THE IMPORTANCE OF GENETIC LITERACY AND EDUCATION IN MEDICINE

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THE IMPORTANCE OF GENETIC LITERACY AND EDUCATION IN MEDICINE

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EDITORIAL
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Editorial: The Importance of Genetic Literacy and Education in Medicine

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Keywords: genetic literacy, genetic education, medical education, medical genetics, medicine

Editorial on the Research Topic

The Importance of Genetic Literacy and Education in Medicine

Genetic literacy is a critical prerequisite for appropriate care for patients with genetic disorders, and includes the literacy on basic concepts in human and medical genetics. Medical genetics is one of the fastest-developing medical specializations, and advances in the development of new, comprehensive genetic and genomic testing methods are becoming increasingly integrated into various parts of medicine. Unfortunately, these advances have not been accompanied by an adequate level of genetic literacy in medical students, non-genetic health professionals involved in the care of patients with genetic disorders, as well as general public, including patients. Consequently, the demands for appropriate, needs-based genetic education on all levels are increasing.

The focus of this Research Topic includes the state of the current level of genetic literacy among medical students, non-genetic health professionals, patients and general public, as well as the current state of activities, options and future directions for genetic education in these groups. Additionally, we addressed the needs and possibilities of genetic education for patients with rare diseases. The Research Topic comprises 10 articles, with as much as 59 eminent authors from 20 countries.

The Research Topic begins with a methods article by Tobias et al., who emphasize the concerns that the current COVID-19 pandemic has raised in individuals with genetic disorders regarding both the viral infection and its specific implications and advisable precautions. These concerns were discussed on the ScotGEN Steering Committee and the Education Committee of the European Society of Human Genetics. Consequently, an up-to-date online hub of genetics-related COVID-19 information resources was created and provided freely online at www.scotgen.org.uk and www.eurogems.org.

Sassano et al. in their original research article summarized the educational initiatives aimed at increasing citizens' literacy in omics sciences worldwide, performing a web search. They identified a variety of initiatives aimed at improving citizens' literacy in omics sciences, with the largest majority carried out in the United States and being web-based. Their results showed heterogeneity among the initiatives as to the dealt topics and the adopted methods.

Considering that the care for patients with rare diseases requires a multidisciplinary approach, Domaradzki and Walkowiak performed an original research, assessing the awareness of rare diseases among nursing, physiotherapy and medical students in Poland using a questionnaire. Although 98% of respondents had heard of the term "rare disease," most students had problems in defining their most common causes and prevalence. Almost 92% of medical students, and 84% of physiotherapy and nursing students did not feel prepared for caring for these patients. The results emphasize the need for better education in this field.

The rewiew article by Liehr summarizes the general background on non-invasive prenatal testing (NIPT), differences of NIPT platforms, advantages and limitations of NIPT, as well as consequences

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of insufficient counselling before and after NIPT. Unfortunately, gynecologists and obstetricians who discuss the use of NIPT with patients may lack specific training on the interpretation of results, although they have a highly qualified background in their specialty area(s). The author emphasizes the importance that the corresponding scientific societies close the potential knowledge gaps quickly and comprehensively to ensure optimal patient care.

In their mini review, Little and Gunter discuss the current literature describing genetic literacy and genetic testing rates for autism spectrum disorders (ASD). They conclude that the current level of the population's genetic literacy is insufficient to ensure the individuals' informed decisions about their genetic information. In addition, only 22% of families undergo genetic testing after diagnosis. Therefore, the authors suggest that improving genetic literacy in ASD populations can also improve attitudes toward genetic testing.

Zimani et al. provide a mini review regarding the current state of educational activities within national genomic projects for different target groups and identify good practices that could contribute to patient empowerment, public engagement, proficient healthcare professionals, and lend support to personalized medicine. The authors reviewed 41 current national genomic projects and identified 16 projects specifically describing the approach to genomic education. Hopefully, the initial efforts made by national genomic projects will result in durable national solutions leading to further implementation of personalized medicine in healthcare systems.

An interesting perspective article by Tobias et al. summarizes how the European Society of Human Genetics is adapting to deliver innovative genetic educational activity. The Society works through many approaches, including educational sessions at the annual conference; training courses in general and specialist areas of genetics; an online resource of educational materials (EuroGEMS); and a mentorship scheme. Their Education Committee is implementing new approaches to expand the reach of its educational activities and portfolio.

In their brief research report, Majstorović et al. evaluate current genomics content in the curriculum of undergraduate and graduate nursing studies programs in Croatia in 2020/2021, and measure the genomic literacy through assessing participants' understanding of genomic concepts critical to nursing practice. Their results indicate that the current genomics content is inadequate and dis-concordant among universities. Moreover, genomic literacy of nursing students was low. The authors emphasize that the curricula for undergraduate and graduate nursing studies programs needs revision and implementation of modern genomics education.

In the original research article by Vidgen et al. a training session, introducing Health Interpreters to genetics was developed and evaluated. The online training was delivered multiple times as a single 2-h session comprising lectures and activities. Participants completed questionnaires to assess the impact of training on knowledge, attitude, self-efficacy, and self-reported practice behaviour. The results show that most respondents and Health Interpreters agreed that the training was useful and acceptable. Increased delivery of training and associated research is needed to assess findings in a larger cohort and to measure the impact on patients.

Finally, Pereza et al. in their original research article perform the first research on the current state of compulsory basic and clinical courses in genetics for medical students offered at medical faculties in six Balkan countries with Slavic languages (Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia). Except for Slovenia, all other countries offer either courses in basic education in human genetics or both basic education in human genetics and clinical education in medical genetics. Unfortunately, due to huge differences in course designs, the authors emphasize the need for future collaboration in reaching a consensus on medical genetics education in Balkan countries.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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ORIGINAL RESEARCH
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Knowledge and Attitudes of Future Healthcare Professionals Toward Rare Diseases

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Caring for patients suffering from a rare disease (RD) requires the special and combined efforts of different healthcare professionals, including nurses, physiotherapists and physicians. Nevertheless, Poland still lacks a national plan for RDs and the undergraduate and postgraduate education of future healthcare professionals on RDs is also inadequate. Thus, the aim of this study was to assess the awareness of RDs among nursing, physiotherapy and medical students in Poland. It shows that although 98% of respondents had heard of the term "rare disease," most students had problems in defining the most common causes of RDs and their prevalence. Students also lacked basic knowledge about the healthcare system for RD patients in the country. While over 95% of future nurses, physiotherapists and physicians assessed their knowledge about RDs as insufficient or very poor, almost 92% of medical students, and 84% of physiotherapy and nursing students, did not feel prepared for caring for RD patients. Furthermore, although the vast majority of respondents declared eagerness to broaden their knowledge on RDs, only 45% of medical students, 76% of nursing students and 88% of physiotherapy students believed that RDs should be included into the medical curricula. Simultaneously, for most students the Internet was the prime source of information on RDs. It is concluded that as caring for RD patients requires a multidisciplinary approach, by identifying the gap in the education of future nurses, physiotherapists and physicians this study shows that there is an urgent need of better education about RDs among future healthcare professionals.

Keywords: genetic literacy, medical education, nursing students, physiotherapy students, medical students, future healthcare professional, rare diseases

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INTRODUCTION

The European Union (EU) defines rare diseases (RDs) as chronically debilitating or life-threatening conditions of a prevalence of less than 5 per 10,000 persons (Eurordis, 2009). While there are approximately 27–36 million people in the EU suffering from as many as 6,000–8,000 different types of RDs (Montserrat and Taruscio, 2019; Czech et al., 2020) they require the special, combined efforts of different healthcare professionals, including physicians, physiotherapists, nurses, psychologists, dieticians or speech therapists. Thus, the implementation of such an interdisciplinary

Abbreviations: RD, rare disease; EU, The European Union; PUMS, Poznan University of Medical Sciences.

approach is strongly required because it can reduce the perinatal and early mortality of RD patients or increase their quality of life.

At the same time, while some 2–3 million persons suffer from RDs in Poland, available data suggests that still many RD patients remain without a diagnosis or proper treatment (Libura et al., 2016; Ministerstwo Zdrowia, 2019). Moreover, due to the minimal training of physicians on RDs, lack of information and awareness about RDs among healthcare professionals, poor communication among health providers and lack of standardized criteria for diagnosis, the search for a diagnosis and therapy often turns into an endless odyssey (Anderson et al., 2013; Black et al., 2015). This is important because misdiagnosis or late diagnosis results in delayed or many unnecessary treatments and hospitalizations, the worsening of an RD patient's condition or his or her premature death. For all these reasons RDs are now widely recognized as an important medical, social and legal problem and an urgent public health issue (Schieppati et al., 2008). Consequently, in June 2009 the Council of the European Union recommended that by the end of 2013 all Member States (MS) should adopt a national plan or strategy for RDs (Council of the European Union, 2009). Moreover, throughout the years the EU has created an operational framework and coordinates several areas of common health policy in the field of RDs, including the classification and codification of RDs and orphan medicinal products, an ICD-10 revision and the creation of European Reference Networks or a European Platform for Rare Diseases registration (Moliner, 2010; Rodwell and Aymé, 2014, 2015; Moliner and Waligora, 2017; Khosla and Valdez, 2018; Montserrat and Taruscio, 2019; Czech et al., 2020). Nevertheless, while a lot has been done in the field of recommendations, in funding, and the reimbursement of orphan drugs in Europe (Kawalec et al., 2016; Zelei et al., 2016; Kolasa et al., 2018; Szegedi et al., 2018), still one of the most urgent areas in both the European and national health policies in the field of RDs is the medical education of healthcare students and professionals (Miteva et al., 2011; Budych et al., 2012; Anderson et al., 2013; Engel et al., 2013; Krajnović et al., 2013; Zurynski et al., 2017). Meanwhile, according to the EU recommendation, social and medical education on RDs should be one of the key areas of each national plan or strategy (Council of the European Union, 2009).

Nevertheless, although only a few MS, i.e., France and Spain, have fully implemented national plans/strategies for RDs according to the EU's recommendations, and the vast majority have already created such plans (i.e., Belgium, Bulgaria, Cyprus, the Czech Republic, Denmark, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Portugal, Romania, the Slovak Republic, Slovenia, the Netherlands, and the United Kingdom), Poland is among the three EU countries, next to Malta and Sweden, that still have not adopted their national plans (Khosla and Valdez, 2018; Montserrat and Taruscio, 2019; Czech et al., 2020). However, according to the recent declaration of the Polish Ministry of Health, Poland should promulgate such a strategy by June 2020 (Ministerstwo Zdrowia, 2019). It is important because one of its strategic points is the improvement of undergraduate and postgraduate education on RDs by including lectures and seminars on RDs during the last 2 years of studies and by creating a system of postgraduate training offering mandatory specialization training sessions and specialized courses on RDs. Simultaneously, nowhere does the document specify or differentiate between the educational needs of undergraduate and graduate students. This is of key importance because previous research projects show that future healthcare professionals in the country lack general knowledge of RDs and there is an urgent need to raise the awareness on RD among medical students and to educate them about such diseases (Kopeć and Podolec, 2015; Jonas et al., 2017; Domaradzki and Walkowiak, 2019; Walkowiak and Domaradzki, 2020). Moreover, although RD patients require interdisciplinary approach, most previous studies focused on the knowledge and awareness on RDs among medical students and general practitioners (Miteva et al., 2011; Byrne, 2012; Kopeć and Podolec, 2015; Wolyniak et al., 2015; Medić et al., 2016; Jonas et al., 2017; Domaradzki and Walkowiak, 2019; Ramalle-Gómara et al., 2020). Meanwhile, although it is physicians who coordinate the process of caring for RD patients the role of other healthcare professionals, including nurses and physiotherapists, in managing of RDs is increasing, especially so that most RDs affect children. Consequently, there is also a need for enhancing genetic literacy on RDs among all healthcare professionals.

It is of special importance, because while medical, nursing and physiotherapy students in Poland receive classes in clinical genetics for at least two semesters, where they are taught about some genetic diseases (i.e., PKU, CF, sickle cell anemia, Huntington disease, Pompe disease, Niemann-Pick disease), the methods and types of materials used in genetic laboratory diagnostics, they do not receive special training in clinical genetics ambulatories. Neither do they receive any particular course on RDs. Moreover, also postgraduate specialization trainings for physicians, nurses and physiotherapists supervised by the Polish Minister of Health give little or no such information on RDs. For example, postgraduate specialization courses in nursing offer only a 1-h lecture dedicated to the National Rare Disease Plan and education in the field of RD. However, neither qualification courses nor specialized courses give any information on caring for RD patients (Walkowiak and Domaradzki, 2020). Thus, the objective of our study was to assess the knowledge and awareness of RDs among nursing, physiotherapy and medical students of the Poznan University of Medical Sciences (PUMS), Poland.

MATERIALS AND METHODS

The study was conducted between October and December 2019 among nursing, physiotherapy and medicine students of the PUMS. However, because it takes 6 years to complete medical studies in Poland, while both nursing and physiotherapy programs are five years long (3-year Bachelor's degree and 2-year Master's degree), this research was conducted among *students* during the 2 final years of their studies. The student participants were recruited during regular classes. A standard questionnaire was used, comprising the topics based on the literature review and the study's aim. The detailed description of the questionnaire

and the method used for its development has been described elsewhere (Domaradzki and Walkowiak, 2019; Walkowiak and Domaradzki, 2020). Briefly, the questionnaire comprised of 28 questions: 22 items referred to respondents' knowledge of and attitudes toward RD and 6 questions that addressed their demographic data, and was divided into four sections. The first questions regarded students' basic knowledge on RDs, such as their definition, etiology and estimated prevalence of RDs worldwide, in the EU and in Poland. Students were also asked to indicate RDs from a list comprising twenty eight diseases: eighteen RDs and 10 more common disorders. We have chosen RDs that are either commonly known conditions (i.e., progeria, Huntington disease, hemophilia or sickle cell anemia) or are included into medical curricula (i.e., Pompe disease, Gaucher disease, Niemann-Pick disease, phenylketonuria). The second section included questions regarding organizational issues, including the Polish rare disease policy and the orphan drug reimbursement system. The third section were questions on students' education about RDs and their self-assessment of the knowledge and competence in the field of RDs. The last section of the questionnaire included questions concerning students' demographic characteristics.

The process of elaborating the questionnaire itself followed the guidelines of the European Statistical System (Eurostat, 2005). A total of 18 subjects were involved in the development of the questionnaire (five nursing students, five medical students, five physiotherapy students, one geneticist, one sociologist and one statistician) who elaborated a list of important issues on RDs, which resulted in developing a questionnaire which was assessed by five external reviewers (one nurse, one physiotherapist, one physician, one geneticist and one sociologist). Second, the questionnaire was pre-tested in face-to-face meetings with another ten nursing, physiotherapy and medicine students, which resulted in the reformulation of four questions. The final version of the questionnaire was again evaluated by another five external reviewers from the same specialties. After receiving final approval, the survey was distributed to all the students who had volunteered. Ethics approval was obtained from the PUMS Bioethics Committee (1018/18). Informed consent was obtained from all individual participants included in the study.

The data collected in the questionnaires were verified and checked for completeness, quality and consistency. Then, they were coded and exported into the statistical packages JASP (Version 0.12.2) and STATISTICA 13.1 (TIBCO, Palo Alto, United States). The results were presented as descriptive statistics. A Likelihood Ratio Chi-square was used to assess the differences in the distribution of answers among the groups. The odds ratio (OR) was calculated to compare one group of students according to different characteristics based on their opinions in relation to other groups of students. The 95% confidence interval (95% CI) was calculated to estimate the precision of the OR. A 5% level of significance was used for all hypothesis tests.

RESULTS

Out of all the 862 students approached, 654 (75.9%) completed the questionnaire (**Table 1**). 208 students who refused to participate did so because they either lacked interest in the study or were unwilling to discuss their knowledge on RDs. The feedback on surveys from the nursing students (NS) was 113/120 (94.2%), from the physiotherapy students (PS)—173/219 (79.0%) and from the medical students (MS)—368/523 (70.4%). The sample consisted of 463 females (70.8%) and 191 males (29.2%), all of Polish origin. 43 students declared having a person suffering from a RD in their family (18.4%). One physiotherapy student suffered from a RD herself, although no such question was asked in the questionnaire.

More than 98% of students in our study groups declared having heard the term "rare disease" (**Table 2**). However, while almost 90% of the medical students and nearly 70% of the physiotherapy students knew what was the most common cause of RDs, among the nursing students it was only 60%. Nevertheless, only about 30% in each group correctly estimated

TABLE 1 | Socio-demographic characteristics of students.

Characteristics	N (%)		
	Nursing students	Physiotherapy students	Medical students
Year of study			
4th nursing and physiotherapy students/5th medical students	56 (49.6)	86 (49.7)	201 (54.6)
5th nursing and physiotherapy students/6th medical students	57 (50.4)	87 (50.3)	167 (45.4)
Gender			
Female	104 (92)	136 (78.6)	223 (60.6)
Male	9 (8)	37 (21.4)	145 (39.6)
Have you ever met a person suffering from RD			
Yes	38 (33.6)	83 (48)	268 (72.8)
No	54 (47.8)	46 (26.6)	65 (17.7)
I do not know	21 (18.6)	44 (25.4)	35 (9.5)
Is anyone in your family suffering from RD?			
Yes	4 (3.5)	14 (8.1)	25 (6.8)
No	99 (87.6)	141 (81.5)	292 (79.4)
I do not know	10 (8.9)	18 (10.4)	47 (12.8)

TABLE 2 | Students' knowledge about rare diseases.

	N (%)			Comparison between groups p		
	Nursing students	**Physiotherapy students**	**Medical students**	**NS vs. PS**	**NS vs. MS**	**PS vs. MS**
Have you ever heard the term "rare diseases"?						
Yes	107 (94.7)	171 (98.8)	365 (99.2)	0.04	0.005	ns
No	6 (5.3)	2 (1.2)	3 (0.8)			
Rare disease is the one that affects less than:						
1 person in 1,000	17 (15)	31 (17.9)	25 (6.8)			
1 person in 2,000	**8 (7.1)**	**11 (6.4)**	**43 (11.7)**	ns	ns	0.04
1 person in 3,000	1 (0.9)	4 (2.3)	11 (3)			
1 person in 5,000	5 (4.4)	23 (13.3)	12 (3.2)			
1 person in 10,000	52 (46)	92 (53.2)	213 (57.9)			
I do not know	30 (26.6)	12 (6.9)	64 (17.4)			
What is the estimated number of rare diseases?						
100–500	17 (15)	24 (13.9)	27 (7.3)			
1,000–2,000	37 (32.7)	50 (28.9)	52 (14.1)			
3,000–5,000	14 (12.4)	33 (19.1)	49 (13.3)			
6,000–8,000	**7 (6.2)**	**24 (13.9)**	**40 (10.9)**	0.03	ns	ns
9,000–10,000	6 (5.3)	11 (6.3)	19 (5.2)			
Over 10,000	9 (8)	18 (10.4)	126 (34.2)			
I do not know	23 (20.4)	13 (7.5)	55 (15)			
At what age group do rare diseases most frequently appear?						
Newborns	29 (25.7)	54 (31.2)	172 (46.7)			
Children	**42 (37.2)**	**63 (36.4)**	**99 (26.9)**	ns	0.04	ns
Adolescents	3 (2.6)	6 (3.5)	10 (2.7)			
Adults	6 (5.3)	7 (4)	8 (2.2)			
They are present in all age groups equally	21 (18.6)	38 (22)	40 (10.9)			
I do not know	12 (10.6)	5 (2.9)	39 (10.6)			
How many people suffer from rare diseases worldwide?						
10–15,000,000	23 (20.3)	27 (15.6)	66 (17.9)			
50–75,000,000	35 (31)	38 (22)	68 (18.5)			
100–150,000,000	15 (13.3)	51 (29.5)	76 (20.7)			
200–250,000,000	5 (4.4)	16 (9.2)	32 (8.7)			
300–350,000,000	**7 (6.2)**	**25 (14.4)**	**35 (9.5)**	0.02	ns	ns
Over 500,000,000	1 (0.9)	1 (0.6)	28 (7.6)			
I do not know	27 (23.9)	15 (8.7)	63 (17.1)			
How many people suffer from rare diseases in Poland?						
500–1,000	22 (19.5)	17 (9.8)	24 (6.5)			
10–15,000	28 (24.8)	43 (24.9)	72 (19.6)			
50–75,000	17 (15.1)	37 (21.4)	61 (16.6)			
100–150,000	11 (9.7)	24 (13.9)	67 (18.2)			
300–500,000	5 (4.4)	17 (9.8)	56 (15.2)			
1 000 000	2 (1.8)	3 (1.7)	6 (1.6)			
2–3,000,000	**4 (3.5)**	**24 (13.9)**	**18 (4.9)**	0.002	ns	0
Over 5,000,000	0	0	6 (1.6)			
I do not know	24 (21.2)	8 (4.6)	59 (16)			
What is the most common cause of rare diseases?						
Infectious and bacterial	5 (4.4)	12 (6.9)	2 (0.5)			
Genetic	**67 (59.3)**	**116 (67)**	**330 (89.6)**	ns	0	0
Autoimmune	26 (23)	36 (20.8)	13 (3.5)			
Mitochondrial	3 (2.7)	7 (4)	4 (1.1)			
Environmental	1 (0.9)	4 (2.3)	2 (0.5)			
I do not know	11 (9.7)	16 (4.6)	17 (4.6)			

(Continued)

TABLE 2 | Continued

	N (%)			Comparison between groups p		
	Nursing students	**Physiotherapy students**	**Medical students**	**NS vs. PS**	**NS vs. MS**	**PS vs. MS**
What percentage of rare diseases are of genetic origin?						
5–10%	19 (16.8)	17 (9.8)	11 (3)			
20%	27 (23.9)	50 (28.9)	54 (14.7)			
50%	28 (24.8)	48 (27.7)	135 (36.7)			
80%	**30 (26.5)**	**52 (30.1)**	**131 (35.6)**	ns	ns	ns
100%	0	1 (0.6)	18 (4.9)			
I do not know	9 (8)	5 (2.9)	19 (5.1)			

Correct answers are written in boldface.

the percentage of RDs of genetic origin. At the same time, physiotherapy students' estimates of the number of RD patients worldwide and in Poland were the most accurate, although only 14% of them gave the correct answers. Similarly, while most students knew that RDs affect mostly the newborns and children, very few students knew the correct prevalence of RDs (NS = 7.1%, PS = 6.4, MS = 11.7) and the number of RDs (NS = 6.2%, PS = 13.9%, MS = 10.9%).

From the presented list of 28 diseases (including 18 RDs), students chose those they considered to be rare diseases (**Table 3**). Among medical and nursing students the most frequently recognized RDs were Pompe disease, Gaucher disease and Niemann-Pick disease, while among physiotherapy students it was Pompe disease, Niemann-Pick disease and Fragile X syndrome. On the other hand, in all three groups the most common disease that was mistaken with RDs turned out to be Munchausen syndrome. The statistical analysis of the frequency of indications for specific RDs in individual groups of students revealed the existence of many statistically significant differences. Future physicians identified more RDs from the list correctly more frequently than nursing students, although in the case of non-RDs it was exactly the opposite: nursing students indicated them as RDs less often than medical students did. Similarly, medical students selected RDs correctly more often than physiotherapy students, although in the case of acromegaly, Fragile X syndrome and Marfan syndrome, the opposite was the case. On the other hand, physiotherapy students scored higher than nursing students. The results of the analysis are ambiguous and indicate evident knowledge gaps in all student groups. Despite the fact that on average future doctors gave the best answers, still they also indicated most of non-RDs, including acquired immunodeficiency syndrome as a RD most often.

Physiotherapy students were of the opinion that RDs constitute a serious public health issue more often than medical and nursing students (**Table 4**). However, more than 75% of medical students also believed that RDs should be prioritized. The difference between all three groups was statistically significant ($p = 0.000$). At the same time, approximately 60% of all students falsely believed that there is a central register of RD patients in Poland. Similarly, more than 40% of nursing students and almost 60% of physiotherapy and medical students believed that orphan drugs are reimbursed in Poland, which is also not true. Simultaneously, it was medical students who knew the name of the European website providing information about RD and orphan drugs best (20.6% vs. 11% PS and 0.9% NS). Finally, approximately one-third of each group knew how many RDs can be treated with drugs.

Some significant differences between groups of nursing, physiotherapy and medical students were observed. While only four nursing students assessed their knowledge about RDs as very good, there was no such person among medical and physiotherapy students (**Tables 5**, **6**). On the other hand, there was a statistically significantly difference between nursing students who rated their knowledge as very poor and other students (LR, $p = 0.01$). Despite this difference, in each group at least 95% of students assessed their knowledge on RDs as insufficient or very poor. Moreover, almost 92% of medical students, and 84% of physiotherapy and nursing students did not feel prepared for caring for RD patients. In turn, 11% of physiotherapy students found themselves prepared to care for such patients. While the vast majority of students declared their eagerness to broaden their knowledge on RDs, only 45% of future doctors believed that such a topic should be included into the medical curricula. In contrast, among nursing students it was 76% and among physiotherapy students 88%. These declarations of future doctors were, statistically, significantly different from those of the nursing and physiotherapy students. While some medical students did not feel prepared to care for RD patients and declared their wish to broaden their knowledge, they did not see the need to include the RDs topics into the curricula. Interestingly, for all three groups of students the Internet was the most important source of information on RDs, although medical students also pointed out the mandatory and elective courses at the university.

As for the year of studies and the faculty, no significant differences between nursing and physiotherapy students were found, whereas among medical students the last year students felt better prepared to care for RD patients than those studying at the penultimate year (**Table 7**). Nevertheless, sixth year students did not answer better than their younger colleagues. Moreover, they completed the survey with the highest number of factual mistakes regarding the recognition of RDs from the list, and the difference between their results and those of the rest of students was considerable.

TABLE 3 | Which of the following diseases are considered to be rare in Poland?

	N (%)			Comparison between groups p		
	Nursing students	**Physiotherapy students**	**Medical students**	**NS vs. PS**	**NS vs. MS**	**PS vs. MS**
Sickle cell anemia	6 (5.3)	33 (19.1)	48 (13)	0	0.01	ns
Cystic fibrosis	15 (13.3)	48 (27.7)	87 (23.6)	0.003	0.009	ns
Acromegaly	19 (16.8)	56 (32.4)	61 (16.6)	0.003	ns	0.004
Hemophilia	9 (8)	20 (11.6)	85 (23.1)	ns	0	0.001
Down syndrome	2 (1.8)	2 (1.2)	19 (5.2)	ns	ns	0.01
Niemann-Pick disease	56 (49.6)	86 (49.7)	242 (65.8)	ns	0	0
Halitosis	12 (10.6)	32 (18.5)	97 (26.4)	ns	0	0.04
Glaucoma	0	3 (1.7)	16 (4.4)	ns	0.003	ns
Progeria	32 (28.3)	60 (34.7)	206 (56)	ns	0	0
Neurofibromatosis	10 (8.9)	52 (30.1)	110 (29.9)	0	0	ns
Craniodiaphyseal dysplasia	18 (15.9)	45 (26)	158 (42.9)	0.04	0	0
Cerebral palsy	6 (5.3)	1 (0.6)	30 (8.2)	0.01	ns	0
Fibromyalgia	38 (33.6)	30 (17.3)	121 (32.9)	0.01	ns	0
Huntington disease	36 (31.9)	64 (37)	169 (45.9)	ns	0.007	0.05
Duchenne muscular dystrophy	35 (31)	49 (28.3)	162 (44)	ns	0.01	0
Acquired immunodeficiency syndrome	6 (5.3)	26 (15)	87 (23.6)	0.007	0	0.02
Munchausen syndrome	59 (52.2)	85 (49.1)	186 (50.5)	ns	ns	ns
Mucopolysaccharidoses	19 (16.8)	51 (29.5)	176 (47.8)	0	0.01	0
Achondroplasia	21 (18.6)	33 (19.1)	102 (27.7)	ns	0.05	0.03
Crohn's disease	12 (10.6)	54 (31.2)	17 (4.6)	0	0.03	0
Pompe disease	58 (51.3)	94 (54.3)	268 (72.8)	ns	0	0
Gaucher disease	56 (49.6)	81 (46.8)	254 (69)	ns	0	0
Fragile X syndrome	48 (42.5)	82 (47.4)	140 (38)	ns	ns	0.04
Marfan syndrome	43 (38.1)	80 (46.2)	109 (29.6)	ns	ns	0
Schizophrenia	1 (0.9)	1 (0.6)	8 (2.2)	ns	ns	ns
Alzheimer's disease	1 (0.9)	1 (0.6)	15 (4.1)	ns	ns	0.01
Osteogenesis imperfecta	18 (15.9)	54 (31.2)	202 (54.9)	0.005	0	0
Phenylketonuria	14 (12.4)	54 (31.2)	155 (42.1)	0	0	0.01

ns, not significant.

DISCUSSON

The results of this study confirm previous findings regarding the unsatisfactory level of knowledge of students of various medical faculties on RDs (Byrne, 2012; Krajnović et al., 2013; Kopeć and Podolec, 2015; Ramalle-Gómara et al., 2015; Wolyniak et al., 2015; Alam et al., 2016; Medić et al., 2016; Jonas et al., 2017; Domaradzki and Walkowiak, 2019; Walkowiak and Domaradzki, 2020). At the same time, while all the nursing, physiotherapy and medical students lacked basic information about RDs the vast majority of our respondents was aware of their knowledge deficits. Interestingly, some differences found between the groups of students were somehow surprising and difficult to explain on the basis of the individual study programs. As students from each faculty receive at least 1 year of training in genetics during the first year of their study where they study about some genetic diseases (i.e., PKU, CF, Huntington disease, sickle cell disease, Pompe disease or Niemann-Pick disease) and basic methods of genetic laboratory tests, it seems that the process of their education is rather random and knowledge about RDs is often passed casually and not in the form of a systematic academic lecture. Consequently, neither the medical nor the nursing or the physiotherapy students receive any special training in RDs.

Thus, this confirms Greb et al. (2009) observation that medical students do not retain knowledge and skills in medical genetics learned during the first years of their education. Also students who enrolled in our study received some lectures on particular types of RDs during lectures and in clinical practice, but they did not have any dedicated courses aimed particularly at RDs throughout the entire course of their studies. The only exception were 20 medical students who had chosen some elective course on metabolic diseases. Nevertheless, all the students' knowledge about RDs was strongly dispersed and it seems that while students possibly know some individual RDs and would be able to present a simplified way of dealing with a given disease, frequently they do not identify it as a RD. Such a claim is supported by the fact that although PKU is one of the most commonly discussed RDs in medical curricula, only 42.1% of MS, 31.2% of PS and 12.4% of NS recognized it as a RD. Moreover, PKU is a model example of RD, as the one in which neonatal screening began and an effective treatment procedure was implemented.

Moreover, these results are even more intriguing as some basic information on genetics is already present in high school

TABLE 4 | Students' knowledge about the healthcare system for RD patients.

	N (%)			Comparison between groups p		
	Nursing students	**Physiotherapy students**	**Medical students**	**NS vs. PS**	**NS vs. MS**	**PS vs. MS**
What is the name of the European website providing information about RD and orphan drugs?						
Rare Disease Foundation	3 (2.7)	19 (11)	10 (2.7)			
NORD	4 (3.5)	7 (4)	4 (1.1)			
EURORDIS	11 (9.7)	30 (17.3)	26 (7.1)			
R.A.R.E	5 (4.4)	15 (8.7)	28 (7.6)			
Orphanet	**1 (0.9)**	19 (11)	**76 (20.6)**	0	0	0.004
Global Genes	1 (0.9)	4 (2.3)	6 (1.6)			
I do not know	88 (77.9)	79 (45.7)	222 (60.3)			
Is there a central register of RD patients in Poland?						
Yes	64 (56.6)	108 (62.4)	228 (61.9)			
No	**10 (8.9)**	**26 (15)**	**15 (4.1)**	ns	ns	0
I do not know	39 (34.5)	39 (22.6)	125 (34)			
What percentage of rare disease can be treated with drugs?						
0%	6 (5.3)	5 (2.9)	1 (0.3)			
5%	**30 (26.5)**	**58 (33.5)**	**117 (31.8)**	ns	ns	ns
10%	22 (19.5)	39 (22.5)	67 (18.2)			
15%	16 (14.2)	28 (16.2)	69 (18.7)			
20%	11 (9.7)	28 (16.2)	33 (9)			
50%	1 (0.9)	9 (5.2)	5 (1.4)			
I do not know	27 (23.9)	6 (3.5)	76 (20.6)			
Are orphan drugs reimbursed in Poland?						
Yes	2 (1.8)	6 (3.5)	7 (1.9)			
Yes, some	**50 (44.3)**	**101 (58.4)**	**220 (59.8)**	0.02	0.004	ns
No	15 (13.3)	46 (26.6)	41 (11.1)			
I do not know	46 (40.7)	20 (11.5)	100 (27.2)			
Do RDs constitute a serious public health issue?						
Absolutely yes	29 (25.7)	77 (44.5)	60 (16.3)			
Yes	67 (59.3)	77 (44.5)	224 (60.9)			
No	6 (5.3)	15 (8.6)	58 (15.8)			
Definitely not	1 (0.9)	2 (1.2)	1 (0.3)			
I do not know	10 (8.8)	2 (1.2)	24 (6.5)			

Correct answers are written in boldface.

programs in biology, where inheritance is discussed in examples of RDs. Nevertheless, it seems that in accord with Williams' observation (Williams, 2019), the structure and content of our current medical education is often outdated. As the current medical system is technologically orientated and market-driven, its socio-cultural aspects have become blurred (Green et al., 2002). In consequence, medical training focuses overly on scientific underpinnings, which is reinforced by the system that rewards students for recalling biomedical minutiae rather than thinking critically and holistically. This observation is exemplified by the relatively small number of medical students who believed that there should be a mandatory course on RDs in medical curricula (45.6%). Nevertheless, while such a biomedical type of training often neglects the psychosocial and humanistic aspects of patient care, it is particularly these dimensions that are required in the case of patients suffering from RDs (Williams, 2019).

Another problem is the general lack of clear guidelines and recommendations at the European Union level. Although teaching standards in medical studies are defined by the Directive 2013/55/EU of the European Parliament and of the Council amending Directive 2005/36/EC on the recognition of professional qualifications (Council of the European Union, 2013), these give only general recommendations to EU member states which shape their medical curricula and set their own examinations independently, deciding whether any mandatory or elective courses on RDs should be included in their teaching programs (McKay, 2019). Also, in Poland the Directive was implemented into the Polish legal system by the Regulation of the Minister of Science and Higher Education in 2019 and determined the standards of teaching medical professionals (Ministerstwo Nauki i Szkolnictwa Wyższego, 2019). Unfortunately, while the document is over 200 pages long, the term RD does not appear in it even once. Thus, as

TABLE 5 | Students' self-assessment of their knowledge about RDs, split faculty.

