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Medical students' knowledge and opinions about rare diseases: A case study from Poland

Jan Domaradzki[1,*], Dariusz Walkowiak[2]

[1] *Department of Social Sciences and Humanities, Poznan University of Medical Sciences, Poznań, Poland;*
[2] *Department of Organization and Management in Health Care, Poznan University of Medical Sciences, Poznań, Poland.*

Summary **While genetics constitutes an important part of medical education, one can observe a lack of knowledge about rare diseases (RD) among medical students and healthcare professionals. Meanwhile, many RD are life threatening and chronically debilitating conditions that significantly reduce patients' quality of life. Most RD patients experience various psychiatric symptoms, behavioral changes and mental retardation. Consequently, physicians should be educated on RD. Thus, the aim of this paper is to assess the knowledge about RD among future physicians. The study was conducted among 346 medical students of Poznan University of Medical Sciences. It showed that while 99.4% of respondents had heard the term 'rare disease' and 90.5% knew its main cause, only 11.5% correctly estimated the prevalence of RD. Moreover, only 35.3% knew what percentage of RD is of genetic character and 24.9% that RD are most common among children. Additionally, very few students knew the number of RD patients in Poland (5.2%). Most respondents believed that it is primarily geneticists (76.6%) and pediatricians (74.3%) who should be uniquely educated and trained in RD. Interestingly, although 95.4% of respondents perceived their knowledge about RD as insufficient or very poor and 92.2% did not feel prepared for caring for RD patients, 45.7% believed that it is not necessary to add an extra course on RD into medical curricula. Thus, as most future physicians do not possess knowledge about RD, there is an urgent need to raise the awareness on RD among medical students and educate them about such diseases.**

Keywords: Rare diseases, medical education, medical students' knowledge

1. Introduction

While there is no accepted definition of rare diseases (RD) it is widely recognized that they affect a small percentage of the population. For example, in the European Union a disease is considered to be rare when the number of people affected is less than 5 per 10,000, *i.e.* no more than 1 in 2,000, while in the United States RD are defined as conditions that affect fewer than 200,000 people and in Japan it is 1 in 2,500 people (*1*). While there have been listed about 6,000-8,000 RD so far (*2*), their prevalence differs significantly between countries or regions and many of them affect only a few people in the world. At the same time it is estimated that approximately 300-350 million people, *i.e.* 6-8% of the global population, suffer from RD worldwide, including 25-30 million in the US and 27-36 million in the EU (*3*). Moreover, it is said that one in every seventeen EU citizens will be affected by RD during their lifetime. These numbers alone suggest that RD patients are numerous and that most healthcare professionals will encounter such patients during their professional career. For all these reasons, in 2009, the Council of the European Union recognized that RD pose a serious 'threat to the health of EU citizens' (*4*). Consequently, they are now considered an important medical and social problem and an urgent public health issue (*5*).

Nevertheless, while some countries, *i.e.* the USA, the United Kingdom, Australia, Japan or Taiwan, have adopted legislation on RD and orphan drugs and promote investments in RD research, many other countries, including Poland, still lack a national strategy

**Address correspondence to:*
Dr. Jan Domaradzki, Department of Social Sciences and Humanities Poznan University of Medical Sciences, Rokietnicka 7, St., 60-806 Poznań, Poland.
E-mail: jandomar@ump.edu.pl

for RD (*6*). Meanwhile, approximately 2.3-3 million people suffer from RD in our country (*7,8*). Moreover, in Poland there is neither a center for registration of RD nor a central register of drugs for such diseases. Yet another problem patients and their caregivers have to struggle with is lack of education of healthcare professionals on RD. Consequently, they are often left without a diagnosis and proper treatment. It is important because while RD are life threatening and chronically debilitating diseases that significantly reduce patients' quality of life, their early detection, diagnosis and therapy enable the patient's daily functioning and increase their quality of life.

