Review

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Incidence and prevalence of 121 rare diseases in China: Current status and challenges

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Summary **In order to ascertain the current status of and challenges posed by the incidence and prevalence of rare diseases in China, this study teases out data on the incidence and prevalence of 121 rare diseases listed in *China's First List of Rare Disease* to provide rationales and references for the development and promotion of rare-disease-related policies. The National Health Commission of the People's Republic of China issued the *Rare Disease Diagnosis and Treatment Guide (2019)* (denoted here as *China's Rare Disease Diagnosis and Treatment Guide*), which cited data on the incidence/prevalence of 21 rare diseases (21 of 121 rare diseases, 17.36%). Data on 68 diseases (56.20%) were found in monographs, literature databases, and official websites. Data on the incidence/prevalence of 70 diseases were compiled, though no data were available for the 51 remaining diseases. There are published data on the incidence/prevalence of only 14 diseases at the national level. Sources of data on the incidence and prevalence of rare diseases mainly include cases counts from hospitals (40.56%), other sources of data (24.48%), screening (20.98%), cross-sectional studies (8.39%), and estimates from models (7.69%). Data on the incidence/prevalence of rare diseases in China are limited and typically lack accuracy, uniformity, and timeliness. Epidemiological data at the national level are greatly lacking, and data are not amenable to comparison. China recently initiated epidemiological studies of rare diseases at the national and regional level. The country will continue to promote, use, and update its list of common rare diseases, actively encourage the coding and registration of cases of rare diseases, and take actions to collect, share, and use that information.**

Keywords: Rare disease, incidence, prevalence, China's Rare Disease Diagnosis and Treatment Guide

1. Introduction

Epidemiological data could indicate the incidence of and changes in rare diseases and lay the foundation for estimation of the rare disease burden for the country or regions, guide the development of orphan drugs, and help with the formulation of rare-disease-related health policies. From the perspective of national health care and social service provision, the population with rare diseases needs to be determined in accordance with their national health care needs and socioeconomic status. The burden of rare diseases is hard to determine because of the difficulty in diagnosis, misclassification, and the lack of appropriate coding; these issues pose major problems with the development of a rare disease health plan. As China works to provide social security to address rare diseases, its top priorities are to enhance the collection

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of epidemiological data, to provide health care, and to register patients.

There is no clear standard for recognition of rare diseases in China due to the large population, the lack of epidemiological data on rare diseases, the variety of rare diseases, and other factors. To enhance the management of rare diseases in China and improve the diagnosis and treatment of rare diseases, to protect the rights of patients with rare diseases, and to provide a reference for policymaking by relevant departments, the National Health Commission of the People's Republic of China, the Ministry of Science and Technology, the Ministry of Industry and Information Technology, the National Medical Products Administration, and the National Administration of Traditional Chinese Medicine issued *China's First List of Rare Disease* in May 2018 (denoted here as *China's Rare Disease List*) (*1,2*). In February 2019, the National Health Commission issued the *Rare Disease Diagnosis and Treatment Guide* (2019) (denoted here as *China's Rare Disease Diagnosis and Treatment Guide*), which cited data on the incidence/prevalence of rare diseases based on China's Rare Disease List (*3*).

The current study is based on *China's Rare Disease Diagnosis and Treatment Guide* and has searched monographs, literature databases and official websites in the field of rare diseases, such as *Treatable Rare Diseases* edited by Chen *et al*., the *Compendium of China's First List of Rare Diseases* edited by Zhang *et al*., the CNKI database, the Wanfang database, and the official website of the Taiwan Health Promotion Administration. Data on the incidence/prevalence of 121 rare diseases in *China's First List of Rare Diseases* have been compiled and the current status of and challenges posed by the incidence/prevalence of rare diseases in China have been ascertained in order to provide references for the formulation of rare-disease-related policies.