	N (%)		
	Nursing students	**Physiotherapy students**	**Medical students**
How would you rate your knowledge about rare diseases?			
Very good	4 (3.5)	0	0
Fair enough	2 (1.8)	9 (5.2)	18 (4.9)
Insufficient	46 (40.7)	97 (56.1)	207 (56.2)
Very poor	61 (54)	67 (38.7)	143 (38.9)
Do you feel prepared for caring for a patient with a rare disease?			
Definitely	0	2 (1.2)	1 (0.3)
Rather yes	3 (2.7)	17 (9.8)	17 (4.6)
Rather not	51 (45.1)	95 (54.9)	152 (41.6)
Definitely not	44 (38.9)	50 (28.9)	185 (50.3)
I do not know	15 (13.3)	9 (5.2)	13 (3.2)
Would you like to broaden your knowledge about rare diseases?			
Yes	94 (83.2)	147 (85)	272 (73.9)
No	3 (2.7)	14 (8.1)	44 (12)
I do not know	16 (14.2)	12 (6.9)	52 (14.1)
Do you think that there should be a mandatory course on rare diseases in medical curricula?			
Definitely yes	26 (23)	55 (31.8)	23 (6.2)
Rather yes	60 (53.1)	97 (56.1)	145 (39.4)
Rather not	12 (10.6)	16 (9.2)	142 (38.6)
Definitely not	2 (1.8)	0	28 (7.6)
I do not know	13 (11.5)	5 (2.9)	30 (8.2)
Did you/do you have any classes about rare diseases during your studies?			
Yes	36 (31.9)	89 (51.5)	282 (76.6)
No	60 (53.1)	76 (43.9)	63 (17.1)
I do not know	17 (15)	8 (4.6)	23 (6.3)
Where do you/did you get your knowledge about RDs from?			
Mandatory courses at the university	12 (10.6)	56 (32.4)	188 (51.1)
Facultative courses at the university	9 (8)	20 (11.6)	82 (22.3)
Scientific literature and research	15 (13.3)	16 (9.3)	72 (19.6)
Scientific conferences, symposia	7 (6.2)	10 (5.8)	36 (9.8)
Internet	62 (54.9)	92 (53.2)	216 (58.7)
Other	3 (2.7)	2 (1.2)	9 (2.5)
I do not search for such information	27 (23.9)	30 (17.3)	42 (11.4)

the expected national plan for RDs suggests the improvement of medical education on RDs, this issue needs to be re-examined. Moreover, it seems that all future healthcare professionals, including nurses, physiotherapists and physicians, should receive basic teaching about RDs, which should include information regarding the prevalence and relevance of RDs to everyday medical care, the concept of the diagnostic odyssey and possible ways of reducing it, the challenges faced by RD patients and their families and sources of information and support for RD patients. At the same time, one must acknowledge McKay's argument that although specific RD and case studies may be used in medical curricula, teaching programs should not focus on any particular RD (McKay, 2019)—the reason being that while it is impossible to teach anyone about all 6,000–8,000 different types of RDs, we should focus on passing knowledge on the prevalence and occurrence of such diseases, patterns of dealing with patients with unusual or unknown symptoms, available sources of getting reliable information on RDs, including web pages, and raising awareness about one's own deficits. This is of key importance because health professionals' false beliefs in their knowledge and skills makes it difficult to change the situation of patients with rare diseases (Pisklakov et al., 2013). However, it may be worth considering Alawi's suggestion and using RDs as teaching models, as a basis for learning fundamental principles of basic science and clinical practice (Alawi, 2019).

Yet another alarming finding was that although last year medical students differed significantly in their self-assessment of being prepared to care for RD patients, they did not answer any better than their younger colleagues did. This is of key importance, because although health professions' self-assessment and reflecting on one's practice can help to set appropriate learning goals and identify one's strengths and weaknesses (Eva and Regehr, 2005), it seems that in contrast to nursing and physiotherapy students many future physicians overrated their knowledge and skills on RDs. This way of looking at one's own competences may also be the reason for

TABLE 6 | The odds ratio of different aspects of nursing, physiotherapy and medical students' self-assessment.

	Odds of being of the opinion that there should be a mandatory course on rare diseases in medical curricula		
	Nursing students vs. physiotherapy students	Nursing students vs. medical students	Physiotherapy students vs. medical students
OR	0.44	3.79	8.62
95%CI	0.24–0.83	2.35–6.12	5.23–14.21
p	**0.005**	**0**	**0**
	Odds of being interested in broadening knowledge about RDs		
	Nursing students vs. physiotherapy students	Nursing students vs. medical students	Physiotherapy students vs. medical students
OR	0.88	1.75	2.00
95%CI	0.46–1.67	1.01–3.01	1.24–3.22
p	0.41	**0.02**	**0.002**
	Odds of being of the opinion that RDs constitute a serious public health issue		
	Nursing students vs. physiotherapy students	Nursing students vs. medical students	Physiography students vs. medical students
OR	0.70	1.65	2.37
95%CI	0.35–1.41	0.93–2.92	1.39–4.05
p	0.16	0.04	**0.001**
	Odds of feeling prepared for caring for a patient with RD		
	Nursing students vs. physiotherapy students	Nursing students vs. medical students	Physiotherapy students vs. medical students
OR	0.22	0.53	2.40
95%CI	0.06–0.77	0.15–1.83	1.23–4.70
p	**0.008**	0.16	**0.005**
	Odds of reporting not searching information about RDs		
	Nursing students vs. physiotherapy students	Nursing students vs. medical students	Physiotherapy students vs. medical students
OR	1.50	2.40	1.60
95%CI	0.83–2.69	1.40–4.11	0.96–2.67
p	0.09	**0.001**	0.03
	Odds of reporting getting get knowledge about RDs from mandatory course at the university		
	Nursing students vs. physiotherapy students	Nursing students vs. medical students	Physiotherapy students vs. medical students
OR	0.25	0.11	0.45
95%CI	0.13–0.49	0.06–0.21	0.31–0.65
p	**0**	**0**	**0**

Statistically signifcant diferences are written in boldface.

TABLE 7 | The odds ratio of feeling prepared for caring for a patient with RD for students during the final 2 years of study.

	Odds of feeling prepared for caring for a patient with RD		
	6th year medical students vs. 5th year medical students	5th year physiotherapy students vs. 4th year physiotherapy students	5th year nursing students vs. 4th year nursing students
OR	10.54	1.81	0.50
95%CI	2.39–46.55	0.67–4.83	0.04–5.68
p	**0.001**	0.12	0.29

Statistically signifcant diferences are written in boldface.

overconfidence bias, a belief universal for many professions that you know more than you really do (Croskerry, 2003). Meanwhile, such inadequate belief in one's knowledge and skills may hinder physicians' future professional development. Moreover, it may cause delays, misdiagnoses and lack of understanding of patients with RD, especially that research projects prove that self-evaluation and self-assessment of medical students are directly connected to the quality of provided health care (Pisklakov et al., 2013). Thus, while self-directed and continuous learning is the core concept that should be fundamental to medical education, it seems that that students should be more aware of their knowledge deficits and should recognize when to recruit additional resources: to obtain a consultation, to recruit additional support, or to refer the problem to another individual who is more competent in this domain (Eva and Regehr, 2005).

All in all, our findings confirm that just as medical curricula contain an insufficient amount of information about RDs so too nursing, physiotherapy and medical students possess inadequate knowledge and skills in this field. Moreover, as many students mistakenly believe that they are trained enough to meet the health needs of RD patients, there is an urgent need of both the improvement of medical education on RDs by including mandatory lectures and seminars into medical curricula and creating a system of postgraduate training offering specialization training sessions on RDs and raising awareness about the deficits in their training and its possible consequences for RD patients.

STUDY LIMITATIONS

Simultaneously, although to our best knowledge this is one of the few studies on the knowledge on RDs among future healthcare professionals in Poland, it also has a few limitations. First, while the response rate was high, the study included students from only one medical university. Second, this study represents solely the opinions of students who agreed to participate in the study. Consequently, the results cannot be generalized for the entire population of future health professionals and more in-depth studies would be required. However, despite these limitations, some advantages of this study should also be acknowledged. Most importantly, as there is a scarcity of previous work on the topic this research helps fill the gap in the research on the knowledge of future healthcare professionals on RDs. Moreover, as it compares the knowledge of nursing, physiotherapy and medical students, it may stimulate further discussion on the need of better education not only of future physicians but also other health professionals whose role in the process of caring for RD patients is also vital.

CONCLUSION

This study shows that there is a serious educational gap in future healthcare professionals about RDs. What is important is that it shows that deficits of knowledge on RDs were present not only among nursing or physiotherapy students but also future physicians. Thus, it confirms that there is an urgent need to include RDs into the medical curricula, which contain an insufficient amount of information about such diseases. Moreover, as caring for RD patients requires a special and combined approach, all healthcare specialists, including physicians, physiotherapists, nurses, midwives psychologists, dieticians or speech therapists should be enrolled in education on RDs. In order to overcome the existing knowledge deficits, it is suggested to include an RD module into the medical curricula and to implement teaching programs similar to those present in such European countries as France, Spain or the United Kingdom. Moreover, a bigger emphasis should be placed on training all medical students in basic genetics and newborn screening. Finally, while self-directed and continuous learning on RDs among healthcare professionals should be promoted, e-learning programs or courses on RDs should be also organized and Polish web pages with reliable information on RDs should be organized.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Poznan University of Medical Sciences Bioethics Committee (1018/18). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JD supervised conceptualization, design of the study and the collection of data. DW performed the statistical analyses. JD and DW critically revised and edited the various drafts of the manuscript and approved the final version before submission. Both authors conducted the literature search and analyses, had full access to all of the study data, discussed the results of the questionnaire, assisted in the interpretation of the data, and wrote the original draft of the manuscript.

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REVIEW
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Non-invasive Prenatal Testing, What Patients Do Not Learn, May Be Due to Lack of Specialist Genetic Training by Gynecologists and Obstetricians?

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Platforms for "non-invasive prenatal testing" (NIPT), or also referred to as "non-invasive prenatal screening" (NIPS) have been available for over 10 years, and are the most recent tools available to obtain information about genetic condition(s) of an unborn child. The highly praised advantage of NIPT-screening is that results can provide early hints on the detection of fetal trisomies and gonosomal numerical aberrations as early as the 10th week of gestation onward, without any need for invasive procedures, such as amniocenteses or alternatives. Understandably, the public along with gynecologists and obstetricians eagerly await these early test results. Their general hope for normal (=negative) test results is also justified, as in >95% of the tested cases such an outcome is to be expected. However, pregnant women can be disappointed and confused, particularly regarding the genetic information and proposed care when the results are positive, and these emotions are also common with false-positive and false-negative NIPT results. Finally, such concerns in understanding the advantages and limitations of this routinely ordered screening tool end up at Clinical Geneticists and Genetic counselors. In this review, general background on NIPT, differences of NIPT platforms, advantages and limitations of NIPT, as well as consequences of insufficient counseling before and after NIPT are summarized. To provide comprehensive care in all pregnancies situations, professionals need a careful attitude toward offering NIPT along with specially training and qualifications in counseling for these procedures. Often it is gynecologists and obstetricians who discuss the use of NIPT with patients; however, although these physicians have a highly qualified background and knowledge in their respective specialty area(s), they may lack specific training on the interpretation of NIPT-screening results. These potential knowledge gaps must be closed quickly and comprehensively by the corresponding scientific societies to ensure optimal patient care.

Keywords: non-invasive prenatal testing, qualified genetic counseling, cell-free placental DNA, massively parallel sequencing, single nucleotide polymorphism whole genomic sequencing, background knowledge, NIPT-shortcuts

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INTRODUCTION

Advances in modern medicine are in parts breathtaking when compared to our limited capabilities only 2, 5, or 10 decades ago. This is especially true for prenatal predictive genetic testing in human reproduction. Today it is hard to imagine reproductive care without many of the tools and approaches now available, which enhance the study and evaluation of the life of the unborn. These enumerable invasive and non-invasive approaches allow examination of the fetus and may detect genetic condition(s) (Hixson et al., 2015). All these evaluation possibilities are, from the pregnant mother's perspective, just options she must choose from to answer the single burning question: "How likely is it that this baby in my womb will be affected or not affected by a (specific) genetic disease?" Or more simply: "Will my baby be okay?" With respect to the desire for negative results and for those who may use these results to decide on an induced abortion in the presence of a fetal anomaly, the pressing need for early test-results is completely understandable (Hixson et al., 2015; Liehr et al., 2017).

Pregnant women seek help, education, and counseling regarding these tests primarily from their gynecologists and obstetricians. Also many national health system regulations require qualified genetic counseling before and after NIPT either from gynecologists or obstetricians, and/or genetic counselor or a medical doctor (MD) with a specialization in Clinical Genetics (which may but must not include gynecologists or obstetricians) (Skirton, 2018). During qualified genetic counseling, a general risk-estimation is performed first for the pregnancy and can simply base on epidemiological data, including family history of disease(s) and/or abortion(s), age, ethnicity, and weight of pregnant woman. Suitable testing options can then be discussed and ideally, after counseling and time for consideration of available options, the pregnant woman/the couple should be allowed to form their own educated decision on the need for further genetic tests, and if so, which one(s) she/they want to undertake for the evaluation of the fetus (National Society of Genetic Counselors' Definition Task Force et al., 2006).

In many countries ultrasonography is part of routine prenatal testing and is offered free of charge for all pregnancies (Hixson et al., 2015). It remains the most straightforward non-invasive method to learn about the condition of an unborn child—test accuracy is estimated at up to 82% (Levi, 2002). First trimester sonography is an important and integral part of comprehensive first trimester screening (FTS) (Anderson and Ghaffarian, 2021). FTS also includes additional biochemical testing of maternal blood for pregnancy-associated plasma protein A (PAPP-A) and free β-human chorionic gonadotropin (β-hCG) (Rink and Norton, 2016), which also take into account maternal age, ethnicity, and body weight. Using FTS, a 91–96% reliable risk estimation for the fetus can be achieved (Hixson et al., 2015). However, if an enhanced risk has been identified, further clarification and/or testing may be required to determine if the underlying problem is one of the more common trisomies of 13, 18, or 21, or any other "genetic problem," or to confirm a false positive finding. Therefore, until recently, the only options available after abnormal sonography were invasive prenatal diagnostic approaches—i.e., amniocentesis (AC), chorionic villi (CVS), and/or umbilical cord blood sampling (CBS), which differ in the tissue examined; in CVS the placenta is studied, whereas in AC and CBS real fetal tissues are examined. Overall, discussions of the procedure and result expectations regarding all aforementioned prenatal testing approaches, which have been available for more than two decades, are well understood by patients and medical doctors (Hixson et al., 2015; Liehr et al., 2017).

However, in the last decade, another, new approach has become routinely available and has subsequently joined the plethora of other prenatal testing approaches—the so called "non-invasive prenatal testing" (NIPT) or also "non-invasive prenatal screening" (NIPS) (Skrzypek and Hui, 2017). This recent development in prenatal diagnostics is based on the so-termed second-generation sequencing approaches for analyzing copy number alterations in free placental DNA in maternal blood plasma (also referenced in the literature as cell-free fetal DNA = cffDNA; see also below) (Liehr et al., 2017). NIPT is advantageous given DNA derived from the placenta (!) during pregnancy can be examined very early (at around 10th week of gestation = w.o.g.) for the most frequent chromosomal aberrations detected in the first and second trimester (Taylor-Phillips et al., 2016). With the widespread utilization of NIPT screening, more and more countries have added the assay as a statutory health insurance benefit, however, in tandem, moral concerns regarding the use of the tests in pregnancy decision making have been raised, e.g., concerns over the use of the results in decision making for or against continuing a current pregnancy (Farrell et al., 2014). In addition, Nigün Dutar (Institute for Prenatal Medicine and Ultrasound, Wuppertal, Germany) recently stated: "The diagnostic gain of the non-invasive prenatal tests is actually very small. On the other hand, the pressure on pregnant women to give birth to a perfect child will increase due to a blood test that is supposedly easy to use" (translated from German site: https://www.aerzteblatt.de/nachrichten/99669/Praenatalmediziner-warnen-vor-breitangelegtem-Einsatz-nichtinvasiver-praenataler-Tests). However, in disagreement with the public suggestion that NIPT may be "a blood test that supposedly easy to use," there are several points as outlined below that must be brought to the attention of the field.

NIPT IS NOT EQUAL TO NIPT

NIPT was developed based on the 1997 finding that in the blood, or more accurately in plasma of a pregnant woman, there is cell free **placenta**-derived DNA along with maternal cell-free DNA (Lo et al., 1997). This DNA derived from the placental syncytiotrophoblast layer is misleadingly referred to as cell-free **fetal** DNA (cffDNA) in literature (Shaw et al., 2020). This free placenta-derived DNA can be detected earliest at ∼4.5 w.o.g. (D'Aversa et al., 2018) and can reach 30% of cell-free DNA in a pregnant woman during the 3rd trimester. Following birth, placental cell-free DNA is removed from maternal blood within hours, and as such, no mix-up of genetic materials from different pregnancies is possible (Lo et al., 1999; Shaw et al., 2020).

In the NIPT-literature, it is often difficult to understand which NIPT protocol, method or evaluation platform was used by the authors, and which genetic aberrations were potentially detectable by a specific test. Generally, it is less cumbersome when commercial NIPT assays are performed because in most cases these vendors declare the use of a second generation sequencing based testing approach and they provide results as Z-scores, with normally high positive predictive values (PPVs) and with detailed sensitivity and specificity of the test:

- A Z-score of more than 3 standard deviations away from the expected value for the DNA fragments derived from a specific chromosome is considered a high-risk-result for trisomy (Palomaki et al., 2011).
- The sensitivity of NIPT for trisomy 21 is generally given as 99.3%, for trisomy 18, 97.4% and for trisomy 13, 97.4%,
- with a specificity of 99.9% for trisomy 21 (Taylor-Phillips et al., 2016).
- Previous PPVs for trisomy 21 were given as 80–90% however, they are now corrected to 45.5% and lower (Skrzypek and Hui, 2017).

Thus, these "standard NIPT" protocols are able to detect trisomies 13, 18, and 21 and gonosomal numerical aberrations. When further copy number alterations are detectable by a NIPT platform, such as trisomies of other chromosomes, or specific microdeletion and microduplication syndromes (MDDs) (Weise et al., 2012), these protocols are marketed as "expanded NIPT" or "NIPT Plus" tests. For these emerging platforms, the data for Z-scores, sensitivity, specificity and PPVs are in most cases hard to find or are not provided (Skrzypek and Hui, 2017; Shaw et al., 2020; Ye et al., 2021).

The following whole genomic sequencing (WGS) based principles are used to perform a NIPT:

(i) shotgun massively parallel sequencing (s-MPS),
(ii) target massively parallel sequencing (t-MPS) and
(iii) single nucleotide polymorphism (SNP) based WGS.

In both MPS based approaches either untargeted (s-MPS) or targeted (t-MPS) regions of the pregnant mother's cell-free DNA are sequenced. An aneuploidy is indicated as an excess (or deficit) in the detected amount of DNA for the studied chromosome compared with the expected result for diploid cases. In this evaluation, maternal and placental DNA cannot be distinguished, and only s-MPS based NIPT tests can be widened to become "expanded NIPT" or "NIPT Plus" tests. In SNP-based NIPT, maternal and placental DNA can be distinguished, and thus the relative contribution of both DNA-types is measured; with this approach "expanded NIPT" can be easily performed (Neveling et al., 2016; Skrzypek and Hui, 2017; Andari et al., 2020). In addition, slightly alternative approaches have been reported, such as the use of real-time polymerase chain reaction before low coverage DNA sequencing (Chen et al., 2013). All current WGS platforms are considered to be suitable for NIPT (Neveling et al., 2016).

Thus, it must be stated that all commercial NIPT tests and all published NIPT data should be analyzed in detail to confirm the underlying approach used for the assay. Optimally, data should be available for sensitivity, specificity and PPVs, as well as cut-off levels, which should include the number of false negative and false positive results to be expected for the corresponding NIPT approach. However, this data is often not readily available, sometimes even impossible to obtain, as in many cases the approaches are patented and quite often, the approach used to obtain and calculate results remains a coveted company secret. Accordingly, it is also difficult to align different publications for NIPT-screening and a paucity of literature is available for such comparisons (Agarwal et al., 2013; Kotsopoulou et al., 2015; Sekelska et al., 2019). While most companies started with NIPTs to offer testing for trisomy 13, 18, and 21 as well as gonosomal aberrations, more and more offer and are now testing for additional genetic conditions (with the anticipated added expense) (Liehr, 2019), and a few platforms also test all chromosomes, but fail to appropriately identify which MDDs were under evaluation by the platform (Health Quality Ontario, 2019).

Even more complexity in testing within the field is exemplified by differences in testing, e.g., Belgium and the Netherlands have offered NIPT since 2017 to all citizens, which are whole genome oriented assays that also include evaluation of genetic material associated with certain monogenic disorders (van Schendel et al., 2017; Žilina et al., 2019). Further evidence of confusion within the field comes from the naming convention used for the first NIPT (also called NIPS) assays, in contrast to testing for single-gene disorders on free placental DNA, referred to as "non-invasive prenatal diagnosis" (NIPD). Thus, as Shaw and colleagues provocatively wrote in 2020: "The distinction between diagnostics and screening has become blurred, and there is a clear need for the education of physicians and patients regarding the technical capabilities and limitations of these different forms of testing. Furthermore, there is a requirement for consistent guidelines that apply across health sectors, both public and commercial, to ensure that tests are validated and robust and that careful and appropriate pre-test and post-test counseling is provided **by professionals who understand the tests offered**." This statement is further supported by the statement of Stefanovic (2019): "**The knowledge and counseling should be substantially improved**. Cell-free DNA screening is not a replacement for diagnostic testing and its use in prenatal testing is complex and limited" (Stefanovic, 2019).

NIPT: ADVANTAGES AND SHORT-CUTS

NIPT is advantageous given DNA derived from placenta during pregnancy can be tested for the most frequent chromosomal aberrations generally detected in the first and second trimester; this can be performed starting around the 10th w.o.g., with a result anticipated within 2 weeks. Thus, information on the health of an unborn child can now be obtained a few weeks earlier than by FTS or invasive approaches. Accordingly, expecting couples have long awaited this new possibility and in only a few years, NIPT has rapidly transformed prenatal care worldwide. Thus, massive reduction in the number of invasive prenatal

procedures performed has already been observed (Shaw et al., 2020). Even with these reported changes in care pathways, surprisingly, the aforementioned is the only relevant summary of all publications regarding the appropriate advantages of NIPT. The following list of potential problems is much longer, and unfortunately, these issues are not as well-known to the public and/or gynecologists and obstetricians when compared with the widespread awareness of the catchy statements often used in favor of the technique (see also **Table 1**).

The list of limitations begins with the understanding that is important to keep in mind: "NIPT is a screening test, with positive results requiring confirmation via invasive testing" (Shaw et al., 2020). In addition, negative NIPT results and a fetus with sonographic findings may need further (invasive) testing (Liehr et al., 2017). As long as no (really reliable) "expanded NIPT" or "NIPT Plus" test is available it must be understood and considered that at a maximum 50% of cases with chromosomal aberrations of the first and second trimester are detectable via NIPT. Accordingly, as reported in 2016, the extensive use of NIPT in United States since 2011 has been associated with a dramatical increase in the rate of newborns with MDDs as compared with previous years (Beaudet, 2016).

Furthermore, the misleading use of the name cffDNA instead of free placental DNA has further implications on the general understanding of this assay. It is known, and confirmed by many "single case reports" in the literature, that genetic and chromosomal conditions of placenta are different from that of the fetus in 2% of cases (in second trimester) and may be even higher in first trimester evaluations (Hartwig et al., 2017). Thus, a negative NIPT can only exclude ∼98% of adverse copy number changes in the fetus, and a positive NIPT for a trisomy can be false positive in up to ∼2% of the cases. The phenomenon of confined placental mosaicism is real, and should be understood when interpreting the NIPT-screening findings or while providing pre/post-test counseling (Lau et al., 2014; Hartwig et al., 2017; Liehr et al., 2017).

In the beginning of NIPT-era, which continues today by some vendors, NIPT is advertised as an assay capable of reducing the risk for invasive tests. This erroneous claim ignores two facts: (i) that invasive testing is still necessary in the case of a positive NIPT; and (ii) that the terrifying data often touted of 1–3% abortion risk associated with CVS, AC or CBS is derived from outdated studies performed in the 1980s/1990s. That is, these data are derived from a time that predated the availability of better suited needles for aspiration and the routine control of the procedure by sonography. Today, the risk of invasive diagnostics is at 0–0.3% (Liehr et al., 2017). This is an important distinction regarding invasive procedural risk, which is critical data pregnant women must be properly informed about when considering available testing options during pregnancy.

False positive results can also derive from maternal (acquired) mosaicism in peripheral blood or come from other tissues excreting cells and cell-free DNA into the plasma of the pregnant woman. Cases have been reported where a previously undetected maternal malignancy was the reason for an abnormal NIPT result (Bianchi et al., 2015; Saes et al., 2019). Other abnormal NIPT outcomes have been reported to result from maternal mosaicism (mos 46,XX/45,X), leading to incorrect conclusions regarding a sex chromosome abnormality in the fetus (Wang et al., 2014). Furthermore, other studies report that MDDs in the mother have been falsely attributed to fetus (Kumps et al., 2020). Lastly, a chromosomally abnormal vanishing twin can also interfere with the NIPT-result; in particular, targeted SNP-sequencing based NIPT cannot distinguish between triploidy and vanishing twin scenarios (Andari et al., 2020).

Finally, it also possible, as observed in 1.58–6.39% of NIPT-tests, that free DNA in the pregnant mother's blood does not contain sufficient placental DNA to achieve an informative test result. This issue is of great concern when performing NIPT-screening in early w.o.g. and/or if mother is obese, because in these situations, the ratio of placental/maternal cell-free DNA is altered, leading to a disadvantage when attempting to detect placental derived DNA (Skrzypek and Hui, 2017). Interestingly, failure rates differ according to the NIPT-technology: NIPT based on MPS have the lowest and targeted SNP-sequencing have highest failure rates (Yaron, 2016).

All the points raised herein must be discussed in a qualified genetic counseling before NIPT is consented and performed. This level of understanding of both the capabilities and limitations of NIPT-screening is only possible if gynecologists and obstetricians either provide this appropriate counseling or refer the pregnant woman/the couple to a counselor or MD with specialization in Clinical Genetics (Skirton, 2018). Logically, such counseling requires considerable care and time, which may be not readily available in routine daily practice of the doctor's office.

CONSEQUENCES OF INSUFFICIENT COUNSELING BEFORE AND AFTER NIPT

The most obvious and worst possible outcome imaginable from a lack of sufficient counseling are that the families consented for NIPT do not understand the implications of the test performed (**Table 1**). The following three examples support the need for appropriate counseling:

- Beaudet (2016) reported an increase of newborns with MDDs after massive introduction of NIPT in United States. This is most logically due to a misunderstanding by pregnant women that a negative NIPT means the baby will be genetically normal, and that all possible genetic aberrations have been "ruled out" by this test, even when there were hints of malformations observed in FTS or sonography.
- In the same vain, are many cases repeatedly observed by the author of this paper: when using MPS-based NIPT it is possible to detect trisomies, but not triploidies. This fact is difficult for laymen to comprehend and in some cases following a normal NIPT, the pregnant women learned of the triploid condition only after an AC. This is likely due to a failure in consultation to explain the limitations of the test, which may lead to a break down psychologically, as without all of the information they were inappropriately

TABLE 1 | Expectations and reality of NIPT.

NIPT	
Expectations	**Reality**
The test can be performed earlier than others	This is correct; it is a screening test
The test includes zero risk for the unborn baby in contrast to invasive testing, which has 1–3% abortion risk	First point is correct; however, nowadays risk of invasive testing is between 0 and 0.3% only
If we do the NIPT there is no need to do invasive testing	In case NIPT is positive an invasive confirmatory test is obligatory In case NIPT is negative but sonography normal invasive confirmatory test is recommended to exclude a placenta mosaicism
The test is based on fetal DNA	The test is based on placenta derived DNA
The test is a quick test and is easy to understand	There are many variants of the test There is a need for detailed pre-test counseling (e.g., to explain that a hidden maternal tumor may be detected) The technical details how the test works are very complicated
The test is equally reliable for all kinds of genetic conditions tested	Highest reliability is available for trisomy 21; all other conditions have lower PPVs In many cases there are no PPVs available for the corresponding tested syndrome
There is a clear answer if baby will be ok.	It is a screening test
The results are available very fast	It lasts ∼2 weeks and in 1.58–6.39% of the cases the tests needs to be repeated due to not sufficient cffDNA in maternal plasma
There is a clear answer if baby will be not ok, e.g., have trisomy 21	2% risk of placenta mosaics; false positive results are possible
It is a test which can exclude all genetic problems	Neither the "normal NIPT" nor the "expanded NIPT" can exclude all possible genetic conditions

convinced up to this moment that the normal NIPT result all but assured them they will deliver a healthy child.

- Similarly catastrophic are prenatal cases that are voluntarily terminated after an abnormal NIPT screening, without any verification by sonography and/or invasive procedures of a false positive finding, which are also reported in literature (Xue et al., 2020).

NIPT is commercialized and advertised as an assay that will provide early information on the unborn child that is quick and with clear answers, which will most often provide the optimal and hopeful anticipated result desired by the pregnant mother: no genetic abnormalities are found. But how well can gynecologists and obstetricians answer questions in cases of a delayed or abnormal result? Here is an example based on the experience of one of ∼25 women, the author was in contact with, and who was interviewed by a German newspaper (Krafft, 2020):

- The woman got a NIPT result that her baby could have a trisomy 18. She did not feel well-informed after getting the result from her obstetrician and was not referred to a genetic counselor to discuss the findings. After AC and nearly ∼8 weeks after the NIPT she received information the baby was okay—the abnormal result was most likely associated with confined placental mosaicism. Her comment to the journalist was "I was psychologically exhausted. For weeks. In retrospect, I think to myself that I should never have taken this test" (translated from Krafft, 2020).

Further examples, known to the author of this paper include situations where pregnant women were desperate for clarity following an abnormal NIPT test; many of them had already received further results after invasive diagnostics and Clinical Genetic counseling, which was in the majority not referred appropriately by their gynecologists and obstetricians; instead they found a suited counselor after performing their own internet research. Problems associated with NIPT-screening results these women did not get a qualified answer from gynecologists and obstetricians are as follows:

- What is a chromosomal mosaic and a supernumerary marker chromosome?
- The pregnant women were told in such cases that a special trisomy was indicated by NIPT, but afterward in AC there was only a hint on a mosaic trisomy and/or a small supernumerary marker chromosome (sSMC) (Liehr, 2021). In such cases genetic specialists need to explain that a mosaic can possibly reduce the expected abnormal phenotype, that an sSMC is in ∼70% of cases a kind of harmless leftover from a trisomic rescue. Yet the author knows five such cases who were in direct contact with him.
- Why is the accuracy and PPV of the test only 5% in my case?
- This question was asked by a pregnant woman, who received the result of a "extended NIPT" with the information—all is okay, but there is a 5% risk for a specific MDD—which could have been 1p36. A molecular cytogenetic test on AC derived cells excluded a corresponding microdeletion and subsequently a healthy child was born. This example highlights the limitations of many extended NIPT platforms, i.e., these companies do not have reliable cutoff rates, and the reporting is somewhat ambiguous, often leading to uncertainty in the results, which is also difficult to reconcile for the patient following a short consultation with a gynecologist or obstetrician, who may also be puzzled by such a test outcome.

CONCLUDING REMARKS

As discussed herein, all of the aforementioned issues are of high ethical impact for societies worldwide. However, a more careful approach for offering NIPT along with a new way of counseling have recently been suggested, which may serve to enhance patient care (Kater-Kuipers et al., 2020). Education and training must ensure that gynecologists and obstetricians can perform their role as the primary provider of NIPT advisement though awareness of all implications for the pregnancy that may be associated with the test results. Concrete normative measures for application of NIPT have already been published (Guidelines of the Royal College of Obstetricians Gynecologists, 2019; American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics, Committee on Genetics, Society for Maternal-Fetal Medicine, 2020); still normative measures for educational level of MDs need to be established by the corresponding national societies. In most countries ongoing education is anyway obligatory for MDs. Thus, corresponding courses providing details on NIPT-testing, -advantages and -limitations should be offered by national medical societies, held by independent laboratory specialists rather than company representatives. Connected with this could be a certificate allowing for offering NIPT only if an MD has this kind of advanced training.

Overall, information from this review, from commercial NIPT providers, and many recent NIPT publications provide evidence that alternative and more reliable approaches such as FTS may be underestimated, and that limitations and issues of NIPT must be widely distributed by appropriate professional societies.

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The author confirms being the sole contributor of this work and has approved it for publication.

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MINI REVIEW
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Mini-Review: Genetic Literacy and Engagement With Genetic Testing for Autism Spectrum Disorder

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As genomic and personalized medicine is integrated into healthcare, the need for patients to understand and make decisions about their own genetic makeup increases. Genetic literacy, or one's knowledge of genetic principles and their applications, measures an individual's ability to apply genetic information to their own treatment. Increased genetic literacy can improve comprehension of genetic tests and therefore increase participation in testing to detect and treat genetic disorders. It can also help providers understand and explain genetic information to their patients. However, current research indicates that the population's genetic literacy is generally low. Because many medical students, providers, and patients cannot adequately apply genetic information to their health, new and beneficial genetic technologies can be underused. More specifically, though genetic testing is recommended at the time of diagnosis for those affected by autism spectrum disorder (ASD), as few as 22% of families undergo genetic testing after diagnosis. While ASD, a neurodevelopmental condition characterized by impaired social communication and restricted interests, has both genetic and environmental risk, genetic testing can give clinicians useful information and help families avoid potentially painful and costly tests, even when many families do not receive a "positive" genetic result through microarrays or gene panels. Improving genetic literacy in populations affected by ASD can also improve attitudes toward genetic testing, thereby ensuring access to genetic health risk information. In this mini review, we discuss the current literature describing genetic literacy and genetic testing rates for ASD.

Keywords: genetic literacy, genetic testing, autism spectrum disorder, neurodevelopmental assessment, science communication

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INTRODUCTION

Since the Human Genome Project completed in 2003, the use of genetic information in healthcare, as well as everyday life, has increased exponentially. In fact, leaders at the National Human Genome Research Institute predict that within the next decade, genetic testing will become a mainstream in healthcare, potentially becoming as commonplace as a complete blood count test (Green et al., 2020). There are increasingly more job opportunities in genetics, ancestry testing and clinical genetic testing is widely available, and individuals are able to participate in many facets

of genetic research (Roberts M. C. et al., 2019). Celebrities have even publicized their genetic health decisions, drastically increasing awareness and interest in preventative genetic testing (Abrams et al., 2016). To prevent misconceptions regarding genetic risk, it is pivotal for the public to be equipped with accurate information and sufficient skills to make decisions about their own health and genomic data.

As genetic research expands, there is little doubt that our genes contribute to a variety of common and rare conditions (Claussnitzer et al., 2020). With the goal of prevention and treatment, genetic testing is often recommended as a way for clinicians to quantify and assess their patients' disease risk. Genetic testing can provide information contributing to prevention and treatment for complex conditions, even though it is not always definitive. Receiving genetic risk information confirming a diagnosis can be comforting for patients and can even contribute to more healthful behaviors (McBride et al., 2010). A 2019 survey of two large research cohort studies in the US found that most participants had positive opinions of genetic testing, with a correlation between more favorable opinions and greater genomics knowledge or personal experience with genetic testing (Saylor et al., 2019). In clinical situations, many patients are not aware of the option for genetic testing or its benefits. The public must often rely on healthcare professionals to educate them and explain sometimes complex genetic results.

