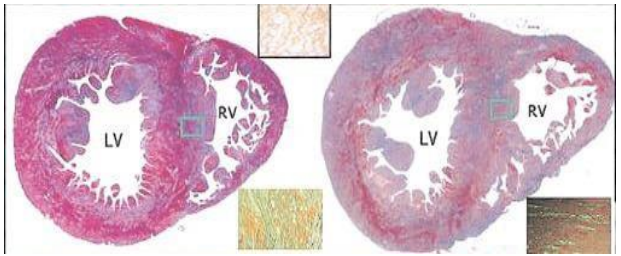
Early diagnosis → Disease subtyping → Clinical trials → Guidance development

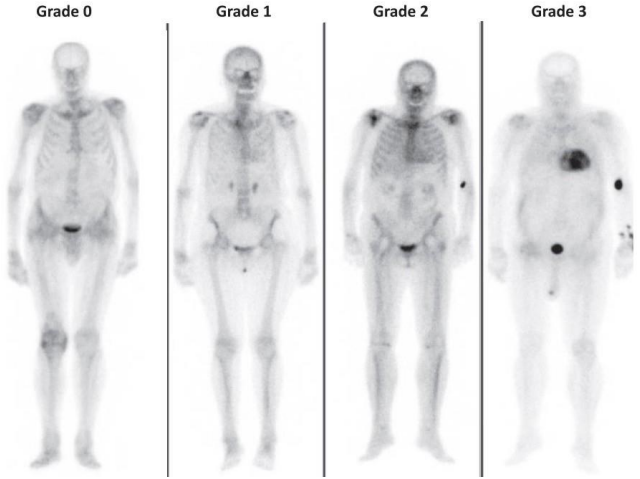


* post-onset of symptoms

Non-invasive diagnosis for ATTR-CM:

- **^{99}Tcm-PYP scintigraphy** with high sensitivity and specificity





Invasive myocardial biopsy → **Non-invasive ^{99}Tcm-PYP scintigraphy 80%**

Diagnostic yield : 20%

The clinical trial and accelerated NDA approval of Tafamidis in China

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

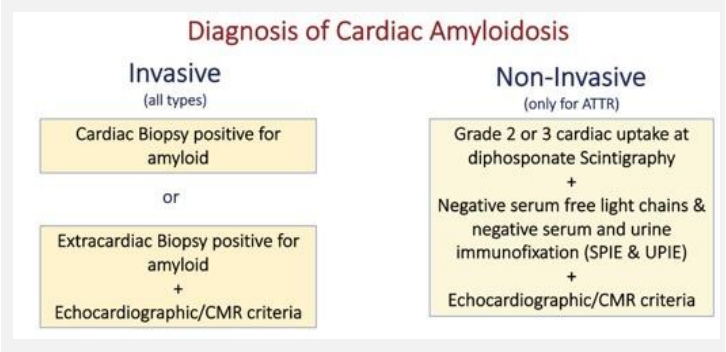
Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*

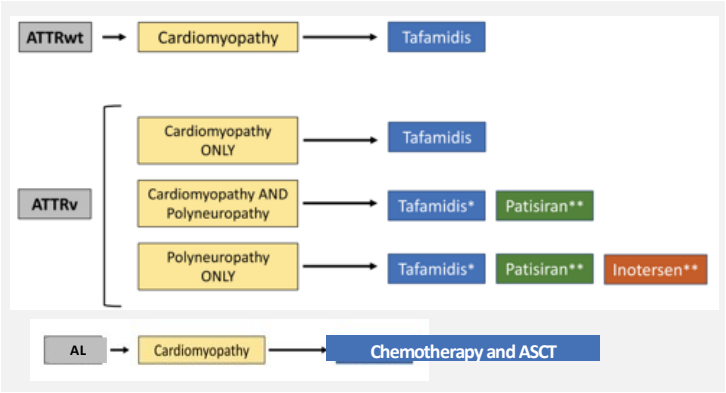
- **PUMCH led the multi-center phase IV clinical trial of Tafamidis and conducted the trial using the NRDRS platform.**
- **Priority review and accelerated NDA approval in China in Sep 2020.**
- **Included by the National Reimbursement Drug List (NRDL) in 2021.**

The first Chinese expert consensus on the diagnosis and treatment of ATTR-CM

- **Guide the healthcare of patients with ATTR-CM**
- **Quality improvement projects have been implemented nationwide**