2. Current incidence/prevalence of 121 rare diseases in China

China's Rare Disease Diagnosis and Treatment Guide cites the incidence/prevalence of 21 rare diseases (21 of 121 rare diseases, 17.36%). Data on 68 diseases (56.20%) were retrieved from the monographs, literature databases and official websites. Data on 70 (57.85%) diseases were compiled, though no data were available for the remaining 51 diseases (42.15%). There are data on the incidence/prevalence of only 14 diseases out of 70 at the national level; data on the other 56 diseases are regional. Details are shown in Table 1. The sources of data on 70 diseases can be divided into 5 categories: cross-sectional studies (national level, regional level), screening (newborn screening and other screening), cases seen at hospitals, estimates from models, and other sources of data. Table 2 shows that data on 70 rare diseases have come from 143 sources, the top 3 of which are cases seen at hospitals (40.56%), other sources of data (24.48%), and screening (20.98%). The sources of data for China's Rare Disease Diagnosis and Treatment Guide are mostly from other sources of data (13.29%) and newborn screening (6.99%). An additional source of data is the number of cases reported to the Taiwan Health Promotion Administration (37.06%).

Newborn screening in China started in the 1980s, and it has developed quickly to cover more diseases with the consecutive issuance of related policies, laws, and supporting documents (*27*). The 20th Anniversary of the Newborn Screening Study Group and the 2018 Newborn Screening Progress Summit were held in November 2018 in Shanghai. At the summit, Professor Zhao of the Children's Hospital, Zhejiang University School of Medicine, said in a special report on "The progress of China's newborn screening" that China's newborn screening covered 97.5% of the country and that tandem mass spectrometry was used in some regions to detect various rare disease (*28*). Newborn screening helps to provide data on the incidence/prevalence of rare diseases. For example, the prevalence of hyperphenylalaninemia is 9.62/100,000 persons (*3*), which is calculated based on screening data from 35 million newborns from 1985 to 2011. Based on 17.96 million pieces of data collected by the Newborn Screening Study Group of the Chinese Preventive Medicine Association, the incidence of phenylketonuria is 8.5/100,000 in China (*12*).

Taiwan established a rare disease reporting system including rare disease incidence, treatment fees, and treatment outcomes in 2000. It also issued the "Regulations on Implementation of Taiwan's Rare Disease and Orphan Drug Act" in 2000 and it stipulated that medical professionals should report any patients with rare diseases or anyone who died from a rare disease to relevant government departments in Taiwan. A disease is deemed to be a rare disease when its incidence is less than 0.01%, it is recognized by the Rare Disease and Drug Review Committee, and it is documented by a relevant department in Taiwan. Only recognized rare diseases are covered by health insurance, which greatly encourages patients to apply for certification and doctors to report the disease. This also guarantees the smooth running of the rare disease reporting system (*29*). The Taiwan Health Promotion Administration updates the number of reported cases every month, and the prevalence of rare diseases is calculated based on statistics prior to December 31, 2018 (*9*) and the population of Taiwan (*30*). Table 2 shows that 53 rare diseases on China's Rare Diseases List were reported in Taiwan.

3. Challenges posed by the incidence/prevalence of rare diseases: Lack of baseline data and comparability within data

Data on the incidence/prevalence of 70 (57.85%) of 121 rare diseases in China's First List of Rare Diseases

Table 1. Incidence and prevalence of rare diseases in China's First List of Rare Diseases