For those without a background in biology, understanding interactions between human health and chromosomal variants can be confusing and overwhelming. At a national level in the US, public understanding of how genetic information contributes to disease risk is generally low. In a survey distributed to 5,404 participants with secondary education, only 1.2% of the sample answered all of the basic genetic knowledge questions correctly (Chapman et al., 2019). Another national survey conducted in 2017 indicated that only half of individuals are aware of genetic testing and approximately a third were aware that genetic testing can contribute to disease treatment (Krakow et al., 2018). Similar trends are seen in healthcare education, with only 29% of a sample of 10,303 physicians reporting they received education in pharmacogenetic testing and only 25% of high school teachers reporting teaching contemporary issues in genetics (Kampourakis, 2016; Sabatello et al., 2019). Given the low rates of genetic knowledge in both the general public and providers, there is an ongoing effort by many organizations to both assess current knowledge rates and work to improve them (Green et al., 2020).

Measuring Genetic Literacy

Genetic literacy, defined as "sufficient knowledge and understanding of genetic principles to make decisions that sustain personal well-being and effective participation in social decisions on genetic issues," is one tool used to measure this phenomenon (Abrams et al., 2015). Importantly, genetic literacy is not the same as genetic knowledge. Those with high genetic literacy are able to understand their genetic testing results, communicate with their providers about genetic testing options, and make decisions about gene-related disease risk (Kampourakis, 2016). In research, genetic literacy has been defined and operationalized in many different ways. It has been measured using a person's pronunciation of medical jargon or their knowledge of genes and heredity (Abrams et al., 2015). Because multiple measures for genetic literacy have been developed and optimized for various situations, it is difficult to adequately assess the public's current genetic literacy rates and factors that influence it (Milo Rasouly et al., 2020). Abrams et al. (2015) proposed a measure of genetic literacy in three domains: Awareness knowledge, how-to knowledge, and principles knowledge. In conjunction, these domains assess the extent to which individuals are familiar with genetics concepts, their ability to apply genetic information to a particular health condition, and their factual genetic knowledge.

The same group assessed this measure in a nationally representative sample, applying genetic literacy to Angelina Jolie's decision to pursue a prophylactic mastectomy following genetic testing in the *BRCA1/2* genes (Abrams et al., 2016). The results indicated moderate genetic knowledge, with the sample answering an average of half of the six factual genetics questions correctly. They also found an interesting interaction between confidence in one's genetic knowledge, media exposure to Jolie's decision, and genetic literacy. Those with high exposure to the news surrounding Jolie's decision felt more confident about their genetic knowledge and their ability to apply this knowledge to the decision for surgery, regardless of their genetic literacy scores. Though it is beneficial for patients to feel confident in their health decisions, high-profile media can skew opinions about genetic health without a factual basis. For example, after the US Food and Drug Administration authorized a direct-to-consumer genetic test for three pathogenic variants in *BRCA1/2* in 2018, thousands of twitter messages relayed either information or opinion on the decision, with the most read being from established media outlets. Tweets from those expressing opinions most often focused on the harms of direct-to-consumer testing, without specifically referencing any research into the nature or frequency of these claims (Roberts M. C. et al., 2019). As discussions and media surrounding genetic health increase, it is important to counter false beliefs with accurate, research-based information. Patients and families with rare genetic diseases, for example, report that they have used social media to find each other and locate or vet potential treatments as they are developed (Iyer et al., 2020), a process which is fraught with the risk of misinformation that could misguide them.

Population Differences in Genetic Literacy

Internationally, genetic knowledge and literacy rates vary as well. A large survey of willingness to share one's genomic data, reporting on 36,268 individuals in 22 countries (Middleton et al., 2020), reported that "only 35.8% of the total sample say that they have some familiarity with the concepts" of DNA, genetics, and genomics; genetic literacy beyond that was not measured. Within the United States, over 30% of the 2,093-person sample indicated that they were unfamiliar with genetic concepts, while approximately 20% indicated they had personal experience with genetics, such as being a patient with a genetic condition or

a genetics professional. This level of personal experience with genetics is relatively high; less than 12% of participants in Japan, Germany, Russia, and Mexico indicated familiarity through personal experience (Middleton et al., 2020). Higher levels in the US could be correlated with the increased use of direct-to-consumer genetic testing, emphasizing the need for genetic education as testing results become integrated into healthcare (Roberts J. et al., 2019).

Though many developed countries indicate relatively high awareness of genetics concepts, most individuals overestimate the impact of our genes on health (Kampourakis, 2016). The most common misconceptions state that genetic testing can control health outcomes, or that it exclusively determines your risk for a condition (Kampourakis, 2016). This is understandable in part because the most sophisticated research in most cases still does not adequately understand the interaction between genes and environment (Green et al., 2020); therefore, many in the public perhaps unsurprisingly attribute overall health to genetics exclusively and believe genetic traits to be immutable (Dar-Nimrod and Heine, 2011; Kampourakis, 2016). However, the belief that genetic information alone determines human traits or separates humans into strict groups ignores the social and environmental impact on human life and behavior. Unfortunately, and importantly, the perpetuation of this belief has led directly to discrimination between social groups when they are seen as genetically distinct and separate (Knerr et al., 2010). For example, genetic researchers in 2005 asserted that mutations in genes related to more adaptive brain development occurred more often in Eurasian than African populations. By suggesting that genes related to brain development are significantly different between ancestral groups, the researchers supported speculation that intelligence can vary by race (Knerr et al., 2010). Though the results were widely criticized within the field, the media only further emphasized the idea of strict and essential differences by genetic ancestry. Improving genetic literacy rates can diminish this perceived difference, educating individuals on the interaction between environment and genetics, and refuting the belief that genes are deterministic (Dar-Nimrod and Heine, 2011).

Genetic literacy rates also vary by social factors, including race, ethnicity, and socioeconomic status. Racial and ethnic minorities are less aware of genetic testing for cancer risk and are less likely to undergo such testing (Krakow et al., 2018). Additionally, individuals who are older or have lower incomes generally have lower genetic literacy and are even less likely to be aware of genetic tests (Krakow et al., 2018). Because those with low genetic literacy are less likely to participate in genetic research, they are less likely to benefit from scientific advances, such as genetic testing (Chapman et al., 2019). A previous study found that individuals undergoing genetic screening who showed low genetic literacy (independent of low genetic knowledge) were more likely to believe misconceptions about genomic medicine and less satisfied with the informed consent process for genetic research (Milo Rasouly et al., 2020). Such disparities in genetic literacy and awareness of genetic testing perpetuate existing health inequities in underserved populations. Without appropriate risk information, these populations are less likely to receive preventative information and adequate treatment.

Given that improving genetic literacy both increases awareness of genetic testing and improves attitudes toward genetic testing and its contributions to research, promoting genetic literacy and genetic testing awareness continues to be a public health goal for large organizations such as the National Human Genome Research Institute (Green et al., 2020).

Genetic Testing for Autism Spectrum Disorder

We suggest that autism spectrum disorder (ASD) is a particular clinical example in which improving genetic literacy is important. Because the diagnosis process can be lengthy and grueling, children are often not diagnosed until years after displaying symptoms, which can impact functioning later in life. As detailed below, genetic testing can be useful in diagnosing ASD by shortening and improving the diagnostic process. However, the uptake of genetic testing in ASD is much lower than it could be, likely due to many factors including insufficient genetic literacy on all sides.

ASD is a neurodevelopmental condition characterized by restricted and repetitive interests as well as impairments in socialization and communication. ASD's etiology is complex as it is influenced by a mix of genetic, epigenetic, and environmental factors. In the US, approximately 1 in 54 children reach the threshold for an ASD diagnosis and the average age of diagnosis is 4.25 years of age (Maenner et al., 2020). The potentially lengthy diagnostic process, often involving developmental pediatricians, neurologists, and geneticists, could mean a child is not diagnosed with ASD for years following initial symptoms. The age at which parents notice symptoms in their children depends on their awareness of ASD; first-time parents who are less aware of typical developmental milestones are less likely to notice developmental delays (Malik-Soni et al., 2021). Caregivers who notice symptoms in a child by 18 months of age are more likely to receive a prompt diagnosis, though many do not seek assessment until 35 months of age (Becerra-Culqui et al., 2018). In a large sample of families in the US and France, parents reported a significant delay between identifying symptoms at 29 months of age and receiving a diagnosis at approximately 55 months of age (Amiet et al., 2014). This gap represents a critical window of opportunity in which the child is missing out on support that can impact their functioning later in life (Li et al., 2016). Given the demonstration that some early behavioral interventions can change the trajectory of ASD (Siller, 2021) and the high frequency of co-occurring conditions which may need separate treatments, expediting the diagnostic process for ASD is imperative.

Because there is a clear genetic link to ASD, genetic testing is recommended by both the American College of Medical Genetic and Genomics and the American Academy of Pediatrics following an ASD diagnosis (Savatt and Myers, 2021). ASD is highly heritable, with estimates of twin heritability ranging from 70 to 90%, and recent advances in genetic research have identified over 100 gene or genetic variants associated with risk for ASD (Johannessen et al., 2016; Genovese and Butler, 2020;

Satterstrom et al., 2020; Savatt and Myers, 2021). As with many other conditions that have a genetic basis, ASD genetic testing can provide families with an expedited and clearer diagnosis, giving them access to appropriate educational or therapy services. Because genetic testing is also used to determine the condition's etiology, it can help children and families avoid other expensive or painful diagnostic tests, such as extensive neuroimaging, and metabolic testing including unnecessary blood draws. Conclusive results from genetic tests can also provide comfort to families affected by ASD. They can ease anxiety and uncertainty, aid medical and legal planning, and even provide a sense of empowerment and reduced negative emotions for the parents (Savatt and Myers, 2021).

Though genetic testing can provide many psychosocial benefits to families, it does not always yield a conclusive result. The first-tier test for ASD, chromosomal microarray or CMA, yields a diagnostic result in only 15–20% of cases (Savatt and Myers, 2021); in addition, the high frequency of copy number variants associated with ASD risk can produce test results which are not straightforward to interpret. The next logical test option is whole exome sequencing, which can increase the diagnostic yield up to 36% for neurodevelopmental disorders overall, making it the preferred genetic test for many clinicians (Srivastava et al., 2019; Martinez-Granero et al., 2021). Even though genetic tests can only provide a diagnostic result in some cases, they can help caregivers and providers identify areas of need and support in the child. In a survey of families who received CMA for ASD, over 60% of families reported that the testing was moderately to very helpful to the child and family (Reiff et al., 2015).

Family Interest in and Referral Rates for ASD Genetic Testing

In a large Turkish sample, 87% of parents stated that they would pursue genetic testing if it could help identify the cause of their child's ASD, and 84% believed that genetic testing referral is a key step in the diagnostic process (Ayhan et al., 2020). However, despite interest in and clinical recommendations for genetic testing, only about 22–28% of families undergo genetic testing in the US (Amiet et al., 2014; Zhao et al., 2019). This unexplained gap in genetic testing uptake is influenced by many factors including the high cost of genetic testing, lack of medical insurance, and low population genetic literacy.

Despite guidelines recommending genetic testing following an ASD diagnosis, referral rates from medical and genetics professionals are low (Amiet et al., 2014; Zhao et al., 2019). Ideally, families who have received an ASD diagnosis would be offered genetic testing and then counseling to determine whether testing is appropriate. However, because families may be referred to multiple medical professionals throughout the assessment, such as a geneticist, pediatrician, neurologist or genetic counselor, there is not always a logical or simple referral method. Many physicians report that they lack the specialized knowledge required to screen and diagnosis children with ASD (Malik-Soni et al., 2021). Medical guidelines also present conflicting information about which provider should offer a referral for genetic testing and when (Barton et al., 2018). As such, providers are left unsure of the specific genetic tests offered to families, and many providers have not received adequate training in treating autistic children and/or are unaware that genetic testing is an option for ASD (Barton et al., 2018; Malik-Soni et al., 2021). For example, the "gold-standard" diagnostic testing is often done by qualified psychologists who are not working with a medical team. As a result, of the majority of parents expressing interest in genetic testing, 83% report that they were not offered a referral by their doctor (Li et al., 2016). Child and adolescent psychiatrists may be better placed to order genetic testing, but a 2021 US survey indicated that only 32.7% had ordered a genetic test in relation to ASD in the previous 12 months (Soda et al., 2021). A mediating factor between low uptake of genetic testing and parental interest and medical guidelines recommending it is likely to be low population genetic literacy, in both families/individuals and providers. Indeed, in the survey of child and adolescent psychiatrists, those who had requested genetic testing related to ASD reported higher self-rated knowledge of genetic testing and higher perceived utility of genetic testing than those who had not (Soda et al., 2021). While this is to be expected perhaps, we suggest that there is work to be done in, for example, addressing the 50% or more of doctors in this survey who did not order genetic testing related to ASD even though they self-reported "good" or "very good" on both knowledge of genetic testing guidelines in psychiatry and knowledge about how to integrate genetic testing into practice (Soda et al., 2021).

DISCUSSION AND FUTURE DIRECTIONS

For individuals and families affected by ASD, high genetic literacy indicates that one understands the genetic and environmental risk factors for ASD and can use this information to determine whether to pursue genetic testing. Parents with a positive association with genetic research are also more likely to support ASD genetic testing for their child (Floyd and Xu, 2017). In addition, those with higher genetic literacy are more willing to apply this knowledge to personal health decisions, potentially lessening the burden of any genetically based disease (Chapman et al., 2019; Mboowa and Sserwadda, 2019). Movements to involve families living with ASD in genetic research are already addressing this goal. One example is the SPARK project, which aims to be "the largest genetic study of autism ever." In addition to creating and providing educational resources, SPARK has established a database that connects autistic individuals to researchers with the goal of developing new supports and treatments (Feliciano et al., 2018). It is important to note that some autistic advocates do not trust genetic or genomic research and have concerns about potentially harmful uses of technologies in this area. Improving interaction between autistic individuals and genetic researchers both fosters a collaborative and trusting relationship between healthcare professionals and their patients and improves accuracy of genetic education, in turn leading to higher genetic literacy.

We thus believe that healthcare will be improved by future research investigating genetic literacy rates in multiple

population samples, and suggest that ASD is an illustrative test case where more research would be beneficial. Sufficient research can be followed by development of targeted genetic education resources addressing populations with lower genetic literacy. Examples include explainer websites targeted to families looking for resources at the time of diagnosis, like https://www.autismspeaks.org/expert-opinion/should-i-or-we-have-genetic-testing-autism or https://www.spectrumnews.org/news/genetic-testing-autism-explained/, or animated explainer videos such as https://youtu.be/LGQUE8fTx_A. Because the current level of genetic literacy is not sufficient to ensure individuals are educated to make informed decisions about their genetic information and health, we also recommend further research investigating genetic literacy and its relationship to attitudes toward genetic testing. Understanding the barriers to genetic literacy and genetic testing will help ensure equitable access to these rapidly expanding genetic technologies.

AUTHOR CONTRIBUTIONS

IL wrote the first draft of the manuscript. CG wrote sections and edited the manuscript. Both authors edited, read, and approved the submitted version.

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A Web Screening on Educational Initiatives to Increase Citizens' Literacy on Genomics and Genetics

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Introduction: Population awareness and empowerment in omics sciences represent a fundamental driver to increase the adoption of evidence-based approaches in personalized medicine. In this context, a pivotal role is played by citizens' literacy, and educational initiatives carried out in this context are key assets to drive future effective interventions. With the present study, we summarized the educational initiatives conducted worldwide aimed at increasing citizens' literacy in omics sciences.

Materials and Methods: We conducted a web search of the educational initiatives aimed at improving citizens' literacy in omics sciences undertaken worldwide, by using three search engines (Google, Bing, and Yahoo Search), in English and in Italian languages.

Results: We identified five initiatives in Europe, 22 in non-European countries, and 13 in Italy. Overall, the majority (69%) were web-based initiatives, while 31% required in-person attendance. The online initiatives included web pages for reading, online lessons/courses, web portals, videos/short movies, animations, and apps for mobile devices. The residential initiatives, on the other hand, included exhibitions, seminars, courses, symposia, information stands in public places, guided visits to research laboratories, and interactive laboratories. All the initiatives were highly heterogeneous in terms of methodologies and the topics addressed.

Discussion and Conclusion: Overall, we identified a variety of initiatives aimed at improving citizens' literacy in omics sciences, with the largest majority carried out in the United States and being web-based. Our results showed heterogeneity among the initiatives as to the dealt topics and the adopted methods. Further research is needed, however, to quantitatively assess the effectiveness of educational initiatives to improve citizens' literacy in omics sciences.

Keywords: citizens, literacy, omics sciences, personalized medicine, initiatives

INTRODUCTION

Advancements in the omics field promise a new era of personalized medicine (PM) in healthcare. A major promise of the "omics" research is that of delivering new information that can transform healthcare through earlier diagnosis, more effective prevention programs, and a higher precision in the treatment of disease (Boccia, 2014). Even though the integration of PM into practice is yet to happen in many health systems and countries worldwide, the exponential growth of knowledge in this field, the increasing costs of new technologies, and, sometimes, the lack of regulation make public health and health systems face a number of challenges (Ricciardi and Boccia, 2017). Among them, health systems should be prepared to face such a profound change in healthcare in order to allow for a better alignment of current research and clinical practice and to allow equitable access to new practices to all citizens and patients. In addition, the adoption of omics technologies and practices will require citizens to be appropriately aware of their benefits, risks, and real utility. This might be achieved through the improvement of literacy of healthcare professionals and citizens (Etchegary and Wilson, 2013; Calabrò et al., 2020). Increasing citizens' literacy requires not only specific initiatives aimed at the appropriate and conscious utilization of the new "omics" technologies but also correct information of users, for example, on the direct-to-consumer genetic tests (DTC-GTs) (Pearce et al., 2019; Hoxhaj et al., 2020; Pastorino et al., 2021). Educational initiatives are therefore needed to allow citizens to acquire correct and reliable information on both the benefits and possible risks of PM in order to make appropriate health decisions supported by healthcare professionals (Ricciardi and Boccia, 2017) and to become active players in the decision-making process (Etchegary and Wilson, 2013), as already highlighted in the *Vision Paper on Personalised Medicine Research and Implementation by 2030* from the International Consortium for Personalised Medicine (ICPerMed) (International Consortium for Personalised Medicine, 2019).

To date, the landscape of existing citizens' literacy initiatives on omics sciences across the world is fragmented and sparse, even though some efforts were put in place for their identification (Genomic Literacy Education and Engagement (GLEE) initiative, 2017). The current knowledge of such initiatives is urgently needed across Europe, however, in order to design future educational initiatives that build up on a common knowledge base. In this context, national authorities in Europe are paying great attention to citizens' literacy in omics sciences. As an example, Genomics England has been carrying out several public engagement activities in the United Kingdom over recent years (Samuel and Farsides, 2018). As for Italy, this is witnessed by the National Plan for Innovation of the Health System based on omics sciences, which addresses literacy of all stakeholders as a prerequisite for the correct implementation of omics sciences into practice (Boccia et al., 2017). To this aim, we attempted to summarize all the educational initiatives aimed at improving citizens' literacy in the field of omics sciences in the context of a project funded by the National Center for Disease Prevention and Control (CCM) of the Italian Ministry of Health through a web screening of ongoing and past initiatives worldwide, with a particular focus on Italy and English-speaking countries.

MATERIALS AND METHODS

Search Strategy

We conducted a web search of online and in-person educational initiatives carried out in European and non-European countries aimed at educating citizens in the field of omics sciences without limit of the age of the target population. An additional focus was dedicated to Italian initiatives.

The search was conducted using the three most used web search engines worldwide: Google, Bing, and Yahoo Search (Statista, 2021). The search was limited to articles published in English and Italian languages and was performed in June 2020.

We used the following terms for the web search in Google using its "advanced search" application[1]: (genetics OR genomics OR omics sciences) AND education AND initiatives AND citizens. The search was repeated with the same terms in the Italian language, as follows: (genetica OR genomica OR scienze omiche) AND formazione AND iniziative AND cittadini. This search strategy was also used as the template for the search in other search engines.

After the launch of the search through the string, we filtered the results according to the categories "all" and "news" in order to find textual records relevant to our research aim and eligibility criteria, and no limits according to file type or date of publication were applied.

Two researchers (GC and MS) independently screened the identified records by title, abstract, and summary, whenever available, in order to identify the eligible initiatives. A database of relevant records from the screening stage was created using an Excel spreadsheet, and full texts or full web pages of these records were further assessed against our research aim and our eligibility criteria by two researchers (GC and MS) independently. Any discrepancy on the inclusion of the identified records was solved by discussion or by the involvement of a third researcher (SB).

Starting from the relevant pages identified, we performed a secondary search for other relevant initiatives that were suggested or mentioned on the web page using web links and articles retrieved at each web page. In addition, we manually searched the list of references of each relevant document and web page, if available.

Eligibility Criteria

Eligible initiatives were those dealing with omics sciences and addressing citizens and those reporting the title and a minimum set of information including the target population, dealt topics, and aim. Initiatives aimed at students and teachers (up to high schools) were also included, while structured courses or degree courses promoted by universities were excluded.

[1]https://www.google.com/advanced_search

Data Extraction and Synthesis of Results

For each eligible initiative, two researchers (GC and MS) independently extracted the following information: name of initiative/project, country (and city for Italian initiatives requiring in-person attendance), period or year, organizer/promoter of the initiative, topic, type of initiative, target population, and type of attendance (in-person or digital). Any discrepancy in data extraction was solved by discussion, or with the involvement of a third researcher (SB) whenever agreement between the first two researchers (GC and MS) was not achieved through discussion.

We summarized the results using a narrative descriptive synthesis (Ryan, 2013), focusing on similarities and differences regarding the following extracted characteristics of the identified initiatives: topic, target population, and type of required attendance. These results were grouped and synthesized according to three categories: European initiatives excluding Italy, non-European initiatives, and Italian initiatives.

Preliminary findings were previously reported in brief elsewhere (Sassano et al., 2020). Here, we summarize the final results of our study.

RESULTS

The search in English language produced 1,871 results (57 on Google, 907 on Bing, and 907 on Yahoo Search), while 1,458 results were yielded through the search in Italian language (51 on Google, 570 on Bing, and 837 on Yahoo Search). Details of the selection process are reported in the flowchart in **Figure 1**. After initial screening, 83 records were further assessed through examination of full texts or full web pages. Lastly, following in-depth examination of the identified records, we included 34 records, with five more identified through secondary search, thus leading to a total of 39 included initiatives: five conducted in Europe excluding Italy (yourgenome, 2017; GenoME, 2018; European Researchers' Night, 2021; Navarrabiomed, 2021; Orphanet, 2021), 22 in non-European countries (HudsonAlpha, 2011, 2021; Genetic Science Learning Center of University of Utah Health Sciences, 2015, 2018; Yale University, 2016; 23andMe, 2021; Cold Spring Harbor Laboratory, 2021a,b; Columbia University Medical Center Division of Molecular Genetics, 2021; Department of Education of the American Museum of Natural History, 2021; DiseaseInfoSearch, 2021; Genes in Life, 2021; Genetic Literacy Project, 2021; Genome, 2021; GenomeQuébec, 2021; iBiology, 2021; MyGenome App, 2021; National Center for Advancing Translational Sciences, 2021; National Human Genome Research Institute, 2021a,b,e; Understanding Genetics, 2021), and 13 in Italy (European Researchers' Night, 2021; Fondazione Telethon, 2021; Genetica biologia e salute, 2021; Istituto Italiano per la Medicina Genomica, 2021; Istituto Superiore di Sanità, 2021; Muse- Museo delle Scienze di Trento, 2021; Museo Tridentino di Scienze Naturali, 2021; Palazzo delle Esposizioni, 2021; Polo d'Innovazione di Genomica Genetica e Biologia, 2021; Portale Italiano delle Malattie Complesse, 2021; Scienze a Scuola, 2021; Università della Calabria, 2021; Zanichelli Aula di scienze, 2021; **Supplementary Tables 1–5**). One of the retrieved initiatives involved several countries, but since it is a web-based initiative, hence with no in-person events around the involved countries, it is reported only once in a single category, according to the country where it was originally founded (Orphanet, 2021).

The five initiatives conducted in European countries other than Italy addressed citizens/general population (yourgenome, 2017; GenoME, 2018; European Researchers' Night, 2021; Navarrabiomed, 2021; Orphanet, 2021; **Supplementary Tables 1**, **2**). Among the non-European ones, 15 initiatives addressed citizens/general population (HudsonAlpha, 2011, 2021; 23andMe, 2021; Cold Spring Harbor Laboratory, 2021a,b; Columbia University Medical Center Division of Molecular Genetics, 2021; DiseaseInfoSearch, 2021; Genes in Life, 2021; Genetic Literacy Project, 2021; iBiology, 2021; MyGenome App, 2021; National Center for Advancing Translational Sciences, 2021; National Human Genome Research Institute, 2021a,b; Understanding Genetics, 2021), six addressed students and/or teachers (Genetic Science Learning Center of University of Utah Health Sciences, 2015, 2018; Yale University, 2016; Department of Education of the American Museum of Natural History, 2021; GenomeQuébec, 2021; National Human Genome Research Institute, 2021e), and one involved both categories (Genome, 2021; **Supplementary Tables 3**, **4**). Among the Italian initiatives, six addressed citizens/general population (European Researchers' Night, 2021; Fondazione Telethon, 2021; Istituto Superiore di Sanità, 2021; Muse- Museo delle Scienze di Trento, 2021; Palazzo delle Esposizioni, 2021; Portale Italiano delle Malattie Complesse, 2021), six addressed students and/or citizens (Genetica biologia e salute, 2021; Istituto Italiano per la Medicina Genomica, 2021; Polo d'Innovazione di Genomica Genetica e Biologia, 2021; Scienze a Scuola, 2021; Università della Calabria, 2021; Zanichelli Aula di scienze, 2021), and one addressed both (Museo Tridentino di Scienze Naturali, 2021; **Supplementary Tables 5**, **6**).

Overall, 31% (n = 12) of the retrieved initiatives required in-person attendance (Yale University, 2016; European Researchers' Night, 2021; Genetica biologia e salute, 2021; Genome, 2021; Istituto Italiano per la Medicina Genomica, 2021; Muse- Museo delle Scienze di Trento, 2021; Museo Tridentino di Scienze Naturali, 2021; National Human Genome Research Institute, 2021e; Navarrabiomed, 2021; Palazzo delle Esposizioni, 2021; Polo d'Innovazione di Genomica Genetica e Biologia, 2021; Università della Calabria, 2021), including exhibitions, seminars, courses, symposia, information stands in public places, guided visits to research laboratories, and interactive laboratories, while 69% (n = 27) were web-based resources (HudsonAlpha, 2011, 2021; Genetic Science Learning Center of University of Utah Health Sciences, 2015, 2018; yourgenome, 2017; GenoME, 2018; 23andMe, 2021; Cold Spring Harbor Laboratory, 2021a,b; Columbia University Medical Center Division of Molecular Genetics, 2021; Department of Education of the American Museum of Natural History, 2021; DiseaseInfoSearch, 2021; Fondazione Telethon, 2021; Genes in Life, 2021; Genetic Literacy Project, 2021; GenomeQuébec, 2021; iBiology, 2021; Istituto Superiore di Sanità, 2021; MyGenome App, 2021; National Center for Advancing Translational Sciences, 2021;

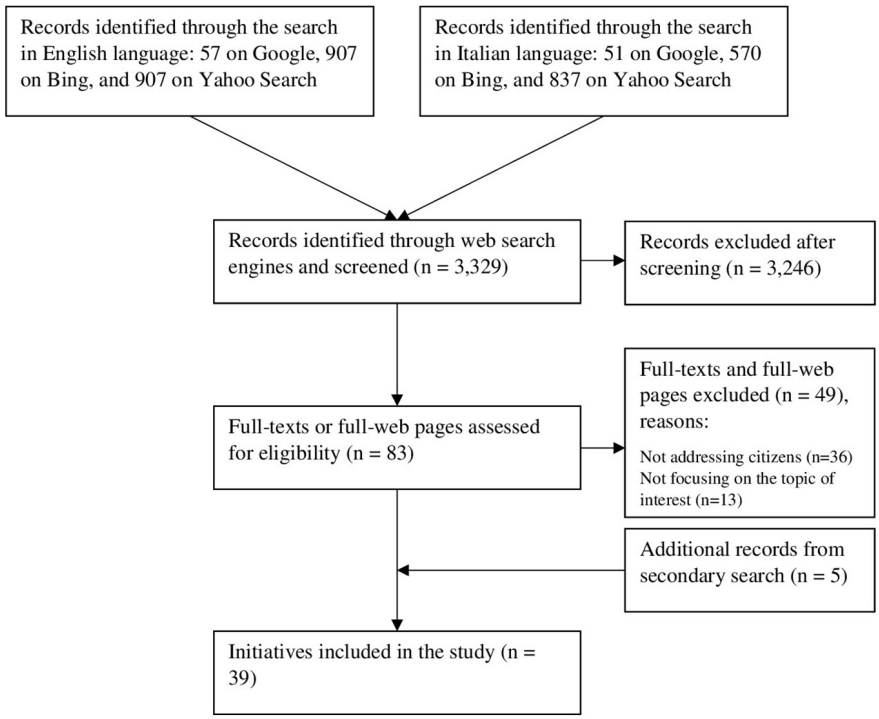

FIGURE 1 | Flowchart of the selection process.

National Human Genome Research Institute, 2021a,b; Orphanet, 2021; Portale Italiano delle Malattie Complesse, 2021; Scienze a Scuola, 2021; Understanding Genetics, 2021; Zanichelli Aula di scienze, 2021). The latter were highly heterogeneous and included web pages for reading and consultation by the public, online lessons and courses, web portals aimed at giving information and advice, videos and short movies, animations, and apps for mobile devices. The identified initiatives focused mainly on genomics, in particular on the following topics: basic concepts of cellular biology and genetics, genetic risks of diseases, modern genome sequencing techniques, genetic tests, and the clustered regularly interspaced short palindromic repeats (CRISPR) technique, which is a gene editing tool (**Supplementary Tables 1–5**).

European Initiatives

We identified five initiatives, of which two were performed in the United Kingdom (yourgenome, 2017; GenoME, 2018), two involved several European countries and cities (also non-European countries in one case) (European Researchers' Night, 2021; Orphanet, 2021), and one was conducted in Spain (Navarrabiomed, 2021; **Supplementary Table 1**). Two initiatives required in-person attendance (European Researchers' Night, 2021; Navarrabiomed, 2021), while three were web-based resources (yourgenome, 2017; GenoME, 2018; Orphanet, 2021), all involving the general population (**Supplementary Table 1**). One of the two in-person educational initiatives was promoted by the European Commission, with the 2018 and 2019 editions of "European Researchers' Night" (European Researchers' Night, 2021), which involved several cities across Europe with events focused on genetics, genomics, or omics sciences. In particular, four identified events were carried out in the United Kingdom, two in Ireland, two in Germany, one in Poland, and one in Spain. The project "European Researchers' Night" allows the organization of scientific events every year, with the aim of making citizens more aware of science and of researchers' daily activities and outputs (**Supplementary Table 2**). The second in-person event was organized by the Spanish company Navarrabiomed, which periodically organizes informative events open to citizens. An example is the event "¿Quieres visitar Navarrabiomed?" on November 6, 2019 (Navarrabiomed, 2021) that offered the general population the opportunity to visit a biomedical research center and understand the organization.

The three web-based resources identified are two websites and an application for tablets, both addressing the general population (yourgenome, 2017; GenoME, 2018; Orphanet, 2021; **Supplementary Table 1**). In detail, the interactive website yourgenome (2017) from the Public Engagement Team and scientists of the Wellcome Genome Campus, United Kingdom, is a resource for the general population to improve knowledge on genetics and genomics. The web platform hosts videos and interactive activities on a number of topics (e.g., DNA, genome sequencing, and DTC-GTs). On the other hand, the application GenoME (available only for Apple iPads) (GenoME, 2018) allows users to explore four Personal Genome Project United Kingdom ambassadors' genetic codes and characteristics, for example, the ethnic origin, eye color, health, smoking habit, and age. Information are presented through animations and videos, and a musical interpretation of the genetic code can

also be listened to by users. This application has the purpose of making citizens improve their knowledge about the human genome and understand how genetic variants could predict some phenotypic traits. Lastly, the Orphanet website is a web portal of rare diseases and orphan drugs, with the aim of spreading high-quality information among all the stakeholders. Orphanet was originally founded in France by the Institut National de la Santé et de la Recherche Médicale (INSERM) in 1997 and co-funded over the years by the European Commission, but gradually expanded to over 40 countries all over the world. Its website hosts an encyclopedia reporting information about rare diseases and the genes involved in their development, orphan drugs, patient associations, centers of excellence for the care of specific diseases, laboratories for the diagnosis of rare diseases, ongoing research projects, clinical trials, and biobanks.

