European Journal of Medical Genetics 66 (2023) 104805

Contents lists available at ScienceDirect

European Journal of Medical Genetics

journal homepage: www.elsevier.com/locate/ejmg

Lack of guidelines and translational knowledge is hindering the implementation of psychiatric genetic counseling and testing within Europe – A multi-professional survey study

Kati Koido [a,1], Charlotta Ingvoldstad Malmgren [b,ac,1], Lejla Pojskic [c,1], Peter Z. Almos [d], Sarah E. Bergen [e], Isabella Borg [f], Nada Božina [g], Domenico A. Coviello [h], Franziska Degenhardt [i], Lana Ganoci [j], Uffe B. Jensen [k], Louise Durand-Lennad [l], Claudine Laurent-Levinson [m], Andrew McQuillin [n], Alvydas Navickas [o], Nikolai P. Pace [p], Milena Paneque [q], Marcella Rietschel [r], Maria Grigoroiu-Serbanescu [s], Maria Johansson Soller [t], Jaana Suvisaari [u], Algirdas Utkus [v], Evelien Van Assche [w], Lily Vissouze [l], Shachar Zuckerman [x], Boris Chaumette [y,ab,1], Kristiina Tammimies [z,aa,1,*]

[a] Department of Physiology, Institute of Biomedicine and Translational Medicine, Faculty of Medicine, University of Tartu, Tartu, Estonia
[b] Department of Clinical Genetics, Karolinska University Hospital, Stockholm, Sweden
[c] Laboratory for Human Genetics, University of Sarajevo - Institute for Genetic Engineering and Biotechnology, Sarajevo, Bosnia and Herzegovina
[d] Department of Psychiatry, University of Szeged, Szeged, Hungary
[e] Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden
[f] Pathology Department, Faculty of Medicine and Surgery, University of Malta, Msida, Malta
[g] University of Zagreb School of Medicine, Department of Pharmacology, Zagreb, Croatia
[h] Laboratory of Human Genetics, IRCCS Istituto Giannina Gaslini, Genoa, Italy
[i] Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Essen, University of Duisburg-Essen, Essen, Germany
[j] University Hospital Centre Zagreb, Department of Laboratory Diagnostics, Division for Pharmacogenomics and Therapy Individualization, Zagreb, Croatia
[k] Department of Clinical Genetics, Aarhus University Hospital, Aarhus, Denmark
[l] Université Paris Cité, INSERM U1266, Institute of Psychiatry and Neuroscience of Paris, Paris, France
[m] Faculté de Médecine-Sorbonne Université, Groupe de Recherche Clinique N°15 - Troubles Psychiatriques et Développement (PSYDEV) & Centre de Référence des Maladies Rares à Expression Psychiatrique, DMU ORYGINE Femmes-Mères-Enfants, Service de Psychiatrie de l'Enfant et de l'Adolescent, Assistance Publique-Hôpitaux de Paris, Sorbonne Université, Paris, France
[n] Molecular Psychiatry Laboratory, Division of Psychiatry, University College London, London, UK
[o] Psychiatric Clinic, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania
[p] Centre for Molecular Medicine and Biobanking, University of Malta, Malta
[q] Center for Predictive and Preventive Genetics, Institute of Molecular and Cellular Biology, Institute for Research and Innovation in Health, University of Porto, Porto, Portugal
[r] Department of Genetic Epidemiology in Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Germany
[s] Alexandru Obregia Clinical Psychiatric Hospital, Biometric Psychiatric Genetics Research Unit, Bucharest, Romania
[t] Department of Clinical Genetics, Karolinska University Hospital, Stockholm and Karolinska Institutet, Stockholm, Sweden
[u] Finnish Institute for Health and Welfare, Department of Public Health and Welfare, Mental Health Team, Helsinki, Finland
[v] Department of Human and Medical Genetics, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania
[w] Department of Psychiatry, University of Münster, Münster, Germany
[x] Medical Genetic Institute, Shaare Zedek Medical Center, Jerusalem, Israel
[y] Université Paris Cité, INSERM U1266, Institute of Psychiatry and Neuroscience of Paris, GHU-Paris Psychiatrie et Neurosciences, Paris, France
[z] Center of Neurodevelopmental Disorders (KIND), Centre for Psychiatry Research, Department of Women's and Children's Health, Karolinska Institute, Region Stockholm, Stockholm, Sweden
[aa] Astrid Lindgren Children's Hospital, Karolinska University Hospital, Region Stockholm, Stockholm, Sweden
[ab] Department of Psychiatry, McGill University, Montreal, Canada
[ac] Center for Research and Bioethics, CRB, Uppsala University, Uppsala, Sweden

* Corresponding author. J9:30 Bioclinicum, Visionsgatan 4, 171 64 Solna, Sweden.
E-mail address: kristiina.tammimies@ki.se (K. Tammimies).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.ejmg.2023.104805
Received 15 February 2023; Received in revised form 25 April 2023; Accepted 23 June 2023
Available online 3 July 2023

ARTICLE INFO

Handling Editor: A. Verloes Koido et al.