Thus, although during the past few years there have been an increasing number of campaigns and initiatives aiming at addressing RD, including celebration of Rare Disease Day on February 29th (which was first organized in 2008 in numerous European countries and in Canada), and creation of many websites dedicated to RD and their particular types, still there can be observed a lack of knowledge about RD among the general population (*9,10*), medical students (*11-16*) and healthcare professionals, including physicians and pharmacists (*17-22*). Consequently, RD patients and their families report that due to physicians' lack of knowledge and disease-related experience they have to become self-experts on their own disease and educate physicians about their condition (*18,23,24*). At the same time, healthcare professionals themselves declare that lack of knowledge is the biggest problem they face while caring for RD patients (*17,19,21,22*). Meanwhile, as RD are very complex and require multi-professional care, it is essential that not only primary-care physicians but also various specialists, including geneticists, neurologists, psychiatrists, immunologists, pediatricians, pharmacists, nurses, dieticians and physiotherapists must be engaged in education on RD (*11,13,25*).

Concurrently, it is important to remember that one of the main factors leading to increased stress in RD patients and their caregivers is delays in receiving a correct diagnosis (*19, 26-28*). For example, a European survey conducted in 2008 showed that after the occurrence of the first symptoms 25% of patients with RD were waiting for an appropriate diagnosis between five and thirty years and 40% of them received an incorrect diagnosis (*26*). The *Rare Disease Impact Report* published in 2013 shows that in the US it takes an average of 7.6 years to receive a proper diagnosis and in the United Kingdom 5.6 years. Moreover, before patients get one, they usually visit up to eight physicians and receive two or three misdiagnoses (*23*). In Australia, some parents of children with RD, while waiting ten or even eighteen years for diagnosis, reported visiting more than ten physicians, and 27.3% had received misdiagnosis (*20*). Walshe and Yealland (*29*) reported that only 30% of patients with Wilson disease were diagnosed at presentation. It is important, because a delay or misdiagnosis leads to worsening of symptoms and disease progression (physical, cognitive, psychological deterioration of the patient or even death or birth of other affected children), results in delays in appropriate treatment or in receiving unnecessary medical interventions, including tests, readmissions and surgeries, and cause additional medical costs (*26*). Therefore, the aim of this paper is to assess the knowledge and awareness about RD among future physicians. Our findings may serve as a point of departure for revision of medical university curricula.

2. Materials and Methods

The study was conducted between January and March 2019 among medical students of Poznan University of Medical Sciences, Poland. The participants were recruited during regular classes. The survey was conducted with a standard questionnaire that was constructed from themes based on a review of the literature and the study aim. It included 28 questions: 22 items referring to respondents' knowledge of and attitudes towards RD and 6 questions that addressed their demographic data. The questionnaire consisted of four groups of questions. The first group were ten questions on the definition, frequency, number and estimated prevalence of RD. The respondents were also asked whether they have ever heard the term 'rare disease'. Other questions referred to epidemiological issues: in which age group RD are the most common, how many people suffer from RD worldwide, in the EU and in Poland. Two questions referred to the etiology of RD. Additionally, students were asked to indicate RD from a list comprised of twenty eight diseases: eighteen rare diseases and ten more common disorders. The rare diseases included were chosen because they are either commonly known rare diseases (*i.e.* haemophilia, progeria, Huntington disease or sickle cell anemia) or students had an opportunity to learn about them during their studies (*i.e.* Niemann-Pick disease, neurofibromatosis, Pompe disease, Gaucher disease).

The second group of six questions concentrated on organizational issues. The respondents were asked about the name of the European website providing information about RD and orphan drugs and whether Poland has a national register of RD patients. They were also asked about the percentage of RD that can be treated with the drugs and whether orphan drugs are reimbursed in Poland. Finally, the respondents were asked whether RD should be considered as an important aspect of Polish healthcare policy and which specialists should possess special knowledge about RD.

The third group of questions contained six questions related to the participants' self-assessment of knowledge and competence in the field of RD. The respondents were asked if they had any classes on RD, how they perceive their knowledge about RD and whether they

would like to broaden it. The authors also wanted to know whether future physicians believed that there is a need to include an obligatory course on RD in medical curricula. Finally, the respondents were asked where they got the information on RD from and whether they felt prepared to care for RD patients.

The last group of questions consisted of six items related to gender, year of studies, marital status, dwelling place, whether the respondents had ever met a patient with RD and had a relative suffering from RD.
Ethics approval and research governance approval were obtained from the Poznan University of Medical Sciences Bioethics Committee (1018/18).