Non-European Initiatives

We identified 22 initiatives carried out in non-European countries (HudsonAlpha, 2011, 2021; Genetic Science Learning Center of University of Utah Health Sciences, 2015, 2018; Yale University, 2016; 23andMe, 2021; Cold Spring Harbor Laboratory, 2021a,b; Columbia University Medical Center Division of Molecular Genetics, 2021; Department of Education of the American Museum of Natural History, 2021; DiseaseInfoSearch, 2021; Genes in Life, 2021; Genetic Literacy Project, 2021; Genome, 2021; GenomeQuébec, 2021; iBiology, 2021; MyGenome App, 2021; National Center for Advancing Translational Sciences, 2021; National Human Genome Research Institute, 2021a,b,e; Understanding Genetics, 2021), and their characteristics are summarized in **Supplementary Table 3**. The vast majority were carried out in the United States (HudsonAlpha, 2011, 2021; Genetic Science Learning Center of University of Utah Health Sciences, 2015, 2018; Yale University, 2016; 23andMe, 2021; Cold Spring Harbor Laboratory, 2021a,b; Columbia University Medical Center Division of Molecular Genetics, 2021; Department of Education of the American Museum of Natural History, 2021; DiseaseInfoSearch, 2021; Genes in Life, 2021; Genetic Literacy Project, 2021; Genome, 2021; iBiology, 2021; MyGenome App, 2021; National Center for Advancing Translational Sciences, 2021; National Human Genome Research Institute, 2021a,b,e; Understanding Genetics, 2021), while one was in Canada (GenomeQuébec, 2021). Overall, three initiatives required in-person attendance (Yale University, 2016; Genome, 2021; National Human Genome Research Institute, 2021e), while 19 were web-based resources (HudsonAlpha, 2011, 2021; Genetic Science Learning Center of University of Utah Health Sciences, 2015, 2018; 23andMe, 2021; Cold Spring Harbor Laboratory, 2021a,b; Columbia University Medical Center Division of Molecular Genetics, 2021; Department of Education of the American Museum of Natural History, 2021; DiseaseInfoSearch, 2021; Genes in Life, 2021; Genetic Literacy Project, 2021; GenomeQuébec, 2021; iBiology, 2021; MyGenome App, 2021; National Center for Advancing Translational Sciences, 2021; National Human Genome Research Institute, 2021a,b; Understanding Genetics, 2021). Among those requiring in-person attendance, two addressed students and/or teachers (Yale University, 2016; National Human Genome Research Institute, 2021e) and one involved also the general population (Genome, 2021; **Supplementary Table 3**). As for the initiatives aimed at teachers and/or students, the National Human Genome Research Institute (NHGRI) in the United States offered to science teachers a short course in genomics during the summer of 2019 in order to improve their knowledge on the field (National Human Genome Research Institute, 2021e). Furthermore, Yale University (United States), during the second Pathways to Genomics and Proteomics Day in 2016, allowed 25 middle and high school students to spend a day focused on omics sciences and PM, with explanations and interactive activities about genomics (Yale University, 2016). Similarly, the exhibition "Genome: Unlocking Life's Code" (Genome, 2021), held in 2013, also addressed the general population and was realized to celebrate the 10th anniversary of the completion of the Human Genome Project. In addition, lectures, symposia, and discussion groups were developed with the aim of exploring the topics of the exhibition and are available to watch on YouTube (**Supplementary Table 4**). Among the identified web-based resources, four addressed students and/or teachers (Genetic Science Learning Center of University of Utah Health Sciences, 2015, 2018; Department of Education of the American Museum of Natural History, 2021; GenomeQuébec, 2021), while 15 addressed the general population (HudsonAlpha, 2011, 2021; 23andMe, 2021; Cold Spring Harbor Laboratory, 2021a,b; Columbia University Medical Center Division of Molecular Genetics, 2021; DiseaseInfoSearch, 2021; Genes in Life, 2021; Genetic Literacy Project, 2021; iBiology, 2021; MyGenome App, 2021; National Center for Advancing Translational Sciences, 2021; National Human Genome Research Institute, 2021a,b; Understanding Genetics, 2021; **Supplementary Table 3**). As for the former, we identified the online course "Genetics, Genomics, Genethics" (Department of Education of the American Museum of Natural History, 2021), held in October 2019, that targeted middle and high school teachers and focused on the relationships between genetics and genomics and the legal, social, and ethical aspects. On the other hand, the Genetic Science Learning Center of University of Utah Health Sciences (United States) set up two websites – Teach.Genetics (Genetic Science Learning Center of University of Utah Health Sciences, 2015) and Learn.Genetics (Genetic Science Learning Center of University of Utah Health Sciences, 2018) – aimed at teachers and students, respectively. Both offer a vast choice of information and resources to support teaching in topics related to genomics and PM. Similarly, on the website of the non-profit organization GenomeQuébec (Canada), there is a platform for the education of high school students, mostly focused on basic genetic concepts (GenomeQuébec, 2021).

Among the 19 web-based resources aimed at the general population, the Educational Resources (National Human Genome Research Institute, 2021b), Fact Sheets about Genomics (National Human Genome Research Institute, 2021c), Talking Glossary of Genetic Terms (National Human Genome Research Institute, 2021f), and Introduction to Genomics (National Human Genome Research Institute, 2021d) sections on the website of the NHGRI (United States) are aimed at informing

citizens about genetics and genomics (details in **Supplementary Table 3**). In addition, to celebrate the 15th anniversary of the completion of the Human Genome Project, the NHGRI launched in April 2018 a campaign called "15 for 15" (National Human Genome Research Institute, 2021a), explaining 15 ways genomics transformed and is transforming the world. We identified additional web resources aimed at improving citizens' knowledge of genetics and genomics through readings or multimedia activities, including "DNA from the Beginning" (translated also in languages other than English) (Cold Spring Harbor Laboratory, 2021a), the application for mobile devices and the website of iCell (HudsonAlpha, 2021) ICell), the website of the private company 23andMe (2021), the platform iBiology (iBiology, 2021), the platform Genes in Life (2021), the website Learning Genetics (Columbia University Medical Center Division of Molecular Genetics, 2021), the interactive application GenomeCache (available for Apple devices) (HudsonAlpha, 2011), the application MyGenome App (available for Apple iPads) (MyGenome App, 2021), and the website Eugenics Image Archive (focused on the American eugenics movement) (Cold Spring Harbor Laboratory, 2021b; **Supplementary Table 3**).

Also, the website Understanding Genetics: Ask-a-Geneticist (Understanding Genetics, 2021) reports questions about genetics by individuals living all over the world, with related answers by graduate and postdoctoral fellows of the Department of Genetics of Stanford University (United States).

In addition, we identified two web resources focused on rare diseases. The first one is the Genetic and Rare Diseases Information Center (GARD, United States) (National Center for Advancing Translational Sciences, 2021), which aims to provide reliable, high-quality, simple, and updated information regarding rare diseases through its website, in English and Spanish. The second one is the website DiseaseInfoSearch (United States) (DiseaseInfoSearch, 2021), which contains a database of more than 10,000 diseases, including genetic ones.

Lastly, we identified the Genetic Literacy Project (GLP, United States) (Genetic Literacy Project, 2021), which is a non-profit association and includes also the Epigenetics Literacy Project and the Genetic Expert News Service (GENeS). The final aim of the association is to promote the diffusion of knowledge about human, animal, and plant genetics and genomics among the general population through the publication on its website of informative articles and videos addressing citizens' literacy in these topics.

Italian Initiatives

The search engine in Italian language produced a total of 13 initiatives carried out in Italy, whose details are reported in **Supplementary Tables 5**, **6** (European Researchers' Night, 2021; Fondazione Telethon, 2021; Genetica biologia e salute, 2021; Istituto Italiano per la Medicina Genomica, 2021; Istituto Superiore di Sanità, 2021; Muse- Museo delle Scienze di Trento, 2021; Museo Tridentino di Scienze Naturali, 2021; Palazzo delle Esposizioni, 2021; Polo d'Innovazione di Genomica Genetica e Biologia, 2021; Portale Italiano delle Malattie Complesse, 2021; Scienze a Scuola, 2021; Università della Calabria, 2021; Zanichelli Aula di scienze, 2021).

Among them, eight required in-person attendance (European Researchers' Night, 2021; Genetica biologia e salute, 2021; Istituto Italiano per la Medicina Genomica, 2021; Muse- Museo delle Scienze di Trento, 2021; Museo Tridentino di Scienze Naturali, 2021; Palazzo delle Esposizioni, 2021; Polo d'Innovazione di Genomica Genetica e Biologia, 2021; Università della Calabria, 2021), while five were web-based resources (Fondazione Telethon, 2021; Istituto Superiore di Sanità, 2021; Portale Italiano delle Malattie Complesse, 2021; Scienze a Scuola, 2021; Zanichelli Aula di scienze, 2021; **Supplementary Table 5**). Among the eight initiatives requiring physical attendance, four addressed students and/or teachers (Genetica biologia e salute, 2021; Istituto Italiano per la Medicina Genomica, 2021; Polo d'Innovazione di Genomica Genetica e Biologia, 2021; Università della Calabria, 2021), three addressed the general population (European Researchers' Night, 2021; Muse- Museo delle Scienze di Trento, 2021; Palazzo delle Esposizioni, 2021), while one addressed both (Museo Tridentino di Scienze Naturali, 2021; **Supplementary Table 4**).

In Italy, a number of initiatives aimed at students and/or teachers took place in recent years (**Supplementary Table 5**). The most recent one is the project "High School Open Days Terni" (Polo d'Innovazione di Genomica Genetica e Biologia, 2021), which took place in Central Italy (Terni, Umbria Region) for 3 days in May 2019. The project aimed to make high school students learn about the research facility named "Polo d'Innovazione di Genomica, Genetica e Biologia" in the city of Terni. Other similar activities included "Vivere la scienza" ("To live science") (Istituto Italiano per la Medicina Genomica, 2021) that took place in Turin (Piemonte Region) in 2018, consisting of interactive activities and laboratories that allowed students to carry out experiments focused on specific genetic topics, such as DNA fingerprinting, enzymes (e.g., β-galactosidase), DNA extraction, PCR technique, and genetic polymorphisms. Similar initiatives were the "Genetica, biologia e salute" ("Genetics, biology, and health") (Genetica biologia e salute, 2021), held in Trento (Trentino Alto Adige Region) in 2009 and addressed middle and high school teachers, with the aim of improving their knowledge in the genetic field. Lastly, an initiative that took place in Southern Italy, titled OpenLab (Università della Calabria, 2021), was undertaken in 2017 by the University of Calabria. OpenLab is an interactive laboratory project funded by the Italian Ministry of University and Research and addresses middle and high school students, aiming to make students learn more about molecular genetics and the human genome.

Among the initiatives aimed at the general population, we identified two exhibitions organized by two Italian museums: the first, entitled "Genoma umano. Quello che ci rende unici" ("Human genome. What makes us unique") (Muse- Museo delle Scienze di Trento, 2021), held in Trento in 2019 and the second one, called "DNA. Il grande libro della vita da Mendel alla genomica" ("DNA. The great book of life from Mendel to genomics") (Palazzo delle Esposizioni, 2021), held in Rome in 2017.

The exhibition in Trento merged biological themes, such as DNA, genetic traits, mutations, and DTC-GTs, with a humanistic and artistic language. The aim of the exposition was to stimulate

the public's interest in such topics while paying attention to the ethical, social, and legal implications (ELSI) as well. On the other hand, the Roman exhibition was focused on the general aspects of genetics/genomics and was supplemented by a series of meetings and seminars open to the public.

Furthermore, among the events promoted by the 2019 and 2018 editions of the project "European Researchers' Night" (European Researchers' Night, 2021) in Italian cities, there were some focused on omics sciences. They are reported in detail in **Supplementary Table 6**.

Lastly, five web-based resources were identified (Fondazione Telethon, 2021; Istituto Superiore di Sanità, 2021; Portale Italiano delle Malattie Complesse, 2021; Scienze a Scuola, 2021; Zanichelli Aula di scienze, 2021; **Supplementary Table 5**). Among them, two addressed students and/or teachers, namely, the projects "Scienze a Scuola" ("Science at school") and "Aula di Scienze" ("Science classroom") (Scienze a Scuola, 2021; Zanichelli Aula di scienze, 2021), while three addressed the general population, which are the "Portale Italiano delle Malattie Complesse" ("Italian Portal of Complex Diseases") (Portale Italiano delle Malattie Complesse, 2021), "Info_rare" (Fondazione Telethon, 2021), and "ISSalute" (Istituto Superiore di Sanità, 2021). These initiatives aim, through dedicated platforms, to provide citizens with useful information on rare and complex genetic diseases. Lastly, in 2009, an event titled "Bioweek: La nuova biologia per la salute della persona e del pianeta" ("Bioweek: the new biology for the health of the person and of the planet") (Museo Tridentino di Scienze Naturali, 2021) that included a series of public events, such as seminars, round tables, public performances, and entertainment, was organized in Trento. This initiative addressed a wide public, including healthcare professionals, students, teachers, and the general population, with the aim of informing about the recent progress and developments of the health sciences and the impact of new biological knowledge on human health and the environment.

DISCUSSION

The need to inform and educate citizens in the omics sciences is a natural consequence of the disruptive development in this field since the sequencing of the human genome (International Human Genome Sequencing Consortium, 2004) imposes the necessity to identify the best tools, in terms of effectiveness and costs, to reach this goal. The aim of our study was to summarize the initiatives aimed at improving citizens' literacy in omics sciences that can be retrieved over the web. Even though the aim was not to assess which countries are at the forefront in citizen engagement on omics sciences, the results suggest that greater attention to this topic is paid in the United States, although the results might be influenced by the search strategy adopted. Most companies providing new technologies such as DTC-GTs are based in the United States, which could be a possible explanation to the greater effort put in place for informing and educating citizens. This is further confirmed by a recent research showing that individuals educated in the United States had a significant better knowledge compared to those in other countries (Chapman et al., 2019). As for Italy, the relevance of increasing citizens' literacy in omics sciences was recognized by authorities through specific national policies implemented over recent years, such as the National Guidelines on Public Health Genomics and the National Plan for Innovation of the Health System based on omics sciences, hence paving the way for specific research projects in this field (Presidenza del Consiglio dei Ministri, 2013; Boccia et al., 2014, 2017; Gazzetta Ufficiale, 2018).

From our study, we reported that a relevant number of initiatives addressed students and/or teachers, who have a crucial role in the spread of knowledge among the youth, revealing particular interest toward the education of future generations. In particular, almost half of the Italian initiatives and one-third of the non-European ones targeted the school population, underlining the importance of informing and educating young individuals. On the other side, all of the European initiatives included in our study were directed to the general population.

As for the type of identified initiatives, a few required in-person attendance, while most of them were web-based resources. In detail, more than half of the European initiatives and more than two-thirds of the non-European ones were web-based. As desirable, given the considerable development and growing use of the Internet and social networks in recent decades, this further underlines proper consideration of such information means, which could make it possible to reach especially younger groups of the population (Anderson and Jiang, 2018). On the contrary, Italy showed a different tendency, with more than half of the identified Italian initiatives requiring in-person attendance, suggesting the need to strengthen the use of digital means for public outreach, even if not neglecting the importance of events with in-person attendance. Both initiatives requiring physical attendance and web-based instruments identified through our search were highly heterogeneous. In detail, the former included exhibitions, seminars, courses, symposia, informative stands in public places, guided visits to research laboratories, and interactive laboratories, while the latter included web pages for reading and consultation by the public, online lectures and courses, web portals aimed at giving information and advice, videos and short movies, animations, and apps for mobile devices.

The heterogeneity among the retrieved resources is further confirmed by the topics addressed. Indeed, even though most of the initiatives focused on basic concepts of cellular biology, genetics, and genetic risks of diseases, some of them paid attention to more specific and complex topics as well, such as modern genome sequencing techniques, genetic tests, and the CRISPR method.

Such heterogeneity of both methods and dealt topics was found for all categories of initiatives included in our study, namely, European, non-European, and the Italian ones. This suggests that the landscape of topics dealt by citizen engagement initiatives in omics sciences, even if largely limited to genomics, is currently vast. In addition, several methods might be useful and effective to improve citizens' literacy in this field; however, quantitative research is needed for a more accurate comparison.

Our work is the first attempt to summarize past and ongoing initiatives addressing citizens in the omics sciences field using

a web search with a systematic and scientific approach. These results might be useful as a knowledge base for the design of future educational efforts. As for Italy, in particular, well-designed initiatives and strategies are requested to implement the National Plan for Innovation of the Health System based on omics sciences (Boccia et al., 2017).

Study Limitations

Our study has several limitations. In particular, the use of only English and Italian languages for our search limited the chance to identify initiatives carried out in countries in which the first language is different. A broader search of initiatives or institutions addressing public engagement more generally in health or health-related research might have allowed us to identify further initiatives, web tools, activities, or events dealing with omics sciences as well. It should also be noted that many events might have not been advertised over the web, thus minimizing the chance for us to identify them through our search. In addition, even though the search engines employed in our study are the most used worldwide, the addition of other search engines or means of communications, such as Baidu or WeChat, might have led to the identification of further initiatives, especially in Eastern countries. To this end, our search strategies might have led to results skewed toward Western countries, with Eastern countries not being represented in our results. Thus, this could limit the comprehensiveness of our findings.

Furthermore, the great heterogeneity between the retrieved resources and sometimes the lack of relevant information did not allow us to perform a precise comparison, even though we reported qualitative information and possible similarities and differences. In addition, due to the lack of data on quantitative measures and indicators reported on the websites, we could not perform a comparison of the effectiveness of the retrieved initiatives on citizens' literacy improvement.

CONCLUSION

Awareness of existing citizen educational initiatives in the field of omics sciences performed so far is essential to design future ones. In our study, we summarized the characteristics of all the events available on the web that can be used as a knowledge base to implement further citizen educational campaigns and initiatives. Nowadays, increasing citizens' literacy in omics science represents a priority for public health since more informed citizens are expected to make more appropriate choices about their health, thus having a positive impact on health systems. Further research is needed, however, in order to assess quantitatively the effectiveness of the different citizen engagement strategies in improving citizens' literacy, for example, assessing the level of knowledge or awareness of omics sciences before and after the initiative using discussion groups, questionnaires, and similar methods.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

SB and GC conceived the study. MS contributed to the study design. GC and MS identified the initiatives and extracted information from the websites/reports, critically discussed and interpreted the results of the review, and contributed equally to the drafting of the manuscript. SB critically reviewed the manuscript. All authors approved the final version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fgene.2021.637438/full#supplementary-material

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METHODS
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Creation and Worldwide Utilisation of New COVID-19 Online Information Hub for Genetics Health Professionals, Patients and Families

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The current COVID-19 pandemic has unfortunately resulted in many significant concerns for individuals with genetic disorders and their relatives, regarding the viral infection and, particularly, its specific implications and additional advisable precautions for individuals affected by genetic disorders. To address this, the resulting requirement for guidance and information for the public and for genetics professionals was discussed among colleagues nationally, on the ScotGEN Steering Committee, and internationally on the Education Committee of the European Society of Human Genetics (ESHG). It was agreed that the creation of an online hub of genetics-related COVID-19 information resources would be particularly helpful. The proposed content, divided into a web page for professionals and a page for patients, was discussed with, and approved by, genetics professionals. The hub was created and provided online at www.scotgen.org.uk and linked from the ESHG's educational website for genetics and genomics, at www.eurogems.org. The new hub provides links, summary information and representative illustrations for a wide range of selected international resources. The resources for professionals include: COVID-19 research related hubs provided by Nature, Science, Frontiers, and PubMed; clinical guidelines; the European Centre for Disease Prevention and Control; the World Health Organisation; and molecular data sources including coronavirus 3D protein structures. The resources for patients and families include links to many accessible sources of support and relevant information. Since the launch of the pages, the website has received visits from over 50 countries worldwide. Several genetics consultants have commented on usefulness, clarity, readability, and ease of navigation. Visits have originated most frequently in the United Kingdom, Kuwait, Hong Kong, Moldova, United States, Philippines, France, and Qatar. More links have been added since the launch of the hub to include

additional international public health and academic resources. In conclusion, an up-to-date online hub has been created and made freely available for healthcare professionals, patients, relatives and the public, providing categorised easily navigated links to a range of worldwide resources related to COVID-19. These pages are receiving a rapidly growing number of return visits and the authors continue to maintain and update the pages' content, incorporating new developments in this field of enormous worldwide importance.

Keywords: COVID–19, online, genetics, education, coronavirus, genomics, resources, data

INTRODUCTION

In December 2019, it was recognised that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was being transmitted through the human population and causing the potentially fatal human coronavirus disease, COVID-19. During the ensuing global pandemic, there has been enormous internet search activity worldwide for online information in relation to the virus and the disease, especially at the times of major announcements made by the World Health Organisation (WHO) (Szmuda et al., 2020a). The response from the scientific community to the COVID-19 pandemic has been rapid and extensive. Many different aspects of the disease have already been investigated and continue to be explored. As a consequence, numerous articles have been written, published, and made widely available (Cevik et al., 2020).

Many highly informative online resources in relation to COVID-19 and to the causative coronavirus have now been created. These include online hubs directly linking to original genetic scientific publications, such as the Frontiers Coronavirus Knowledge Hub in addition to those provided by Nature Journals, Science Journal, Pubmed LitCovid, the RCSB (Research Collaboratory for Structural Bioinformatics) Protein Data Bank and institutions such as the National University of Singapore. Other websites have been established to provide more summarised information for professionals, such as Nextstrain (with its animated representations of sequence-based coronavirus global epidemiological data) and also the European Reference Networks. Many of these COVID-19 information resources have been relatively recently created and may not all be well known or easily located online amongst other websites.

Although many COVID-19-related resources are accessible by the public it has been reported that many of the information sources are not easily accessible by that audience (Szmuda et al., 2020b). There are, however, several excellent COVID-19-related resources that have been created specifically for the public and, in particular, for patients affected by genetic disorders. These include the COVID-19 resources provided by Unique, the Genetic Alliance and the Contact organisation. Relevant and helpful online resources have also been created by national specialist organisations and major institutions such as the British Society for Genetic Medicine, US Centers for Disease Control and Prevention (CDC), UK National Health Service, European Centre for Disease Prevention and Control, New York's Mount Sinai Icahn School of Medicine, University of Hong Kong, Clinic Barcelona University Hospital and the World Health Organisation.

The Scottish Genetic Education Network (ScotGEN) was created by the four Scottish centres for Clinical Genetics, collaboratively with Scottish Universities, and was launched in 2005. It links all of those individuals who teach genetics for healthcare in Scotland and its website (www.ScotGEN.org.uk) provides a shared national online hub for relevant learning and teaching resources (Scottish Genetic Education Network, 2021). These encompass a wide range of genetics and genomics educational topics, including educational genomics apps (Tobias and Tobias, 2015). The website thus provides extensive information, in addition to many carefully selected web-links, for professionals and patients, to facilitate understanding of genetics and its application to everyday practice (Scottish Genetic Education Network, 2021).

Objectives

In view of the quantity and quality of individual COVID-19-related resources that had become established online around the world that were of great interest and usefulness to clinical and non-clinical genetics professionals and to the public, it was perceived by the authors, including educators and genetics health professionals, that it would be highly beneficial to create a freely accessible centralised online hub, providing direct links to a range of free, high-quality, informative and up-to-date websites. Also, given the large range of information sources available online, including some that may be less suitable for the public (Szmuda et al., 2020b), the authors have created an accompanying guide to a range of those online sources that have been generated for the public (including affected individuals and their family members).

The authors have, in this way, created an online hub providing (a) a page of concisely described links aimed at professionals, including links to websites providing regularly updated highlights (and comprehensive searches) of peer-reviewed original scientific research articles and (b) a page of similarly annotated links for patients and their families. These were added, prominently, to the existing educational web pages of the Scottish Genetic Education Network at www.ScotGEN.org.uk (Scottish Genetic Education Network, 2021).

MATERIALS AND METHODS

Initial Selection of Linked Sources

In selecting online resources to be linked directly from the new ScotGEN COVID-19 pages, a method was used that was similar to that which had been previously used in creating the EuroGEMS.org website (Tobias and Tobias, 2020). Approximately 35 websites were initially considered. The web resources were initially identified by: personal web-searches; personal use of the resources; suggestions from professional colleagues; checking the websites of major organisations in the field of genetics designed for professionals and also for patients; consulting other resources often used as reference sources by major international organisations; and the COVID-19-specific literature hubs run by major scientific publishers. Decisions with regard to source inclusion were made by this article's lead and corresponding author, based on the following inclusion criteria for online resources: (a) free-to-access, (b) high-quality (containing information that was judged as being reliable and free of obviously misleading information), (c) containing up-to-date links, without broken URLs (or "404 errors") that would suggest a failure to maintain and update the online resource, (d) useful (judged as being likely to be helpful to and understandable by the viewer), and (e) informative (providing relevant information and details). Fulfilment of all criteria was regarded as essential for inclusion. The criteria and content were discussed in detail with other professional colleagues.

In order to facilitate navigation by a user, the sources were grouped, as planned, into a page of COVID-19 Resources for genetics professionals and a separate page for patients and families affected by genetic disorders. In addition, to aid online navigation, for each linked online source, a short summary of its content and representative image was included, in addition to its title.

The new web pages and their content were discussed with a large group of clinical genetics colleagues in the West of Scotland Centre for Genomic Medicine, which serves a population of approximately 3 million. These colleagues included clinical genetic counsellors and consultants who each have many years of experience in discussing and explaining scientific concepts to members of the public, including patients and their relatives, verbally and also in printed and electronic form. The new web pages were also shown to two family doctors (general

TABLE 1 | Website names and URLs for all of the websites to which links are provided in the new web-page entitled "COVID-19 Resources for Healthcare Professionals" on the www.ScotGEN.org.uk website.

Website	Current URL
European Reference Networks (ERNs) and patient organisations	http://international.orphanews.org/summary/editorial/nl/id-200327.html
General Practitioner / GP Notebook: COVID-19 resources	https://gpnotebook.com/covid19.cfm
NHS Education for Scotland: COVID-19 Learning Materials	https://learn.nes.nhs.scot/27993/coronavirus-covid-19
European Centre for Disease Prevention and Control	https://www.ecdc.europa.eu/en
World Health Organisation	https://www.who.int
Nature Journals Coronavirus hub	https://www.springernature.com/gp/researchers/campaigns/coronavirus
Science Journal Coronavirus hub	https://www.sciencemag.org/collections/coronavirus?IntCmp=coronavirussiderail-128
LitCovid (NIH curated Coronavirus literature hub)	https://www.ncbi.nlm.nih.gov/research/coronavirus/
The Frontiers Coronavirus Knowledge Hub	https://coronavirus.frontiersin.org/?utm_campaign=sub-cov-cco&utm_medium=fhpc&utm_source=fweb
The National University of Singapore (School of Public Health) COVID-19 Research hub	https://sph.nus.edu.sg/covid-19/research/
Coronavirus—The Science Explained—An overview from the UKRI	https://coronavirusexplained.ukri.org/en/
Horizon	https://horizon-magazine.eu/topics/health
Nextstrain	https://nextstrain.org
RCSB Protein Data Bank	http://www.rcsb.org

TABLE 2 | Website names and URLs for all of the websites to which links are provided in the new web-page entitled "COVID-19 Resources for Patients and Families" on the ScotGEN.org.uk website.

Website	Current URL
Coronavirus—The Science Explained	https://coronavirusexplained.ukri.org/en/
Unique Website	https://www.rarechromo.org/covid19update/
WellChild Website	https://www.wellchild.org.uk/2020/03/18/ten-ways-to-keep-my-child-with-complex-health-needs-safe/
Genetic Alliance & Rare Disease UK pages	https://geneticalliance.org.uk/news-events/
The "Contact" Organisation	https://www.contact.org.uk/advice-and-support/coronavirus-information-for-families-with-disabled-children/
European Centre for Disease Prevention and Control	https://www.ecdc.europa.eu/en/COVID-19/national-sources
UK NHS Guidelines	https://www.nhs.uk/conditions/coronavirus-covid-19/
US Guidelines (CDC)	https://www.cdc.gov/coronavirus/2019-ncov/index.html
Fight COVID-19 (Hong Kong University)	https://fightcovid19.hku.hk
Facts and Resources (Mount Sinai, New York)	https://www.mountsinai.org/about/covid19
Clinic Barcelona (University Hospital): COVID-19	https://www.clinicbarcelona.org/en/assistance/diseases/covid-19
World Health Organisation	https://www.who.int
Detailed review of the origin of COVID-19	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7995093/
NHS UK: Coronavirus vaccine	https://www.nhs.uk/conditions/coronavirus-covid-19/coronavirus-vaccination/coronavirus-vaccine/
NHS Inform. The coronavirus vaccine. Side effects.	https://www.nhsinform.scot/covid-19-vaccine/the-vaccines/side-effects-of-the-coronavirus-vaccines
Oxford University Hospitals: COVID-19 FAQs	https://www.ouh.nhs.uk/working-for-us/staff/covid-staff-faqs-vaccine.aspx

practitioners) and five individuals who were not healthcare professionals. The pages were also discussed with the members of the ScotGEN Steering Committee and with the Education Committee of the European Society of Human Genetics. Where appropriate, any suggested additional COVID-19-related websites meeting the selection criteria were added if they had not already been incorporated.

Technical Aspects of Web-Page Creation

The webpages were created using a "waterfall" methodology, which involves the step-by-step completion of a linear (non-circular) sequence of stages and is a method often used in the development of educational websites and software. The first stage of development was research into different sites and familiarisation with the development stack which was already being used for the website. Two new pages (a professional resource list and a patient resource list) would be added to the website, as well as a modification to the homepage as an internal link. Low fidelity wireframes were then created, using some elements of the User Interface (UI) which already existed in other pages of the site in order to maintain consistency. First prototypes of the webpages were then implemented using the Bootstrap CSS library, as this was the language used for front-end development on the remainder of the website, maintaining the appearance of the website as well as maximising the loading efficiency of the webpages. Mobile optimisation was incorporated by hiding the image on each row which allows for larger text display if the screen is smaller. Web page speed was analysed using Google PageSpeed Insights (Google PageSpeed Insights, 2021).

In order to increase accessibility to potential users, additional links to the website were placed on the appropriate web-pages of the existing educational genetics web pages run on behalf of the European Society of Human Genetics at www.EuroGEMS.org (ESHG Genetic Educational Materials and Sources, 2021). Thus, a prominent link was placed on that website's page for genetics professionals and also on the page for patients and families affected by genetic conditions.

In order to be able to monitor visitor numbers to the new pages, a General Data Protection Regulation (GDPR)-compliant online service (Statcounter) was used (Statcounter, 2021).

RESULTS

The new pages were created as planned, with the page for genetics professionals containing a variety of informative resources (**Table 1**). These included sources relating to (a) COVID-19-related practical advice for healthcare, (b) Nature, Science, Frontiers, LitCovid (PubMed), and RCSB Protein Data Bank (PDB) hubs for Coronavirus research publications, (c) the COVID-19 pages of international organisations such as the World Health Organisation, European Centre for Disease Prevention and Control, and European Reference Networks, and (d) Nextstrain. Each of these websites contain much relevant information. For example, the RCSB PDB now contains data for a large number of structures for coronavirus molecules, including 3D molecular data delineating the structure of the coronavirus spike protein bound to ACE2 or to antibodies. The PDB data are freely available and are linked to the relevant research publications.

In a similar way, the new web page for patients and their families contains descriptions of, and direct links to, several relevant organisations, such as Unique, Genetic Alliance, WellChild and Contact, providing advice regarding COVID-19 for individuals with rare genetic disorders, that includes practical guidance, resources and sources of assistance. The relevant resources for the public, to which links are provided, also include those provided by the WHO, the European Centre for Disease Prevention and Control and the US Centers for Disease Control and Prevention (CDC), in addition to the Fight-COVID-19 website of Hong Kong University and the Facts and Resources web pages of Mount Sinai Medical School in New York. The full list of included websites is outlined in **Table 2**. The authors would welcome recommendations for additional links.

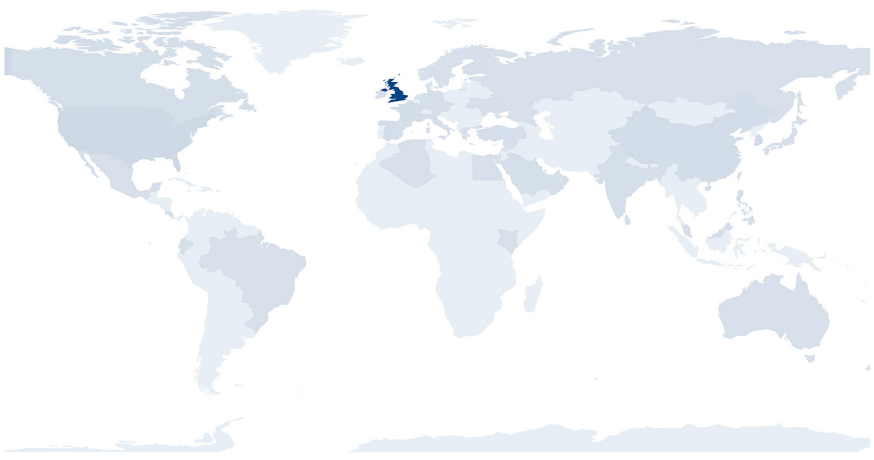

FIGURE 1 | Countries and regions of origin of visitors to the new COVID-19 web pages in the first year since launch. The intensity of shading relates to the proportion of total visits.

TABLE 3 | Countries or region of origin and respective proportions of website visits, in the first year since launch of the COVID-19 webpages.

Country or region	% of page views
United Kingdom	78.9
United States	3.5
Korea, Republic of	2.2
China	1.5
Kuwait	1.4
France	1.3
Spain	1.1
Saudi Arabia	0.8
Hong Kong	0.7
Germany	0.7
India	0.6
Canada	0.6
Philippines	0.5
Netherlands	0.4
Finland	0.4
Denmark	0.4
Malaysia	0.4
Turkey	0.3
Moldova, Republic of	0.3
Italy	0.3
Singapore	0.3
Qatar	0.3
Japan	0.3
New Zealand	0.2
Ireland	0.2
Costa Rica	0.2
Sweden	0.1
Oman	0.1
Israel	0.1
Egypt	0.1
Algeria	0.1
Czech Republic	0.1
Brazil	0.1
Bangladesh	0.1
Australia	0.1
Austria	0.1
Ukraine	0.1
Taiwan	0.1
Syrian Arab Republic	0.1
Russian Federation	0.1
Puerto Rico	0.1
Norway	0.1
Mexico	0.1
Malta	0.1
Luxembourg	0.1
Sri Lanka	0.1
Kenya	0.1
Greece	0.1
Europe	0.1
Estonia	0.1
Ecuador	0.1
Bahrain	0.1
United Arab Emirates	0.1

TABLE 4 | Names and URLs of the 10 most frequently used exit links from the new COVID-19 ScotGEN pages, together with the respective proportions of the total visits to external websites.

Website visited	% of total	Exit link (URL used)
Nature—Coronavirus research	22.2	https://www.springernature.com/gp/researchers/campaigns/coronavirus
UKRI Coronavirus Explained	20.8	https://coronavirusexplained.ukri.org/en/
LitCovid NCBI Journal Articles	11.1	https://www.ncbi.nlm.nih.gov/research/coronavirus/
Science—Coronavirus research	8.3	https://www.sciencemag.org/collections/coronavirus?IntCmp=coronavirussiderail-128
Unique. Rarechromo.org	6.9	https://www.rarechromo.org/covid19update
NHS Education for Scotland	5.6	https://learn.nes.nhs.scot/27993/coronavirus-covid-19
World Health Organisation	4.2	https://www.who.int/
RCSB Protein Data Bank	4.2	http://www.rcsb.org/
British Soc. for Genetic Medicine	2.8	https://www.bsgm.org.uk/
National University of Singapore	2.8	https://sph.nus.edu.sg/covid-19/research/

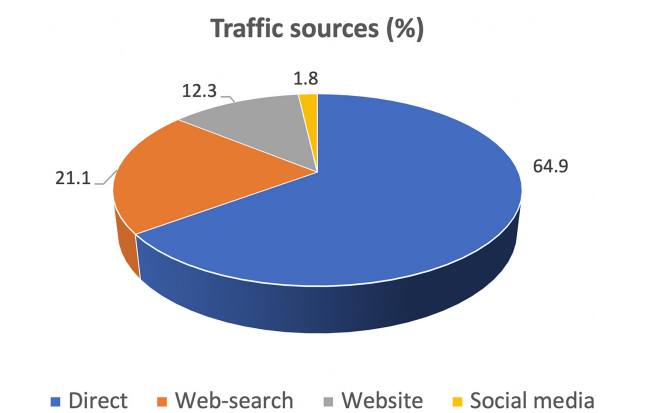

FIGURE 2 | Proportions of visits to ScotGEN's COVID-19 web pages attributable to different website traffic sources.