Keywords:
Psychiatric disorders
Neurodevelopmental disorders
Clinical genetic and pharmacogenetic testing
Genetic counseling
Healthcare implementation

ABSTRACT

Genetic research has identified a large number of genetic variants, both rare and common, underlying neurodevelopmental disorders (NDD) and major psychiatric disorders. Currently, these findings are being translated into clinical practice. However, there is a lack of knowledge and guidelines for psychiatric genetic testing (PsychGT) and genetic counseling (PsychGC). The European Union-funded COST action EnGagE (CA17130) network was started to investigate the current implementation status of PsychGT and PsychGC across 35 participating European countries. Here, we present the results of a pan-European online survey in which we gathered the opinions, knowledge, and practices of a self-selected sample of professionals involved/interested in the field.

We received answers from 181 respondents. The three main occupational categories were genetic counselor (21.0%), clinical geneticist (24.9%), and researcher (25.4%). Of all 181 respondents, 106 provide GC for any psychiatric disorder or NDD, corresponding to 58.6% of the whole group ranging from 43.2% in Central Eastern Europe to 66.1% in Western Europe. Overall, 65.2% of the respondents reported that genetic testing is offered to individuals with NDD, and 26.5% indicated the same for individuals with major psychiatric disorders. Only 22.1% of the respondents indicated that they have guidelines for PsychGT. Pharmacogenetic testing actionable for psychiatric disorders was offered by 15%. Interestingly, when genetic tests are fully covered by national health insurance, more genetic testing is provided for individuals with NDD but not those with major psychiatric disorders.

Our qualitative analyses of responses highlight the lack of guidelines and knowledge on utilizing and using genetic tests and education and training as the major obstacles to implementation. Indeed, the existence of psychiatric genetic training courses was confirmed by only 11.6% of respondents. The question on the relevance of up-to-date education and training in psychiatric genetics on everyday related practice was highly relevant.

We provide evidence that PsychGC and PsychGT are already in use across European countries, but there is a lack of guidelines and education. Harmonization of practice and development of guidelines for genetic counseling, testing, and training professionals would improve equality and access to quality care for individuals with psychiatric disorders within Europe.

1. Introduction

Conditions of the brain, including major psychiatric disorders and neurodevelopmental disorders (NDD), have a strong genetic component, and they arise due to complex and heterogeneous combinations of genetic and environmental factors (Anttila et al., 2018; Jacquemont et al., 2022). Genome-wide association studies (GWAS) for these conditions have identified a range of associated single nucleotide polymorphisms (SNPs), e.g., for attention-deficit hyperactivity disorder (ADHD) (Ditte et al., 2022), autism spectrum disorder (ASD) (Grove et al., 2019), schizophrenia (Trubetskoy et al., 2022), mood disorders (including major depressive disorder (MDD) and bipolar disorder (BD)) (Coleman et al., 2020). However, due to the small effect sizes, individually, these SNPs do not have any clinical utility yet. Calculating the cumulative burden of these associated SNPs alleles weighted by the magnitude of the effect sizes into a polygenic risk score (PRS) gives a single estimate of the common polygenic burden for one individual. However, the current consensus in the field is that PRS within psychiatry does not have sufficient predictive power for diagnosis or to communicate individual risks in the context of genetic counseling (International Society of Psychiatric Genetics 2019). PRSs have been proven useful in research on the genetic relatedness of different psychiatric and medical disorders, and they might be of future value for studying the effectiveness of preventive measures and the selection of treatments (Lewis and Vassos 2022).