No.	Rare disease	National Diagnosis and Treatment Guide published data (*3*)		Other published data	
		Incidence/100,000 persons	Prevalence/100,000 persons	Incidence/100,000 persons	Prevalence/100,000 persons
1	21-hydroxylase deficiency	/	/	3.08 (Dongguan, Guangzhou) (*4*) 3.03 (Liuzhou, Guangxi) (*5*)	/
2	Albinism	5.56	/	/	5.13 (*6*)
3	Alport syndrome	/	/	/	/
4	Amyotrophic lateral sclerosis	0.6 (Hong Kong)	3.1 (Hong Kong)	0.6 (Hong Kong) (*7*) 0.51 (Taiwan) (*8*)	3.04 (Hong Kong) (*7*) 3.33 (Taiwan) (*9*)
5	Angelman syndrome	/	/	/	0.29 (Taiwan) (*9*)
6	Arginase deficiency	/	/	/	0.43 (Zhejiang) (*10*)
7	Asphyxiating thoracic dystrophy	/	/	/	0.00 (Taiwan) (*9*)
8	Atypical hemolytic uremic syndrome	/	/	/	0.068 (Taiwan) (*9*)
9	Encephalitis autoimmune	/	/	/	/
10	Autoimmune hypophysitis	/	/	/	/
11	Autoimmune encephalitis	/	/	/	/
12	β-ketothiolase deficiency	0.10 (Zhejiang)	/	/	/
13	Biotinidase deficiency	/	/	/	0.025 (Taiwan) (*9*)
14	Cardiac ion channelopathies	/	/	/	/
15	Primary carnitine deficiency	/	2.4 (Shanghai) 3.1 (Zhejiang) 1.1 (Hong Kong) 0.8 (Taiwan)	1.27 (Yancheng, Jiangsu) (*11*)	2.5 (*12*) 0.60 (Taiwan) (*9*)
16	Castleman disease	/	/	/	/
17	Charcot-Marie-Tooth disease	/	/	/	1.44 (Taiwan) (*9*)
18	Citrullinemia	/	/	8.66 (Taiwan) (*13*)	0.32 (Taiwan) (*9*)
19	Congenital adrenal hypoplasia	/	/	/	0.081 (Taiwan) (*9*)
20	Congenital hyperinsulinemic hypoglycemia	/	/	/	0.29 (Taiwan) (*9*)
21	Congenital myasthenic syndrome	/	/	/	/
22	Congenital myotonia	/	/	/	/
23	Congenital scoliosis	/	/	/	202.43 (Luohe, He'nan) (*14*) 295.98 (Female, Luohe, He'nan) (*14*) 110.63 (Male, Luohe, He'nan) (*14*)
24	Coronary artery ectasia	/	/	/	656 (Beijing) (*15*)
25	Diamond-Blackfan anemia	/	/	/	/
26	Erdheim-Chester disease	/	/	/	/
27	Fabry disease	/	/	/	1.34 (Taiwan) (*9*)
28	Familial mediterranean fever	/	/	/	/
29	Fanconi anemia	/	/	/	/
30	Galactosemia	/	0.53 (Zhejiang)	0.25 (Taiwan) (*12*)	0.11 (Taiwan) (*9*)
31	Gaucher disease	1.24 (Shanghai)	/	/	0.15 (Taiwan) (*9*)
32	Generalized myasthenia gravis	/	/	/	/
33	Gitelman syndrome	/	/	/	/
34	Glutaric acidemia type I	1.67	/	0.77 (Zhejiang) (*12*)	
35	Glycogen storage disease (type I, II)	2 (Taiwan)	/	1 (Taiwan) (*12*)	3.0 (8 provinces in China) (*16*)

Note: Unless otherwise indicated, data are national data from China.

Table 1. Incidence and prevalence of rare diseases in China's First List of Rare Diseases (continued)