International Use of the ScotGEN COVID-19 Web Pages

The new COVID-19 pages on ScotGEN's website have already attracted many visitors from around the world. The visitors to the website include countries in North and South America (e.g., Brazil), Africa (e.g., Algeria), Europe, Asia (e.g., Kuwait, Japan and Singapore), and New Zealand.

The web pages were made publicly available on 24th April 2020. Using data from Statcounter.com (Statcounter, 2021), since launch of the COVID-19 webpages (approximately 1 year ago)

the website has received approximately 7175 page views (or 19–20 per day, on average), including those visits (representing approximately 64% of the total) that could not be recorded as a result of the reported rejection or blocking of cookies by internet browsers and users (Sullivan, 2020). Of the visits to the new pages that could be recorded, 53.8% of visits were to the page for patients and families, with the remaining 46.2% to the page for professionals. The websites' visitors have originated in over 50 countries (see **Figure 1** and **Table 3**) and the frequency of "returning visits" has increased by over fivefold, over a 6-month period (Statcounter, 2021).

The websites most frequently visited from the new pages are those for Nature Journals Coronavirus Research (from the professionals' page) and UKRI Coronavirus Explained (from the page for patients and their families) (**Table 4**).

Most visitors reached the ScotGEN pages directly via URL (64.9%) but just over a third reached the pages in other ways: 21.1% via web searches (for terms including "covid learning resources," of which 79.3% were performed using Google, 18.9% by Bing, 0.6% by DuckDuckGo, 0.6% by Ecosia and 0.6% by Yahoo), 12.3% via website referral and 1.8% from social media sources, principally Facebook and Twitter (**Figure 2**).

The exit links that were most frequently used, in order of decreasing frequency, were: Nature Journal coronavirus research (22.2%), UKRI Coronavirus Explained (20.8%), PubMed's LitCovid COVID-19 Articles (11.1%), Science Journal coronavirus research (8.3%), and the Unique/rarechromo.org (6.9%) website that provides guidance for individuals affected by rare genetic disorders and their families.

Testimonials

Feedback received with regard to the new pages has been highly positive, including, for example, the following comments from genetics consultants: "Looks very good to me"; "Very useful and what a good idea to bring all the resources together like this"; "Easy to navigate and what I have read is very readable and clear"; "Excellent"; and "Fabulous." Those comments were received after the webpages were presented in detail to many clinical genetic professionals, highly experienced in communicating with patients and their relatives.

DISCUSSION

Two new web-pages have been created on the ScotGEN website that have already been used by a large number of individuals from over 50 countries, worldwide. It is envisaged that providing a range of links to useful COVID-19 resources, in particular those relating to genetics, from a single hub, together with a brief summary of each website's content, will make it easier and quicker for visitors to access a range of sources of information relevant to them. This would appear to be the case already, from the feedback received, by the rapidly increasing number of returning visitors and their wide geographical distribution.

The web pages' links are continually checked to ensure the absence of "404" or "page not found" errors and where necessary, URLs are updated. New links have continued to be added since the original launch of the web pages on 24th April 2020, providing easy access for professionals and the public to additional information provided from sources located around the world. The authors would, however, welcome emailed suggestions for additional links to high-quality freely accessible online COVID-19 information sources.

Further development is planned, including the provision of additional resources and the further growth of the web pages' content.

The authors hope that readers will inform other individuals, including colleagues and members of the public, of the pages' existence, in order to maximise the number of people who can benefit from this free information hub.

DATA AVAILABILITY STATEMENT

The latest version of the information hub presented in the article, together witht its full content and all of its links to online resources, are freely available online at www.ScotGEN.org.uk. Please direct any further inquiries to the corresponding author.

AUTHOR CONTRIBUTIONS

AT and ET conceived, designed and created the COVID-19 web pages, analysed the data, created the figures and tables, and wrote the manuscript. JB, RC, ZM, and MP assisted with the page content selection and the incorporation and hosting of the web pages on the ScotGEN website and the acquisition of the necessary ScotGEN funding. All authors read and approved the final manuscript.

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Increasing Genomic Literacy Through National Genomic Projects

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Genomics is an advancing field of medicine, science, ethics, and legislation. Keeping up to date with this challenging discipline requires continuous education and exchange of knowledge between many target groups. Specific challenges in genomic education include tailoring complex topics to diverse audiences ranging from the general public and patients to highly educated professionals. National genomic projects face many of the same challenges and thus offer many opportunities to highlight common educational strategies for improving genomic literacy. We have reviewed 41 current national genomic projects and have identified 16 projects specifically describing their approach to genomic education. The following target groups were included in the educational efforts: the general public (nine projects), patients (six projects), and genomic professionals (16 projects), reflecting the general overall aims of the projects such as determining normal and pathological genomic variation, improving infrastructure, and facilitating personalized medicine. The national genomic projects aim to increase genomic literacy through supplementing existing national education in genomics as well as independent measures specifically tailored to each target group, such as training events, research collaboration, and online resources for healthcare professionals, patients, and patient organizations. This review provides the current state of educational activities within national genomic projects for different target groups and identifies good practices that could contribute to patient empowerment, public engagement, proficient healthcare professionals, and lend support to personalized medicine.

Keywords: genomic education, national genomic projects, personalized medicine, genomic medicine, patients, healthcare professionals, public, genomic literacy

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INTRODUCTION

The field of genetics has, in the last few decades, provided an ever-increasing amount of tools to improve the health of individuals. At the same time, being a fast-advancing field of medicine, genetics has faced a continuous need to keep target groups adequately informed in order to enable them to access state-of-the-art health care. With the vast scientific advances of the last 20 years, such as the next generation sequencing, that have made sequencing of the whole genome accessible to the general public, the complexity of what is possible to determine, predict, prevent, and/or cure in human health has increased exponentially. Consequently, genomic, rather than genetic, literacy is now needed.

Genomic literacy is defined as "the capacity to obtain, process, understand, and use genomic information for health-related decision-making" (National Research Council, 1996; Institute of Medicine (US) Committee on Health Literacy, 2004; Hurle et al., 2013; Whitley et al., 2020), and, for this, a basic understanding of biology, inheritance as the etiology of hereditary diseases, and the concept of personal data management is needed (Dar-Nimrod and Heine, 2011; Stern and Kampourakis, 2017; Jackson et al., 2018; Hulsen et al., 2019; Youssef et al., 2019). These objectively complex topics need to be adjusted to the level of understanding of the target group before education can begin. For example, topics, such as personalized medicine of complex disorders and the genomics of rare diseases, need to be tailored in different ways for physicians and patients (Bennett et al., 2017; Goetz and Schork, 2018; Stoller, 2018; Ferreira, 2019; Ramalle-Gómara et al., 2020). Similarly, ethical, social, and legal aspects of genomics may be adjusted to different audiences (Taneri, 2011; Callier et al., 2016; Hartman et al., 2020; Wolf et al., 2020).

Genomic literacy is increasingly important due to the growing popularity of direct-to-consumer tests, an implementation of genomic medicine in routine healthcare and the necessity of public support for genomic research and is a prerequisite for an efficient implementation of personalized medicine, which has so far already changed the diagnostics and treatment of patients with rare diseases and cancer (World Health Organization, 2002; Dressler et al., 2014; ACMG Board of Directors, 2016; Brittain et al., 2017).

Currently, many governmental, non-governmental, and international organizations contribute to genomic education, through measures such as the incorporation of genomic topics into formal education, funding of educational institutions, the incorporation and establishment of training programs for genomic professionals, and through providing online provisions for the public and professionals and addressing the public through media engagement, etc. (Bennett et al., 2017; Goetz and Schork, 2018; Hyland and Dasgupta, 2019; Sabatello et al., 2019; Whitley et al., 2020).

To speed up the process of implementing personalized medicine, individual countries have established national genomic projects with various goals as previously reviewed (Kovanda et al., 2021). In order to achieve the main aims of genomic projects, such as determining normal and pathological genomic variation, improving infrastructure and finally implementing personalized medicine, it is crucial to increase genomic literacy among the public, patients, and professionals on relevant scientific and ethical issues (Bennett et al., 2017; Nakamura et al., 2017; Goetz and Schork, 2018; Ha et al., 2018; Hyland and Dasgupta, 2019; Sabatello et al., 2019; Wright et al., 2019; Whitley et al., 2020).

Therefore, national genomic projects, by addressing their major goal of promoting personalized medicine, substantially help genomics to enter into public awareness and thereby aid existing educational infrastructures in achieving genomic literacy.

Our goal was to review how education and promoting genomic literacy are addressed by the currently on-going national genomic projects, how these measures supplement existing genomic education, and to identify good practices of how they have been tailored to the key target groups of the projects educational outreach.

RESULTS

The 41 currently active national genomic projects were identified and analyzed through a systematic on-line search as previously described (Kovanda et al., 2021). As reviewed previously, the currently active national projects are very diverse and reflect the needs and resources of individual countries (Kovanda et al., 2021). The main aims of these projects are determining normal genomic variation (90%), pathological genomic variation (71%), improving infrastructure (59%), and achieving personalized medicine (37%). A total of 16 projects (39%, 16/41) specifically declared education as one of their aims (**Table 1**).

The projects with educational aims had three primary target groups; the general public (nine projects), patients (six projects), and professionals involved in genomics (all 16 projects; **Figure 1**), reflecting the projects' general aims (Kovanda et al., 2021).

The various solutions addressing the many challenges of genomic education reflect the specific project aims and will be further discussed below. In addition to classic approaches, such as workshops and other educational events, there is a clear trend toward the utilization of online educational resources. The various educational resources are presented here according to the target groups and respective educational resources (**Figure 1**).

The General Public

The public represents the most diverse group of stakeholders and includes individuals of all ages, education levels, professions, religions, and ethnicity. Nine of the national genomic projects specifically stated their efforts toward increasing the genomic literacy of the public.

The most common approaches among the projects targeting the general public include educational events, online platforms, and media and social media engagement (**Table 1**; **Figure 1**). Australia and the United Kingdom stated provisions for community engagement. Finland plans to empower its citizens to make informed decisions about genetic testing and study participation with the implementation of guidelines on the use of genomic data and online platforms, such as an educational genome portal, online genome tools, and virtual health services, which would enable users to interact with and use their genomic information. France, the United Kingdom, Canada, and Finland have begun to integrate genomic education into primary and secondary education by updating school curricula, providing teachers with specialized training or utilizing online educational platforms (LaRue et al., 2018; Whitley et al., 2020).

Primary Education Level

Primary education level is important and in many ways (simplification, emphasis on fundamental principles, and interesting examples of benefit to patients) similar to genomic education of the general public. For example, projects by the United Kingdom

TABLE 1 | Webpage resources of national genomic projects.

Country	Project names	Webpages/resources
Armenia	The Armenian Genome Project	http://armeniangenome.am/
Australia	Australian Genomics	https://www.australiangenomics.org.au/, https://www.genomicsinfo.org.au/
	Rare Cancers Australia – Your Cancer Journey	https://www.rarecancers.org.au/page/66/your-cancer-journey
Brazil	Brazilian Initiative on Precision Medicine BIPMed	http://bipmed.github.io/
Canada	Génome Québec – Education Platform Génome Québec Éducation et formations	http://www.genomequebec-education-formations.com/education-en
	Genome Canada	https://www.genomecanada.ca/
Cyprus	Center of Excellence in Biobanking and Biomedical Research	https://biobank.cy/
Finland	Finland's Genome Strategy Working Group Proposal	https://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/74712/URN_ISBN_978-952-00-3598-3.pdf?sequence=1&isAllowed=y
France	Plan France Médecine Génomique 2025	https://pfmg2025.aviesan.fr
Japan	Platform Program for Promotion of Genome Medicine | Japan Agency for Medical Research and Development	https://www.amed.go.jp/en/program/list/14/01/001.html
New Zealand	Genomics Aotearoa	https://www.genomics-aotearoa.org.nz, https://github.com/GenomicsAotearoa
Poland	Genomic map of Poland	http://www.ecbig.pl/page/genomic-map-of-poland/
Qatar	Qatar Genome Programme	https://qatargenome.org.qa/node/5
Saudi Arabia	Saudi Human Genome Program	https://shgp.kacst.edu.sa/index.en.html#program-objectives
Slovenia	Slovenian Genome Project	http://genom.si/
Switzerland	SPHN – Swiss Personalised Health Network	https://sphn.ch/
United Kingdom	Genomics England and Genomics Education Programme	https://www.genomicsengland.co.uk/ https://www.genomicseducation.hee.nhs.uk/
Uruguay	Urugenomes	http://urugenomes.org/en/the-project/

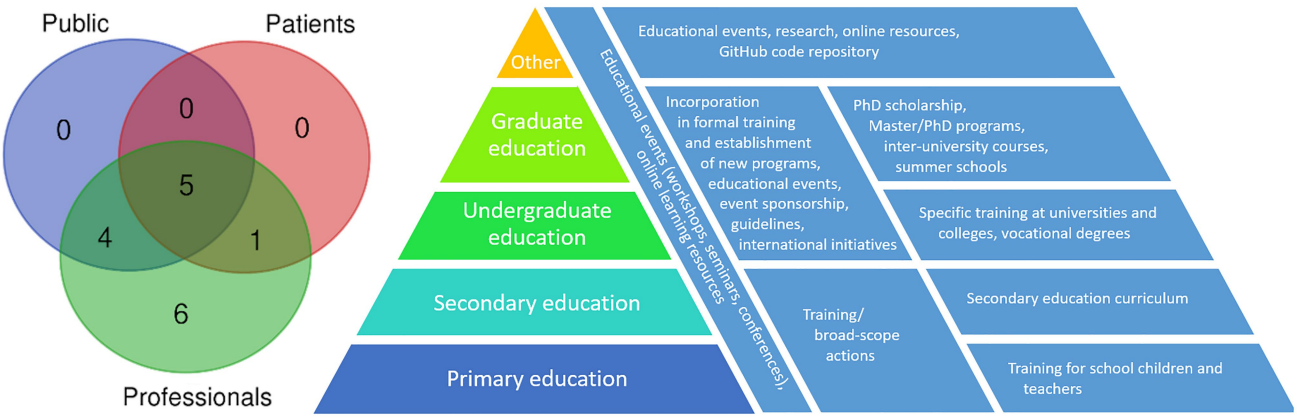

FIGURE 1 | Overlap between the target groups of 16 national genomic projects and educational solutions and resources according to the level of education.

and France have implemented provisions tailored for students and teachers at the primary education level. These include organized workshops for school children and implemented university training courses for teachers (LaRue et al., 2018). These types of initiatives are designed both to educate children about genomics and to invoke critical thought about the benefits and drawbacks of genomic research. Additionally, these classical educational measures are supplemented by online platforms with resources for children and teachers.

Secondary Education Level

Genomic education at the secondary level is also an important measure toward increasing genomic literacy of the public since students not only use this knowledge in their later career but also often transfer their knowledge to their parents and other family members (Dressler et al., 2014). Students, who receive genomic education, are also more likely to participate in genomic research and request research results (Sabatello et al., 2019). Five projects included provisions for secondary education. Genome Quebec, a subsidiary of Genome Canada, offers an online platform for high school students and teachers, which doubles as an all-ages educational provision. Finland proposes incorporating genomic education into existing health education, thus providing students with sufficient resources to make informed decisions about their healthcare in the future.

Undergraduate Education

Good general genomic undergraduate education of science majors is necessary to recruit the next generation of genetic counselors, clinical and laboratory geneticists, and genetic nurses (Garber et al., 2016; Bennett et al., 2017; Whitley et al., 2020). Australia, Brazil, France, Slovenia, Switzerland, and the United Kingdom addressed undergraduate stakeholders. Brazil, Slovenia, Switzerland, and the United Kingdom organized educational events for students and healthcare professionals. Australia and France additionally introduced undergraduate and graduate programs, including transdisciplinary vocational programs, tailored for genomic professionals.

Patients

Six projects included provisions for patients, focusing mostly on genomic education *via* workshops, online platforms, outreach programs, and informed consent provisions (**Table 1**; **Figure 1**).

Genomics England was one of the first projects to establish the Patient and Public Involvement Network, which tasked with the review of the educational resources and consent process. Patients were actively involved in the process of creating educational material and consent literature, including members of minority ethnic groups and youth. Their representatives were additionally involved through the Ethics Advisory Committee and other key institutions of the project in the management of the data access process, a crucial issue for study participants. Similarly, Australian Genomics put forward the Genomics in the Community Project in collaboration with Patient Advocacy Groups, focusing on analysis, curation, and preparation of educational material for patients and the public, on the topic of insurance and data privacy, an area where existing material was found to be insufficient.

Genome Canada and the Canadian Organisation for Rare Diseases are developing outreach programs aimed at patients with rare diseases to better understand the community of patients and tailor diagnostic and therapeutic approaches. Slovenian Genome Project will develop national guidelines for genomic medicine that will address genomic research and treatment, data management, interpretation of genetic results, biobanking, commercial genetic tests, and special interest groups. The project will develop national medico-ethical and legal frameworks for genomic medicine.

Australian Genomics designed the platform CTRL, a dynamic consent provision that enables the study participants to tailor and control the consent process, to receive news and study updates, and to contact the researchers. Rare Cancer Australia, a charity organization, offers a comprehensive online platform for patients with rare cancers with educational resources and tools for finding health services and clinical trials, a "Patient Treatment Found," patient support services and support groups, and Radio Rare, a patient community-focused podcast.

Professionals

All 16 projects included the education of professionals in genomic as their aim, reflecting its utmost importance (**Table 1**; **Figure 1**). As professional education includes several levels of formal education, the particular approaches to this challenge are discussed both under appropriate educational levels and as particular solutions implemented in the projects.

Graduate and Post-graduate Level

The majority of projects addressed the needs of graduate and postgraduate students with several projects establishing Master or PhD programs, focusing on building capacity and expertise in genomic medicine (Australia, France, Qatar, Slovenia, the United Kingdom, etc.). For example, Health Education England implemented a master's degree in genomic medicine, targeting doctors and other healthcare professionals, with bioinformatics training utilizing the Genomic England dataset. Slovenia recently implemented a master PhD program for Genomic Counselors. Qatar implemented a master program in Genetic Counseling and a master and PhD program in Genomic Medicine. Australian Genomics established the Genomics Education Network of Australasia (GENA) to facilitate collaboration between providers of genomic education and implement new tools for genomic education, including a technical report of the overview of education programs for healthcare professionals involved in genomic medicine (McClaren et al., 2018). This report specifically identified the need to coordinate the implementation of new programs in response to the development of new technologies (McClaren et al., 2018). Other, broad higher-level educational resources include those of Cyprus that will establish the Centre of Excellence in Biobanking and Biomedical Research and Uruguay that implement tailored programs for researchers in collaboration with the University of Seoul.

Continuing Professional Development

We have identified five projects with tailored provisions for doctors and nurses that supplement existing specializations in genetics that are already part of formal education in countries such as Belgium (Hanquet, 2018). In addition to doctors and nurses, recent efforts have broadened the scope of professional genomic education to include non-medical healthcare workers that are nevertheless crucial for the development of genomics (Bennett et al., 2017). The projects specifically defining other target healthcare workers named diverse professionals, such as analysts, laboratory technicians, genetic counselors, researchers, pharmacists, data-scientists, bioinformatics engineers, system-administrators, government employees, industry staff, managers, etc. The professionals mentioned above can be loosely grouped under three categories – laboratory professionals, professionals in informatics, and others, such as research and development professionals, however, as shown by the approaches employed by national genomic projects these categories almost inevitably overlap to a large extent.

Common approaches to the education of working professionals consist of online and in-person educational events, such as workshops, seminars, lectures, summer schools, conferences, and training programs or initiatives. These approaches are similar to those included in the formal education of healthcare workers with the advantage of being more accessible to different professional profiles.

Specifically, Finland, Poland, and Saudi Arabia proposed strategies and programs to train existing healthcare professionals and develop new personnel in the field of genomics. Similarly, Australia's National Health Genomics Policy Framework proposes strategies to increase the number of genetic professionals, increasing access to genetic professionals, and promote formal knowledge exchange with partnerships and networks (Australian Health Ministers' Advisory Council, Australia, and Department of Health, 2017). Genomics Education England organizes an interactive course on the basics of genomic medicine in clinical practice aimed at nurses, general practitioners, other healthcare workers and scientists. Canada and Slovenia plan to organize educational events, including seminars, workshops, conferences, and courses on genomic data translation. Slovenian Genome project aims to create an online educational platform eSLOG. Finland plans to introduce guidelines, support tools, and databanks, to increase an utilization of genomic data for disease risk stratification. Similarly, Urugenome will implement a comprehensive training program for healthcare workers, particularly addressing the need for data analysis expertise, inclusion and report criteria for doctors, and ethical considerations. Finally, Brazil offers a biannual BIPmed workshop on technical development and current research, tailored for students, researchers, and managers from the public and private sector.

Six projects specifically describe provisions for bioinformatics engineers, solidifying the importance of data analysis and management for genetic testing and implementation of personalized medicine. The educational process for bioinformatics engineers is currently very diverse, which results in vastly different qualifications and carrier paths for professionals working in data analysis (Hanquet, 2018). France proposes implementing undergraduate and graduate transdisciplinary programs with recognized job titles such as biostatistics, data mining, and analysis. Their strategy proposes standardizing data analysis by providing modified training programs in bioinformatics and biostatistics and creating new job titles. Similarly, Japan's Platform Program for Promotion of Genome Medicine aims to implement personalized medicine and disease prediction by educating engineers and researchers in bioinformatics and biostatistics, facilitating data management, data sharing, and genomic research of multifactorial diseases. Armenian Genome aims to promote education in bioinformatics and genomics by organizing workshops, seminars and providing research opportunities for researchers and students. New Zealand's Genome Aotearoa implemented a comprehensive bioinformatics training program, which offers workshops and summer schools, and established a code repository within the GitHub online platform.

Illustrating the significance of competency in genomic medicine for other professionals involved in education, media and decision-making, Australia, Brazil, France, Poland, Switzerland, and the United Kingdom offer training programs and educational events for teachers, journalists, industry staff, insurance scientists, bioethicists, managers, and administrative staff.

An example to be followed, Genomics Aotearoa formulated the Guidelines for Genomic Research with Māori to equip researchers, ethics committee members and other professionals with a framework of ethical, social, and cultural considerations relevant to the Māori community of New Zealand.

Limitations

The study faces several limitations, as previously described (Kovanda et al., 2021). Firstly, the authors gathered information available on the websites of the currently ongoing national genomic projects. Only the information available in the English language has been included, and we would like to recognize that our analysis may not reflect the full or final scope of the individual projects. The projects substantially differ in terms of their general scope and budgets. Additionally, the information on whether the impact of their educational measures will be evaluated was not available. We would like to emphasize that the primary focus of this review are the educational measures that are part of national genomic projects and recognize that many additional countries implement large scale national or even international initiatives and programs in genomic education outside the scope of their respective national genomic projects.

DISCUSSION

Genomic literacy empowers individuals to make informed decisions about their health, minimizes misconceptions about genomic testing and research, and leads to greater understanding and neutral perception of human diversity (Dressler et al., 2014).

In the context of national genomic projects, genomic education is primarily meant to increase project visibility and raise awareness about the implications of participation for the public and patients. The national genomic projects, discussed here, provide an opportunity to supplement the existing genomic education of professionals in their respective countries, facilitating the integration of personalized medicine into clinical practice (Wilcox et al., 2018). In medical terminology, national genomic projects' educational measures are needed, but not themselves sufficient to achieve genomic literacy. Indeed, the scale of the effort needed implies each of the different existing measures (national, international, and project-type) can successfully contribute toward achieving genomic literacy.

The main challenges for genomic education of the public are limited financial resources, insufficient infrastructure, a lack of a unified approach, and the complexity of genomic medicine (Dressler et al., 2014).

Consequently, provisions for the public are often either broad or target a specific subgroup of the public (**Figure 1**). Indeed, in a 2014 study of genomic researchers and ELSI advisors, no consensus was reached on who should oversee the education of the public, what the target audience is and what topics should be presented (Dressler et al., 2014; Whitley et al., 2020). Providing opportunities for genomic education may not directly translate into an uptake of such opportunities or the use of the knowledge obtained, and it

would be helpful to the field if educational measures could be evaluated in terms of their final impact.

Patients are the stakeholders most directly affected by genomics, and their adequate literacy on this topic is a fundamental step in the implementation of personalized medicine. Patient awareness regarding ELSI issues, especially data privacy, is a prerequisite of informed consent (Dressler et al., 2014). In addition to patients with rare diseases and cancer, genomic literacy is also important for patients with common non-communicable diseases, as low literacy puts these patients at a risk of not receiving personalized preventive care. On the other hand, an appropriate communication and interpretation of results represent unique challenges from the positions of the patient, parents/caretakers, and physicians/genetic councilors (Nakamura et al., 2017; von der Lippe et al., 2017; Stoller, 2018; Mboowa and Sserwadda, 2019).

The final and most complex group of stakeholders addressed by genomic projects is the healthcare and other professionals involved. In addition to doctors and nurses, professionals involved in genomics include laboratory analysts, informatics engineers, data scientists, administrators, legislators, ethics experts, and others, whose education presents additional challenges.

Due to the ever-increasing demand, substantial efforts to train genomic professionals exist independently of national genomic projects in many countries such as Belgium (Bennett et al., 2017; Hanquet, 2018). For an efficient implementation of genomic medicine, healthcare professionals both require and request educational resources that enable them to keep up to date with the current state-of-the-art in genomics (Ha et al., 2018; Hyland and Dasgupta, 2019; Cerovic et al., 2020). Several studies of European and United States physicians have illustrated that, although non-genetic physicians frequently see patients with rare diseases in their practice, they often lack formal education in genomic medicine, feel unprepared to order genetic tests, to interpret genomic data, and to effectively communicate the results to the patients (Rubanovich et al., 2018; Cerovic et al., 2020; Ramalle-Gómara et al., 2020). Similarly, nurses often lack the necessary genomic literacy. A 2018 survey of 18 countries showed that the integration of genomic education into nurse training was inconsistent and varied in scope (Calzone et al., 2018).

To facilitate an introduction to personalized medicine, medical students should be introduced to genomic medicine early on, with courses covering both preclinical and clinical medicine (Plunkett-Rondeau et al., 2015; Wilcox et al., 2018). Nationwide educational measures, such as the implementation of undergraduate and graduate programs, modification of school curriculum, and other large scale provisions, necessitate greater funding and collaboration between government institutions, universities, patient advocacy groups, etc. Several national genomic projects offer various solutions to supplement existing national educational structures (from primary to higher education), like establishing novel vocations or study programs or resorting to stand-alone solutions such as online resources and repositories for different professionals that can easily be tailored to specific groups.

Additionally, international collaboration contributes to achieving genomic literacy of professionals in genomics, by providing an overview of the state-of-the-art, access to new technology and databases, educational material, and other resources. Indeed, half of the national genomic projects included international provisions such as international conferences, courses for international students, collaboration in established international institutions and through open science initiatives, and organizing international projects. In these efforts, we have identified that the existing international initiatives, such as The Global Alliance for Genomics and Health (GA4GH), Elixir, ERN, Orphanet, etc., provide helpful educational resources and infrastructure for life science information (ELIXIR, n.d.; GA4GH, n.d.; Orphanet, n.d.; Public Health – European Commission, 2016). The adoption of existing international infrastructures (e.g., GA4GH, which provides policy frameworks and technical standards for secure and responsible data sharing), by national genomic projects, will hopefully translate to their national genomic education strategies in the future.

Finally, the educational provisions implemented by national genomic projects reflect the variability in the projects' goals and unique national situations regarding genomics (Kovanda et al., 2021). The common approaches, presented in this mini-review, reflect the unique needs of different stakeholder groups, ethnic and cultural diversity, regulatory and legal genomic policies, and infrastructural capacities of the individual countries (Dressler et al., 2014; Mboowa and Sserwadda, 2019; Pastorino et al., 2019; Whitley et al., 2020). Due to the scope and the heterogeneity of genomics, as well as funding constraints, the most projects implemented cost-effective broad strategies, like educational events, online platforms, and community engagement projects, to educate the general public and patients, while professional training events, online platforms and tools, and an establishment of clinical guidelines and standards were used for educating of genomic professionals. Reflecting this variability, the predicted impact of increasing genomic literacy through genomic projects includes various factors contributing to developing personalized medicine, such as improved diagnostic capabilities, faster time to diagnosis of rare diseases, citizen and patient empowerment, greater visibility of genomic professions, and increased participation in genomic projects' acquisition of normal and pathological genomic variability.

CONCLUSION

In conclusion, we provide evidence of diverse educational activities across current national genomic projects, which reflect the differences in the goals of national genomic projects and specific national requirements. Examples of common approaches include workshops for healthcare workers, online information repositories for the general public and rare disease patients and families, and the development of guidelines, standards and national programs for implementation of genomic education into formal education. Hopefully, initial efforts made by national genomic projects will result in durable national solutions leading toward further implementation of personalized medicine in healthcare systems.

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All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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The Role of the European Society of Human Genetics in Delivering Genomic Education

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The European Society of Human Genetics (ESHG) was founded in 1967 as a professional organisation for members working in genetics in clinical practice, research and education. The Society seeks the integration of scientific research and its implementation into clinical practice and the education of specialists and the public in all areas of medical and human genetics. The Society works to do this through many approaches, including educational sessions at the annual conference; training courses in general and specialist areas of genetics; an online resource of educational materials (EuroGEMS); and a mentorship scheme. The ESHG Education Committee is implementing new approaches to expand the reach of its educational activities and portfolio. With changes in technology, appreciation of the utility of genomics in healthcare and the public's and patients' increased awareness of the role of genomics, this review will summarise how the ESHG is adapting to deliver innovative educational activity.

Keywords: education, genomics, European Society of Human Genetics, Education Committee, EuroGEMS, massive open online course, courses/diffusion, mentorship

INTRODUCTION

The European Society of Human Genetics (ESHG[1]) was established in March, 1967, by a small group of European geneticists attending a conference in Chicago, United States (Renwick and Edwards, 1995). The first symposium of the new society was held in Copenhagen, Denmark, in November 1967, with invited lectures on genetic polymorphisms and a session for contributed papers. In 1993, the Society started to publish its own Journal, the European Journal of Human Genetics, which now appears monthly. The Society now has over 3,000 members, composed of Clinical Geneticists, Genetic Counsellors, diagnostic laboratory and research scientists, students and individuals from other disciplines with an interest in human and medical genetics.

From its inception to present, the Society has always considered education at the core of its remit. Within its statutes, the purpose of the Society is stated to 'strive for the integration of scientific research and its implementation in the clinical field as well as for (postgraduate) education of specialists and the public in all areas of medical and human genetics'.[2] As demonstration of this commitment, the Society formed 'the Education Committee (EduComm) to disseminate the knowledge, training and teaching of modern human genetics and genomics to the general public, students, postgraduate scientists and to genetic and medical professionals'. The current, recently expanded, core membership of EduComm consists of 13 members (eight women and five men) working in 10 countries across Europe.

EduComm challenges itself to oversee a portfolio of the highest quality education and training in genomics. This has primarily been aimed at the members of the ESHG. However, there is a recognition of an additional responsibility to provide resources to health professionals and scientists working outside of genomics. Engagement and educational interaction with members of the public is also within the remit of the group. However, until now, this has not been the primary focus and we will consider how this can be addressed in more detail later. EduComm is committed to provide a broad range of educational resources. The education portfolio has targeted all levels of expertise, from a basic level understanding of genomics (where there are the greatest needs) to high-level expert training often delivered through the state-of-the-art educational symposia at the annual conference.

EduComm has sought to provide oversight and guidance for a portfolio of training courses that meet the needs of the membership (**Table 1**). The Society has placed a high emphasis on ensuring that these courses are affordable, aiming to ensure equitable access and the highest educational quality. Through the EuroGEMS[3] website (Tobias and Tobias, 2020), EduComm has facilitated access by multiple audience types to a wide range of the existing high-quality, free and online educational resources in genetics and genomics, including apps and massive open online courses (MOOCs). The Committee also provides input into the ESHG Scientific Program Committee to suggest educational content for the annual conference.

TABLE 1 | Current educational courses co-organised and/or supported by ESHG (https://www.eshg.org/courses.0.html).

Course	Location	Co-organisers
Introduction to the statistical analysis of genome-wide association studies	London, United Kingdom	University of Surrey
Clinical Genomics and NGS Course	Bertinoro, Italy	University Residential Center of Bertinoro
Eye Genetics Course	Bertinoro, Italy	University Residential Center of Bertinoro
Basic and Advanced Course on Genetic Counselling	Bertinoro, Italy	University Residential Center of Bertinoro
Course in Hereditary Cancer Genetics	Bertinoro, Italy	University Residential Center of Bertinoro
Cardiac Genetics Training Course	Manchester, United Kingdom Antwerp, Belgium	Manchester Centre for Genomic Medicine University of Antwerp
Basics in Human Genetic Diagnostics – A course for Clinical Laboratory Geneticists in education	Various	University of Jena
Manchester Dysmorphology Course	Manchester, United Kingdom	Manchester Centre for Genomic Medicine
Goldrain Course on Clinical Cytogenetics	South Tyrol, Italy	
Pharmacogenetics	Slovenia	University of Ljubljana
Next-generation	Netherlands	Maastricht University
Reproductive Genetics		Medical Center

The analysis of genomic information forms an increasingly important component in the diagnosis, treatment and prevention of disease. At present, genomic medicine is only an integral part of service provision in a few countries, yet this adoption is set to expand. The ESHG has a role to support this expansion. Better use of technology and data is a prerequisite for supporting and enabling key educational developments. The COVID-19 healthcare crisis accelerated the transition to digitalisation by the rapid establishment of virtual conferences and meetings and a widespread move to online teaching. For successful integration, it is important that educators make the most of the opportunities afforded by digital education, including apps and MOOCs.

CHALLENGES TO DELIVERING GENOMIC EDUCATION

The ESHG is just one of many organisations operating to provide educational support to health professionals and to engage with the public and patients. It is important that it targets its resources for maximal impact.

Genetic professionals face the challenge of finding a balance between their own continuous professional development and mainstreaming genomic education for other specialties. Most individuals who have a genomic test as part of their diagnostic

[1]https://www.eshg.org/
[2]https://www.eshg.org/index.php?id=54
[3]https://www.eurogems.org

process will, in future, have this requested, and the results managed, by non-genetic specialists. The relative lack of education in genomics for non-specialists is a challenge for implementation. Ensuring access to this expertise, training and education is complex. Many approaches with a major educational component have been adopted and led by genetic specialists, including online networks like Dyscerne (Douzgou et al., 2016b), expert resources for rare conditions, such as Orphanet (Aymé, 2003) and the educational programmes of the European Reference Networks (ERN; Tumiene and Graessner, 2021).

The ESHG is keen to understand and address the disparities in the access to training and education of health professionals in some nations and across ethnic groups. EduComm is aware of and concerned about these disparities and is defining strategies to reduce these, by facilitating access to genetic information in different languages and exploring strategies to better integrate minorities in ESHG activities. The roles of different professionals in genomics, including genetic counsellors, can be promoted through education, explaining the key skills of this workforce which has not been equally represented or formally recognised in all European countries.

