

# Rare diseases in developing countries: Insights from China's collaborative network

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## Abstract

Rare diseases (RDs) are complex conditions and a worldwide healthcare challenge. The healthcare policymakers in developing countries lack templates from countries at the same level of development. This article introduced and discussed the combination of top-down strategies and bottom-up interventions in addressing RDs in a developing country, China, as an example. The government leads the formulation of laws, policies, and guidance to coordinate national resources, while local authorities and nongovernment organisations (NGOs) are responsible for policy localisation and complement policy gaps. This article may inspire other developing countries of improving RD healthcare.

## KEYWORDS

bottom-up interventions, developing countries, healthcare policy-makers, rare diseases, top-down strategies

## Highlights

- China's collaborative network addresses rare diseases through top-down policies and bottom-up interventions.
- National rare diseases diagnosis and treatment network established in 2019.
- Medical insurance covers RD drugs, with price negotiations reducing costs.
- Local authorities explore flexible models, like the "1 + N" copay model.
- Non-governmental organisations contribute to advocacy and support for RD patients.

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## 1 | INTRODUCTION

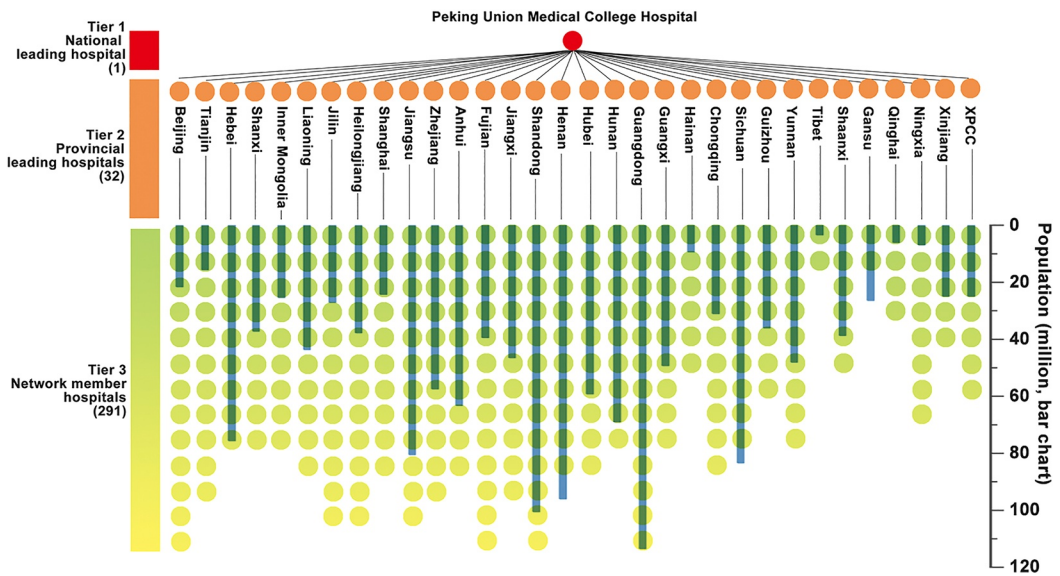
Rare disease (RD) has no universal definition, whose concept varies even among different countries/regions.<sup>1</sup> In the United Kingdom (UK), RD is defined as a condition that affects less than 1 in 2000 people, according to the 2021 UK Rare Diseases Framework.<sup>2</sup> In comparison, the European Union (EU) defined RD as conditions with a prevalence of not more than 50 per 100,000,<sup>3</sup> while the American Orphan Drug Act (1983) defined RDs as disorders affecting fewer than 200,000 individuals nationally, equivalent to an incident rate of 86 per 100,000 at that time.<sup>4</sup> There are more than 7000 types of RDs,<sup>5</sup> and this number is increasing with new conditions being identified by the latest research and techniques. It is estimated that approximately 10% of the entire world population are RD patients; however, the prevalence of most RDs remains elusive, and 90% of them lack effective treatments.<sup>6</sup> From the first glance of these definitions and epidemiology, RD is an extremely complicated challenge with significant regional and/or genetic heterogeneity and difficulties in diagnosis and treatment. There even appears 'health emigration' seeking competent healthcare from other countries.<sup>7</sup> Due to limited cases, insufficient research input and clinical training, and unprofitable drug development, advances in the field of RD are unsatisfactory, necessitating urgent policy intervention.

