Research Square

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Rare disease awareness and perspectives of physicians in China: a questionnaire-based study

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Abstract

Background There are over 16.8 million rare disease patients in China, representing a significant challenge for the healthcare system and society. Rare disease patients often experience delayed diagnosis, misdiagnosis, or improper treatment, which may be due to the lack of rare disease awareness among physicians. Results A total of 224 physicians from different hospitals in China participated in the questionnaire, and 9 rare disease experts were interviewed with open-ended questions. Most physicians (83.5%) were from Tertiary hospitals, which have over 500 beds. Only 5.3% of physicians were moderately or well aware of rare diseases. Most physicians (80.1%) had suspected their patients to have rare diseases less than 3 times. There was a strong support for special legislations for rare diseases and orphan drugs. Further, multinomial logistic regression (MLR) was used to determine whether hospitals, gender, and career length has an impact on perspectives and awareness. It was shown that male physicians were more likely to think newborn screening is important ($p<0.05$). The longer the career length is, the more likely physicians believe that their previous education has not provided sufficient information about rare diseases and that their hospital has paid enough attention to rare diseases. Physicians from Tertiary A hospitals were more likely to rate the affordability of orphan drugs high. In addition, nine experts believed that rare disease awareness is essential for early diagnosis and timely treatment. These experts also made recommendations on how to improve rare disease awareness through medical school education and continuing training. Conclusions Our study highlighted the importance of improving rare disease awareness among physicians in China. Recommendations about how to improve rare disease awareness in medical school education and establish an online ‘information hub’ are made for considerations of policy-makers.

Background

There are at least 16.8 million rare disease patients in China, representing a significant challenge for the healthcare system that should not be neglected. In addition to the disease burden, rare disease patients often face the lack of treatment options, financial burden, and psychological stress [1]. Moreover, rare disease patients often experience delayed diagnosis: 5–6 years and 3–10 different physicians before a diagnosis [2–40. Previous studies showed that approximately 30% of patients and families attributed delayed diagnosis to the lack of rare disease awareness and knowledge among physicians, as well as the limited availability of genetic testing [2, 3, 5]. As shown in a previous study, 78.8% of rare disease patients believed that they did not receive proper care due to the lack of rare disease awareness and knowledge among physicians [6].

At the beginning of 2020, our group in cooperation with Seven-Pansy Rare Disease Community, Guangzhou Medical University, and Shenzhen University, did an investigation and study on rare disease cognition. It aims to understand the status of China's rare disease field, provide a basis for relevant departments to issue relevant policies, and provide reference for medical research and development. In addition to the patients with rare diseases and the public, the survey participants joined the group of physicians. After more than 3 month of research, we collected 224 valid questionnaires from physicians.

Questionnaires for the public are still being collected. The research report shows that the physicians' awareness of rare diseases still needs to be improved. There are obvious differences between physicians and patients in the diagnosis of rare diseases, the degree of physician follow-up, and the degree of medical burden. The academic qualifications of the physicians in this survey are much higher than average of Chinese physicians. The number of years of medical practice reflects the richer experience in medical treatment, but even so, only 5.3% of physicians were moderately or well aware of rare diseases.

In-depth understanding of the problems encountered by the rare disease group in various aspects, reveal the relationship between the various parties involved in the rare disease, so as to put forward more targeted and feasible opinions and suggestions, and submit them to relevant policy research and decision-making departments.

Results

Questionnarie of physicians

A total of 224 physicians participated in this study. The demographic information of these physicians are summarized in Table 1. Out of 224 physicians, 104 (46.4%) were male and 120 (53.6%) are female. Thirty-four physicians (15.2%) were under the age of 30, 132 (58.9%) were between 30 to 45, 52 (23.2%) were between 46 and 60, and only 6 (2.7%) were over 60 years old. Hospitals in China are organized according to a 3-tier system that recognizes a hospital's ability to provide medical care, medical education, and conduct medical research. Based on this, hospitals are designated as Primary (< 100 beds), Secondary (100–500 beds), or Tertiary institutions (> 500 beds). Further, based on the level of service provision, size, medical technology, medical equipment, and management and medical quality, these 3 grades are further subdivided into 3 subsidiary levels: A, B and C. Out of 224 physicians, 163 (72.8%) were from Tertiary A (the highest level), 16 (7.1%) from Tertiary B, 8 (3.6%) from Tertiary C, and only 35 (15.6%) from Primary or Secondary hospitals. Out of 222 physicians responded, 81 (36.5%) practiced between 5 and 15 years, 71 (32.0%) practiced between 16 and 30 years, 49 (22.1%) under 5 years, and 21 (9.5%) over 30 years.