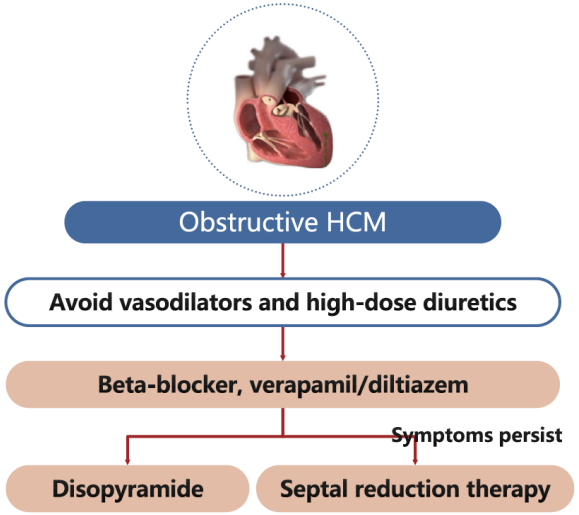
- **From 2018 to 2023**
- **The number of confirmed ATTR-CM cases nationwide had a 20-fold increase**
- **The risk of in-hospital mortality decreased by 30%**



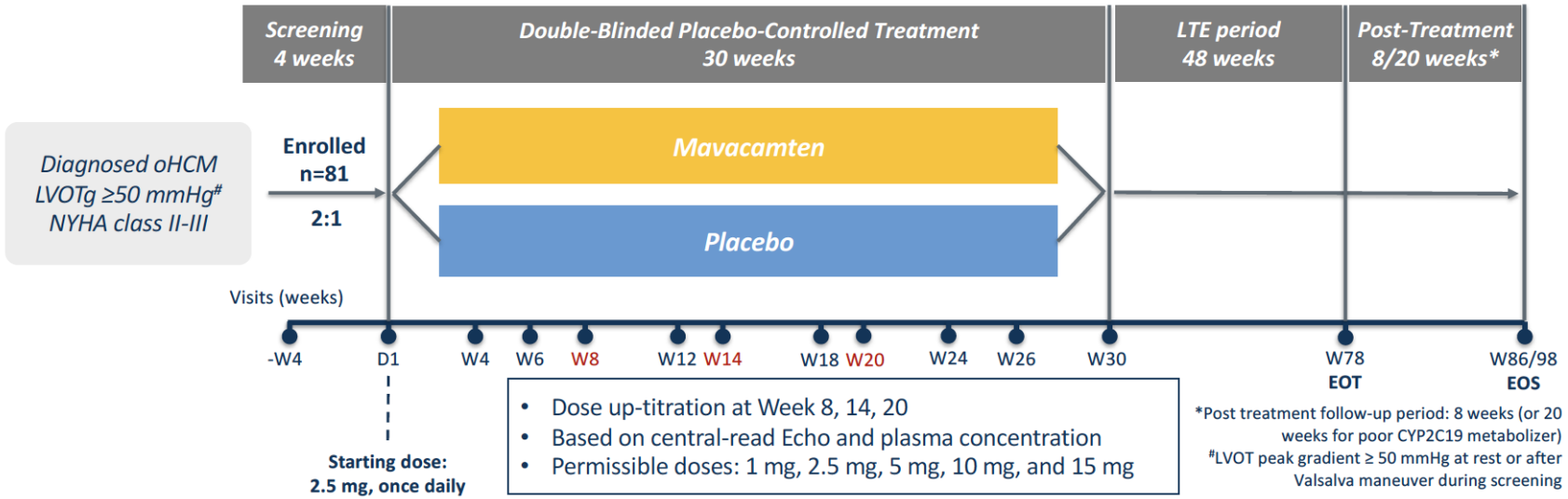


Obstructive Hypertrophic Cardiomyopathy (HCM)

- HCM is a myocardial disorder characterized by primary left ventricular (LV) hypertrophy.
- The prevalence of HCM in the Chinese population is about 80 per 100,000 adults.
- Treatment goals: relieving clinical symptoms, improving cardiac function, delaying disease progression, and reducing death.
- No agency-approved therapy available in China.