No.	Rare disease	National Diagnosis and Treatment Guide published data (*3*)		Other published data	
		Incidence/100,000 persons	Prevalence/100,000 persons	Incidence/100,000 persons	Prevalence/100,000 persons
36	Hemophilia	20 (Male, Blood group A); 4 (Male, Blood group B)	2.73 (China mainland)	/	2.7 (China mainland) (*17*) 5.5 (Male, China mainland) (*18*) 2.0 (Blood group A, 8 provinces in China) (*16*) 8.1 (Male, Taiwan) (*19*) 6.4 (Hong Kong) (*20*)
37	Hepatolenticular degeneration	/	/	/	2.85 (8 provinces in China) (*16*)
38	Hereditary angioedema	/	/	/	0.034 (Taiwan) (*9*)
39	Hereditary epidermolysis bullosa	/	/	/	0.30 (Taiwan) (*9*)
40	Hereditary fructose intolerance	/	/	/	/
41	Hereditary hypomagnesemia	/	/	/	/
42	Hereditary multi-infarct dementia	/	/	/	/
43	Hereditary spastic paraplegia	/	/	/	0.48 (Taiwan) (*9*)
44	Holocarboxylase synthetase deficiency	/	/	/	/
45	Hyperhomocysteinemia	/	/	/	/
46	Homozygous familial hypercholesterolemia	/	/	/	0.20 (Taiwan) (*9*)
47	Huntington's disease	/	/	/	1.23 (Taiwan) (*9*)
48	Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome (HHHS)	/	/	/	/
49	Hyperphenylalaninemia	/	9.62	12.67 (Yancheng, Jiangsu) (*11*)	9.62 (21)
50	Hypophosphatasia	/	/	/	0.017 (Taiwan) (*9*)
51	Hypophosphatemic rickets	/	/	/	0.52 (Taiwan) (*9*)
52	Idiopathic cardiomyopathy	/	/	/	/
53	Idiopathic hypogonadotropic hypogonadism	/	/	/	/
54	Idiopathic pulmonary arterial hypertension	/	/	/	1.56 (Taiwan) (*9*)
55	Idiopathic pulmonary fibrosis	/	/	/	/
56	IgG4 related disease	/	/	/	/
57	Inborn errors of bile acid synthesis	/	/	/	0.013 (Taiwan) (*9*)
58	Isovaleric acidemia	0.63	/	0.63 (Shanghai) (*12*) 0.27 (Taiwan) (*12*)	0.047 (Taiwan) (*9*)
59	Kallmann syndrome	/	/		0.20 (Taiwan) (*9*)
60	Langerhans cell histiocytosis	/	/	/	/
61	Laron syndrome	/	/	/	0.021 (Taiwan) (*9*)
62	Lever hereditary optic neuropathy	/	≥ 1.092 (Xingtai, Hebei)	/	/
63	Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency	0.40	/	/	/
64	Lymphangioleiomyomatosis	/	/	/	/
65	Lysinuric protein intolerance	/	/	/	/
66	Lysosomal acid lipase deficiency	/	/	/	0.0042 (Taiwan) (*9*)
67	Maple syrup urine disease	/	0.72 (China mainland) 1 (Taiwan)	0.72 (Shanghai) (*12*) 0.56 (Zhejiang) (*12*) 1 (Taiwan) (*12*)	0.12 (Taiwan) (*9*)
68	Marfan syndrome	/	/	/	0.75 (8 provinces in China) (*16*)

Note: Unless otherwise indicated, data are national data from China.

Table 1. Incidence and prevalence of rare diseases in China's First List of Rare Diseases (continued)