3. Results

Out of all 523 students approached, the questionnaire was completed by 346 students (66.1%). 177 students who did not complete the questionnaire refused to participate in the study and their refusals were motivated by an unwillingness to discuss their knowledge on RD and/or lack of interest in the study. Feedback on surveys from fifth year students was 201/272 (73.9%) and from sixth year – 145/251 (57.7%). The sample consisted of 212 females (61.3%) and 134 males (38.7%), all of Polish origin (Table 1). 58.1% of respondents were fifth year students and 41.9% sixth. The majority of the respondents were single (60.7%), while 27.4% were cohabiting and 10.7% were married. Most respondents lived either in large agglomerations with a population of over 500 thousand (43.1%) or in big towns with 101-500,000 inhabitants (20.2%). 72.5% of the respondents declared having met a patient suffering from RD and 78.3% did not have a RD relative in his or her family.

Table 1. Socio-demographic characteristics of students

Characteristics	N (%)
Year of study	
5	201 (58.1)
6	145 (41.9)
Gender	
Female	212 (61.3)
Male	134 (38.7)
Marital status	
Single	210 (60.7)
Cohabiting	95 (27.4)
Married	37 (10.7)
Widowed	0 (0)
Divorced	4 (1.2)
Domicile	
Under 10,000 inhabitants	41 (11.8)
10-50,000 inhabitants	54 (15.6)
51-100,000 inhabitants	32 (9.3)
101-500,000 inhabitants	70 (20.2)
Over 500,000 inhabitants	149 (43.1)
Have you ever met a person suffering from RD	
Yes	251 (72.5)
No	62 (18)
I do not know	33 (9.5)
Is anyone in your family suffering from RD?	
Yes	25 (7.2)
No	271 (78.3)
I do not know	50 (14.5)

While almost all of the respondents declared having heard the term 'rare disease' (99.4%) and knew its main cause (90.5%), only 11.5% correctly estimated the prevalence of RD (Table 2). Even fewer knew the number of RD (10.4%). Moreover, only ¼ knew that RD are most common among children (24.9%). Very few students were also aware of the number of patients suffering from RD in the world (9.5%), in the EU (9%) and in Poland (5.2%). One third of future physicians knew what percentage of RD is of genetic character (35.3%).

The respondents were also presented a list of twenty eight diseases and asked to select those they considered to be rare (Table 3). The most recognized RD were: Pompe disease (72.8%), Gaucher disease (69.1%) and Niemann-Pick disease (65.6%). Least often were indicated acromegaly (17.3%) and sickle cell anemia (13.9%). On the other hand, the most common diseases that were mistaken with RD were Munchhausen syndrome (50.9%), fibromyalgia (33.2%), halitosis (27.8%) and acquired immunodeficiency syndrome (24.9%).

Future physicians also lacked practical information on RD (Table 4). For example, barely 19.4% knew the name of the European website providing information about RD and orphan drugs. Moreover, 61.6% falsely believed that Poland has a central register of RD patients and less than one third knew the percentage of RD that have an approved drug treatment (31.5%); 59.2% knew that only some orphan drugs are reimbursed in our country.

Finally, the authors also evaluated students' perception of their knowledge about RD (Table 5). Surprisingly, although 95.4% of future physicians perceived their knowledge about RD as insufficient (56.6%) or very poor (38.7%) and 92.2% did not feel well prepared for caring for RD patients, almost half of the respondents (45.7%) believed that it is not necessary to add an extra course on RD into medical curricula. At the same time, 75.1% declared eagerness to increase their knowledge about RD and 78% believed that RD constitute a serious public health issue and should be prioritized. What is important from an educational perspective is that while 51.7% of the respondents declared getting their knowledge about RD from mandatory courses and 22% from elective courses, the Internet was a major source of information for 59.8%.

At the same time, the respondents believed that it is primarily geneticists (76.6%) and pediatricians (74.3%) who should be uniquely educated and trained in RD (Table 6). Thus, although RD patients frequently experience psychological distress, behavioral changes and mental deterioration and are often confused with psychiatric patients, only 22.5% of future physicians