The challenges of rare disease policies in China are closely intertwined with economic development and uneven resource allocation. As a developing country, China boasts vast territory, the world's second-largest population (estimated 20 million RD patients), and is home to as many as 56 ethnic groups. Its expansive regions offer abundant natural resources, albeit with uneven distribution. Meanwhile, significant variations in geography, economics, and even culture across regions pose complexities in policy development and implementation. Among them, the impact that stands out the most is from China's economic transformation, which can be traced back to the renowned "reform and opening up" strategy proposed by Deng Xiaoping in the 1970s.<sup>8</sup> This transformation has brought about profound economic improvement while also leading to the widening income disparity between coastal and inland regions.<sup>9</sup> Qin and Hsieh emphasised the crucial role of economics in guiding the allocation of medical resources.<sup>10</sup> When this law comes to RDs, this influence is significantly amplified compared to other common diseases. According to Zhang's report,<sup>11</sup> the percentage of RD patients in Beijing, Shanghai, and Chongqing who can receive a local diagnosis is 96.6%, 93.8%, and 71.3%, respectively. In contrast, 100% of patients in Tibet and 83.7% of patients in Inner Mongolia need to travel long distances to receive diagnoses in other provinces.

There have been some networks addressing RD challenges in developed countries/regions. However, to the best of our knowledge, there is a notable gap in literature focussing on the collaborative efforts of developing countries, especially China's rapid establishment of its collaborative network in the past 5 years. This article aims to bridge this gap by providing a comprehensive perspective on China's unique combination of top-down strategies and bottom-up interventions in addressing the RD challenges. Furthermore, we delve into the roles of local authorities and organisations in reacting to and implementing these policies. Through this exploration, we offer a fresh perspective that could be instrumental for other developing countries with similar developmental trajectories.

## 2 | GOVERNMENT POLICY IS AN INDISPENSABLE GUIDER AND A POWERFUL REGULATOR

Denying the importance of the government's top-down legislation and guidance in healthcare is narrow-minded and short-sighted. All countries have endorsed at least one binding treaty that incorporates the right to health,<sup>12</sup> for example, the European Reference Networks (ERNs).<sup>13,14</sup> There is a growing recognition that a robust healthcare system and centralised coordination are crucial for advancing health equality. RDs, being exceptional conditions, particularly require governmental support. However, compared to the aforementioned first official document on RDs in the United States (US) dating back to 1983,<sup>4</sup> China was incapable of having sufficient input in RDs before the 21st century, resulting in a dearth of statistics, standard diagnoses, and therapies. In 2006, Zhaoqi Sun, a deputy of



**FIGURE 1** The hierarchical structure of the China National Rare Diseases Diagnosis and Treatment Collaborative Network 2019. Each dot represents one hospital. The overlapped bar chart and scale on the right indicate the provincial population in 2019, which is sourced from statistical bulletins published by the provincial statistical bureaus in that year. XPC: Xinjiang Production and Construction Corps.

National People's Congress (NPC), raised the first proposal appealing for RD legislation.<sup>15</sup> After a decade of persistent efforts, in 2018, the National Health Commission (NHC) of China, in conjunction with five other departments, jointly released the ground-breaking 'first list of rare diseases' based on 15 million hospitalisation cases, encompassing 121 types of RDs.<sup>16</sup> This monumental epidemiologic investigation would have been unfeasible without national-level involvement. Since then, the promotion of relevant policies and attention devoted to RDs across all sectors of society have been rapidly increasing.