Table 1

Demographic information of participants of the questionnaire for physicians. Only specialties with more than 4 participants were shown. Hospitals in China are organized into a 3-tier system: Primary (< 100 beds), Secondary (100–500 beds), or Tertiary institutions (> 500 beds). Moreover, based on size, medical equipment, medical technology, management, service provision, and medical quality, each tier are further divided into 3 levels: A, B and C.

Gender	**Male (n = 104, 46.4%)**
	Female (n = 120, 53.6%)
Age (years)	< 30 (n = 34, 15.2%)
	30–45 (n = 132, 58.9%)
	46–60 (n = 52, 23.2%)
	> 60 (n = 6, 2.7%)
Hospital	Tertiary A (n = 163, 72.8%)
	Tertiary B (n = 16, 7.1%)
	Tertiary C (n = 8, 3.6%)
	Secondary A (n = 22, 9.8%)
	Secondary B (n = 1, 0.4%)
	Primary A (n = 4, 1.8%)
	Primary B (n = 4, 1.8%)
Career length (years)	< 5 (n = 49, 22.1%)
	5–15 (n = 81, 36.5%)
	16–30 (n = 71, 32.0%)
	> 30 (n = 21, 9.5%)
Specialty	Pediatrics (n = 13, 6.3%)
	Radiology (n = 22, 10.6%)
	Surgery (n = 18, 8.7%)
	Orthopedics (n = 10, 4.8%)
	Internal Medicine (n = 10, 4.8%)
	Dermatology (n = 10, 4.8%)
	Cardiology (n = 9, 4.3%)

Gender	Male (n = 104, 46.4%)
	Nephrology (n = 5, 2.4%)
	Neurology (n = 5, 2.4%)
	Obstetrics and Gynecology (n = 8, 3.9%)
	Oncology (n = 9, 3.9%)
	Other (n = 88, 42.5%)

As to self-evaluated level of rare disease awareness, one hundred and sixteen physicians (51.8%) were ‘aware of, but did not know much about’ rare diseases, 85 (37.9%) ‘knew a little bit’ about rare diseases, and 11 (4.9%) were ‘not aware of’ rare diseases. Only 11 (4.9%) ‘moderately aware of’ rare diseases, and 1 (0.4%) ‘well aware of’ rare diseases. A previous study in Spain showed that 15% of physicians have a good knowledge about rare diseases [7], significantly better than a total of 5.3% in this study. These results indicated a significant lack of awareness of rare diseases among physicians in China. Considering the fact that most physicians were from Tertiary hospitals with > 500 beds and located in big cities, the rare disease awareness among average physicians in China would be even worse. On the question ‘Have you ever suspected that a patient suffered from a rare disease?’, 91 of 221 respondents (41.2%) chose ‘once or twice’, while 86 (38.9%) chose ‘never’. Only 44 (19.9%) chose ‘over three times’. Out of 220 respondents, 121 (55%) thought that less than 10% of their patients had rare diseases, while 79 were not sure. Only 20 (9.1%) thought over 10% of their patients had rare diseases. Out of 218 respondents, 203 physicians (93.1%) thought rare disease patients were more difficult to manage. Out of 221 respondents, 133 thought their hospitals had not paid enough attention to rare disease patients. Out of 222 respondents, 119 (53.6%) physicians encountered one to five types of rare diseases, and 66 (29.7%) never encounter any. Only 17 (7.7%) encountered more than 10 types, while 20 (9.0%) encountered six to nine types. The combined total of physicians who encountered rare disease patients at least once was 83.3%, similar to the number among physicians in Spain (90%) [8]. Out of 182 respondents, 89 physicians (48.9%) had no rare disease patients in the past year, 44 (24.2%) had one or two rare disease patients, and 27 (14.8%) had three to five rare disease patients. Only 10 (5.5%) had six to ten rare disease patients, and 8 (4.4%) had over ten rare disease patients. Four physicians were not sure which diseases were rare diseases. Out of 177 respondents, 112 physicians (63.3%) had not treated any rare disease patients, 35 (19.8%) treated one to two, 19 (10.7%) treated three to five, 8 (4.5%) treated six to ten, while 3 (1.7%) treated over ten. Out of 222 respondents, 131 physicians (59%) ‘strongly’ supported special legislations for rare diseases, and 84 (37.8%) ‘moderately’ supported. Only 7 (3.2%) were neutral or negative on legislations for rare diseases. These results highlighted the urgent need and wide support for special legislations for rare diseases. Out of 219 respondents, 126 physicians (57.5%) ‘strongly’ supported special legislations for orphan drugs, and 80 (36.5%) ‘moderately’ supported. Only 13 (5.9%) were neutral or negative on legislations for rare diseases. Out of 222 respondents, 103 physicians (46.4%) supported special insurance programs for rare diseases, 95 (42.8%) suggested inclusion of rare diseases into the Critical illness insurance program, a national insurance program in China. Only 8 (3.6%) thought