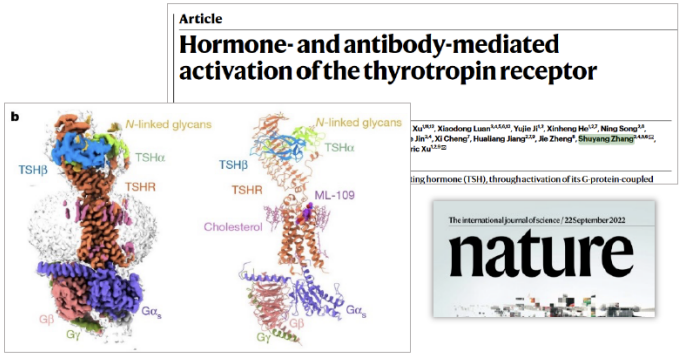
Study design of the clinical trial of Mavacamten in patients with HCM



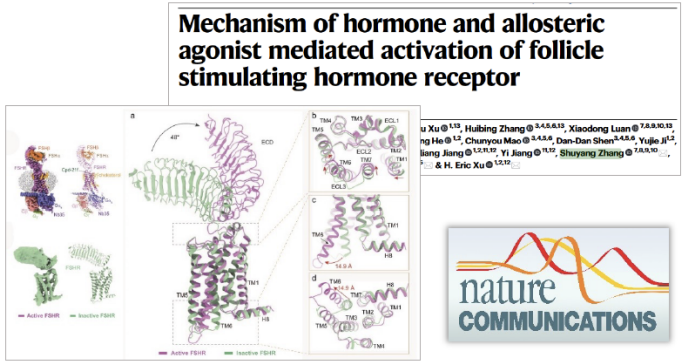
Structural biology-based drug development for RDs

Nomination for the "Top 10 Advances in Chinese Life Sciences in 2022"

Structural basis for the clinical development of antibodies or small molecule drugs for the treatment of rare pituitary diseases



Structural basis for the development of small molecule drugs targeting the glycoprotein hormone receptor

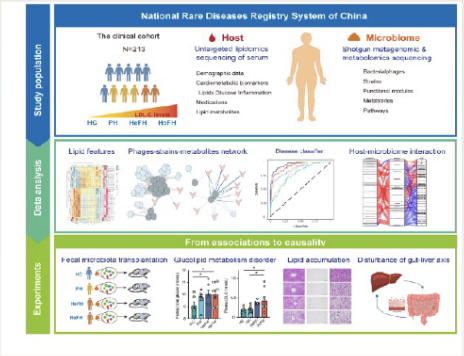


Nature 2021; *Nat Commun* 2023

Drug development for familial hypercholesterolemia

Lipid-lowering therapy for both rare dyslipidemic diseases and common chronic diseases

Driven by clinical problems



A 15-year early-onset coronary heart disease registry cohort:

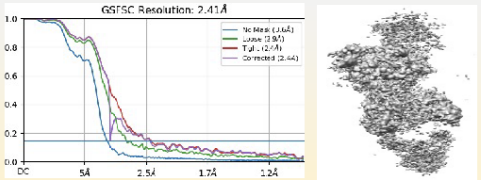
23 familial hypercholesterolemic families

Multi-omics discovery of targets

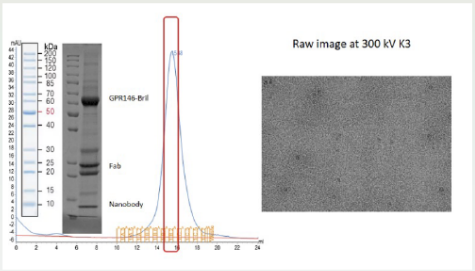
Carrying out research on the domestic PCSK9 monoclonal antibody drug Inusi injection

Mapping of fh immunity and enterobacteria in the Chinese population

Modification of novel PCSK9 antibodies based on new targets



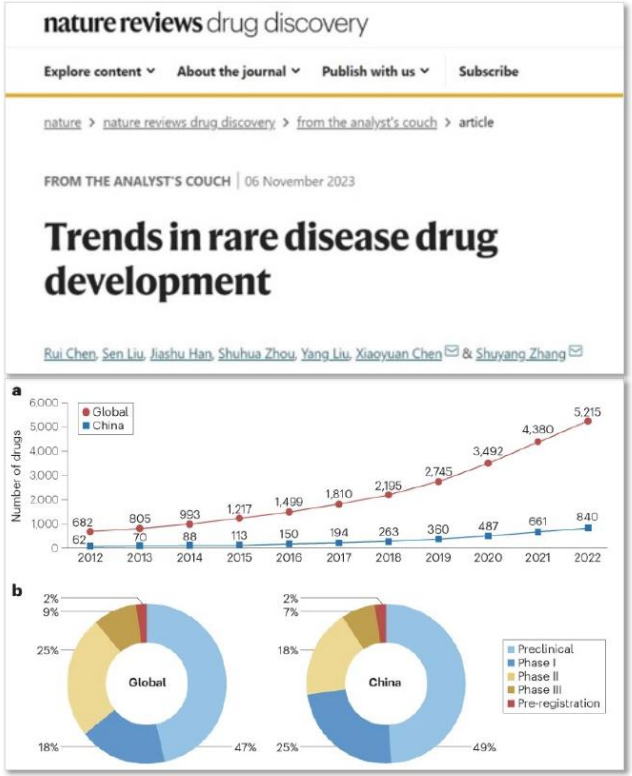
New drug development with intellectual property rights