The increasing digitalisation of educational resources has facilitated their global outreach but has also modified the learning experience. Traditional healthcare education and development included experiential learning and contact with the patient (for example, ward rounds), aspects less feasible in digitalised environments as they include sharing patient-sensitive data. There is an urgent need to ensure that these resources are available in different languages, with information governance and straightforward navigation by health professionals, patients and the public. The translation of the EuroGEMS website (see below) and its inclusion of multi-language resources will increase access to such resources.

Whilst online education is a powerful adjunct, many learners experience difficulty in concentrating for extended periods. Instead, short periods of engaging interactively-delivered information are fundamental to the success of online learning. Despite its cost, face-to-face teaching and experiential work remain a vital part of training and should be supported.

Research funding is not equally distributed across countries within the EU (Lynch and Borg, 2016). This may reduce the opportunities for a highly capable trainee to undertake research within their country. Some rare diseases cluster in specific geographical areas, and local research and educational resources are imperative to improve care for that specific disorder. The overlap between research and teaching is symbiotic; centres without research will encounter greater difficulties in providing leading-edge teaching.

In future, health professionals in genomics will be more actively involved in clinical trials and in treating patients. This is true of laboratory staff also, who will need to reduce test turnaround times and analyse biomarkers that indicate response or resistance to treatment. It is imperative that educational resources support the change in professional roles and ensure that up to date accurate information is available. Examples of resources in this area are starting to emerge, like Treatable-ID,[4] which provides easily accessible information in the form of an app on treatable causes of intellectual disability.

EDUCATIONAL COURSES

Given the broad background, levels of experience and knowledge of ESHG members, educational courses, organised or supported by the Society, have tried to reflect the needs of the different groups. They support some of the core competencies that provide an appropriate framework for genetics education of health professionals across national boundaries (Skirton et al., 2010). The courses seek to disseminate best standards of good clinical, laboratory and data analysis practice in genetics. The topics span basic sciences to clinical delivery of Genomic Medicine and Genetic Counselling. The courses have adopted a mixed approach, including lectures, workshops, case discussions and presentations and importantly a forum to meet and share experiences and create a relaxed interactive environment for faculty and delegates. This has been more challenging throughout the COVID-19 pandemic where some courses have moved to an exclusively online format. However, this shift will likely allow a mixed approach to these courses in future, permitting many individuals to participate in a virtual capacity, whereas others will attend in person and be able to experience the full benefit of small group work and face-to-face interaction. The online format greatly democratises accessibility to courses, where financial and several other factors can prevent travel, attendance and participation for many individuals, and it will allow more flexible, greater and longer-term use of the resources.

Recent courses have been designed to consider newer areas of genomics, including pharmacogenetics, genomic sequencing, bioinformatics, statistical genetics and new technologies in prenatal medicine. Many of the courses encourage participants from non-genomic specialties to attend; for example, the cardiac genetics course has an attendance comprising 50% cardiologists. Plans are in development to expand the course portfolio to include precision medicine and biochemical genetics. Many courses are delivered in partnership with other professional societies to increase their reach and to reduce duplication.

Dysmorphology workshops and courses have been a mainstay of the ESHG portfolio (Donnai, 2017). These have been crucial in educating professionals in a field which is integral to the care of patients and families with rare inherited developmental disorders (Douzgou et al., 2016a). The interactive forum created by the dysmorphology courses forged an environment from which the Young Geneticists' Network and the European Society of Human Genetic–Young Committee (ESHG-Y) were founded. In this way, the representation of young geneticists in the decision-making process of the ESHG was achieved and highlighted their specific educational and training requirements.

The five-day course 'Introduction to the statistical analysis of genome-wide association studies (GWAS[5])' has been running yearly since 2016. The course covers basic statistical theory

[4]https://www.treatable-id.org/
[5]https://www.eshg.org/index.php?id=104

in GWAS, quality control, imputation, population stratification, trans-ethnic GWAS and principles of Mendelian Randomisation. Due to Covid-19, the course moved to an online live format, whilst maintaining the same content and expanding the audience. The digital platform enabled hands-on computer exercises with supervision and feedback in real time. The course, initially targeting postdoctoral researchers, has seen ~60% PhD student audience, contributing to advanced training of early career researchers in Europe and other countries worldwide.

EuroGEMS

Purpose and Content

To provide high-quality educational resources for genetics and (increasingly-importantly) non-genetics health professionals and the general public, an educational website at www.EuroGEMS.org has been established on behalf of EduComm (Tobias and Tobias, 2020). With high-speed, high-bandwidth, secure-socket-layer hosting, it provides content summaries and direct links for a wide range of carefully selected international online educational genetic and genomic resources, for audiences of all levels, including the public.

General inclusion criteria used in resource selection are as follows: (a) free-to-access, (b) informative, (c) containing up-to-date unbroken links, and (d) of high quality and free of obviously misleading information. Resources were chosen to include those used from personal experience and following discussions with many professional colleagues, including EduComm and the ESHG Board. Links to >110 educational resources (many from outside Europe) were thus included, categorised in web pages according to target audience. A brief summary of content and purpose was provided for each resource. The website's content has undergone recent detailed peer review (Tobias and Tobias, 2020).

Design to Include Non-genetics Specialists

For non-genetics health professionals, such as primary-care physicians and non-genetics ('mainstreaming') specialists, a web page was added with information and links, including Gen-Equip, Orphanet, GeneReviews, Unique and Contact, a range of free genomic MOOCs and several smartphone apps (described below).

Genomic Education for the Public

A large part of EuroGEMS provides public education, including pages for patients and their relatives. These pages contain, for example, well-established online directories of rare conditions and support organisations, such as Unique, Contact, Orphanet, EURORDIS and MedlinePlus-Genetics, with more general genetics educational resources, including a range of animated videos. Other pages comprise multiple resources for primary and secondary/high school teachers, including animations and professionally filmed videos of children relating experiences of rare disorders. Pages and links of general interest are as follows: a web page of Ethical, Legal & Social Implications (ELSI) resources; links provided within several pages to many non-English and multi-language resources; access to sets of genetics-relevant COVID-19-related educational resources; and links to several MOOCs.

International Use

EuroGEMS has received visits from 120 countries, with 47% of web page visits originating in European countries with a non-English primary language and 21% from outside Europe (**Table 2**). The frequency of returning visits has markedly increased, now three-fold greater (in January–March, 2021) than in the first 3 months. Although the majority (55.2%) of the website's visitors have accessed it directly *via* its URL, a large proportion (23.7%) reached it *via* the ESHG website. The users categorised by total page views are as follows: genetics professionals: 23.5%, students: 22.2%, secondary schools: 16.2%, patients and families: 13.9%, non-genetics health professionals: 10.3%, primary schools: 8.4% and ELSI: 5.4%.

Evaluation

Highly appreciative feedback regarding EuroGEMS was received from clinical professionals, teachers and the public, internationally (including from Australia, South Africa and Saudi Arabia). Comments have included 'really easy to use and well organised'; 'very useful'; and 'fantastic and I look forward to using it for the rest of my career'.

Further Development of EuroGEMS

Since the website's launch, its numerous links have been regularly updated and further international resources and a page for non-genetics health professionals have been added. Supported

TABLE 2 | The 10 countries/areas inside and 10 outside the continent of Europe from which visits to EuroGEMS.org have most frequently originated.

Country/Area	Proportion (%) of total page views
Within the continent of Europe	
United Kingdom	29.8
Italy	5.2
Belgium	3.8
France	3.4
Spain	3.2
Sweden	3.2
Portugal	3.1
Germany	3.0
Turkey	2.9
Netherlands	2.5
Outside Europe	
United States	5.2
Canada	1.9
Australia	1.6
India	1.4
Brazil	0.8
Israel	0.7
China	0.7
Saudi Arabia	0.7
Egypt	0.6
Japan	0.6

Data: Statcounter (Accessed March 16, 2021).

by the ESHG, translation of EuroGEMS into non-English languages is underway, commencing with Spanish.

Massive Open Online Courses

Links within EuroGEMS to a range of MOOCs provide worldwide access to these free public-oriented extensive, cutting-edge courses, covering genetics, genomic medicine, cancer genomics, clinical bioinformatics and sequencing technologies. Designed for non-genetics healthcare professionals and the public, the MOOCs are provided on dedicated interactive online platforms and contain many short video lectures and articles, plus web links, glossaries, self-assessment quizzes and educator-moderated discussion forums. The enormous global access to the courses provided by such online delivery has, for example, enabled the genomic medicine MOOC[6] (created by author EST and Glasgow University colleagues), to educate 805 learners (including the public, hospital physicians, primary-care practitioners, students and scientists) in 97 countries, in the first 3 months post-launch.

Smartphone Apps

The smartphone and tablet apps linked from EuroGEMS include a (Guy's Hospital) cancer genetics referral guide for general practitioners, the Treatable-ID app (mentioned above) and a set of five free educational apps designed and coded by an EduComm member (Tobias and Tobias, 2015). This set comprises an illustrated glossary for genomics and bioinformatics terminology, greatly expanded since launch, and also self-assessment quiz apps for terminology and genetic inheritance mechanisms. Downloaded free-of-charge from Apple and Android app stores these have been used by >5,000 individuals in >70 countries (05/04/2021).

ANNUAL CONFERENCE

Each year the Society convenes a conference in different cities across Europe. The focus each year is to consider research at the forefront of human genetics. Equally important and integral to the conference programme is an educational track, which provides educational symposia and workshops across a broad range of topics. The EduComm has added to the programme half-day courses on specific topics with a focus on important basic standards, including accurate description of variants, describing phenotypes (Human Phenotype Ontology), variant classification, databases and data sharing. These initiatives will complement other courses provided by collaborating organisations, for example, the HVP/HUGO Variant Effect Prediction Training Course.[7] The conference also includes a wide-ranging ELSI-related multi-session track entitled Ethical Legal and Psychosocial Aspects in Genetics led by the ESHG Public and Professional Policy Committee.

MENTORSHIP

The EduComm established a mentorship scheme to broaden the opportunity for young ESHG members to benefit from interaction with another centre. The mentorship scheme will especially support individuals from economically disadvantaged countries or where genetics services are less well developed. The successful candidates will combine attendance at the annual conference with a visit to the centre of an established international leader in any field of genomics or relevant subject area. We hope that this scheme will act as an adjunct to the ERN clinical exchange programmes and foster long-term supportive relationships between the mentor and the young Society member, enhancing their career progression.

PUBLIC AND PATIENT EDUCATION IN GENOMICS

The ESHG has previously had a more limited role in educating the wider non-scientific public in genomic and precision medicine. Interaction with school children has previously been at the centre of the approach to public engagement taken by the ESHG. Currently, events are hosted for school children aligned to the annual conference.

Many ESHG members work with patient advocacy groups providing expert scientific and medical advice. Through this, the accurate information can be shared with affected individuals, their families and carers for a broad range of rare conditions where there is less knowledge within the healthcare system. Additionally, ESHG-Y members are supporting the translation of the Unique[8] patient guides into seven languages. Social media can act as a form of knowledge and information exchange and has been adopted by many patient organisations. Several organisations have established websites and are leading condition-specific, educational strategies, e.g., for Myhre syndrome.[9]

THE DNA DAY ESSAY CONTEST

DNA Day, April 25, is commemorated internationally as a celebration of genetics. The ESHG sponsors a DNA Day Essay contest in European high schools. The contest is designed as a learning tool and a means to promote knowledge of genetics within Europe. It intends to challenge students to examine, question and reflect on the importance and social implications of genetic research and its applications. Essays are expected to contain substantive, well-reasoned arguments indicative of a depth of understanding of the issues. The essays received have been of excellent quality with award winners from throughout Europe.

[6]https://www.futurelearn.com/courses/harnessing-the-power-of-genomics-in-medicine
[7]VEPTC.variome.org
[8]https://rarechromo.org/
[9]https://www.myhresyndrome.org

CONCLUSION

The challenges and opportunities to meet the needs of its members, health professionals, scientists, patients and the public, with the increasing adoption of genomics in healthcare, are enormous. The ESHG is just one organisation contributing to education and training in genomics. Work with the educational committees of other international genomic societies (e.g. the American Society of Human Genetics), universities, hospitals, patient support groups and commercial partners to deliver and support educational activities will be important to maximise the impact of genomic and precision medicine. Taking flexible, complementary approaches to the education and training of individuals, irrespective of their experience, role and location, will be key to the success of creating a genomics-literate society.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material; further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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BRIEF RESEARCH REPORT
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The Importance of Genomic Literacy and Education in Nursing

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Genetic discoveries and technological advances have been changing nursing care delivery, which modifies the roles and practices of nursing in society. Although the need for education of nurses in the field of genomics has been recognized in the 1960s, many countries still have no clear guidelines in this field of education and training. The purpose of this study was to evaluate current genomics content in the curriculum of undergraduate and graduate programs of studies in nursing in Croatia, and to measure the genomic literacy of Croatian undergraduate nursing students through assessing participants' understanding of genomic concepts most critical to nursing practice. The curriculum of undergraduate and graduate programs of nursing classes of 2020/2021 were independently analyzed by the authors. For measuring the knowledge of essential genomic concepts among nurses, a Genomic Nursing Concept Inventory (GNCI©) instrument was employed. Results indicate that the current genomics content, for undergraduate and graduate nursing programs in Croatia, is inadequate and not concordant among universities. Moreover, the genomic literacy of Croatian undergraduate students (Undergraduate program 10) was found to be low. Scores across respondents ranged from 3 to 22 (out of possible 31), with a mean scale score 9.8 (SD 5.3) (31.6% correct). We can conclude that the curriculum for undergraduate and graduate programs of Studies in nursing should be revised to implement the latest genomic practices and approaches to genomics education while nurses should acquire an adequate level of genomic literacy in order to produce desired outcomes of competency in nursing practice.

Keywords: curriculum, education, genomics, literacy, nursing

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INTRODUCTION

Development in genomics and its implementation in the healthcare system worldwide has been steadily increasing (Skirton et al., 2010; Murakami et al., 2020). Moreover, genomic knowledge has been applied in different areas: promotion of health, prevention of injuries and diseases, diagnostics, therapy, patient counseling, support and education (International Society of Nurses in Genetics, 2020). Nurses, as the largest professional group in healthcare system and as a primary contact with patients, have a significant role in the interpretation of genomic data relevant to the care of the patient (World Health Organization, 2016). However, international studies demonstrate a lack of nurses' genomic literacy, and confidence in applying this information to their work (Skirton et al., 2012; Godino et al., 2013; Umberger et al., 2013; Donnelly et al., 2017; Read and Ward, 2018; Wright

et al., 2018). Although the urgency for education of nurses in the field of genetics was recognized in the early 1960s (Brantl and Esslinger, 1962), many countries, including Croatia, still have no clear guidelines in aforementioned field of education and training (Mc Cormick and Calzone, 2017). This is evident throughout the insufficiently represented genomic curriculum contents (Prows et al., 2005; Giddens and Brady, 2007; Collins and Stiles, 2011; Daack-Hirsch et al., 2012; Giarelli and Reiff, 2012; Calzone et al., 2014; Camak, 2016).

In Croatia, the education of nurses at the academic level is organized at the undergraduate and graduate studies. The harmonization of undergraduate studies is prescribed by the Common compulsory part of the undergraduate study program of nursing (core curriculum) (Ministry of Science and Education Republic of Croatia, 2014). This document is in line with the provisions of Directive 2005/36/EC (EUR-Lex, 2020). Core curriculum prescribes 47 compulsory courses during 3 years [158 European Credit Transfer and Accumulation System (ECTS)] in the field of nursing care, basic and social sciences. These courses constitute 87.7% of the program, whereas the remaining 22 ECTS credits are designed by each higher education institution. Nurses with a Bachelor degree learn to independently determine individuals basic human needs, plan, implement, record, and evaluate health care, participate in diagnostic and therapeutic procedures and conduct education. The graduate-level program lasts 2 years (120 ECTS) and is designed exclusively by the higher education institution that runs the program. Nurses with a Master's degree work at all levels of health and social care, independently plan and organize all work processes in the field of nursing care, participate in research processes and complex diagnostic and therapeutic procedures. Moreover, the Proposal of the Standard of Occupations, the Croatian Classification Framework, prescribes the key tasks and competencies of the Master of Nursing. The Framework emphasizes that implementing evidence-based knowledge is the key to successful nursing practice, as well as conducting research on the latest advances in healthcare, which may include genomics (Croatian Qualifications Framework, 2017).

In order to assess the readiness for integrating genomics into nursing curriculum in Croatia, we conducted a survey study with two specific aims: 1) to evaluate the current genomics content in both undergraduate and graduate nursing programs in Croatia (academic year 2020/2021), and 2) to measure the genomic literacy of Croatian undergraduate nursing students through assessing their understanding of core concepts in genomics which are most critical to nursing care.

MATERIALS AND METHODS

Evaluation of the Current Genomics Content in the Curriculum

The authors first collected curriculums of all compulsory, additional and elective courses in undergraduate and graduate programs, reviewed them, and determined how many of those curriculums included a genomic component. Undergraduate programs were explored through the National Information System for Application to Higher Education Institutions (National Information System for Application to Higher Education Institutions, 2021; Working group, 2013), and graduate programs through the university websites (**Supplementary Material S1**). The types of courses in the undergraduate study of nursing are divided into compulsory courses which are prescribed by the core curriculum (47 courses, 158 ECTS) and additional courses (22 ECTS) which are designed by the university. Additional courses can be organized as compulsory and elective courses.

TABLE 1 | Characteristics of the participants (n = 53).

Variable	N (%)
Gender	
Male	6 (11.3)
Female	47 (88.7)
Employment	
Yes	10 (18.9)
No	43 (81.1)
Number of years in nursing	
0	43 (81.1)
1–5	4 (7.5)
6–10	3 (5.7)
>10	3 (5.7)
Acquired knowledge about genomics through	
Literature on genomic topics	24 (45.3)
Previous genomic course	3 (5.7)
Previous genomic workshop	1 (1.9)
Other resources	27 (50.9)
Curricular progression	
1st year	39 (73.6)
2nd year	8 (15.1)
3rd year	6 (11.3)

Measuring the Genomic Literacy of Croatian Undergraduate Nursing Students

Study Design

The anonymous online survey was conducted over 2-month period (March 2021–May 2021). It was approved by the Institutional Review Board of Undergraduate program 10. Inclusion criteria were students attending the Undergraduate nursing program 10 (1st–3rd year), Faculty of Medicine at the time of the survey administration and their willingness to participate in the study. There were no age or sex restrictions for participation.

Instrument

Survey data were collected using an online open-source software survey program Limesurvey. It consisted of demographic data shown in **Table 1** and the 31 multiple-choice questions that constitute the Genomic Nursing Concept Inventory (GNCI©) (Ward, 2011). The GNCI© is an internationally validated questionnaire developed for assessment of genomic literacy among nurses across four topical categories (Genome Basics, Mutations, Inheritance Patterns, Genomic Healthcare) and eighteen foundational genomic concepts (Ward, 2011; Ward et al., 2014; Ward et al., 2016a). Permission to use the

TABLE 2 | Curriculum for Undergraduate studies in nursing (academic year 2020/2021) in Croatia.

University		Enrollment quota		Courses				
		Full–time study program	Part–time study program	Compulsory	Additional		Genomics included as	
					Compulsory	Elective	Part of subject*	Independent subject
1	Undergraduate program 1	95	30	48	1	23	+	-
2	Undergraduate program 2	30	80	54	7	42	+	-
3	Undergraduate program 3	30	120	48	2	16	+	-
4	Undergraduate program 4	30	0	58	12	8	+	-
5	Undergraduate program 5	0	21	49	2	18	+	+
6	Undergraduate program 6	42	60	47	0	25	+	-
7	Undergraduate program 7	41	20	50	3	10	+	-
8	Undergraduate program 8	47	0	51	4	9	+	-
9	Undergraduate program 9	33	117	47	0	31	+	-
10	Undergraduate program 10	73	30	47	0	9	+	+
Total		421	478	499	31	191		

No defined learning outcomes and a number of hours related to genetic content.

TABLE 3 | Curriculum for Graduate studies in nursing (academic year 2020/2021) in Croatia.

University		Enrollment quota		Courses			
		Full–time study program	Part–time study program	Compulsory	Elective	Genomics included as	
						Part of subject*	Independent subject
1	Graduate program 1	0	20	110	60	+	-
2	Graduate program 2	0	40	50	57	+	-
3	Graduate program 3	30	150	13	10	+	-
4	Graduate program 4	0	20	25	5	-	-
5	Graduate program 5*	0	0	32	11	+	+
6	Graduate program 6	28	46	16	19	-	-
7	Graduate program 7	15	15	15	18	-	-
8	Graduate program 8	20	70	20	13	+	+
9	Graduate program 9	20	30	9	13	-	-
Total		113	391	290	206		

*No defined learning outcomes and a number of hours related to genetic content; **academic year 2020/2021 not enrolled.

instrument was obtained from the author of the GNCI©. The survey was translated into the Croatian language.

Data Analysis

Data were analyzed using SPSS® version 25 software (IBM Corp., Armonk, NY, United States). Descriptive statistics were used to determine trends in the demographic data. Each of the 31 GNCI© questions was scored as correct or incorrect and a total number of correct answers (range 0–31) was calculated for each participant. Mean scores for the four topical categories were calculated using a specified item data in each category.

RESULTS

Evaluation of the Current Genomics Content in the Curriculum

Table 2 shows the core curriculum for undergraduate studies (academic year 2020/2021) in Croatia. Ten universities in Croatia provide either full–time or part–time undergraduate study program, which enrolled 899 students in academic year 2020/2021. The nominal distribution among compulsory, additional and elective courses was similar between universities (**Table 2**). Genomics is included as a part of subject at each university, mainly throughout the Pediatrics course, with no defined learning outcomes and a number of hours related to genetic content. Only two undergraduate nursing programs (Undergraduate programs 5 and 10) provide independent genomic courses for Bachelor of nursing students.

Table 3 shows the curriculum for graduate studies (academic year 2020/2021) in Croatia. Nine universities in Croatia provide either full–time or part–time program, which enrolled 504 students in academic year 2020/2021. The nominal distribution among compulsory and elective courses vary a lot between universities (**Table 3**). Genomics modules are taught as part of other subject-matter courses (**Table 3**). Graduate programs 6 and 9 do not integrate any genomics content in their nursing curriculum. Curricula contents were not available

TABLE 4 | GNCI© item scores, topical category scores and total score.

Topical category	Domain	Item	Concept	Number of correct answers (%)
Genome Basics	Genome composition/ organization	2	DNA sequence = the order of nucleotides	37 (69.8)
		4	All cells contain an entire set of genes	5 (9.4)
		5	Genome organization (amount of DNA in the human genome)	21 (39.6)
		8	Organization of DNA (genome-chromosome-gene nucleotide)	6 (11.3)
	Homo and heterozygosity	13	Heterozygosity = two functionally different gene alleles	4 (7.5)
		29	People with AD diseases are usually heterozygous for the mutation	15 (28.3)
	Gene function/ expression	1	Gene function/expression	7 (13.2)
		6	Central dogma (product of DNA transcription-translation = protein)	9 (17.0)
		9	Specific role of a gene in determining a trait (produces a protein)	10 (18.9)
		11	Nature of gene expression (distinct from gene sequence)	13 (24.5)
	Genotype-phenotype association	7	Meaning of 'genotype' (distinguished from phenotype)	15 (28.3)
	Human genome variation	3	>99% of DNA sequence of unrelated people is identical	8 (15.1)
		20	All people have the same set of genes (e.g., BRCA)	11 (20.8)
	Mean score of topical category			**12.4 (SD = 8.8)**
Mutations	Mutations and disease	19	Genetic heterogeneity (people with the same genetic condition may have unique mutations)	14 (26.4)
		21	DNA alterations cause disease by altering protein production	15 (28.3)
	Germline and somatic mutations	18	Distinguishing germline and somatic mutations	2 (3.8)
	Mean score of topical category			**10.3 (SD = 7.2)**
Inheritance	Dominance	10	The meaning of dominance	13 (24.5)
	Autosomal inheritance	24	Autosomal disorders are inherited equally by males and females	14 (26.4)
	Autosomal dominant inheritance	30	Calculating inheritance risk in AD disease	23 (43.4)
		31	Inheritance risk is fixed and independent of number of offspring	20 (37.7)
	Autosomal recessive inheritance	15	Parents of offspring with AR conditions are obligate carriers	14 (26.4)
		16	Calculating inheritance risk in AR disease	25 (47.2)
	X-linked inheritance	17	Understanding inheritance of X-linked disorders	20 (37.7)
	Multifactorial inheritance	25	Multifactorial etiology of complex diseases	12 (22.6)
	Mean score of topical category			**17.6 (SD = 4.5)**
Genomic healthcare	Family health history	23	Identifying red flags (risk factors)	10 (18.9)
		26	Utility of family history to predict risk for complex disease	17 (32.1)
	Pharmacogenomics	12	Mutations can cause people to respond unpredictably to drugs	34 (64.2)
		27	A drug receptor is a protein (genetics and pharmacodynamics)	15 (28.3)
		28	Genes influence drug response via their effect on proteins	11 (20.8)
	Genetic testing	14	Meaning of a positive screening test	27 (50.9)
		22	Purpose of carrier testing	8 (15.1)
	Mean score of topical category			**17.4 (SD = 9.6)**
Mean total score				**14.7 (SD = 8.2)**

for all courses at the Graduate programs 4 and 7. Only two graduate nursing programs (Graduate programs 5 and 8) provide independent genomic courses for Master of nursing students.

Measuring the Genomic Literacy of Croatian Undergraduate Nursing Students

Initially, 189 students were invited to participate in the study, whereas 108 students clicked on the survey link. Sixty-eight inventories had missing responses to one or more test items. Those were excluded from analysis, which resulted in a final sample of 53 students. Ages ranged from 19 to 40 years (median 23.5 years). Most respondents identified as female (88.7%), were currently unemployed (81.1%), reported to be in the first year of their studies (73.6%) and acquired knowledge in genomics primarily by reading the literature (**Table 1**).

For each participant, a total number of correct answers (range 0–31) was calculated. Scores across all respondents ranged from 3 to 22, with a mean scale score of 9.8 (SD 5.3) (31.6% correct). Topical category scores were highest on "Inheritance" (33.2%), and lowest on "Mutations" (19.5%). A description of each item, along with the number of correct answers and the mean score of topical category is provided in **Table 4**. In relation to questions, student scores were highest in response to DNA sequence (Question 2, 69.8% answered correctly). In contrast, lowest scores were in distinguishing germline and somatic mutations (Question 18, 3.8% answered correctly).

DISCUSSION

Evaluation of the Current Genomics Content in the Core Curriculum

This study represents the first evaluation of the current genomics content in the curriculum of undergraduate and graduate program of Studies in nursing in Croatia (academic year 2020/

2021). Data were derived from the curriculum of ten undergraduate and nine graduate nursing programs. Our findings show that the genomics is marginalized in the education of nurses, both at the undergraduate and graduate levels.

Our findings corroborate that genomics curriculum is less developed at the undergraduate than the graduate level likely because graduate programs are mandated by the Ministry of Education (Ministry of Science and Education Republic of Croatia, 2014) to include genomics content to comply with European Directive 2005/36/EC) (EUR-Lex, 2020). The Directive prescribes in detail the minimum requirements for a 3-year education of nurses, 4,600 h of theoretical and clinical training, and compulsory courses in the field of nursing care, basic and social sciences. Representatives of all higher education institutions conducting undergraduate nursing study programs in Croatia organized in 2013 a working group for the harmonization of nursing study programs with the provisions of Directive 2005/36/EC. Besides, the working group has developed a core curriculum that defines each compulsory course at the undergraduate level (Working group, Ministry of Science and Education Republic of Croatia, 2014). During the development of the core curriculum, the working group did not follow the results of numerous studies showing a low level of genomic knowledge (Bankhead et al., 2001; Bottorf et al., 2005; Maradiegue et al., 2005; Tomatir et al., 2006). Neither recommendations of The European Society of Human Genetics (ESHG) to facilitate the development of genomic health care in the European community were adopted into the core curriculum (The European Society of Human Genetics, 2008). A review of the directive shows that genomics is only mentioned in the education study program for veterinary surgeons as part of the specific subjects related to basic science (EUR-Lex, 2020). As the significance of genomics in the education of nurses was not recognized, the opportunity to incorporate basic competencies in genomics (The European Society of Human Genetics, 2008) into the core curriculum was missed. However, curricula of the Undergraduate programs 5 and 10, include genomics both, as a part of other subject and as an independent subject. In all other universities' curricula, genomics is present only as a part of compulsory courses. No expected learning outcomes are specified nor are guidance about the number of hours genomics should occupy in the total course schedule. At the graduate level, the situation is similar. Among nine universities, only Graduate programs 5 and 8 offer genomics both as part of the subject and independent subject.

Although the Undergraduate programs 5 and 10, as well as graduate programs 5 and 8, represent Croatian Universities that recognize the importance of genomic education among nurses, when compared to examples of good practice at the international level (e.g., The University of Texas Permian Basin, 2020), their programs are still insufficient. Namely, outcomes at the international level include higher levels of knowledge, which enables skills acquisition and the development of attitudes, content is focused on incorporating genomics knowledge and technologies in nursing practice, obligatory and recommended materials are from the field of nursing practice, and the curriculum is entirely based on established competencies.

Measuring the Genomic Literacy of Croatian Undergraduate Nursing Students

Our results indicate that the genomic literacy of Croatian undergraduate nursing students (Undergraduate program 10) is low. Interestingly, the majority of participants that initially clicked the survey link gave up during the survey, because, as stated in their reasons, "it was too difficult." This could signal a genomic knowledge deficit among the students we recruited to survey. The reason for this can perhaps be found in the fact that most of the participants were first-year students, and did not attend any genomic course that may improve their understanding of genomics (e.g., compulsory Pediatrics course or an elective course Human Genetic Disease).

With a mean total score of 9.8 (SD 5.3; score range 3–22; 31.6% correct answers), our results are marginally lower in comparison to the results of other studies that utilized the GNCI© instrument. Namely, Wright et al. reported a mean score of 13.3 (SD 4.60; score range 3–29) (Wright et al., 2019), McCabe et al. 13.7 (SD 4.9; score range 5–26; 44% correct answers) (McCabe et al., 2016), while Ward et al., reported a mean score of 12.85 (SD 4.64; score range 3–28; 41.5% correct responses) (Ward et al., 2016b), and finally, Read and Ward published 14.9 (SD 5.3; score range 4–31; 48% correct answers) (Read and Ward, 2016). To reflect on the results of the other studies that used different methods for genomic literacy assessment, the integrative reviews by Wright et al., and Godino et al., were analyzed (Godino et al., 2013; Wright et al., 2018). The reported conclusions of these studies are similar, declaring inadequate genomic competency among nurses, which closely correlates with a level of their genomic literacy. The authors underline the importance of assessing actual content knowledge using a validated inventory instrument e.g., GNCI rather than self-reports to best capture genomic literacy in future studies. However, considering motivation as a very important factor in the learning process (Ferreira et al., 2011), the estimation of self-reported motivation and/or perceived knowledge should also be included.

LIMITATIONS

The results of this study should be interpreted in light of several limitations. Namely, curricula contents were not available for all courses at the websites of all universities (Graduate programs 4 and 7), while the available curricula were not concordant among universities. Furthermore, the curricula analyzed either did not provide information on the number of hours devoted to genomics or if listed, did not specify how student knowledge was assessed. Measuring the genomic literacy of Croatian undergraduate nursing students was limited by the Covid-19 pandemic. Online impersonal assessment made it difficult to motivate students and ended with poor recruitment and participation of students. It resulted in small sample size, mostly consisting of first-year students, from a single nursing program. In addition,

the participation of second and third-year students in small numbers prevented the previously planned comparison of knowledge between students of different years of study. Nonetheless, although the survey response rate was lower than expected, our study findings provide a valuable snapshot of genomic literacy among under/graduate nursing students.

FINAL RECOMMENDATIONS AND CONCLUSION

Based on the results of our research, it is necessary to create the preconditions for efficient and effective implementation of genomics in the education of nurses in Croatia. The inclusion of genomics should be harmonized throughout the curriculum, with well-defined outcomes that should be coordinated with international documents prescribing the competencies of nurses in the field of genomics, respecting the specifics of each country. Existing curricula should be reviewed to ensure only genomics concepts that are relevant to nursing practice are added to improve literacy. Moreover, the assessment of genomic literacy throughout the validated questionnaires should be accomplished before the development of the curriculum so that course content can be directed to knowledge deficits. Furthermore, our recommendation would be to implement the genomic content from the beginning of the studies in order to adopt the basic knowledge, which should be upgraded during continuous education. The genomic content at the graduate level should be harmonized with the outcomes that students acquire upon completion of the study program. Besides, elective genomic courses should be offered to students who want to acquire more knowledge and skills related to genomics. Since it is essential to weave genomics throughout the curriculum, it is necessary to support teachers in this area. We must not forget the nurses who completed their education according to curricula that did not include genomic content. Multifactorial barriers to increasing the amount of genomics content in nursing curricula include: insufficient genomics knowledge base of most nursing faculty, limited numbers of faculty in various programs who view genomics as relevant to nursing practice, perceived inability to add more content to an already crowded curriculum, and a lack of regulatory agencies of nursing requiring competency in genomics as part of the licensure.

Due to the fact that research is carried out with a small student population, mostly in their first year of undergraduate, our plan would be to replicate the research on the national level, which means recruiting each University in Croatia that provides a nursing Program, using the GNCI© questionnaire, which would allow scaling up the results with adequate sample size. Moreover, this would provide insight into genomic literacy among Croatian nursing students and serve as a good starting point for the development of a nationally adapted curriculum.

Overall, more must be done to ensure that Croatian nurses have an adequate level of genomic literacy (knowledge of the role of the genomic factors in health and disease, understanding of the utility and limitations of genomic testing and information, upholding the rights of all individuals to informed decision making) to deliver optimal nursing care. Study programs have to be in line with modern clinical nursing practice, which definitely require the implementation of genomics into the curriculum, either as a part of a compulsory course or/and a separate one. Also, we believe that mandatory non-formal education, prescribed by the Croatian Chamber of Nurses is a good ground for the inclusion of genomic content as well. Finally, genomics is increasingly important in all areas of clinical nursing practice, and the effectiveness of courses and curricula in developing genomic competence among students is of high priority for evolving modern nursing practice.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Board of Juraj Dobrila University of Pula. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DM and JV conceived the study. AB contributed to the study design. DM identified the extracted information from the websites. MŠ translated the survey. ID collected and analyzed survey data. DM, AB, and JV reviewed, critically discussed and interpreted the core curriculum and the results of the survey. DM and AB contributed to the drafting of the manuscript. JV and MŠ critically reviewed the manuscript. All authors read and approved the final version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fgene.2021.759950/full#supplementary-material

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Current State of Compulsory Basic and Clinical Courses in Genetics for Medical Students at Medical Faculties in Balkan Countries With Slavic Languages

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Introduction: In this study we aimed to perform the first research on the current state of compulsory basic and clinical courses in genetics for medical students offered at medical faculties in six Balkan countries with Slavic languages (Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia).