that the Basic Medical Insurance Systems for Urban and Rural Residents is sufficient, and 4 (1.8%) suggested special subsidies from the government (Figure.1A). Out of 222 respondents, 114 physicians (51.4%) rate newborn screening as ‘essential’, 80 (36%) as ‘very important’, 25 (11.3%) as ‘important. Only 3 (1.4%) rated it as ‘not that important’, and none c selected ‘useless’ (Figure.1B). Out of 216 respondents, 107 physicians (49.5%) rated the availability of orphan drugs as ‘moderate’, 39 (18.1%) selected ‘good’, and 29 (13.4%) selected ‘very good’ (Figure.1C). Only 29 (13.4%) selected ‘poor’ and 12 (5.6%) selected ‘very poor’. As to the affordability of orphan drugs, 116 physicians (53.0%) selected ‘mediocre’, 49 (22.4%) selected ‘bad’, and 21 (9.6%) selected ‘very bad’ (Figure.1D). Only 14 (6.4%) and 19 (8.7%) selected ‘very good’ and ‘good’, respectively. Out of 222 respondents, 195 (87.8%) selected ‘yes’ to the question ‘do you need information about rare diseases?’ This number is similar to a previous study in Belgium (83–97%) [9]. As to the question ‘does your previous education and training did not provide sufficient information about rare diseases?’, out of 222 respondents, 77 (34.9%) selected ‘moderate’, 72 (32.4%) selected ‘not sufficient’, and 13 (5.9%) selected ‘useless’. Only 45 (20.3%) and 15 (6.8%) selected ‘very useful’ and ‘sufficient’, respectively.

As to organizations of rare disease patients, 96 physicians heard about China-Dolls Center for Rare Disorders, a non-government organization established in 2008 for patients with osteogenesis imperfecta. Forty-nine physicians heard about the Seven Pansy Rare Diseases Community, a national organization in China dedicated to raise rare disease awareness and provide scientific information and support. As shown in Figure.2A, international sources, e.g., NORD (10.7%), Orphanet (11.6%), Global Genes (8.5%), EURORDIS (4.5%), were not as well-known in China. It has been shown that among pediatricians in Australia, the percentage of awareness of Orphanet, NORD, and EURORDIS was 50%, 35%, and 21%, respectively [10]. This discrepancy may be partly due to the language barrier. Eighty-five physicians (37.9%) have not heard about none of the listed organizations. As to ‘What kind of information do you need?’, 186 respondents (83.0%) chose ‘diagnosis’, 167 (74.6%) for both ‘screening’ and ‘treatment’ (Figure.2B). Interestingly, 106 out of 220 respondents (48.1%) only wanted to know information about rare diseases that can be possibly cured. As to the information source, 163 (72.8%) selected academic conferences, 152 (67.9%) chose the internet, 141 (62.9%) selected medical school education (Figure.2C). Interestingly, only 61 (27.2%) selected patients, and 46 (20.5%) selected patient organizations.