Development of drugs based on the structure of GPR146, which will become new drugs with clinical potential

Not only is it valuable for rare diseases, but it can also help with lipid-lowering therapy for common diseases

Drug development blossoms for RDs in China



I. Over the past five years, the number of RD drugs under development in China has increased significantly, with an average annual growth rate of 34%, exceeding the global growth rate of nearly 42%

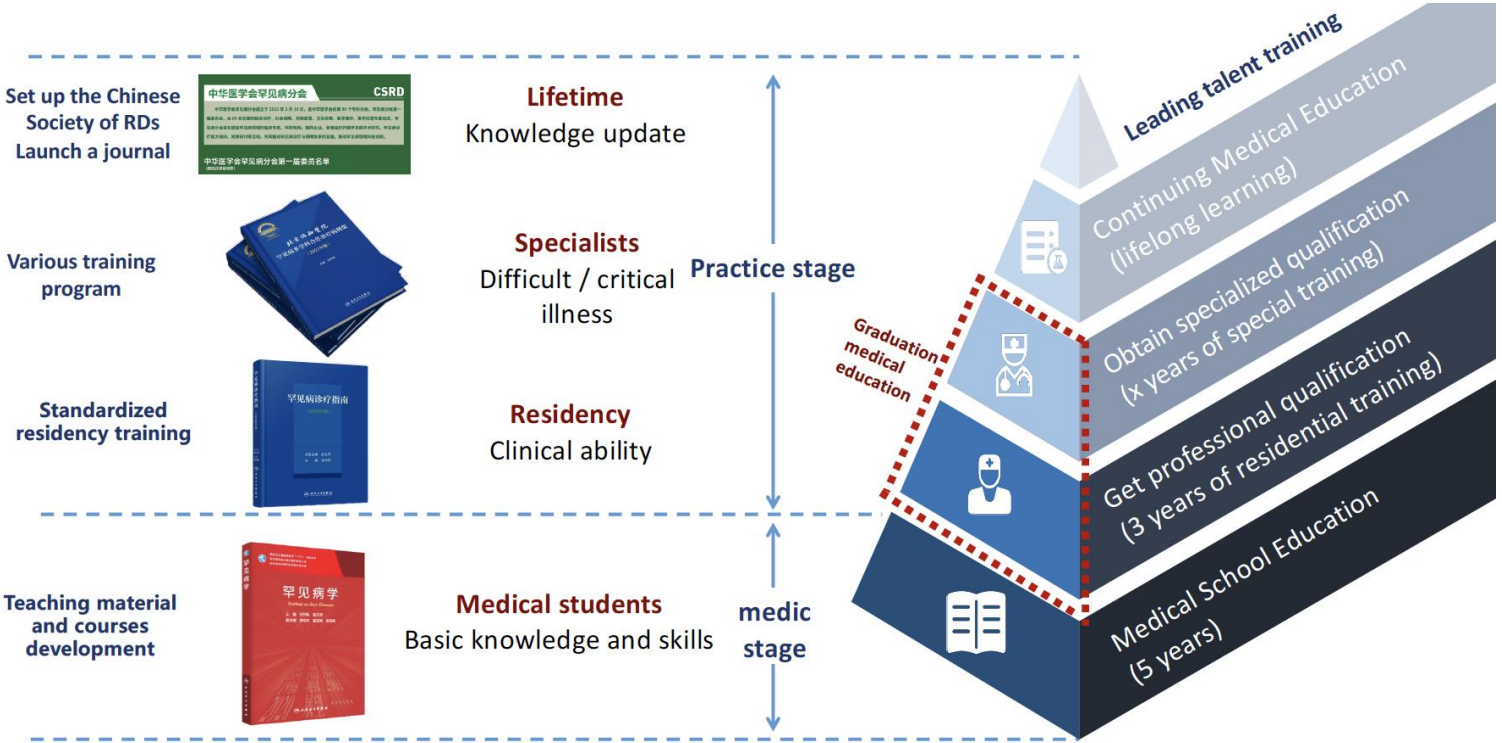
II. By the end of 2022, there will be a total of 840 RD drugs under development in China, most of which are in the preclinical stage.