No.	Rare disease	National Diagnosis and Treatment Guide published data (*3*)		Other published data	
		Incidence/100,000 persons	Prevalence/100,000 persons	Incidence/100,000 persons	Prevalence/100,000 persons
69	McCune-Albright syndrome	/	/	/	0.089 (Taiwan) (*9*)
70	Medium-chain acyl-CoA dehydrogenase deficiency	/	0.66	0.67(China mainland) (*13*) 0.28 (Zhejiang) (*12*) 1.43 (Shanghai) (*22*) 2.13 (Shandong) (*22*) 0.38 (Taiwan) (*13*)	0.034 (Taiwan) (*9*) 0.74 (Shanghai) (*12*)
71	Methylmalonic acidemia	10 (North China)	3.57 (China mainland) 1.16 (Taiwan)	1.27 (Yancheng, Jiangsu) (*11*)	3 (Shanghai) (*12*) 1.5 (Zhejiang) (*12*) 0.22 (Taiwan) (*9*)
72	Mitochondrial encephalomyopathy	/	/	/	/
73	Mucopolysaccharidosis	/	/	/	0.46 (Taiwan) (*9*)
74	Multifocal motor neuropathy	/	/	/	/
75	Multi acyl-CoA dehydrogenase deficiency	/	/	/	/
76	Sclerosis multiple	/	/	/	3.4 (Male, 8 provinces in China) (*16*) 6.3 (Female, 8 provinces in China) (*16*) 7.02 (Taiwan) (*9*) 4.8 (Hong Kong) (*23*)
77	Multiple system atrophy	/	/	/	0.65 (8 provinces in China) (*16*)
78	Myotonic dystrophy	/	/	/	0.70 (Taiwan) (*9*)
79	N-acetylglutamate synthase deficiency	/	/	/	/
80	Neonatal diabetes mellitus	/	/	/	0.0042 (Taiwan) (*9*)
81	Optical neuromyelitis	/	/	/	/
82	Niemann-Pick disease	/	/	/	0.059 (Taiwan) (*9*)
83	Nonsyndromic hearing loss	/	/	/	/
84	Noonan syndrome	/	/	/	/
85	Ornithine transcarbamylase deficiency	/	/	/	0.089 (Taiwan) (*9*)
86	Osteogenesis imperfecta	/	/	/	11.3 (8 provinces in China) (*16*) 1.45 (Taiwan) (*9*)
87	Parkinson's disease (early-onset; young-onset)	/	/	/	7.39 (Taiwan) (*24*)
88	Paroxysmal nocturnal hemoglobinuria	2.7 (Mudanjiang, Heilongjiang) 1	/	0.21 (*13*) 0.041 (*25*) 0.063 (6 provinces in China) (*25*)	0.614 (*25*) 0.8 (8 provinces in China) (*16*) 1.419 (6 provinces in China) (*25*) 0.45 (Taiwan) (*9*)
89	Peutz-Jeghers syndrome	/	/	/	/
90	Phenylketonuria	8.47	/	8.5 (*12*) 1.82 (Taiwan) (*12*)	9.62 (*12*) 1.17 (Taiwan) (*9*)
91	POEMS syndrome	/	/	/	/
92	Porphyria	/	/	/	0.44 (Taiwan) (*9*)
93	Prader-Willi syndrome	/	/	/	1.22 (Taiwan) (*9*)
94	Primary combined immunodeficiency	/	/	/	/
95	Primary hereditary dystonia	/	/	/	/
96	Primary light chain amyloidosis	/	/	/	/

Note: Unless otherwise indicated, data are national data from China.

Table 1. Incidence and prevalence of rare diseases in China's First List of Rare Diseases (continued)

No.	Rare disease	National Diagnosis and Treatment Guide published data (*3*)		Other published data	
		Incidence/100,000 persons	Prevalence/100,000 persons	Incidence/100,000 persons	Prevalence/100,000 persons
97	Progressive familial intrahepatic cholestasis	/	/	/	0.059 (Taiwan) (*9*)
98	Progressive muscular dystrophy	25.95	/	21.93 (*13*)	/
99	Propionic acidemia	/	0.6~0.7		0.055 (Taiwan) (*9*)
100	Pulmonary alveolar proteinosis	/	/	/	/
101	Pulmonary cystic fibrosis	/	/	/	0.064 (Taiwan) (*9*)
102	Retinitis pigmentosa	/	/	/	23.38 (Beijing rural areas) (*26*) 26.43 (*13*)
103	Retinoblastoma	/	/	/	/
104	Severe congenital neutropenia	/	/	/	/
105	Severe myoclonic epilepsy in infancy	/	/	/	0.25 (Taiwan) (*9*)
106	Sickle cell disease	/	/	/	/
107	Silver-Russell syndrome	/	/	/	/
108	Sitosterolemia	/	/	/	0.017 (Taiwan) (*9*)
109	Spinal bulbar muscular atrophy	/	/	/	/
110	Spinal muscular atrophy	/	/	/	1.71 (Taiwan) (*9*)
111	Spinocerebellar ataxia	/	/	/	4.41 (Taiwan) (*9*)
112	Systemic sclerosis	/	/	/	/
113	Tetrahydrobiopterin deficiency	/	/	/	0.021 (Taiwan) (*9*)
114	Tuberous sclerosis complex	/	/	/	2.16 (Taiwan) (*9*)
115	Tyrosinemia	/	/	/	0.042 (Taiwan) (*9*)
116	Very long-chain acyl-CoA dehydrogenase deficiency	/	/	/	/
117	Williams syndrome	4.26 (Hong Kong)	/	/	1.07 (Taiwan) (*9*)
118	Wiskott-Aldrich syndrome	/	/	/	0.064 (Taiwan) (*9*)
119	X-linked adrenoleukodystrophy	/	/	/	/
120	X-linked agammaglobulinemia	/	/	/	/
121	X-linked lymphoproliferative disease	/	/	/	/

Note: Unless otherwise indicated, data are national data from China.