To identify parameters that have impact on rare disease awareness and perspectives, the correlation between Q1-6 and Q7-15 were analyzed. First, in Q4, hospitals were categorized into 9, and 72.8% of physicians were in the Tertiary A hospitals. Therefore, hospitals were re-categorized into Tertiary A and non-Tertiary A hospitals to ensure that each category has sufficient samples. Then, age (Q3) and career length (Q5) was correlated ($R^2 = 0.79$). To avoid collinearity, only gender (Q2), hospital (Q4), and career length (Q5) were analyzed as parameters. Finally, multinomial logistic regression (MLR) was used to determine whether hospitals, gender, and career length has an impact on perspectives and awareness (results summarized in Table 2). As to rare disease awareness, although age is better predictor with an Akaike information criterion (AIC) value of 456.604, no factors had a significant impact. This may be because few physicians were moderately or well aware of rare diseases, which would affect assumptions

of MLR. As to Q11 (does your hospital pay enough attention to rare disease patients?), only career length has a significant impact with an AIC value of 289.4388, and p value of 0.0009. The longer their career length is, the more likely physicians have a positive response. As to Q12 (how many rare disease patients have you met?), gender has significant impact (AIC = 491.425, $p = 0.02$). Specifically, compared to '>10', female physicians were more likely to respond 'none'. As to Q13 (do you support special legislation for rare diseases?), no factors had a significant impact. Similarly, no factors had a significant impact on Q16 (do you support special legislations of orphan drugs?), Q17 (perspectives on medical insurance), Q18 (the availability of orphan drugs), and Q21 (do you need rare disease information?). Interestingly, hospitals had a significant impact on Q19 (affordability of orphan drugs) with an AIC value of 570.3079 and a p value of 0.017. Physicians from Tertiary A hospitals were more likely to rate the affordability of orphan drugs high. This may be explained by the fact that Tertiary A hospitals had more resources and insurance subsidies from the government. As to perspectives on newborn screening (Q20), gender and career length had significant impact (AIC = 442.2492, $p < 0.05$). Female physicians were less likely to think newborn screening is important. Notably, very few respondents believed newborn screening to be useless, which may affect assumptions of MLR. As to Q22 (does your previous education and training provide sufficient information about rare diseases?), career length was a good predictor (AIC = 612.4972, $p < 0.05$). The longer the career length is, the less likely they believe previous education to be useful. This may be explained by the fact that the amount of information about rare diseases in medical school education and job training had gradually increased over time. As to Q25 (do you only want information about rare diseases that can be possibly cured?), career length was also a good predictor (AIC = 290.00995, $p < 0.01$). Interestingly physicians with less than 5 years or over 30 years of experience were more likely to respond positively, while physicians with 5–30 years of experience had no preference.

Table 2

Impact of demographic information on rare disease awareness and perspectives. First, in Q4, hospitals were initially categorized into 9, and 72.8% of physicians were in the Tertiary A hospitals. Therefore, hospitals were re-categorized into Tertiary A and non-Tertiary A hospitals to ensure that each category has sufficient samples. Then, age and career length were correlated ($R^2 = 0.79$). To avoid collinearity, only gender, hospital, and career length were analyzed as parameters. Then, a MLR analysis was performed with SPSS. Akaike information criterion, AIC.