III. In terms of therapeutic areas: rare neurological disorders (12%), respiratory disorders (8%), digestive/metabolic disorders (7%), and immune system disorders (6%).

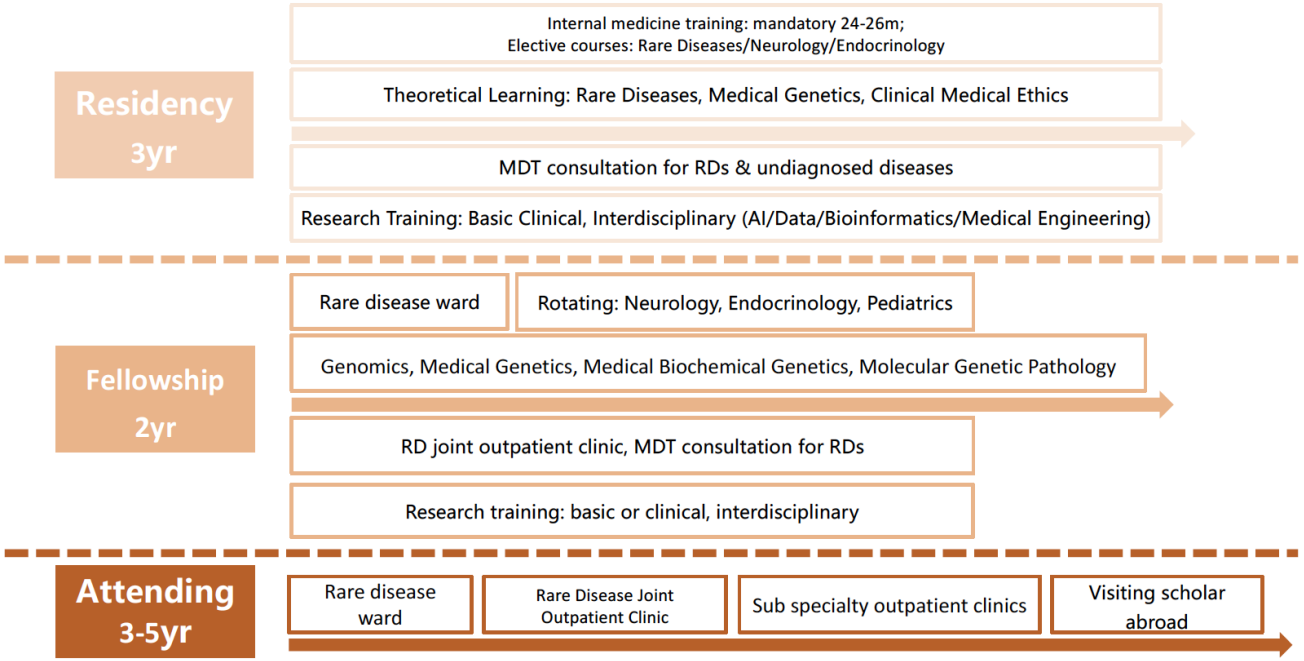
IV. Biologics account for almost half (49%) of the RD pipeline, with proteins (20%), cytostatics (16%), and nucleic acids (9%) rounding out the top three.

Medical Education for Rare Diseases

The three stages: medical school, graduate, and continuing medical education



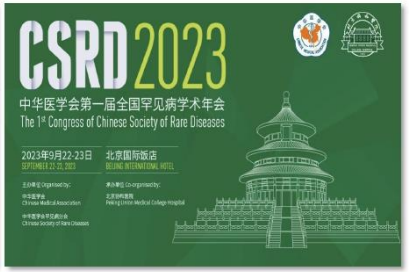
Graduate medical education: Clinician Training Program at the Dept. of RDs, PUMCH



The Rare Disease Branch of the Chinese Medical Association: Chinese Society of Rare Diseases (CSRD)