Table 2. Sources of data on the incidence/prevalence of 70 rare diseases in China

Source of data	Number of diseases (n = 21)	Sources of detailed data [No. (%)]								
		Cross-sectional study		Screening		Cases seen at hospitals		Estimates from models	Some other source of data*	Total
		National level	Regional level	Newborn screening	Other screening	Statistical table of reported cases of rare diseases in Taiwan	Other case counts from hospitals			
In guidelines	21 (17.36)	1 (0.70)	1 (0.70)	10 (6.99)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	19 (13.29)	31 (21.68)
Not in guidelines	68 (56.20)	0 (0.00)	10 (6.99)	16 (11.19)	4 (2.80)	53 (37.06)	5 (3.50)	11 (7.69)	16 (11.19)	112 (78.32)
Total	70 (57.85)	1 (0.70)	11 (7.69)	26 (18.18)	4 (2.80)	53 (37.06)	5 (3.50)	11 (7.69)	35 (24.48)	143 (100)
		12 (8.39)		30 (20.98)		58 (40.56)				

**Note*: Other sources of data mainly include systematic reviews, meta-analyses, and expert opinions.

have been compiled, though no data are available on the incidence/prevalence of the 51 remaining diseases (42.15%). There are no available data on 107 diseases (88.43%) at the national level. Baseline data on the incidence/prevalence of rare diseases in China are lacking, and some data are not updated in a timely manner. For instance, data on the prevalence on hemophilia in *China cited in China's Rare Disease Diagnosis and Treatment Guide* were calculated based on survey data from 1986 to 1989. However, the prevalence of hemophilia varies differently in different countries and even in the same country at different times because of economic and other factors. Clearly, the data cited in *China's Rare Disease Diagnosis and Treatment Guide* do not accurately represent the current prevalence of hemophilia in China (*3*).

In addition, the sources of data are disparate. Few data come from cross-sectional studies (8.39%); only one source of data was a national cross-sectional study. Most data are from other sources (24.48%). Data in the form of expert opinions are subjective, which will lead to the rather large differences in the incidence/prevalence of a disease and a lack of comparability. In *China's Rare Disease Diagnosis and Treatment Guide*, an expert estimate of the incidence of paroxysmal nocturnal hemoglobinuria is 1/100,000. However, the estimated incidence is 0.21/100,000 in the *Compendium of China's First List of Rare Diseases* edited by Zhang *et al*. (*13*) while it is only 0.041/100,000 (*25*) according to Wang based on the number of reported cases of rare diseases in the China Biological & Medical Literature Database and the population size according to the Sixth National Census. The prevalence of methylmalonic acidemia in Taiwan is 1.16/100,000 (*3*) according to *China's Rare Disease Diagnosis and Treatment Guide*, but it is only 0.22/100,000 based on the number of cases of rare diseases reported to the Taiwan Health Promotion Administration (*9,30*).

Moreover, the incidence/prevalence of some rare diseases is too high. Patients from across the country visiting noted hospitals for treatment might be one reason for this. Other reasons include obvious regional differences, the sample size, or a limited number of interview respondents. More data need to be collected at the national level. Pan studied 106,305 patients who underwent coronary arteriography at Beijing Fuwai Hospital from January 2009 to May 2014 and found that the prevalence of coronary artery ectasia was 656/100,000 (*15*). Li *et al*. conducted a cross-sectional study of 15,000 children in Luohe, Henan and found that prevalence of congenital scoliosis was 202.43/100,000, which is far higher than 65-100/100,000 as indicated by the WHO (*31*). In general, there are few data on the incidence/prevalence of rare diseases in China, and the data that are available lack accuracy, uniformity, and timeliness. Epidemiological data at the national level are greatly lacking, and data are not amenable to comparison.