The NHC comprehensively designed coordinated policies consisting of three aspects: healthcare, medical insurance, and pharmaceuticals. In terms of healthcare, only 1 year after releasing the list (2019), the NHC introduced the 'national rare diseases diagnosis and treatment collaborative network'.<sup>17</sup> This initiative established a systemic and hierarchical network comprising 324 hospitals (Figure 1), including a national leading hospital (Peking Union Medical College Hospital), 32 provincial leading hospitals, and 291 network member hospitals. To expedite progress of RD diagnosis and treatment, the proportion of network member hospitals in most provinces exceeds the corresponding proportion of the population relative to the total population. The establishment of this network also serves as a prerequisite for the follow-up policy implementation. Regarding medical insurance, the NHC has approved 60 RD drugs for market, with 45 of them being covered by national medical insurance.<sup>18</sup> In 2021, a total of seven RD drugs successfully underwent price negotiation between the NHC and manufacturers, resulting in an average price reduction of 65%. One example is the previously expensive life-saving drug Nusinersen Sodium Injection for patients with spinal muscular atrophy. It used to cost ¥700,000 (equivalent to £80,000) per dose but now a self-afforded cost of ¥30,000 (equivalent to £3500) per dose after being covered by the national medical insurance.<sup>19</sup> Through state financial support, the scope of diseases covered by medical insurance has been expanded, benefiting RD patients. The government has also increased its investment in pharmaceutical research and local accessibility. The largest national research funder, the National Nature Science Foundation of China (NSFC), has established a special fund for RDs starting in 2021.<sup>20</sup> Also, the National Medical Products Administration (NMPA) prioritised the approval of new RD drugs. Furthermore, to ensure local accessibility of drugs, the NHC requested that there must be at least one RD drug-distributed pharmacy in a prefecture-level city.<sup>21</sup>

A critical sign of developing countries is their relatively low per capita income. Moreover, China owns a huge population and a relatively late start of industrialisation. Government-led top-down coordination plays a positive role in centralising resources for focused tasks at an early stage. Meanwhile, the localisation of policies and bottom-up self-directed development are another important components, which will be introduced in the next section.

### 3 | EXPLORATION OF LOCAL MODELS AND NON-GOVERNMENT ORGANISATIONS

Complicated local conditions make the China national government allow local authorities to have great flexibility in exploring local models. For example, the Qingdao local authority proposed the '1 + N' copay model according to its financial situation.<sup>22</sup> In this context, '1' refers to the government's leading role in providing funding (medical insurance, medical assistance, and negotiating price reductions with pharmaceutical companies) to ensure that the majority of the expenses for RD patients are covered. "N" refers to the involvement of other social entities to supplement any policy gaps, such as pharmaceutical companies providing free medication to charities or fundraise via social donations. With this model, patients can access medication at low or even no cost.

Furthermore, patient communities have always been pivotal bottom-up driving forces behind the advancement of policies, research, pharmaceuticals, and social advocacy for RDs. The Haemophilia Home of China (<http://web.bjxueyou.cn>) founded in 2000 is the first rare disease nongovernmental organisation (RDNGO) in China. By the end of 2021, there were more than 130 RDNGOs with established identities and regular activities. These RDNGOs largely facilitate the social recognition and discussion on RDs. Additionally, their work filled the gaps left by the limited early-stage engagement of the government. A prominent example is the China-Dolls Centre for Rare Disorders (CCRD, <http://chinadolls.org.cn/>), which focuses on serving patients with osteogenesis imperfecta (OI). In 2009, the CCRD set up the first special fund for RDs in China. The China-Doll Rare Disease Care Fund helped over 1300 patients within 10 years. Three consecutive China-Doll National Patient Conferences raised social attention on OI and have been reported by over 100 media outlets. In 2012, the CCRD collaborated with Renmin University of China to conduct research on the survival status of the RD population, covering more than 20 types of RDs, and contributed to incoming larger-scale research and policy establishment.<sup>23</sup> Between 2012 and 2014, the CCRD hosted Youth Cooperation Camps and cultivated over 60 young leaders who speak up for the community. The CCRD has become a highly influential RDNGO.

Briefly, the local authorities and RDNGOs are not only pivotal for implementing and localising central policies and supplementing policy gaps but also a nonnegligible force in promoting progress in RD diagnosis, treatment, and social caring.

### 4 | CONCLUSION

Our study offers a unique insight into China's collaborative approach to rare diseases, emphasising the synergy between top-down governmental strategies and grassroots interventions. While we highlight China's significant progress, it's crucial to note the limitations, such as reliance on published data which might not capture all grassroots challenges. This work is especially valuable for policymakers, healthcare professionals, and researchers in developing countries. It underscores the importance of a collaborative approach in addressing healthcare challenges and serves as a reference for nations with similar developmental contexts.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

## ETHICS STATEMENT

This research, which does not involve human participants, has no requirements for informed consent. Clinical Trials and Animal Research: Our study does not involve clinical trials or research using animals. Therefore, these ethical considerations are not applicable to our work.

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