Table 2. Students' knowledge about rare diseases

Items	N (%)
Have you ever heard the term 'rare diseases'?	
Yes	344 (99.4)
No	2 (0.6)
Rare disease is the one that affects less than:	
1 person in 1,000	24 (6.9)
1 person in 2,000	**40 (11.5)**
1 person in 3,000	11 (3.2)
1 person in 5,000	12 (3.5)
1 person in 10,000	196 (56.7)
I do not know	63 (18.2)
What is the estimated number of rare diseases?	
100-500	25 (7.2)
1,000-2,000	50 (14.5)
3,000-5,000	46 (13.3)
6,000-8,000	**36 (10.4)**
9,000-1,000	18 (5.2)
Over 10,000	119 (34.4)
I do not know	52 (15)
At what age group do rare diseases most frequently appear?	
Newborns	166 (48)
Children	**86 (24.9)**
Adolescents	10 (2.9)
Adults	8 (2.3)
They are present in all age groups equally	37 (10.7)
I do not know	39 (11.2)
How many people suffer from rare diseases worldwide?	
10-15,000,000	63 (18.2)
50-75,000,000	65 (18.8)
100-150,000,000	69 (19.9)
200-250,000,000	28 (8.1)
300-350,000,000	**33 (9.5)**
Over 500,000,000	27 (7.8)
I do not know	61 (17.65)
How many people in the EU suffer from rare diseases?	
5,000,000	106 (30.6)
15,000,000	53 (15.3)
20,000,000	34 (9.85)
30,000,000	**31 (9)**
40,000,000	29 (8.4)
Over 50,000,000	20 (5.8)
I do not know	73 (21.1)
How many people suffer from rare diseases in Poland?	
500-1,000	23 (6.6)
10-15,000	67 (19.4)
50-75,000	58 (16.8)
100-150,000	58 (16.8)
300-500,000	55 (15.9)
1,000,000	6 (1.7)
2-3,000,000	**18 (5.2)**
Over 5,000,000	6 (1.7)
I do not know	55 (15.9)
What is the most common cause of rare diseases?	
Infectious and bacterial	2 (0.6)
Genetic	**313 (90.5)**
Autoimmune	12 (3.5)
Mitochondrial	1 (0.3)
Environmental	2 (0.6)
I do not know	16 (4.6)
What percentage of rare diseases are of genetic origin?	
5-10%	11 (3.2)
20%	52 (15)
50%	126 (36.4)
80%	**122 (35.3)**
100%	18 (5.2)
I do not know	17 (4.9)

Correct answers are written in bold characters.

Table 3. Which of the following diseases are considered to be rare in Poland?

Items	N (%)
Sickle cell anemia	48 (13.9)
Cystic fibrosis	84 (24.3)
Acromegaly	60 (17.3)
Haemophilia	82 (23.7)
Down syndrome	18 (5.2)
Niemann-Pick disease	227 (65.6)
Halitosis	96 (27.8)
Glaucoma	16 (4.6)
Progeria	195 (56.4)
Neurofibromatosis	103 (29.8)
Craniodiaphyseal dysplasia	147 (42.5)
Cerebral palsy	30 (8.7)
Fibromyalgia	115 (33.2)
Huntington disease	160 (46.2)
Duchenne muscular dystrophy	154 (44.5)
Acquired immunodeficiency syndrome	86 (24.9)
Munchausen syndrome	176 (50.9)
Mucopolysaccharidoses	161 (46.5)
Achondroplasia	90 (26)
Crohn's disease	16 (4.6)
Pompe disease	252 (72.8)
Gaucher disease	239 (69.1)
Fragile X syndrome	133 (38.4)
Marfan syndrome	99 (28.6)
Schizophrenia	8 (2.3)
Alzheimer's disease	15 (4.3)
Osteogenesis imperfecta	188 (54.3)
Phenylketonuria	140 (40.5)

Table 4. Students' knowledge about healthcare system for RD patients

Items	N (%)
What is the name of the European website providing information about RD and orphan drugs?	
Rare Disease Foundation	8 (2.3)
NORD	4 (1.1)
EURORDIS	21 (6.1)
R.A.R.E	27 (7.8)
Orphanet	**67 (19.4)**
Global Genes	6 (1.7)
I do not know	213 (61.6)
Is there a central register of RD patients in Poland?	
Yes	213 (61.6)
No	**14 (4)**
I do not know	119 (34.4)
What percentage of rare disease can be treated with drugs?	
0%	1 (0.3)
5%	**109 (31.5)**
10%	61 (17.6)
15%	65 (18.8)
20%	31 (9)
50%	5 (1.4)
I do not know	74 (21.4)
Are orphan drugs reimbursed in Poland?	
Yes	7 (2)
Yes, some	**205 (59.3)**
No	28 (11)
I do not know	96 (27.7)
Do RD constitute a serious public health issues?	
Absolutely yes	59 (17)
Yes	211 (61)
No	54 (15.6)
Definitely no	0
I do not know	22 (6.4)