Establishment of CSRD
February 19, 2023 Beijing

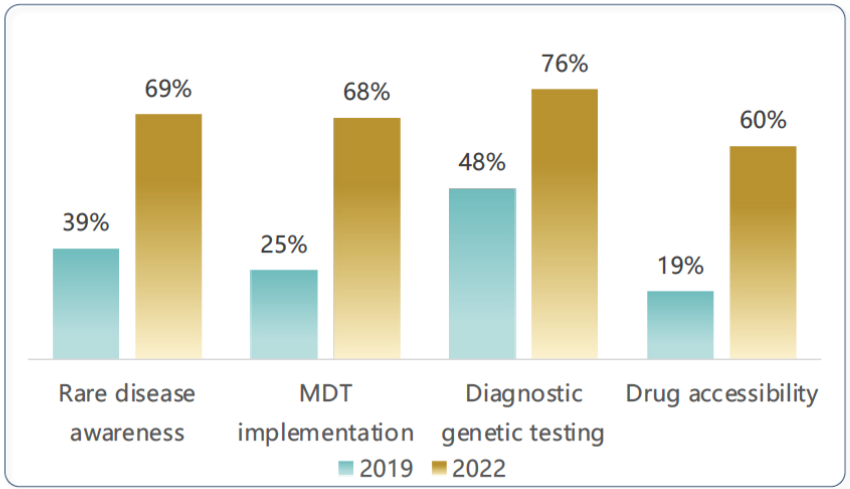
The annual congress of CSRD



Education and training programs improve healthcare for RDs nationwide

Nationwide surveys on RDs in 2019 and 2022

Rare disease awareness, MDT development, genetic testing, and drug accessibility significantly improved



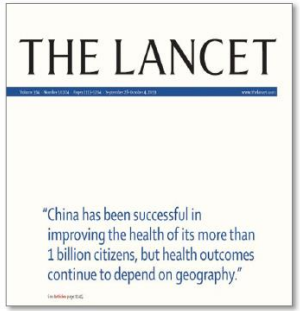
2019

13,000 doctors nationwide

2022

40,000 doctors nationwide

The China model contributing to the evolving landscape of RD healthcare and research worldwide



Orphan drug development in China: progress and challenges

On Aug 26, 2019, the National People's Congress (NPC) Standing Committee approved the new revision of the Drug Administration Law of China that allows orphan drug approval to be based on evidence from foreign clinical trials through the green channel mechanism with priority review and accelerated approval. Medical institutions can now legally purchase small amounts of urgently needed orphan drugs from overseas markets.[1] This is welcome news for China's 16 million patients with rare diseases.[2]

Rare diseases are a public health issue in China, as orphan drugs from foreign countries will be legally available. Since 2018, 37 urgently needed orphan drugs qualified for accelerated and simplified approval by the NMPA.[4] Through the green channel approval process, Peking Union Medical College Hospital legally purchased mitotane for adrenal cortical carcinoma, with the help of the China Alliance for Rare Diseases, which comprises more than 50 entities ranging from medical institutes, universities, academic institutions, and companies.[6] A challenge is that medical providers still hesitate to preorder these drugs because of their

"The Chinese model worthy of learning from the countries in the world"