Materials and Methods: The study was conducted from June to September 2021. One representative from each country was invited to collect and interpret the data for all medical faculties in their respective country. All representatives filled a questionnaire, which consisted of two sets of questions. The first set of questions was factual and contained specific questions about medical faculties and design of compulsory courses, whereas the second set of questions was more subjective and inquired the opinion of the representatives about mandatory education in clinical medical genetics in their countries and internationally. In addition, full course syllabi were analysed for course aims, learning outcomes, course content, methods for student evaluation and literature.

Results: Detailed analysis was performed for a total of 22 medical faculties in Bosnia and Herzegovina (6), Croatia (4), Montenegro (1), North Macedonia (3), Serbia (6), and Slovenia (2). All but the two medical faculties in Slovenia offer either compulsory courses in basic education in human genetics (16 faculties/courses) or clinical education in medical genetics (3 faculties/courses). On the other hand, only the medical faculty in Montenegro offers both types of education, including one course in basic education in human genetics and one in clinical education in medical genetics. Most of the basic courses in human genetics have similar aims, learning outcomes and content. Conversely, clinical courses in medical genetics are similar concerning study year position, number of contact hours, ECTS (European Credit Transfer and Accumulation System) and contents,

but vary considerably regarding aims, learning outcomes, ratio of types of classes, teaching methods and student evaluation.

Conclusion: Our results emphasise the need for future collaboration in reaching a consensus on medical genetics education in Balkan countries with Slavic languages. Further research warrants the analysis of performance of basic courses, as well as introducing clinical courses in medical genetics to higher years of study across Balkan countries.

Keywords: genetic education, medical genetics, human genetics, medical education, compulsory course, genomic medicine, medical students, medical faculty

INTRODUCTION

Medical genetics is one of the most complex, comprehensive and multidisciplinary medical specialties covering all stages of life and organ systems, simultaneously placing a special emphasis on ethical, legal and social implications of genetic testing. Moreover, the integration of the fascinating advancements in the development of genetic and genomic testing methods into various parts of medicine occurs at an accelerated pace. Therefore, most countries in Europe, especially Western Europe, have long recognised not only the importance of introducing medical and laboratory genetics as separate medical specialties, but have also put effort into raising the level of genetic literacy among medical students as the future health professionals who will be involved in the care of patients with genetic disorders (Tobias et al., 2021).

The Balkan area is a geographical region in the south-eastern part of the European continent, associated with different cultural and historical classifications. One of these includes the classification according to the languages spoken in specific countries, such as Slavic, Romance, Turkish and other languages. Countries with Slavic languages include Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, North Macedonia, Serbia and Slovenia. In fact, these countries are not only associated by Slavic language but also similar higher education and health systems.

Unfortunately, Balkan countries with Slavic languages have encountered many historical obstacles that have left inevitable consequences in terms of significant delays in both introducing medical and laboratory genetics as medical specialties, as well as recognising genetic education at medical faculties as an indispensable tool for future physicians of the 21st century. Consequently, the advances in medical genetics internationally have not been accompanied always by an adequate level of application in clinical practice nor raising genetic literacy among medical students locally in the Balkans. Furthermore, most countries have not yet introduced medical or laboratory genetics as medical specialties, which inevitably reflects on the (poor) position of genetic education in the integrated undergraduate and graduate medical education system.

Genetic education of medical students is a critical prerequisite for appropriate care for patients with genetic disorders (Bennett et al., 2017; Hyland and Dasgupta, 2019). Because medical genetics is both a basic science and a clinical specialty, appropriate genetic education of medical students should include the literacy on basic concepts in human genetics, as well as clinical concepts in medical genetics (Robinson and Fong, 2008). However, the current situation for genetic education opportunities for medical students at medical faculties in the afore-mentioned Balkan countries is not known. Considering this, as well as the fact that Balkan countries with Slavic languages are associated by more similarities than separated by simply geographical boundaries, the aim of this study was to analyse the current state of compulsory basic and clinical courses in genetics for medical students offered at medical faculties in these countries.

MATERIALS AND METHODS

Inclusion of Representatives From Different Balkan Countries

This retrospective study was conducted from June to September 2021. To investigate the current state of basic and clinical compulsory courses in genetics for medical students at medical faculties in Balkan countries in which Slavic languages are spoken, the study was designed so that one representative from each of the selected countries was invited to collect and interpret the data for all medical faculties in their respective country.

An additional four representatives from four different Balkan countries with Slavic languages (Bosnia and Herzegovina, Montenegro, North Macedonia, and Serbia) were contacted *via* e-mail in June 2021 with a letter of invitation to participate in the study. The representatives were chosen based on their expertise, as well as national and international excellence in the field of both basic human genetics and clinical medical genetics. The letter of invitation contained all the relevant information regarding the research, including an explanation of the background, aims, materials and methods. In addition, in this invitation letter, the representatives were sent and asked to fill a questionnaire about the basic and clinical compulsory courses in genetics offered in their respective countries at medical faculties for medical students and a due date was provided. All six representatives (Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia and Slovenia) filled the questionnaire and were sent a second e-mail with the request to send the full syllabi for each course mentioned in the

questionnaire. The second e-mail also contained a detailed explanation of the reasons for requesting the full course syllabi (evaluation of course aims, learning outcomes, course content, methods for student evaluation and mandatory literature).

All representatives participated in the research voluntarily. Considering that this research is a retrospective study, no approval of ethical committees was necessary.

Questionnaire

A short questionnaire was designed with the aim of collecting the relevant data about basic and clinical compulsory courses in genetics for medical students at medical faculties in Balkan countries in a concise and uniform manner. The questionnaire consisted of two sets of questions.

The first set of questions was factual and contained specific questions about mandatory education, including the names of the medical faculties in their respective countries and titles of basic and clinical compulsory courses in genetics offered at each medical faculty for medical students. In addition, for each course, the representatives were asked to grade the appropriateness of the study years on which the courses are offered at each faculty (level too low/appropriate/too high), number of contact hours (insufficient/appropriate/too high), and ECTS (underestimated/appropriate/overestimated).

The second set of questions was more subjective and inquired the opinion of the representatives about mandatory education in clinical medical genetics in their countries and internationally. The questions were: "Do you think that there should be a single, uniform curriculum for all compulsory courses in medical genetics in your country?", "Do you think that there should be a single, uniform curriculum for all compulsory courses in medical genetics internationally?", "Is medical genetics recognized as a medical specialty in your country? If yes, from which year", "Is laboratory genetics recognized as a medical specialty in your country? If yes, from which year", and "What are the main obstacles for optimization of the courses in your country?".

Full Course Syllabi

Data extracted, analysed and compared from full course syllabi were course aims, learning outcomes, course content, methods for student evaluation and literature.

RESULTS

Representatives of six Balkan countries with Slavic languages (Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia) participated in the research. Detailed analysis was performed for the total number of medical faculties in these countries, which is 22 (Bosnia and Herzegovina 6, Croatia 4, Montenegro 1, North Macedonia 3, Serbia 6, Slovenia 2). All but two medical faculties (Faculty of medicine, Universities of Ljubljana and Maribor in Slovenia) offer either compulsory courses in basic education in human genetics (16 faculties/courses) or clinical education in medical genetics (3 faculties/courses). On the other hand, only one medical faculty offers both types of education, including one course in basic education in human genetics and one in clinical education in medical genetics (Faculty of Medicine, University of Montenegro, Podgorica). Data on the 20 medical faculties that offer compulsory courses in genetics for medical students is shown in **Tables 1**, **2**.

Basic Courses in Human Genetics

General Features

A total of 17 compulsory basic courses in human genetics are offered at 17 medical faculties in five countries (Bosnia and Herzegovina 6, Croatia 1, Montenegro 1, North Macedonia 3, Serbia 6) (**Table 1**). While most courses are similar according to their position in the study years (15 in the first year, two in the second year), the courses vary considerably regarding the number of contact hours (45–135) and ECTS (4–9). Furthermore, the representative of Croatia stated that a small percentage of the compulsory course "Medical biology", which is offered on all four medical faculties in the country, is dedicated to the basics of human genetics but this is not reflected in the title of the courses and is therefore not presented in **Table 1**.

Representatives of Bosnia and Herzegovina, Montenegro and North Macedonia agree that the position of the courses regarding the study years is too low. On the contrary, the representative of Serbia considers that the positions for the basic courses are appropriate in their country but emphasises the importance of introducing additional mandatory education in clinical genetics in the later study years. A special emphasis should be placed on the Faculty of Medicine, University of Split (Croatia), where the title of the basic course "Immunology and Medical Genetics" does not reflect its content, which is a mixture of both basic and clinical topics.

In addition, representatives of Bosnia and Herzegovina (regarding medical faculties in Banja Luka, East Sarajevo and Mostar), Croatia, Montenegro and Serbia agree that the number of contact hours and ECTS is appropriate for the respective courses. On the other hand, the representatives of Bosnia and Herzegovina (regarding medical faculties in Sarajevo, Tuzla, Zenica and Mostar) and North Macedonia state that the number of contact hours and ECTS in insufficient.

Analysis of Full Course Syllabi

The analysis of full course syllabi across different Balkan countries (indicated in **Table 1**) revealed many similarities with only a few differences, which can be attributed to the freedom of each course coordinator, as well as specificities of the faculties' full curricula. The only exception is the course "Immunology and Medical Genetics" at the Faculty of Medicine, University of Split (Croatia), which contains mostly basic topics with a hint of practical topics, and a consequently unclear aim and learning outcomes of the course and was therefore excluded from further comparison. Also, the title of the course "Medical genetics" at the Faculty of Medicine, University of Mostar (Bosnia and Herzegovina) would correspond more to a "Human Genetics" type of course according to their aims, learning outcomes and contents. The mandatory literature is similar for all courses (Cooper, 2000), and, additionally, at certain medical faculties, the course coordinators have their own accredited handbooks.

TABLE 1 | Basic courses in genetics offered at medical faculties for medical students in Balkan countries with Slavic languages.

Country	Names of medical faculties in country	Titles of the compulsory courses offered at each medical faculty	Number of contact hours in course	Number of ECTS for the course	Study year at which the course is offered
Bosnia and Herzegovina	Faculty of Medicine, University of Banja Luka	Human Genetics	75	6	1st
	Faculty of Medicine Foca, University of East Sarajevo	Cell Biology and Human Genetics	135	9	1st
	Faculty of Medicine, University of Sarajevo	Cell Biology and Human Genetics	75	6	1st
	Faculty of Medicine, University of Tuzla	Biology with Human Genetics	75	7	1st
	Faculty of Medicine, University of Zenica	Medical Biology with Human Genetics	50	5	1st
	School of Medicine, University of Mostar	Medical Genetics	45	4	2nd
Croatia	Faculty of Medicine, University of Split	Immunology and Medical Genetics	95	6	2nd
Montenegro	Faculty of Medicine, University of Montenegro, Podgorica	Human genetics	90	6	1st
North Macedonia	Faculty of Medicine, SS. Cyril and Methodius University, Skopje	Human genetics	60	5	1st
	Faculty of Medical Sciences, Goce Delcev University, Stip	Human genetics	45	4	1st
	Faculty of Medical Sciences, State University, Tetovo[a]	Human genetics	45	4	1st
Serbia	Faculty of Medicine, University of Belgrade	Human Genetics	75	6	1st
	Faculty of Medical Sciences, University of Kragujevac	Human Genetics	60	6	1st
	Faculty of Medicine, University of Novi Sad	Biology with Human Genetics	75	8	1st
	Faculty of Medicine, University of Niš	Molecular and Human Genetics	75	7	1st
	Faculty of Medical Sciences, University of Prishtina[b]	Human Genetics	75	7	1st
	Medical Faculty of the Military Medical Academy, University of Defence in Belgrade	Human Genetics	75	7	1st

[a]*Teaching in performed in Albanian language.*
[b]*Temporary headquarers in Kosovska Mitrovica.*

TABLE 2 | Clinical courses in medical genetics offered at medical faculties for medical students in Balkan countries with Slavic languages.

Country	Names of medical faculties in country	Titles of the compulsory courses offered at each medical faculty	Number of contact hours in course	Number of ECTS for the course	Study year at which the course is offered
Croatia	Faculty of Medicine, University of Zagreb	Medical Genetics	45	4	6
	Faculty of Medicine, University of Rijeka	Medical Genetics	45	3	5
	Faculty of Medicine, University of Osijek	Medical Genetics	45	4	6
Montenegro	Faculty of Medicine, University of Montenegro, Podgorica	Clinical genetics	60	4	5

The aims were highly similar between courses, and mostly referred to the basic principles of modern biology and genetics (e.g. cell, biology, molecular biology, developmental biology and human genetics), focusing on the important molecular mechanisms that are important to human health, as well as the diagnosis and therapy of human diseases. Furthermore, learning outcomes were also comparable regarding knowledge, skills, and attitudes, although the biggest differences can be attributed to the level of performance required from the student. Moreover, the course content is again similar with certain specificities; however, the topics are relevant for medical students and up to date for the field of modern human genetics. The topics cover a wide array of content, from the structure of nucleic acids and chromosomes to the basics of genetic disorders aetiology (e.g. gene mutations, chromosome aberrations, epigenetic modifications) and modern methods for detection of genetic disorders. Finally, the biggest differences are present in the methods for student evaluation, especially in terms of grading and number of tests used. Although student evaluation is based mostly on the assessment of knowledge, some courses use only written exams, whereas others use both written and oral exams. With a few exceptions, the acquisition of skills is not assessed in most courses, i.e., assessment does not reflect the expected learning outcomes regarding skills.

Clinical Courses in Medical Genetics

General Features

A total of four compulsory basic courses in medical genetics are offered in two countries (Croatia—Faculties of Medicine,

University in Rijeka, Osijek and Zagreb, and Montenegro—Faculty of Medicine, University in Podgorica) (**Table 2**). Two of the courses are offered at the fifth year and two at the sixth year of study. All four studies are similar according to the number of contact hours (45–60) and ECTS (3–4).

All representatives agree that the position of the respective courses in the study year is appropriate. On the other hand, the representative of Montenegro stated that the number of contact hours and ECTS in insufficient for their course, whereas the representative of Croatia agrees that it is appropriate.

Finally, an additional course offering mandatory education in clinical genetics is integrated with pediatrics at the Faculty of medicine, University in Maribor (Slovenia). However, the program is focused only on genetics in the paediatric period and was therefore excluded from further analysis. In addition, in Slovenia at the Faculty of Medicine, University of Ljubljana some of the medical genetic topics are included in other basic or clinical courses.

Analysis of Full Course Syllabi

Unlike the basic courses in human genetics, the four clinical mandatory courses in medical genetics (**Table 2**) are similar only regarding the course contents, whereas they vary considerably with respect to the aims, learning outcomes, types of classes, ratio of types of classes, teaching methods and methods for student evaluation. The mandatory literature for the courses offered at the medical faculties of Zagreb, Osijek and Podgorica is the same (Turnpenny and Ellard, 2012), whereas the course "Medical Genetics" offered at the Faculty of Medicine, University of Rijeka has its own accredited mandatory literature.

The course "Medical Genetics" offered at the Faculty of Medicine, University of Rijeka (Croatia) consists of 17 h of lectures, 15 h of seminars and 13 h of practicals. The entire course is conducted exclusively through active learning methods and is designed and performed through case-based reasoning, thus achieving both clinical reasoning and a simulation of the actual physician-patient relationship in practice. The learning outcomes were determined and derived in accordance with key competencies according to Core Competences in Genetics for Health Professionals in Europe published by the European Society of Human Genetics specifically for physicians who are not specialists in medical genetics (ESHG European Society of Human Genetics, 2008; Čargonja et al., 2021). The final exam is delivered in the form of patient management problems, evaluating knowledge, skills, and attitudes at the same time.

The course "Medical Genetics" offered at the Faculty of Medicine, University of Zagreb (Croatia) consists of 20 h of lectures, 5 h of seminars and 20 h of practicals. Practicals are conducted at the clinics for pediatrics and the final exam is a written test. On the other hand, the third course delivered in Croatia, "Medical Genetics" at the Faculty of Medicine, University of Osijek (Croatia) consists of 27 h of lectures and 18 h of seminars.

Finally, the course "Clinical Genetics", which is delivered at the Faculty of Medicine, University of Podgorica (Montenegro) resembles the course "Medical Genetics" at the Faculty of Medicine, University of Rijeka regarding the aim and learning outcomes, although it has more contact hours, thus enabling a wider approach in topics. The final exam consists of the practical and oral part.

Reflections on Uniform Curricula Locally and Internationally

The representatives of all six countries agree that there should be a single, uniform curriculum for all compulsory courses in medical genetics in their respective countries. The representative of Bosnia and Herzegovina believes that it would allow easier cooperation and coordination of program. However, the representatives of Croatia and Slovenia believe that although a common framework would be helpful, some variations and freedom should be allowed between faculties due to specificities in medical genetics practice in each country and curricula of other subjects. The representative of Croatia emphasises that this curriculum should not be provisory but should also be aligned with the already existing document Core Competences in Genetics for Health Professionals in Europe published by the European Society of Human Genetics specifically for physicians who are not specialists in medical genetics (ESHG).

The representatives demonstrated more variation in their answers to the question on whether a there should be a single, uniform curriculum for all compulsory courses in medical genetics internationally. For example, the representatives of Croatia, Montenegro and Serbia think that a common framework for the Balkan area would be more appropriate due to the local specificities and different level of genetic services. On the contrary, the representatives of North Macedonia and Slovenia believe that there should be a common framework, although adapted to national health systems, which would enable common standards of knowledge for the European Union health systems, whereas the representative of Bosnia and Herzegovina thinks that a single uniform curriculum for all compulsory courses internationally would lead to better optimization of the scientific plan. Finally, all representatives agree that variations and freedom should be allowed to each course coordinator.

Opportunities for Training in Medical and Laboratory Genetics in Balkan Countries

Medical Genetics as a Medical Specialty

Of the six included countries, medical genetics is offered as a medical specialty only in North Macedonia (from 2015) and Slovenia (from 2002). In Montenegro and Serbia, clinical genetics is offered as a sub-specialist education after a previously completed specialty (e.g. in pediatrics, internal medicine, gynaecology, etc.). Neither of the previously mentioned opportunities are offered in Bosnia and Herzegovina and Croatia.

Laboratory Genetics as a Medical Specialty

Similar to the opportunities for medical genetics training, laboratory genetics is available as a medical specialty in North Macedonia and Slovenia. In the case of North Macedonia,

training in medical genetics was previously available only for biologists at the Medical faculty, University in Skopje; however, a new specialty—Clinical laboratory genetics, was introduced in 2012, which is open to health professionals, including medical doctors. In Montenegro, training in laboratory genetics is recognized in terms of the necessary conditions for work in genetic laboratories but residents need to perform their training in other countries considering that it is not available in their country. Neither of the previously mentioned opportunities are offered in Bosnia and Herzegovina and Croatia.

Obstacles for Optimization of Clinical Courses in Medical Genetics in Balkan Countries

In the final question, the representatives were asked to share their opinion on the main obstacles for optimization of the courses in their respective countries.

The representative of Bosnia and Herzegovina shared a detailed evaluation on the current situation in their country, including that knowledge of medical genetics among teaching staff is very limited considering that there are no specialists in medical and laboratory genetics. In addition, financial challenges are obvious, especially in organizing laboratory work, such as demonstrations. Finally, the representative emphasises the inconsistencies of the entire education system as a separate issue.

The representative of Croatia believes that the fact that mandatory clinical courses in medical genetics are even offered in Croatia is a success of its own considering there is no training in medical or laboratory genetics. The biggest issue for their optimization is the lack of sufficient awareness of clinical decision makers about the importance of medical genetics and its place in modern medicine, which contrasts with great agility among medical faculty teachers towards the introduction of medical genetics in clinical practice, especially at the Faculty of Medicine, University of Rijeka. The fact that clinicians underestimate the necessity that medical students learn about medical genetics and do not integrate genetic contents or discuss patients with genetic disorders with their students represents the greatest obstacle for proper implementation of medical genetics in clinical practice in Croatia. One of the possible reasons for this is the low level of genetic literacy among different specialists. The representative of Montenegro, who believes that the small population of the country does not enable the sustainability of all types of education and that there is insufficient awareness of decision makers about the importance of medical genetics and its place in modern medicine, shared a similar opinion. In addition, the representative of Serbia thinks that better synchronization is needed between basic, laboratory and clinical aspects of medical genetics, both in education and in practice in their country. Finally, the Slovenian representative believes that there is a disconnection between medical faculties, which are dominated by non-medical scientists involved in teaching and decision making, and clinical centres, which are the seats of actual genetic medical practice.

DISCUSSION

In the present study, we evaluated the current state of compulsory basic and clinical courses in genetics for medical students offered at medical faculties in six countries associated by Slavic languages, including Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia. With the help of representative authorities in both human and medical genetics from each country, we performed the first such study in the Balkan peninsula, which was of the utmost importance for gaining insight into the present situation, as well as planning for future directions in mandatory genetics education at medical faculties for medical students in this area. A detailed analysis of each country revealed that Bosnia and Herzegovina and Serbia precede in the number of medical faculties (six in each country), and are followed by Croatia (4), North Macedonia (3), Slovenia (2), and Montenegro (1). Except for Slovenia, all other countries offer some sort of compulsory courses in genetics for medical students: either courses in basic education in human genetics (Bosnia and Herzegovina, North Macedonia, Serbia) or both basic education in human genetics and clinical education in medical genetics (Croatia and Montenegro). However, in the case of Croatia, basic education in human genetics is offered at just one medical faculty, whereas clinical education in medical genetics is offered at three different medical faculties. Therefore, currently the best example for an integrative approach to medical students' comprehensive education in genetics is represented by the Faculty of Medicine, University of Podgorica in Montenegro, which offers basic education in human genetics in the first year of study and clinical education in medical genetics at the fifth year of study.

Basic Courses in Human Genetics

Compulsory basic courses in human genetics are offered at 17 medical faculties in five countries (Bosnia and Herzegovina 6, Croatia 1, Montenegro 1, North Macedonia 3, Serbia 6). Interestingly, except for Croatia, which represents a special case, and Slovenia, which does not offer any type of basic education in human genetics, this result indicates that mandatory education in human genetics is offered at every medical faculty in Bosnia and Herzegovina, Montenegro, North Macedonia, and Serbia. Most of the courses (15) are offered in the first year of study, with highly similar aims, learning outcomes and course content. Although the mandatory literature is also similar, commendably, certain course coordinators also have their own accredited handbooks, emphasising and encouraging the importance of allowing freedom to each course coordinator. All these results indicate high awareness of the importance of basic sciences in modern medicine in these countries and represents an excellent basis for the introduction of clinical courses in medical genetics in the later years of study, like in Montenegro.

As indicated, Croatia represents a special case because although a compulsory course "Medical biology" is offered at all four medical faculties in the country, covering certain topics of the basics of human genetics, this is not reflected in the title of the course and was therefore excluded from further analysis.

However, an initiative might be launched at the national level to rename the courses to reflect their contents in a more accurate manner (e.g. Medical biology with human genetics). We also encountered certain illogicality at the Faculty of Medicine, University of Split, where the title of the basic course "Immunology and Medical Genetics" does not reflect the content and should therefore be renamed and separated from immunology. In addition, after the modification of the course aims, learning outcomes and contents, the course should be moved to a higher year of study, as is the case with the remainder of medical faculties in the country. It is unclear how this artificial merging of two highly diverse courses occurred considering that this not in line with the Croatian national curriculum.

Although the representatives of Bosnia and Herzegovina, Montenegro and North Macedonia believe that the position of the courses are too low in the study year, the representative of Serbia considers that the position is appropriate and that an additional clinical course should be introduced at the higher years of study.

Clinical Courses in Medical Genetics

The current situation regarding compulsory clinical courses in medical genetics is completely different than for basic courses in human genetics. Generally, clinical courses in medical genetics are highly underrepresented in Balkan countries. Specifically, only four compulsory clinical courses are offered in just two countries—at three medical faculties in Croatia and one in Montenegro. Interestingly, neither country offers medical or laboratory genetics as a medical specialty. In addition, although these courses are similar with regards to study year position (fifth or sixth year), number of contact hours (45–60), ECTS (3–4) and contents, they vary considerably with respect to the aims, learning outcomes, types of classes, ratio of types of classes, teaching methods and methods for student evaluation. Not only do the courses vary between Croatia and Montenegro, but they also vary substantially between the medical faculties in Croatia. For example, students attend practicals only at the pediatrics departments at the Faculty of medicine, University in Zagreb, whereas at the Faculty of medicine, University of Osijek, students do not have practicals at all. On the other hand, at the Faculty of medicine, University of Rijeka, the course is based on clinical reasoning and is aligned with key competencies according to Core Competences in Genetics for Health Professionals in Europe published by the European Society of Human Genetics specifically for physicians who are not specialists in medical genetics (ESHG European Society of Human Genetics, 2008; Robinson and Fong, 2008). The course content, teaching methods (primarily case-based reasoning) and methods of evaluation were analysed in detail on two generations of medical students and the results, which were previously published (Čargonja et al., 2021), confirmed that needs-based education not only increases the knowledge of medical students, but also helps develop positive attitudes and self-confidence, which is crucial for proper patient care. It is noteworthy to emphasise that the same course at the same medical faculty was among the most problematic in the entire medical study several years ago and received constant negative feedback from students. The main reason for this criticism from students was highly justified since the course contained mostly basic topics in human and laboratory genetics, such as detailed descriptions of methodology and even performance of molecular-genetic methods of genetic testing, which is not relevant for future physicians. All of this is in line with the adult learning theory, in which motivation and purposefulness of content is crucial (Thammasitboon and Brand, 2021). However, the course was completely altered with the new course coordinator and is now in tune with the actual requirements of medical professionals at the end of their integrated undergraduate and graduate education.

Obstacles for Optimization of Clinical Courses in Medical Genetics in Balkan Countries

The reasons for such low integration of compulsory clinical courses in medical genetics at the medical faculties for medical students in Balkan countries are numerous. The Balkan area is a highly specific geographic area in Southeast Europe and is sometimes associated with different cultural and historical explanations. First, this is an area which is synonymous with conflict and violent confrontation, which undoubtedly slowed down the progress and development of certain Balkan countries. The best evidence for this is Slovenia, which is the only country that did not suffer substantial war consequences and was the first of the Balkan countries included in this study to introduce both medical and laboratory genetics specialties and experience profound progress in the application of the most modern technologies in genetic testing to everyday clinical practice. In fact, specialists in medical and laboratory geneticists from Slovenia are the ones who are nowadays helping professionals in other Balkan countries develop medical and laboratory genetics with their knowledge, experience, and clinical services. Second, a direct consequence of the afore-mentioned concerns are economic issues of the Balkan countries, which are still evident in the present time (emphasised by the representatives of Bosnia and Herzegovina and Croatia) and does not allow for the same opportunities for the procurement of expensive modern genomic technologies as in the Central and West European countries. Third and final, considering the substantial delay in medical genetics in comparison with West European countries, most diagnostic genetic laboratories were led by non-medical professionals, especially biologists and molecular biologists, who were consequently also the first course coordinators of clinical courses in medical genetics (especially in Croatia). Considering that non-medical professionals did not associate the contents in their courses with clinical practice, future physicians did not see the benefits of medical genetics in clinical practice. When these students became physicians, they could not integrate medical genetics into their clinical teachings, leading to a consequently huge gap and a vicious circle between basic scientists and clinicians, which is still ongoing.

In this study, the representative of each country shared their opinion on this topic for their country and these are in line with the afore-mentioned issues. With certain specificities in their

answers, all representatives agree that the biggest issue in each country is insufficient awareness of decision makers (be they clinical or basic professionals) about the importance of medical genetics and its place in modern medicine.

Directions for the Future

In terms of the basic courses in human genetics, although they are highly similar on paper (with respect to biggest differences in the methods for student evaluation, as expected), further research would require the analysis of course performance. Therefore, future research would require peer-review and attendance of all courses to evaluate the transfer of content to students, especially in the context of analysing the achievement of course aims and learning outcomes, as well as applied teaching and learning methods (e.g. the application of active learning methods and better horizontal integration with clinical courses). Future studies should also analyse vertical integration with clinical courses to allow for updates in the curricula. Also, feedback from student evaluation of the courses must be considered because student opinion is crucial for advancing any curriculum or syllabus.

For the clinical courses, Balkan countries are in desperate need of introducing these to higher years of study consequent to the rapid development of medical genetics and its integration into all fields of modern medicine. However, course coordinators should bear in mind that it is crucial that their courses are aligned with the minimum core competencies for future physicians and that the education is needs-based. Otherwise, if medical students do not see usefulness, purposefulness, and application of the course contents in their future clinical practice, opposite, unwanted effects might be achieved. Therefore, it would be important to follow the rules of adult-learning theory and apply active learning methods (e.g. clinical reasoning) and critical thinking to the maximum extent (Wolyniak et al., 2015; Čargonja et al., 2021). Although representatives of all six countries agree that a consensus in the form of a national and/or regional Balkan curriculum might benefit medical faculties, it is important to allow freedom to each course coordinator to align the course with national and local specificities.

Additionally, vertical and horizontal integration of medical genetics with other clinical courses would be of the utmost importance and continuous emphasis on the importance of genetics through other medical specialties to medical students is indispensable for their understanding of the importance genetics has in modern medicine. Thus, genetic education of clinicians of other specialties might help prevail this obstacle.

Finally, only two countries offer medical and laboratory genetics as a medical specialty (North Macedonia and Slovenia), and in addition to introducing mandatory genetic education for medical students and clinicians, the remaining countries should focus on the introduction of both specialties for postgraduate students.

CONCLUSION

In the present study, we performed the first research on the current state of basic and clinical courses in genetics for medical students offered at medical faculties in six Balkan countries with Slavic languages (Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia). Except for Slovenia, all other countries offer some sort of compulsory courses in genetics for medical students at a total of 20 medical faculties: either courses in basic education in human genetics (Bosnia and Herzegovina, North Macedonia, Serbia) or both basic education in human genetics and clinical education in medical genetics (Croatia and Montenegro). Most of the basic courses in human genetics are similar concerning their aims, learning outcomes and course content. On the other hand, clinical courses in medical genetics are offered only at three medical faculties in Croatia and one in Montenegro. In addition, although these courses are similar with regards to study year position, number of contact hours, ECTS and contents, they vary considerably with respect to the aims, learning outcomes, ratio of types of classes, teaching methods and student evaluation. Further research warrants the analysis of performance of basic courses, as well as introducing clinical courses in medical genetics to higher years of study across Balkan countries. Increasing genetic literacy in medical genetics in clinicians of other medical specialties is also crucial. Finally, this study emphasises the need for collaboration and is the first step towards breaking the years-long barriers that have prevented the consensus on medical genetics education in Balkan countries with Slavic languages, all for the benefit of future physicians and their patients.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

NP—study design, questionnaire development, data collection and analysis, manuscript writing and revision. RT—data collection and analysis, manuscript revision. DP-K data collection and analysis, manuscript revision. OM—data collection and analysis, manuscript revision. IN—data collection and analysis, manuscript revision. ŽP—data analysis, manuscript revision. SO—study design, questionnaire development, data collection and analysis, manuscript revision. BP—study design, questionnaire development, data collection and analysis, manuscript revision.

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Evaluation of a Genetics Education Program for Health Interpreters: A Pilot Study

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Health Interpreters enable effective communication between health practitioners and patients with limited knowledge of the predominant language. This study developed and evaluated a training session introducing Health Interpreters to genetics. The online training was delivered multiple times as a single 2-h session comprising lectures and activities. Participants completed questionnaires (pre-, post-, and 6-months follow-up) to assess the impact of training on knowledge, attitude, self-efficacy, and self-reported practice behaviour. Questionnaires were analysed using descriptive statistics, Fisher's Exact, or independent *t*-test. In total, 118 interpreters participated in the training sessions. Respondent knowledge improved, with gains maintained at 6-months ($p < 0.01$). There were no changes in self-efficacy, and attitudes. Training did not change self-reported practice behaviour, but there was notable pre-existing variability in participants' methods of managing unknown genetic words. Most respondents agreed that training was useful (93%) and relevant (79%) to their work. More respondents reported learning more from the case study activity (86%) than the group activity (58%). Health Interpreters found the training acceptable and demonstrated sustained improvement in knowledge of genetic concepts. Increased delivery of this training and associated research is needed to assess findings in a larger cohort and to measure the impact on patients.

Keywords: genomics, genetics, education, medical interpreter, health interpreter, culturally and linguistically diverse, implementation, evaluation

INTRODUCTION

Health Interpreters provide a vital service within health systems for patients with limited knowledge of the predominant local language. Their involvement in clinical care is associated with improved quality of healthcare (Karliner et al., 2007). Relaying clinical information accurately to patients is a well-known barrier to effective clinical care, even to native speakers (Meuter et al., 2015). Patients with limited proficiency in the local language may experience further barriers, especially in a

situation with technical terminology or high stress (Booth and Tickle, 2003; Cohen et al., 2005). In Australia, 22.2% of households speak one of over 300 languages-other-than-English (LOTE), including sign-languages (Australian Bureau of Statistics, 2016). Mandarin (2.5%), Arabic (1.4%), Cantonese, Vietnamese and Italian (1.2%) are the most common LOTE (Australian Bureau of Statistics, 2016). Since 2008, Australia's public health services have provided Health Interpreters, free of charge, for patients with limited English at the request of the patient or clinician (Australian Commission on Safety and Quality in Healthcare, 2008). Clinicians are discouraged from using non-professional interpreters (e.g. family members) (Queensland Health Interpreter Service, 2007), as use of non-professional interpreters in health settings is associated with poorer clinical outcomes (White et al., 2018).

Over the last decade genomic testing in clinical care has been increasing (Gaff et al., 2017; Burns et al., 2019; Stark et al., 2019; Vidgen et al., 2021). Training in genetic and genomic terminology for Health Interpreters and non-specialist interpreters who work in medical settings has been identified as an unmet area of need to improve patient outcomes (Krieger et al., 2018; Lara-Otero et al., 2019; Uebergang et al., 2021). This was supported by anecdotal reports of challenges in working with health interpreters from clinicians within the local genetics service. In Australia, interpreters of common LOTE working in medical settings have additional qualifications, with training delivered in the LOTE and a qualification as a certified specialist health interpreter (National Accreditation Authority for Translators and Interpreters, 2020a). However, interpreters working with a LOTE with limited diffusion in the community do not have access to additional language-specific health interpreter training. These interpreters work as paraprofessionals as either certified provisional or recognized practising interpreters (National Accreditation Authority for Translators and Interpreters, 2020a). Language skills in specialist areas of medicine come from work-based practice or post-certification professional development.

Post-qualification training of non-genetic health professionals in genetic and genomic concepts is common for physicians, nurses, and allied health professionals (Talwar et al., 2017). This approach in professional upskilling in genetics and genomics has been effective in improving knowledge and, in some cases, has been demonstrated to positively impact clinical practice (Blazer et al., 2004; Carroll et al., 2009; Metcalf et al., 2010). These finding suggest a similar approach could benefit other trained professionals including interpreters. While internationally there are examples of health interpreter training in prenatal and paediatric genetic terminology (Roath et al., 2019; Roath et al., 2020), we could not identify any examples of general genetics training available to Australia's Health Interpreters. Interpreters are required to participate in professional development activities, including short courses, as part of their certification for continued practice in Australia (National Accreditation Authority for Translators and Interpreters, 2020b). However, there is little research into the impact of short courses and one-off training sessions on their professional development.