Table 5. Students' self-assessment of their knowledge about RD

Items	N (%)
How would you rate your knowledge about rare diseases?	
Very good	0
Fair enough	16 (4.6)
Insufficient	196 (56.7)
Very poor	134 (38.7)
Do you feel prepared for caring for a patient with a rare disease?	
Definitely yes	1 (0.3)
Rather yes	15 (4.3)
Rather not	144 (41.6)
Definitely not	175 (50.6)
I do not know	11 (3.2)
Would you like to broaden your knowledge about rare diseases?	
Yes	260 (75.1)
No	38 (11)
I do not know	48 (13.9)
Do you think that there should be a mandatory course on rare diseases in medical curricula?	
Definitely yes	23 (6.6)
Rather yes	138 (39.9)
Rather not	136 (39.3)
Definitely not	22 (6.4)
I do not know	27 (7.8)
Have you had any classes about rare disease during your studies?	
Yes	264 (76.3)
No	60 (17.3)
I do not know	22 (6.4)
Where do you get your knowledge about RD from?	
Mandatory courses at the university	179 (51.7)
Faculty courses at the university	76 (22)
Scientific literature and research	67 (10.7)
Scientific conferences, symposia	35 (10.1)
Internet	207 (59.8)
Other	9 (2.6)
I do not search for such information	41 (11.8)

Table 6. Which physicians should be uniquely trained in RD?

Speciality	N (%)
Family physician	158 (45.7)
Pediatrician	257 (74.3)
Neurologist	126 (36.4)
Geneticist	265 (76.6)
Psychiatrist	78 (22.5)
Immunologist	171 (49.4)
Other:	
Neonatologist	24 (6.9)
Oncologist	4 (1.2)
Gynecologist	3 (0.9)
Every physician regardless of specialization	84 (24.3)

said that also psychiatrists should be trained in RD. Surprisingly, however, 24.3% believed that all physicians, regardless of their specialization, should possess such knowledge.

4. Discussion

While our understanding of genetically based human diseases has increased significantly and genetics constitutes an important part of medical education, still many educational programs lack specific courses dedicated to RD. Consequently, medical students often do not receive necessary training in RD (*11-16*).

This research confirms that medical students receive little education on RD and that the problem of inadequate training in RD during medical studies does exist. Although nearly all students taking part in the study were aware of such diseases and knew that the vast majority of RD are caused by genetic factors, they lacked basic knowledge about their epidemiology. Moreover, many had even problems with distinguishing rare from common diseases. Most respondents also lacked knowledge about the organization of the health care system for RD patients in our country, as neither did they know the name of the most important website that gathers and provides information about RD and orphan drugs nor about the Polish central register of RD patients. Nevertheless, what is most alarming is that while the vast majority of future physicians were aware of their insufficient knowledge about RD and did not feel prepared for caring for such a patient, still many did not see the need to add extra classes on RD into medical curricula. What is even more intriguing is that while most respondents perceived RD as a serious public health problem, they stressed that it is mainly geneticists and pediatricians who should be uniquely educated and trained in RD.

These results confirm the findings from previous studies, such as, for example, other research conducted among Polish medical students in Szczecin revealed that although the majority (87.8%) had heard about RD during their studies, only 20.7% knew their correct definition. 58.1% did not know their prevalence and 67.4% the number of RD (*16*). Only 25% of healthcare students from la Rioja, Spain knew the definitions of RD and orphan drugs and the majority did not believe that research or funding for RD should be prioritized (*12*). While medical students in Serbia recognized many problems related to drug provisions for RD patients they demonstrated a moderate level of knowledge about RD and did not consider them an important social problem (*15*). Also, many Pakistani pharmacy students from Karachi lacked knowledge about RD (*14*). All these results confirm that RD receive little attention in medical curricula and that the problem of inadequate training in RD during medical studies is a fact.

This is even more important because while knowledge about RD is not retained throughout medical studies, it also does not improve during clinical courses. Thus, as many young physicians acknowledge that they are not adequately trained in RD, they are also afraid that they cannot serve the needs of patients suffering from these diseases. This is why the Council of the European Union stresses the need for 'adequate

education and training for all health professionals to make them aware of the existence of these diseases and of resources available for their care' and 'development of medical training in fields relevant to the diagnosis and management of rare diseases, such as genetics, immunology, neurology, oncology or pediatrics' (*4*). Thus, it acknowledges the need for future healthcare professionals to be well prepared for a possible encounter with RD patients. The problem is, however, that many universities neglect training their students in RD.