- -The President of the United Nations General Assembly

The United Nations Conference on Rare Diseases

Shuyang Zhang
Peking Union Medical College Hospital

Brick by brick, building hope: The Chinese approach for rare diseases

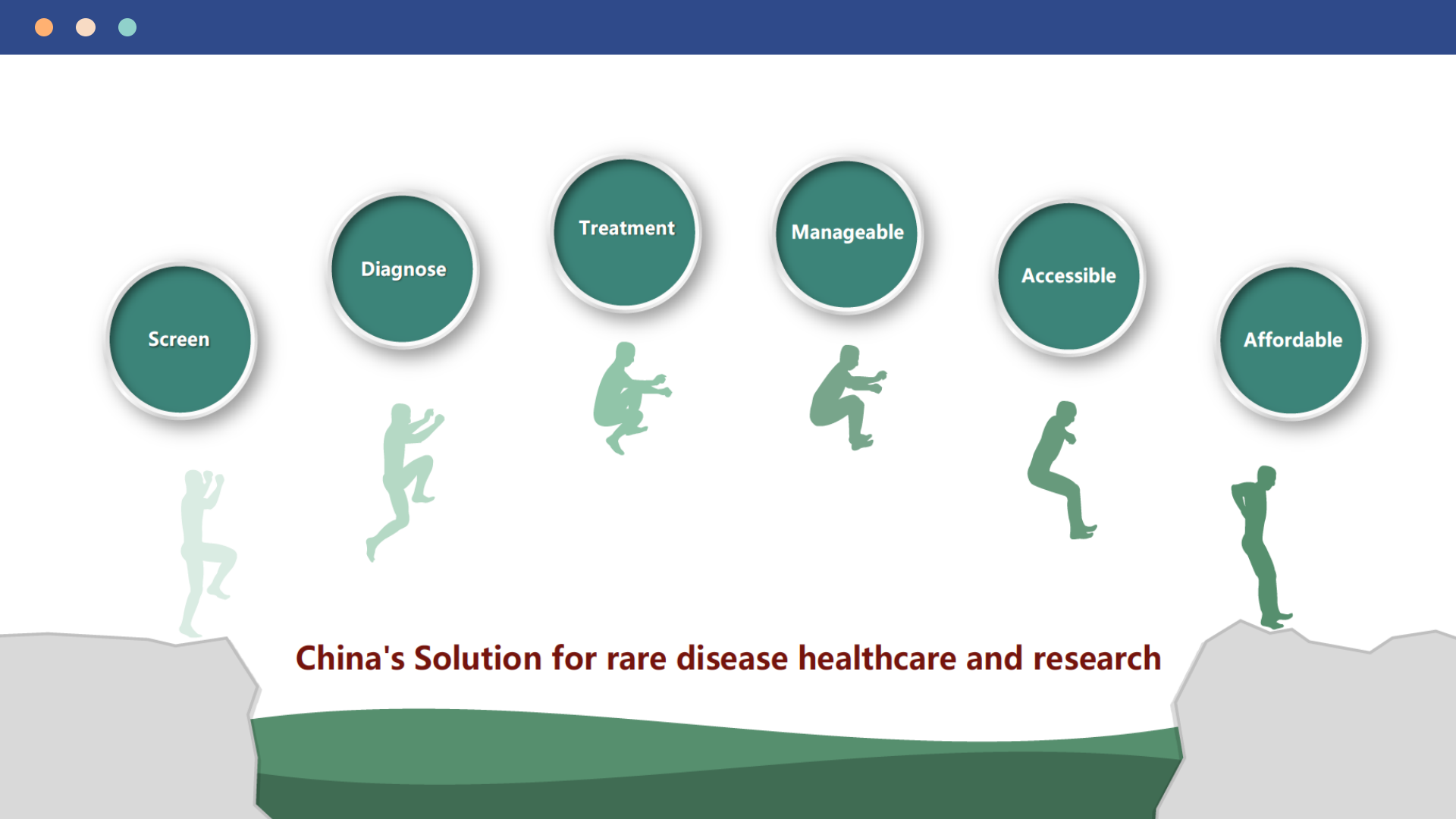
Rare diseases pose a significant medical challenge and a societal issue. In China, due to the large population, rare diseases may not be as rare as one might think. My entry into the field of rare diseases was prompted by a patient I encountered in the outpatient clinic—a person suffering from homozygous familial hypercholesterolemia. He tragically passed away due to early-onset coronary heart disease. Through years of dedication, we have utilized global rare disease catalogs to draw attention to and increase understanding of rare diseases, encouraging more individuals to become involved in the field and transforming the management approach.

In 2023, Peking Union Medical College Hospital established the Rare Disease Medical Department. Leveraging the advantages of multidisciplinary consultations, the time for diagnosing rare diseases at Peking Union Medical College Hospital has been reduced from an average of 4 years to a swift 4 weeks. Medical costs have decreased significantly by more than 90%. Additionally, we have established three large rare-disease data platforms, biobanks, and clinical databases. Based on these, we have outlined a preliminary rare disease map for the Chinese population, serving as a basis for policy formulation. Simultaneously, scientific research based on data

***Med:* Rare Disease Day: Amplifying voices, advocating hope**

"Leading the world's model for the diagnosis and treatment of rare diseases collaborative mode"

- -President of the International Association for Undiagnosed Diseases


Screen
Diagnose
Treatment
Manageable
Accessible
Affordable
China's Solution for rare disease healthcare and research

Durhane Wong-Rieger, PhD

President & CEO

Canadian Organization for Rare Disorders

durhane@raredisorders.ca

Canadian Organization for Rare Disorders