Rare disease awareness	No factors with statistical significance
Does your hospital pay enough attention to rare disease patients?	Career length (AIC = 289.4388, p = 0.0009
	The longer their career length was, the more likely physicians had a positive response
How many rare disease patients have you met?	Gender (AIC = 491.425, p = 0.02)
	Compared to '>10', female physicians were more likely to respond 'none'.
Do you support special legislation for rare diseases?	No factors with statistical significance
Do you support special legislation of orphan drugs?	No factors with statistical significance
Perspectives on medical insurance	No factors with statistical significance
Availability of orphan drugs	No factors with statistical significance
Do you need rare disease information?	No factors with statistical significance
Affordability of orphan drugs	Hospital (AIC = 570.3079, p = 0.017)
	Physicians from Tertiary A hospitals were more likely to rate the affordability of orphan drugs high.
Perspectives on newborn screening (AIC = 442.2492, p < 0.05)	Gender (AIC = 442.2492, p < 0.05)
	Female physicians were less likely to believe newborn screening to be important.
Does your previous education and training provide sufficient information about rare diseases?	Career length (AIC = 612.4972, p < 0.05)
	The longer the career length was, the less likely they believe previous education to be useful.
Do you only want information about rare diseases that can be possibly cured?	Career length (AIC = 290.00995, p < 0.01)
	Physicians with less than 5 years or over 30 years of experience were more likely to respond positively, while physicians with 5–30 years of experience had no preference.

Interviews of rare disease experts

A total of 9 experts in the field of rare diseases were interviewed with exploratory questions. Notably, all of these experts were from Tertiary A hospitals located in big cities, such Beijing, Shanghai and Chengdu. As to how rare disease awareness facilitates fast and accurate diagnosis, most experts (7/9, 77.8%) agreed that such an awareness will point physicians to the right direction and then with additional information they may be able to reach a diagnosis. Even realizing the possibility of rare disease will help them refer patients to larger hospitals where patients are more likely to be diagnosed. Sometimes, physicians without rare disease awareness may neglect crucial evidence that can help diagnosis. Consequently, some patients were misdiagnosed as other common diseases with similar symptoms for long before a correct diagnosis was made. All experts agreed that physicians generally lacked the rare disease awareness, which was a major reason of misdiagnosis. Three experts (33.3%) suggested to establish a rare disease referral hub in each hospital, which collects potential rare disease patients and refer them to larger hospitals. The majority of Chinese population do not live in big cities that have large hospitals and experts. Also, it is unrealistic to provide comprehensive rare disease information to all physicians in smaller hospitals. Such a rare disease referral hub is not expected to incur significant burden to hospitals, therefore, it is feasible and should significantly help the diagnosis and treatment of rare diseases.

All experts believed that current medical school education had not provided enough information about rare diseases. The French National Plan for Rare Diseases stipulated that medical school curriculum should include education in rare diseases [11]. Such stipulations do not exist in China, but all experts recommended inclusion of rare disease topics in medical school curriculum. Five experts (55.6%) recommended that in medical school education and continuing training, topics about a specific type of pathology and related common diseases should also mention potential related rare diseases. Also, case studies of the diagnosis pathway of a rare disease were suggested by seven experts. All experts believed that it would not be practical to include each rare disease in medical school education or continuing medical education. Therefore, the consensus is to adopt a method based on principles and organization of knowledge. Instead of solely teaching students the knowledge of rare diseases, more focus should be put on the ability to exclude common diseases and collect relevant information for diagnosis, as well as the knowledge of how to find information about treatment options upon diagnosis.

As to information sources of rare diseases, seven experts listed medical literature as the major source. Alternative sources included academic conferences, the internet, and patients. Interestingly, all experts mentioned the concept of ‘learning from the patients’, while only 20.7% of physicians listed patients as their information source in the questionnaire. These experts believed that rare disease patients were extremely active in learning about their conditions and scientific breakthroughs in the field, and thus sometimes could teach physicians much. One expert mentioned the experience of one patient explaining the relative strength and weakness of AAV gene therapy versus gene editing for Pompe disease. In general, these experts believed that current information source is not comprehensive and mainly targets experts instead of front line physicians. Six experts (66.7%) expressed that an ideal information source would be a search engine that one can submit symptoms and test results, and obtain possible diseases and treatment options in return. The output could also be recommendations on additional tests and evidence one should look for. Contact information of potential experts or hospitals for referral would be

beneficial as well. Another feature of this search engine is a review system that other users can upvote, downvote, and comment on the output so that it can be optimized. Additionally, the search engine should be fully accessible to at least physicians with or without a cost.