Consequently, during their medical encounter RD patients and their families have to struggle with an insufficiency or lack of knowledge about RD among healthcare professionals. This, in turn, results in lack of or delayed diagnosis, as sometimes patients have to wait up to ten or even twenty years for the correct diagnosis (*19,20,22,23,26-28*). Delayed diagnoses or misdiagnoses usually result in many unnecessary visits to different health specialists, delays in appropriate treatment or in receiving unnecessary medical interventions, including tests, medications, readmissions and surgeries, which cause additional medical costs, worsening of symptoms and disease progression (physical, cognitive, psychological deterioration of a patient or even death) (*26*).

Moreover, although most RD are of genetic character, due to many psychiatric, emotional and behavioral symptoms they cause they present a challenge for psychiatrists who, are a core part of the treatment team for both the RD patient and his or her family. For that reason there is a great need to alter the awareness about RD among physicians in general and psychiatrists in particular (*30*). As many RD have multiple neuropsychiatric manifestations and serious psychosocial implications, both for the patient and the family, psychiatrists are among those medical specialists who should be uniquely educated and trained in the field of RD, especially because that approximately 75% of all RD appear in early childhood leading to permanent disability or premature death. That is why a timely and correct diagnosis is critical for the effective clinical management of RD characterized by psychiatric symptoms and, often, the psychiatrist is the best place to offer this. After that the treatment will require an integrated and collaborative approach between multiple specialists.

Thus, it should be emphasized that since many RD patients experience various psychiatric symptoms, behavioral changes and mental retardation, psychiatrists seem to be those medical practitioners who should be uniquely educated and trained in RD. The reason is that although approximately 80% of RD are of genetic character, living with RD is a serious source of stress and has a detrimental effect on mental well-being for both RD patients and their carers (*24,26-28*), leading to attentional problems, anxiety, low mood, emotional exhaustion, neurocognitive dysfunctions, depression or suicidal ideations. Moreover, mental health problems are often significantly higher in patients suffering from RD than in the general population (*23,30-35*). Research on phenylketonuria indicates that more than one third of patients meet the criteria for psychiatric diagnosis (*36*). Akil *et al*. (*37*) reported psychiatric symptoms at the onset in two thirds of patients with Wilson disease. In the case of cystic fibrosis it has been suggested that all patients and their families should have a chance to be under a psychiatrist's care (*38*). Yet another reason why psychiatrists should be educated and trained in RD is that such diseases are frequently characterized by various neuropsychiatric symptoms, including apathy, social withdrawal, psychosis, delusions or hallucinations, anxiety or aggressive behaviors. Consequently, RD patients are often misdiagnosed as psychiatric patients and often assigned such labels as having schizophrenia, bipolar disorder or other neurodegenerative diseases, including Alzheimer's or Parkinson's disease. Reports show that patients suffering from Niemann-Pick disease type C or classical hyperhomocysteinaemia were misdiagnosed with late-onset schizophrenia (*39*). Some metabolic disorders (but also genetic ones) in their initial phase are manifested by psychiatric symptoms, which in some cases are the only manifestation of the disease (*39-41*).

Although this study brings new insight into the state of knowledge of Polish medical students about rare diseases, it also has a few limitations. Since only 66.1% of medical students from Poznan Medical University of Medical Sciences completed the questionnaire, the results may hinder generalization of the entire population of future doctors. Consequently, a more in-depth study would be required to help clarify the issues of education for RD. However, some advantages of this study should also be acknowledged. Most importantly, as RD seem to be neglected by medical education and there is a scarcity of previous work on the topic, it gives some highlight on the knowledge of medical students about RD. Hopefully, this study may not only stimulate further research on the topic but also provoke discussion on the need of better education of future physicians, including psychiatrists on RD.

5. Conclusions

While the majority of future physicians lack basic knowledge both about the epidemiology and the prevalence of rare diseases and the organization of the Polish health care system for RD patients, there is an urgent need to raise awareness on RD among medical students and educate them about such diseases. It is of special importance because while most of the respondents did not feel prepared for caring for such patients, they did not believe that RD constitute an important public health issue and that they should be well educated in this area.

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