4. The development and promotion of a national rare disease information platform: Standardized data collection and information sharing

The issuance of *China's First List of Rare Diseases* is a milestone in China's efforts to address rare diseases, and it symbolizes the country's commitment to address the social security concerns of patients with rare diseases (*1*). China has made demonstrable progress in policymaking with regard to rare diseases over the past 2 years, and several policies and laws have addressed scientific research, diagnosis and treatment, drug access, and medical care for rare disease (*32*). China is also studying rare diseases epidemiologically: In September 2016, a Clinical Cohort Study of Rare Diseases (Project No.: 2016YFC0901500) was finalized as a specialized medical research project under the national plan for R&D in key areas as formulated by the Ministry of Science and Technology; the aim is to have more than 20 research institutes collaborate in establishing the first national rare disease registry and to register over 50,000 patients with more than 50 diseases (*33*). The project also aims to integrate clinical and biological information and to conduct a large-scale cohort study (*34*). The National Rare Disease Registry (NRDR) was officially launched in June 2017, and more than 100 rare diseases were registered with the NRDR as of August 2018. As of April 29, 2019, information on 35,374 cases of rare diseases was registered. Case registration as part of the project is 70.75% complete (*35*).

Some localities have also addressed rare diseases; two examples are Shandong Province and Beijing. Shandong launched a "Project to Study and Attempt to Control Rare Diseases in China (No.: 2013BAI07B00) as part of the National Program to Support Science and Technology under "the Twelfth Five-year Plan" (2011-2015). Shandong conducted a large-scale thorough study of rare diseases and established a clinical database of rare diseases (*36*). The province also collected data on 10,063 cases of rare diseases and more than 1,000 clinical samples (*37*). In collaboration with research institutes in Shandong and 6 other provinces, the Shandong Association for the Prevention and Treatment of Rare Diseases conducted an epidemiology study of rare diseases in nearly 100 tertiary hospitals in China. Findings indicated that a total of 40,589 patients with rare diseases (2.27% of all hospitalized patients) were seen by 93 hospitals in the 7 provinces. Hospitals diagnosed 952 diseases, and at least half of them were congenital diseases (*38*). On March 1, 2017, the Association and the Shandong Health and Family Planning Commission began registering cases of rare diseases in China. The two organizations initially registered 68 diseases and nearly 1,700 cases, and their efforts are expanding (*37*). The Rare Disease Branch of

the Beijing Medical Association has conducted studies of rare diseases since 2013; using the rare diseases included in European websites related to rare diseases as a template, the Rare Disease Branch has collected and analyzed 404,312 cases from tertiary hospitals in Beijing. As a result, the Rare Disease Branch has identified 1,423 rare diseases (*38*). In 2014, the Rare Disease Branch conducted a "Study on establishing an ICD-10 coding library for rare diseases in China" (*39*). Preliminary research by the Rare Disease Branch yielded information on 121 diseases in China's First List of Rare Disease, including the number of inpatients, disease distribution by province/municipality, age group, and the rate of repeated hospitalization at 96 level A tertiary hospitals. Although national epidemiological data are lacking, information on diseases in the database has been data-mined, which is also an effective approach for an epidemiological study (*40*).

5. Conclusion

Data on the incidence/prevalence of 121 rare diseases in *China's First List of Rare Diseases* are lacking, and sources of data are disparate. China has made preliminary efforts to examine the epidemiology of rare diseases and it has achieved some success, but the completeness, accuracy, uniformity, and timeliness of data need to be improved further. Close cooperation by every party is needed, and several measures should be taken to advance the epidemiological study of rare diseases. In the future, China will promote the use of a uniform rare disease list in its national health care system and ensure that the list is continuously updated. The coding of rare diseases should be actively promoted to improve their traceability in the national health system. Related measures should be encouraged at the national level, and sources of data like government and health care providers should be used extensively to improve the management of rare diseases. National and local offices for registries should be established for specific rare diseases and groups. In accordance with national laws, the governmental health care system should devise tools or measures and allocate funds for additional research projects (*41*), promote the collection of data from every valid source (including clinical facilities), and share more information on rare diseases such as their incidence and prevalence. Information on diagnosis and treatment should be made more accessible to the public (*42*).

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