All experts expressed the concern for the high cost of orphan drugs, especially gene therapy. Nevertheless, all of them acknowledged the cost involved for developing and manufacturing an orphan drug. In 1983, the United States passed the Orphan Drug Act which provide tax incentives, enhanced patent protection and marketing right, and clinical research subsidies to pharmaceutical companies that develop orphan drugs. The number of orphan drugs significantly from 38 before 1983 to over 600 in 2019. Many other countries and districts pass similar laws to stimulate orphan drug development. All experts believed that legislation of an orphan drug act in China will remarkably accelerate orphan drug development and potentially lower the cost. Similar to the 224 physicians in the questionnaire, most experts (7/9, 77.8%) believed that a special rare disease insurance program would be the best option. One expert mentioned the Orphan Reinsurer and Benefit Manager (ORBM), a program being proposed in the United States to address the ultra-high cost of orphan drugs. Under the ORBM, payment is carved out by the primary insurer, which may be vulnerable to financial challenges of orphan drugs. ORBM aims to address the issue of payment timing, therapeutic performance risk, and actuarial risk [12].

Experts also commented on the biggest challenge when handling rare disease patients. One common issue is the lack of rare disease awareness among patients, families, and many frontline physicians. Symptoms of many rare diseases are non-obvious and even difficult to explain, which are thus often ignored, resulting in significant delay in diagnosis and management. Another difficulty is the lack of reliable, up-to-date, and accessible information source. Most experts (8/9, 88.9%) believed that the language barrier creates much challenge while physicians searching for relevant information. Although international organizations, such as Orphanet, NORD, established systems of reliable and comprehensive information about rare diseases, it is not readily accessible for Chinese physicians, most of whom do not speak English. Further, although only 19% of physicians the questionnaire rated the availability of orphan drugs as ‘poor’ or ‘very poor’, all experts expressed the concern over the lack of treatment options. As to the discrepancy, seven experts believed that it was because ‘most physicians do not know the existence of orphan drugs in Western countries’.

Discussion

At present, there are more than 7,000 rare diseases known in the world, of which only 5% are medicated; among the 350 million rare disease patients in the world, there are estimated to be about 20 million rare disease patients in China [13]. However, due to insufficient disease awareness and lack of effective treatment options, patients with rare diseases have long faced the dilemma of low diagnosis and treatment rates. It is urgent to popularize disease knowledge and improve the level of diagnosis and treatment of rare diseases [14].

Due to the extremely low prevalence and incidence, the small number of patients, and the scattered population of patients, most rare diseases require multidisciplinary, interdisciplinary clinical experts and medical genetic experts only through collaboration can accurate diagnosis and treatment be achieved [15]. Thus, empowering physicians is a huge project that requires more support and help from government departments and all walks of life. Major hospitals should establish regular rare disease diagnosis expert teams and formulate scientific and effective training plans so that doctors will no longer have nothing to do with rare diseases.

The establishment of a rare disease registration platform can form a rare disease knowledge base, realize multi-level sharing of rare disease data, reduce the time for physicians to diagnose, and improve the accuracy of diagnosis [16]. At the same time, the establishment of the system is conducive to the formation of unified rare disease registration technical standards and norms, uniting superior units to form a collaborative network of rare diseases, carrying out rare disease registration research nationwide, and establishing a rare disease direct reporting system [17]. The establishment of a new genetic counseling system will also help patients with rare diseases find and diagnose them as soon as possible. Previous report has pointed out that about 80% of rare diseases are genetic, which means that most undiagnosed patients need to consult a medical geneticist to shorten the diagnosis time [17]. Through the establishment of pre-diagnosis centers in genetic clinics or information collection and remote consultation for patients in rural and remote areas, patients can quickly and effectively obtain genetic diagnosis and consultation. At the same time, genetic diagnosis and consultation also require multidisciplinary and interdisciplinary clinical experts. According to industry insiders, my country currently lacks medical talents with multidisciplinary development. Training genetic counselors can solve the problems caused by the shortage of talents in this area [18].