Here we describe an interactive training session aimed to introduce Health Interpreters to basic genetic and genomic concepts and their clinical application. This study's objective was to evaluate the training sessions' effectiveness in improving Health Interpreters' knowledge, attitude, confidence, and practice behaviour using genetic and genomic terms in their professional practice.

MATERIALS AND METHODS

Context

The training involved an interactive workshop-style session, delivered in English to a mixed language cohort of professionally qualified interpreters (see **Supplementary Material S1** for health interpreters in the Australian context). It gave Health Interpreters that participated an introduction to key genetic and genomic terms that are applicable to clinical practice. The objective was for participants to be able to recognise genetic and genomic terms, in English, that are commonly discussed in clinical consultations. From the awareness and knowledge gained through the training, participants were encouraged to explore options for interpreting these words in the language(s) they interpret in their own time. The session was delivered three times using the online Zoom meeting platform (Zoom Video Communications, 2020) between July and August 2020. The online platform and method were selected due to local restrictions on in-person meetings caused by COVID-19. The training and associated evaluation was intended to assess changes in Health Interpreters knowledge and comfort in the use of genetic and genomics concepts in their professional practise (**Figure 1A**). Participants could claim professional development points for attending, which contributes towards continued certification by the National Accreditation Authority for Translators and Interpreters (Australia).

A genetic counsellor (LFF) and a genomic research academic with tertiary teaching experience (MEV) designed the content and format of the training session. The training content was based on the experiences of genetic counsellors working with interpreters in clinical practise. Interpreter service providers were consulted regarding the training session structure and delivery. The 2-h training session was comprised of three lectures and two activities (**Figure 1B**).

Participants and Recruitment

Interpreter service providers, which Queensland Health contracts to provide interpreters for the public health service, advertised the training session using promotional materials provided by Queensland Genomics (the sponsors). These providers advertised the training sessions to their contractors through direct email, newsletters, and social media posts.

Training session participants were recruited to the evaluation study *via* an invitation email with a webpage link to both the participant information sheet and the questionnaire. The email for the pre-training session questionnaire was sent to registered participants 1 week prior to the training session. The post-

A

	Input	Activities	Outputs	Impact
Training	Training development Queensland Genomics funding Stakeholder perspectives on training session	Design training session Delivery of training session to medical interpreters	Medical Interpreters attendance at training session Recording of training session	Increase Medical Interpreters knowledge and comfort in the use of genetic and genomics concepts
Evaluation	Evaluation process development Queensland Genomics funding Medical Interpreter testing of evaluation	Design evaluation and questionnaires Delivery of evaluation to training session attendees	Attendees complete questionnaires	

B

Topic	Activity	Time	Key points / Key learning objectives
Introduction	-	15 min	– Welcome and housekeeping – Rationale and structure of the session – Icebreaker poll
Genomics terms	Lecture	15 min	**An introduction to the concepts of genetics and genomics** – DNA, genes, chromosomes, and genomes – Repetition of concepts using 'library analogy' – How genes can cause health problems
Small group discussion	Group activity	20 min	**Reflecting on concepts delivered in Genomic Terms lecture** Groups to discuss (maximum 4 people per group): "What parts of the presentation made sense you?" "What parts of the presentation didn't make sense to you" "How would you find more information on these terms?"
Break	-	5 min	
Genetics in the Clinic: Part 1	Lecture	25 min	**Concepts discussed in a genetic counselling session** – Medical history and family trees, – Main inheritance patterns (autosomal dominant, autosomal recessive, and x-linked recessive)
Case studies with quizzes	Individual activity	20min	**Genetic diseases case studies (3 cases presented)** Case studies reflects on concepts in previous lecture – Family tree with explanation of case study presented – Multiple choice question using online polling for response – Explanation of correct choice by presenter
Genetics in the Clinic: Part 2	Lecture	10 min	**Types of genetic testing results** – Pathogenic mutations, variants of uncertain significance, and nothing identified
Wrap-up	-	10 min	– Final question and answers – Wrapping up training session

FIGURE 1 | Summary of the training session and evaluation; **(A)** program logic for training session and evaluation, and **(B)** training session structure.

session questionnaire invitation was sent to participants immediately after completing the training sessions and was open for 1-week. The 6-months follow-up questionnaire invitation was sent to participants 6-months after the training session with the questionnaire open for responses for 1-week. Completing the surveys was voluntary and not a prerequisite for attending the training session or receiving professional development points.

Data Collection and Procedures

The training sessions were evaluated using online questionnaires: pre, post, and 6-months follow-up. The questionnaire applied the Theoretical Domains Framework (Atkins et al., 2017) as the underlying concept to frame questions to investigate participant changes: knowledge, attitudes, self-efficacy, self-seeking behavior for education, and self-reported practice behaviour. The questionnaires were intended to be linked through a self-determined code. Participants were asked to create a 7-character code using; first three letters of the month they were born, the last two numbers of their phone number, and the last two letters of the city they were born (**Supplementary Material S2**).

Each of the three questionnaires administered the same core 31-items, with post- and 6-months follow-up having additional questions. The response options for the questions included; rating scale, 5-point Likert scale, multiple-choice, and open text boxes. The core questions contained: 8-items assessing demographic information; 3-items assessing self-efficacy of understanding and

interpreting genetic terms; 3-items assessing attitude on the importance of genetic health services to themselves or their family and their professional practice; 7-items evaluating self-assessed practice behaviours when interpreting genetic terms in a clinical appointment; and 10-items assessing knowledge of genetic concepts.

The knowledge questions were from a validated knowledge tool (Fitzgerald-Butt et al., 2016). In this study 10 of the 18-items from the validated knowledge tool were used (item numbers in the original publication: 1, 3, 4, 9, 12, 13, 14, 16, 17, and 18) (Fitzgerald-Butt et al., 2016). Item 16, "Humans have 20 pairs of chromosomes", was validated as a false statement (Fitzgerald-Butt et al., 2016). A questionnaire tester in this study identified an inability to answer the question since it is true to state that humans have 20 pairs of chromosomes. However, it is false to state that humans have only 20 pairs of chromosomes. The investigators changed the item wording to "humans have 24 pairs of chromosomes" to create an unambiguously false statement.

In addition to the core questionnaire items, the post-questionnaire had an additional 10-items evaluating the participants' training session experience (total 43-items in the post-questionnaire). The 6-months follow-up questionnaire had an additional 5-items capturing the experience of interpreting genetic concepts in the 6-months since the training session (total 36-items in the 6-months follow-up) (**Supplementary Material S2**).

Items, other than knowledge questions, were customised for this questionnaire. Before use, the follow-up questionnaire was pilot tested by Health Interpreters ($n = 11$) and all questionnaires were reviewed by content experts ($n = 3$). The follow-up questionnaire contained the same core questions as the pre- and post-questionnaires. Only the questions related to the training evaluation which were specific to the post-questionnaire were not included in the pilot test.

Data Analysis

Descriptive statistics were used to summarise data characteristics for the questionnaire responses. Association between demographic variables and questions related to the domains self-efficacy, attitude, and self-reported behaviour were compared using Fisher's Exact test. Mean changes in knowledge between questionnaires were analysed with an independent *t*-test. For the 6-months follow-up questionnaire, comparisons were done for each of the domains between, 1) participants that sought additional education (self-seeking behaviour) and 2) participants that had post-intervention appointments, and those that did not.

For the analysis, the variables were collapsed into two or three categories. The variables age, years working as a Health Interpreter, and language interpreted were collapsed into three categories. The language categories were Asian, European and other languages (included African, Oceanian and Middle-Eastern) with languages categorised based on the region of language origin. For example, Spanish originated in Europe, so it is classified as a European language. Variables related to past training and work experience were reduced to two categories, with "unsure" combined with "no". Likert scale questions for self-efficacy, attitude, and self-reported behaviour were reduced to two categories. The categories that expressed overall ease, positive attitude, and agreement were combined (e.g. strongly agree and agree), as were those that expressed overall difficulty, negative attitude, and disagreement (e.g. strongly disagree, disagree and undecided). Responses collected in open text fields for self-reported practice behaviour were thematically analysed by manual coding (MEV and PRM), using process previously described (Nowell et al., 2017). Results from the statistical analysis were considered to be significant when $p \leq 0.05$. Analyses were conducted in Stata (version 15.1) (StataCorp, 2017).

RESULTS

Questionnaire Responses

There were 180 registered participants, with 118 participating in the training sessions. The pre-questionnaire was sent to 180 registered participants, 37 started answering the questionnaire (response rate 20.5%), but four were excluded as they were incomplete. There were 33 complete responses to the pre-questionnaire. Of the 118 participants who attended the sessions, 48 (response rate 40.7%) and 24 (response rate 20.3%) started the post and 6-months follow-up questionnaires, respectively. After excluding incomplete responses, 43 post responses and 22 6-months follow-up responses were included in the analysis. Of the respondents, six completed all three questionnaires as identified *via* the self-determined code. Given the very low sample size of linked data ($n = 6$), paired analysis suited to longitudinal datasets was not possible due to a lack of power in the analysis. Unpaired statistical methods were used for the analysis of this data.

Training Session Participant and Questionnaire Respondent Demographics

Training session participants ($n = 118$) interpreted 49 spoken languages, 26 of these languages were interpreted by one participant. No sign language interpreters attended. The majority of training session participants interpreted Asian languages (59.8%), with Mandarin (24%), Vietnamese (13%), Arabic (6%), and Korean (6%) being the most common. Interpreter languages (by region) were similar between training session participants and the questionnaire respondents (**Table 1**).

There was no statistical difference between demographic variables of the questionnaire respondents across the three response points (**Table 1** and **Supplementary Material S3**, **Supplementary Table S1**). Respondents tended to be women (pre: 90.9%; post: 90.7%; 6-months follow-up: 72.7%) with more than 6 years interpreting experience (pre: 54.5%; post: 62.8%; 6-months follow-up: 50%), and without educational experience of genetics or genomics (pre: 57.6%; post: 57.1%; 6-months follow-up: 77.3%) (**Table 1**). Over a quarter of respondents had

TABLE 1 | Socio-demographic characteristics and professional experience of questionnaire respondents, and languages interpreted by training session participants.

Demographic variables	Training session participants N (%)	Questionnaire respondents		
		Pre N (%)	Post N (%)	6-months follow-up N (%)
Age		**N = 33**	**N = 43**	**N = 22**
25–44	—	10 (30.4)	13 (30.2)	7 (31.8)
45–64	—	19 (57.6)	21 (48.8)	8 (36.3)
65 plus	—	4 (12.1)	9 (20.9)	7 (31.8)
Gender		**N = 33**	**N = 43**	**N = 22**
Female	—	30 (90.9)	39 (90.7)	16 (72.7)
Number of years working as a Health Interpreter		**N = 33**	**N = 43**	**N = 22**
Not a Health Interpreter	—	5 (15.2)	3 (7.0)	3 (13.6)
0–5 years	—	10 (30.3)	13 (30.2)	8 (36.3)
6 years or more	—	18 (54.5)	27 (62.8)	11 (50.0)
Before the training session, did you have any training in genetics?		**N = 33**	**N = 43**	**N = 22**
None at all	—	19 (57.6)	25 (58.1)	17 (77.3)
Some in high school or university	—	10 (30.3)	13 (30.2)	3 (13.6)
Professional development or continued education	—	4 (12.1)	5 (11.6)	2 (9.1)
What language(s) are you qualified to interpret? †	**N = 122**	**N = 34**	**N = 44**	N = 23
Asian language	73 (59.8)	18 (52.9)	25 (56.8)	14 (60.9)
European language	23 (18.9)	8 (23.5)	10 (22.7)	5 (21.7)
Other	25 (20.5)	7 (20.9)	9 (20.5)	4 (17.3)
African language	7 (5.7)	4 (11.8)	4 (9.1)	1 (4.3)
Middle-Eastern language	15 (12.3)	2 (5.9)	4 (9.1)	3 (13.0)
Oceanian language	3 (2.5)	1 (2.9)	1 (2.3)	0
No response	1 (0.8)	1 (2.9)	0	0
Professional experience		**N = 33**	**N = 43**	**N = 22**
Have you interpreted for a specialist genetic clinician (clinical geneticist or genetic counsellor)?—Yes	—	9 (27.3)	12 (27.9)	7 (31.8)
Have you interpreted genetic or genomic terms for a health service client before who was not a specialist genetic clinician (clinical geneticist or genetic counsellor)?—Yes	—	4 (12.1)	13 (30.2)	6 (27.3)
Have you had personal experience outside your professional role (e.g. you, a friend or family member) with a serious genetic condition?—Yes	—	6 (18.2)	15 (34.9)	5 (22.7)
Since completing the training session, have you had a client appointment where you interpreted genetics terms?—Yes	—	—	—	4 (18.2)
Since completing the training session, have you participated in any additional learning about genetics and genomics?				**N = 22**
Yes	—	—	—	13 (59.1)
Materials provided from the training session	—	—	—	8 (36.4)
Other materials not provided in the training session	—	—	—	1 (4.5)
Both materials provided from the training session and materials not provided in the training session	—	—	—	4 (18.2)
Since completing the training session, in how many appointments have you interpreted genetic terms?				**N = 4**
1 to 3	—	—	—	2 (50.0)
4 to 6	—	—	—	1 (25.0)
6 or more	—	—	—	1 (25.0)

†Some training session attendees and questionnaire respondents interpreted for multiple languages from multiple regions. The percentage is based on the number of languages by region spoken by participants, not the number of participants.

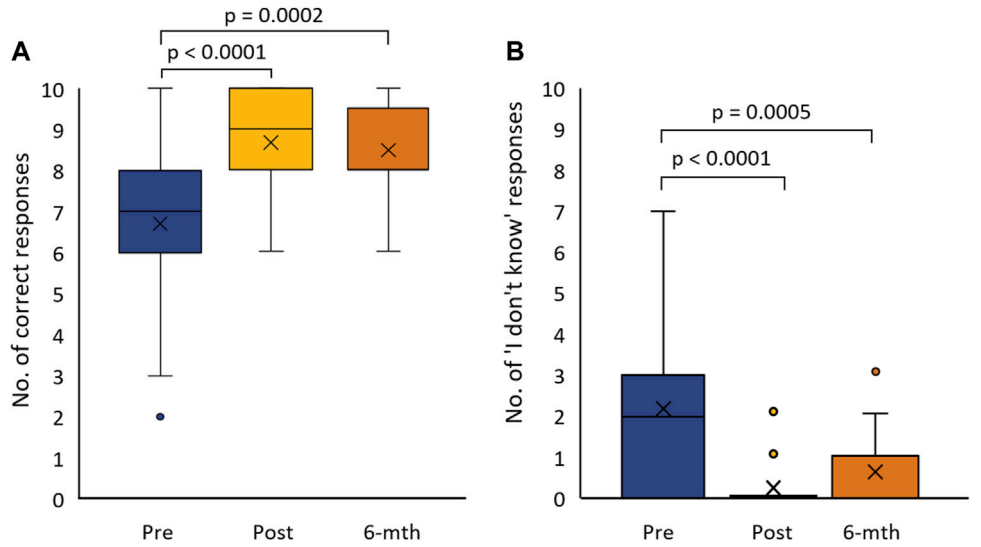

FIGURE 2 | Box-plot of questionnaire respondent knowledge pre-post and 6-months follow-up from the training session: **(A)** the number of correct responses to knowledge questions (Total 10 questions), and **(B)** the number of times respondents selected the 'I do not know' response option for knowledge questions.

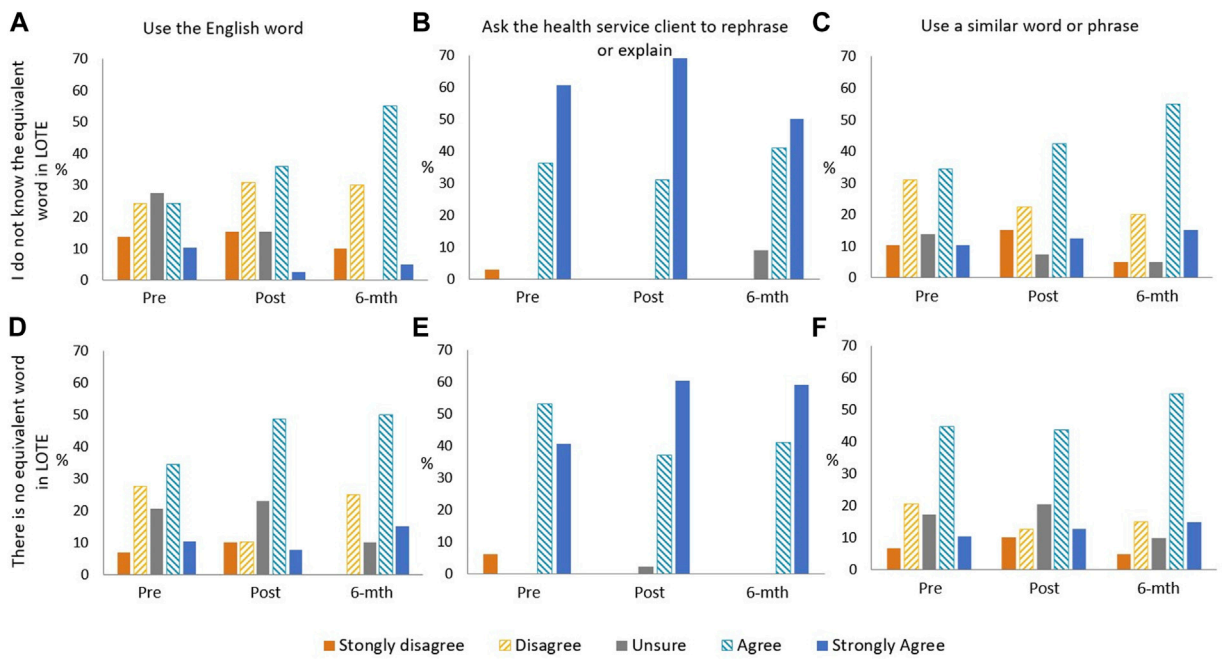

FIGURE 3 | Bar graphs of questionnaire respondent level of agreement of practice behaviours when: they do not know the English word used: **(A)** use the English word, **(B)** ask health service client to rephrase or explain, **(C)** use similar word or phrase; and there is no equivalent word in LOTE, **(D)** use the English word, **(E)** ask health service client to rephrase or explain, **(F)** use a similar word or phrase.

TABLE 2 | Thematic summary of open response questions related to practice behaviour.

Themes	Codes	Pre N (%)	Post N (%)	6-months follow-up N (%)
		N = 36[a]	**N = 49[a]**	**N = 23[a]**
Ask clinician for clarification[‡]	• Simplify or use layman terms • Use different terms • Use examples	12 (36.4)	23 (53.5)	8 (36.4)
The Health Interpreter chose LOTE alternative[b]	• Use simplified terms • Give extended description	8 (24.2)	7 (16.3)	4 (18.2)
Use imagery	• Drawings • Pictures/images • Scans	3 (9.1)	5 (11.6)	3 (13.6)
Health Interpreter look-up	• LOTE word • Information source for patient	3 (9.1)	2 (4.7)	0
Client resources from clinician	• Write down keywords in English for patient's reference • Ask for written materials on the patient's behalf	3 (9.1)	2 (4.7)	3 (13.6)
Use English word[b]	• Use English word	2 (6.1)	2 (4.7)	2 (9.1)
Use physical or verbal indicators	• Body language • Sign language[c] • Change speed or tone of speech	2 (6.1)	2 (4.7)	1 (4.5)
Repeat back	• Get patient to explain understanding back to the health professional • Prompt patient to ask clarifying questions of the health professional	1 (3.0)	4 (9.3)	1 (4.5)
Interpreter self-education	• Speak to the health professional before the appointment • Prior or post-self-learning	1 (6.1)	2 (4.7)	2 (4.5)
		N = 28[d]	**N = 38[d]**	**N = 18[d]**
Multiple themes	• Provided multiple options selected based on circumstances • Provided two or more themes done in tandem	6 (21.4)	11 (28.9)	5 (27.8)

[a]*Number of coded responses.*
[b]*Option given in set response questions.*
[c]*All questionnaire respondents interpret for spoken languages.*
[d]*Number of respondents that responded to the question.*

previously interpreted for genetic health services (pre: 27.3%, post: 27.9%; 6-months follow-up: 31.8%).

Between Questionnaire Analysis to Assess Changes Over Time

Knowledge of basic and applied genetic concepts improved significantly after the intervention (pre mean = 6.7, post mean = 8.7; pre-post *t*-test $p < 0.0001$) and remained consistent in the 6-months follow-up (6-months follow-up mean = 8.5; pre-post *t*-test $p = 0.0002$) (**Figure 2A**). Compared to the pre questionnaire, the "I do not know" response rate significantly reduced after the training session in the post (pre mean = 1.5, post mean = 0.2; pre-post *t*-test $p < 0.0001$) and 6-months follow up questionaries (pre mean = 1.5, 6-months follow-up mean = 0.6; pre-post *t*-test $p = 0.0005$) (**Figure 2B**). While there was an increase in this response option between post and 6-months follow-up, the change did not reflect a change in overall knowledge. There was no statistically significant difference in self-efficacy or attitude (**Supplementary Material S3**, **Supplementary Table S2**).

There was no change in self-reported behaviour after attending a training session. "Asking the clinician to rephrase or explain" was the most common action for "words not known by the interpreter" and "words that do not have an equivalent in LOTE", for both multiple-choice (**Figures 3B & E**) and open response questions (**Table 2**). The overall agreeability of using an English word or interpreter selected explanation of terms has a bimodal distribution pattern (**Figures 3A,D,E &F**). Some respondents provided a mix of options for managing unknown words or words without an equivalent in LOTE in the open response question. Others indicated that asking the clinician to clarify was their only acceptable strategy, using terms such as "mouthpiece" and "conduit" to emphasise the clinician's responsibility for judgment and explanations.

Post-Intervention Self-Seeking Behaviour (Education) and Professional Experience Analysis

In the 6-months after the training session, over half of the respondents sought additional learning on genetics, either from materials provided by the training session or through other sources ($n = 13$, 59.1%) (**Table 1**). However, there was no statistical significance for knowledge, self-efficacy, attitude, or self-reported behaviour between those who exhibited self-seeking behaviour (education) and those who did not.

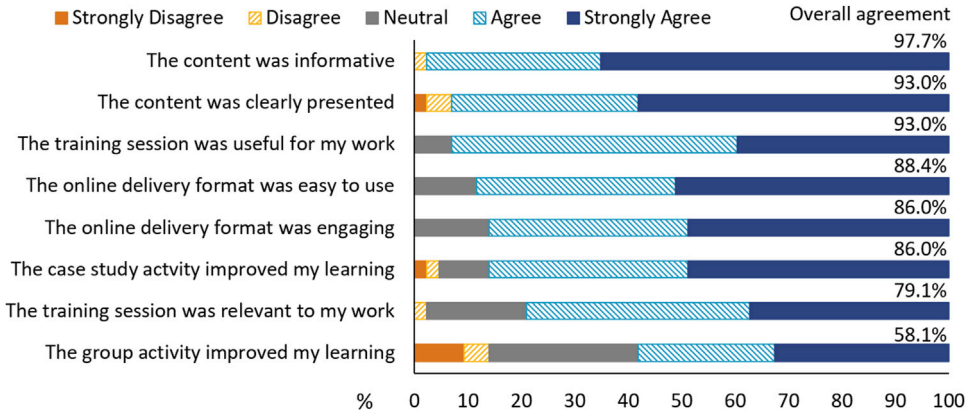

FIGURE 4 | Respondent perspectives of the training session. "Overall agreement" is provided as a percentage and is the combined percentage of "agree" and "strongly agree".

TABLE 3 | Recommendations for developing training in genetic concepts for Health Interpreters.

Recommendation	Description
Audience background	Health Interpreters do not necessarily come from a scientific or medical background. Educators should not assume prior knowledge. More than 50% of questionnaire respondents had no prior genetics education. Up to 15% interpreted languages of limited diffusion and did not have specific Health Interpreter qualifications
Pace of delivery	Multiple short sessions covering a single topic over weeks or months were suggested by respondents as a preferred pace of delivery to help with the information uptake
Resources	Use a flipped classroom format by providing resources before training (i.e., presentation slides). These can assist participants during sessions delivered in real-time or used as a reference point later
Clinical interaction examples	Information on what they can expect from clinical interactions that involve genetics was a desired inclusion for respondents. This content could be in the context of genetic health service appointments and other specialties. Although in this study, most respondents' appointments, where genetics was encountered during 6-months follow-up, were with non-genetic medical specialties
Disease-based examples	Reinforcing concepts by health condition examples was preferred
Family context	Providing content in a way that engages Health Interpreters to think about genetics in the context of their own family. Participants engaged with content when explained in the context of their own family
Activities	Respondents felt the presenter walkthrough of case studies and the associated use of quizzes was beneficial to their learning. Other activity styles suggested by respondents were role-play and group discussion of case studies or clinical scenarios
Analogies	Respondents indicated that the use of analogies, such as comparing the human genome to a library, was effective in supporting their learning

Those respondents that had client appointments in the 6-months follow-up period ($n = 4$) identified having appointments with specialists in; genetics (1 appointment, $n = 2$), allergies and immunology (1 appointment, $n = 1$), breast and endocrine surgery (1 appointment, $n = 1$), gynaecology (2 appointments, $n = 1$), maternity and neonatal medicine (2 appointments, $n = 1$), and paediatrics (3 or more appointments, $n = 1$). No appointments were identified for general practice, or with specialists in cardiology, endocrinology, neurology, oncology, or nephrology. Most appointments where respondents interpreted genetic or genomic terms utilised telehealth or telephone communication. Due to COVID-19 restrictions on in-person appointments during the 6-months follow-up period, this may not represent the usual interpreter experience. Those respondents that had appointments after the training session where they used genetics terms considered it easier to understand genetic and genomic terms in English than those respondents that did not have appointments after the training session (Appointments = 75.0%; No appointments = 23.5%, $p = 0.088$) (**Supplementary Material S3**, **Supplementary Table S2**).

Program Evaluation

Respondents had high levels of overall agreement that the training session was clearly presented (93.0%) and informative (97.7%), with it being useful to their work (93.0%), with slightly fewer respondents considering it relevant to their work (79.1%) (**Figure 4**). Respondents felt that case studies within the training session improved learning (86.0%) more than the group activity (58.1%) (**Figure 4**). The difference was similarly reflected in the open responses. The use of case studies and quizzes were the most popular activities in the open response questions as they allowed respondents to reflect on the content of the presentations. The use of group discussions was not as well-received due to technical execution using the online platform, in particular communication

methods in and between rooms, and the topic discussed (**Figure 1**). Respondents indicated that they would prefer group discussion on interpreter experiences and expectations during genetic consultation, or role-plays as alternative learning techniques.

Respondents felt the training session could be improved by delivering the content at a slower pace or over multiple sessions. Respondents identified that providing information or slides for the presentations before the training session would assist with participant expectations and support participant learning of complex topics. Respondents also indicated that they would like more examples of different diseases and more details on clinical interactions with genomics (**Table 3**).

DISCUSSION

Health Interpreters are an essential part of the equitable provision of quality healthcare to people with limited English language skills (Karliner et al., 2007). The use of Health Interpreters is associated with a range of improvements in clinical care for patients with limited English, including; improved clinical outcomes for patients, increased rate of access to health care, decreased admissions and improved patient satisfaction (Jacobs et al., 2001; Bernstein et al., 2002; Karliner et al., 2007).

Continuing professional development of health professionals, including the use of short educational interventions, is a common mechanisms for upskilling health workers (Samuel et al., 2021). The outcome metrics used to measure the success of professional development in healthcare vary considerably between studies depending on the theoretical domains applied to assess change, but changes in knowledge, practise behaviour or patient outcomes are often the focus (Samuel et al., 2021). These types of educational interventions are similarly used in the professional upskilling of Health Interpreters.

Genomics is being implemented across health services with increasing frequency, creating more medical appointments where these complex concepts are discussed. To improve patient outcomes, training in genetic and genomic terminology for Health Interpreters has been identified as an unmet area of need (Krieger et al., 2018; Lara-Otero et al., 2019; Uebergang et al., 2021). While there are some programs for Health Interpreter training in genetic sub-specialties (Roath et al., 2019; Roath et al., 2020), at the time of publication, there hasn't been evaluation of their effectiveness.

In other studies assessing educational interventions in genetics training for healthcare workers, improved respondent knowledge is consistently observed despite variations in the mode of delivery and duration (Talwar et al., 2017). This was similarly observed in our evaluation of a genetics training session for Health Interpreters, with respondents' knowledge increasing and being maintained 6-months after the training session. Maintenance of knowledge after an educational intervention does not always occur (Kempegowda et al., 2018). Although the use of "I do not know" response to knowledge questions increased between the post and 6-months follow-up questionnaires, it did not correspond to a change in overall knowledge. However, it may indicate waning confidence in responding to knowledge-based questions. Educational interventions that involve 6-months follow-up, either by formal or self-directed learning, or where participants have professional experience during the 6-months follow-up period further improve knowledge retention and duration of knowledge retention (Masny et al., 2003; Lauer et al., 2014), which reflects adult education principles (McNeil et al., 2006).

The questionnaire assessed self-efficacy and attitude to self/family and professional practice in the context of genetics and genomics. There was no change in either domain observed in this study. Self-efficacy is context-specific within individuals, with day-to-day circumstances influencing perception and confidence about professional practice (Zamani-Alavijeh et al., 2019). The neutrality and lack of change in self-efficacy in professional practice could be attributed to situational variability encountered with the core task of interpreting complex terms between the clinical practitioner and non-English speaking clients.

Attitudes to the use of genetics in clinical settings by non-genetic health professionals are dependent on multiple factors including: their clinical specialty, clinical utility of testing in case management, and clinician's consideration of the individual patient's needs (Carroll et al., 2009; Paul et al., 2018). The Health Interpreters' unchanging neutral attitude to genetics in professional practice could reflect the low number of appointments where they use genetics and genomics terminology. In responses to the training session experience, we saw very high overall agreement that the training session was "useful" (93.0%). However, fewer people agreed that it was "relevant" to their work (79.1%). Health Interpreters do not specialise in specific disciplines, rather they work across all areas of medicine. Therefore, it may take time to come across appointments that use this newly acquired knowledge and change attitudes towards relevance to their work. It is also possible that Health Interpreter attitudes will not change, as this group may perceive all medical terms to be equally important to their professional practice.

The presenters did note that participant questions during the training session often referenced their personal history and/or their family members' histories rather than their professional practice or clients. This indicates that a number of participants found personal relevance in training by connecting genetic concepts and health services utility to their own family. Incorporating personal family elements may be a way of engaging participants in educational interventions in genetic and genomic concepts.

As is experienced with medical language in general, the English terminology for genetics and genomic concept often do not have equivalent words in LOTE. It is part of an interpreters' professional practise to manage how terms are delivered, for example through the selection of equivalent words or requesting clarification by the speaker. When the interpreter is unaware of an equivalent word, or it does not occur in the LOTE, asking the clinical client for clarification is the preferred method identified by participants in this study. This practice reflects the Australian training practices and the

interpreters' professional code of ethics (Australian Institute of Interpreters and Translators, 2012). There was a bimodal distribution pattern in the responses to self-reported practice behaviour for using the English word and selecting LOTE equivalent - indicating that individual interpreters have different practice behaviour or perspectives. This practice reflects discourse analysis studies of interpreters in health settings that demonstrate how altering messages varies between interpreters (Gutierrez et al., 2017; Gutierrez et al., 2019). These differences in interpreting practice do not appear to be associated with language or culture but rather the individual (Krieger et al., 2018; Lara-Otero et al., 2019). They may be linked to broader concepts, such as the school of thought associated with initial interpreter training and the individual's past professional experience. Equally, this may reflect individual clinical appointment differences, such as cultural compatibility or the rapport established between the interpreter and the non-English speaking client, rapport with the clinician, or confidence in the interpreted medical topic.

Future Education Recommendations

There is a lack of professional development opportunities for Health Interpreters in Australia and so there was strong support for this training, with requests from Health Interpreters to increase the scope of training to include other medical specialties. To meet the demand for training, the delivery format may need to be adjusted as using live online sessions may not be practical. This mode restricts availability for some users due to the inflexible timing of sessions, has high resource requirements for delivery, and requiring participants to have a reliable internet connection and an interruption-free environment. Other studies of genetic education have demonstrated effective knowledge increase in non-genetic health professionals when using self-directed online training programs and on-demand recorded sessions tailored to the needs of the specific health profession (Wallen et al., 2011; Kaur et al., 2019). The impact of these other learning formats is unknown for Health Interpreters and would require further investigation if applied to their profession. Here we outline some considerations for developing training in genetic concepts for Health Interpreters based on the presenters' experiences and participant feedback (**Table 3**). Whilst technically challenging, future evaluation studies should aim to explore the impact of Health Interpreter educations not only on participants, but also on outcomes for patients and clinical services.

Limitations

The original design of this research was a linked longitudinal study. The main limitation was the insufficient amount of paired data for analysis, which necessitated unpaired methods for analysis. The analysis type weakens both the power and the longitudinal inference of the results. There were moderate responder rates for each individual survey but very low repeat responder rates. To maintain responder anonymity, we did not collect responder contact details. This meant we could not provide targeted reminders to those who did not complete follow-up surveys and could not provide professional development incentives for participating in the research. The researchers would consider methods for re-contacting participants to improve repeat response rates in the future. There is potential responder bias as only 18–32% of training participants completed each of the questionnaires. Based on the response rate and survey findings we would suggest that the evaluation method and domains explored be reassessed to determine if these metrics are suitable for the assessment training in the context of continuing professional development for Health Interpreters.

CONCLUSION

Research has identified that improving Health Interpreters' knowledge of genetic and genomics concepts would improve their client interactions during genetic counselling sessions (Krieger et al., 2018; Gutierrez et al., 2019; Uebergang et al., 2021). This study demonstrated that short training sessions can be an effective way of improving Health Interpreter knowledge of genetic and genomic concepts relevant to the clinical practice of genetic health services. Here we demonstrate the first step - that the intervention positively impacts a Health Interpreter's knowledge. The next step in determining the intervention's value is examining the impact of Health Interpreter training on medical appointments where genetics is discussed from the perspective of the patient, the interpreters, and the clinical staff.

DATA AVAILABILITY STATEMENT

The data generated by the study will be made available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was approved by the QIMR Berghofer Human Research Ethics Committee (P3471). Participants were provided with an online written information sheet before starting the online questionnaire and confirm their willingness to participate via the radio button before starting each of the questionnaires.

AUTHOR CONTRIBUTIONS

SNI, LFF, and MEV conceptualised the study. SNI, LFF, EE, NW, KC, KS, AM-L, and MEV administer and directed the project *via* a working group. MEV, LFF, SB, KF, PR-M developed the surveys. MEV, LFF, KC, KS, and PR-M ran the training and evaluation. MEV and PR-M analysed the data. MEV drafted the manuscript with review and editing by LFF, SNI, EE, KC, KS, JB, LH, GH, AM-L, GP, DR, SB, KF, PR-M, and NW.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fgene.2021.771892/full#supplementary-material

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