In China, due to the imbalance of medical information and resources, the many basic medical needs of patients with rare diseases urgently need to be met. It is even more necessary to rely on the help of patient organizations to provide a patient in seeking medical advice, knowledge popularization, patient care, and rehabilitation support. A platform for communication and voice, appealing to all sectors of society to pay attention to and support the group of patients with rare diseases.

Conclusions

These results highlight the importance of improving rare disease awareness among physicians in China. Recommendations about how to improve rare disease awareness in medical school education and establish an online ‘information hub’ are made for considerations of policy-makers.

Methods

Ethics, consent, and permission

The study was approved by the Institutional Ethics Committee of Guangzhou Medical University. The study was approved by the Institutional Ethics Committee of the Guangzhou Medical University, China. A questionnaire and a list of open-ended questions for interviews were designed in Chinese. Potential participants were invited to participate in this study, and only those who signed the informed consent participated in this study. All the participants acknowledged: 1) the sponsor of the study; 2) the objectives of the study; 3) the affiliation of the investigators; 4) that they can decline to answer any of the questions; 5) that the information collected will only be used for academic research; 6) that they can quit the study at any time; 7) that the results will be published in a scientific journal without seeking their approval of the manuscript; 8) that they will participate in this study anonymously; and 9) that they will not be paid for participating in this study.

Data collection and analysis

Physicians were invited through advertisements on social media and websites. All questionnaires were completed between March to April 2020. Rare disease experts were invited for an interview through Seven-Pansy Rare Disease Community, a national rare disease organization in Shanghai. All interviews were conducted over the phone between April to May 2020. The interviews were audio recorded with the interviewees' permission and transcribed verbatim for further analysis. R was used to analyze data, p value < 0.05 (two-tailed tests) to denote statistical significance. Multinomial logistic regression was used to determine parameters that have an impact on awareness and perspectives.

List Of Abbreviations

National Organization for Rare Disorders (NORD), European Organization for Rare Diseases (EURORDIS), Canadian Organization for Rare Diseases (CORD)

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Ethics Committee of the Guangzhou Medical University, China. All participants signed the informed consent and agreed to participated this study voluntarily.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XL, LO, and SZ designed the study. ZL and JZ collected the data. XZ, BL, JZ performed statistical analysis. LO wrote the manuscript.

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Figures

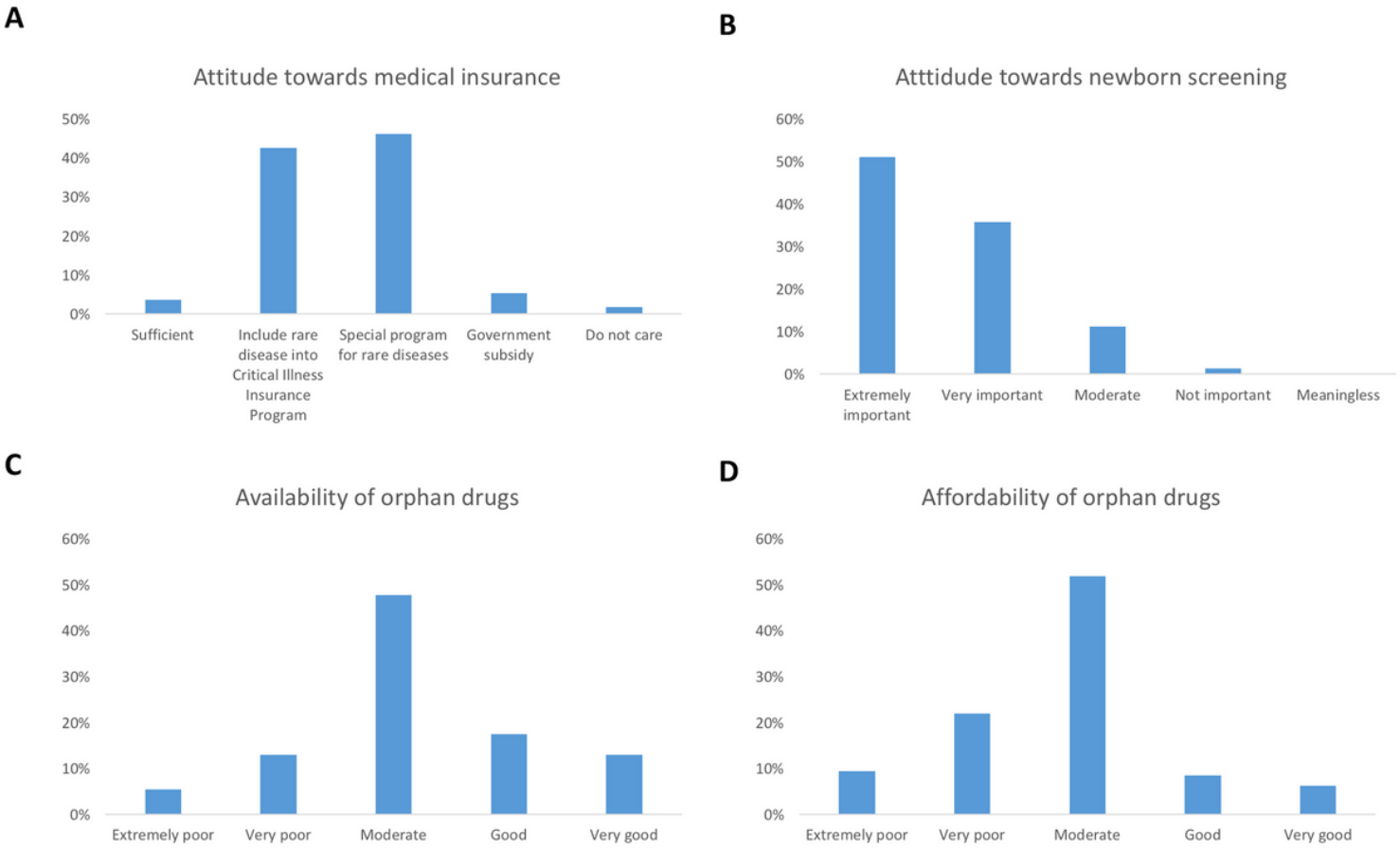

Figure 1

Attitude of physicians towards orphan drugs, medical insurance, and newborn screening.

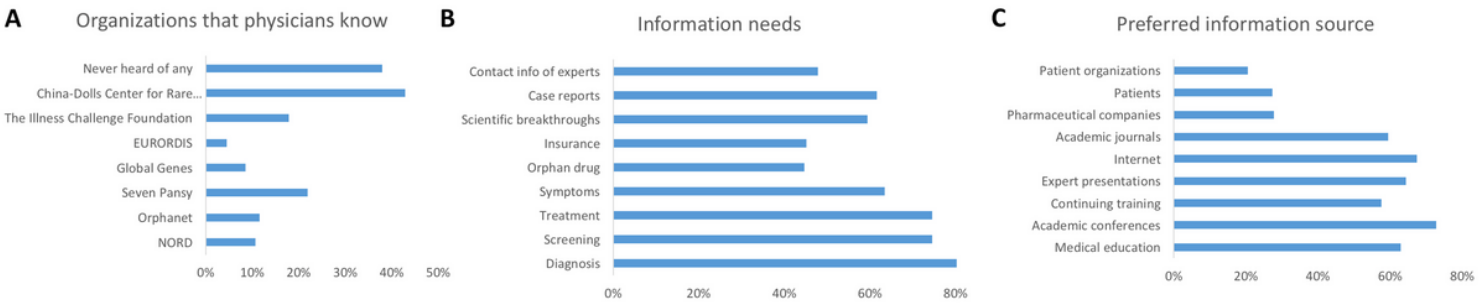

Figure 2

Information needs of physicians. (A) Patient organizations that physicians had heard of. (B) Information needs of physicians were listed in comparison with those of patients and care-givers from the first questionnaire. (C) The preferred information source of physicians.