In contrast to common SNP discoveries, the identification of rare copy number variants (CNVs) and rare damaging gene-disrupting variants with large effect sizes can directly impact the affected individuals and is worth being identified in clinical practice (Finucane et al. 2021). Especially for individuals with NDDs and schizophrenia, many recurrent rare CNVs associated with genomic disorders have been identified (Vorstman and Scherer 2021). Furthermore, whole exome and genome sequencing (WES and WGS, respectively) studies have also pinpointed a large number of genes affected by rare gene-disrupting variants in these conditions; again, many of the genes indicated risk across the disorders, e.g., for ASD and ADHD (Satterstrom et al., 2019); ASD (Trost et al., 2022); BD (Palmer et al., 2022); schizophrenia (Singh et al., 2022). The International Society of Psychiatric Genetics consensus statement on genetic testing (GT) (International Society of Psychiatric Genetics 2019) concludes that for NDDs, chromosomal microarray (CMA) testing should be performed to detect high-risk CNVs. If none is found, WES should be used to search for pathogenic variants in known risk genes. The statement notes that experts have not reached a consensus about routine GT in schizophrenia; some experts advocate CNV testing for those with histories of developmental delay and other NDD features (Foley et al., 2020) or with early onset (Brownstein et al., 2022). Sequencing study of extreme phenotype demonstrates a significant burden of rare variants in severe, treatment-resistant schizophrenia and suggests a future role for clinical sequencing in this condition (Zoghbi et al., 2021). All in all, the clinical translation of rare genetic findings remains still challenging (Vorstman and Scherer 2021).

Genetic counseling (GC) should always be offered before and after clinical GT to help people understand the implications and ethical considerations around GT and results. A major aim of pre-test GC is facilitating the patient's informed choice regarding GT. By definition, GC is a process of helping people understand and adapt to the medical, psychological, and familial implications of genetic conditions and abnormalities (Resta et al., 2006). Recent studies have shown that offering GC can benefit individuals affected by major psychiatric disorders by increasing the patient's empowerment and self-efficacy even when no GT is available (Semaka and Austin 2019; Austin 2020).

There is limited information and guidelines on how GT and GC are implemented in the health care of individuals affected by NDDs and major psychiatric disorders in Europe. Furthermore, how the current education streams facilitate implementing these practices in the future is unknown. Therefore, a network financed by the European Union COST Action, EnGagE (Enhancing Psychiatric Genetic Counseling, Testing, and Training in Europe, CA17130), was initiated in 2018. The overall goal of EnGagE was to provide a platform to discuss and facilitate the implementation of the translation from psychiatric genetics research into patient care. In a pan-European multidisciplinary context, researchers, psychiatrists, geneticists, and genetic counselors work together to extend knowledge about opportunities and pitfalls regarding GT and GC for psychiatric disorders and provide information about clinical translation (Chaumette et al., 2021). The EnGagE consortium

has members from 35 European countries. One of the objectives of the action was to survey the current clinical implementation of psychiatric genetic counseling (PsychGC) and psychiatric genetic testing (PsychGT) across the participating countries.

Here, we present the results from this survey in which we gathered the opinions, knowledge, and practices of a self-selected sample of professionals involved or interested in PsychGC and PsychGT. Additionally, we analyzed factors that facilitate or prevent the implementation of GT and GC for the conditions and provided information for training and education needs.

2. Materials and methods

2.1. Survey design

Members of the EnGagE network designed the survey with 43 questions grouped into four sections - (1) general information about the respondent person/institution, (2) GC, (3) GT, and (4) training for GC and GT (Supplementary Table 1). The survey was piloted among the network members for two weeks, followed by minor linguistic and semantic modifications before distribution outside the network. The validated survey questionnaire was accessible online between February 2021 and June 2021. The survey and data collection were done using Survey & Report, version 4.3.10.5. Information regarding the purpose of the study and how the data would be used and stored was given at the beginning of the survey, and all respondents provided informed consent to start the survey. The estimated time to complete the survey was approximately 20 min. The study and the survey were reviewed and approved by the Swedish Ethical Review Authority (dnr 2020–03291). Groups less than 5 respondents are not shown in the tables.

2.2. Recruitment of respondents

The recruitment of the respondents was done in several steps. First, email recruitment was sent out to all EnGagE members (n = 105 from 35 European countries), followed by email recruitment to all individuals who have been part of the earlier EnGagE activities. EnGagE members were asked to send the information and distribute the questionnaire to their countries, relevant networks, and stakeholders in the third round. The targeted networks are briefly described in Supplementary Table 2.

2.3. Data cleaning and analysis

Survey response data was downloaded from the Survey & Report system and processed using Microsoft Excel and R program version 4.2.1. The demographic information is presented using descriptive statistics. Countries were mapped to their corresponding European regions based on the EuroVoc classification of Northern Europe: Denmark, Estonia, Finland, Latvia, Lithuania, Norway, Sweden; Western Europe: Austria, Belgium, France, Germany, Ireland, Netherlands, Switzerland, United Kingdom; Central and Eastern Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Montenegro, North Macedonia, Poland, Romania, Serbia, Slovenia; and Southern Europe: Cyprus, Greece, Italy, Malta, Portugal, Spain, Turkey. Additionally, we included Israel in the Southern European region (Fig. 1A).

The respondent rates per region and total were presented in count and percentages. We also tested differences between the regions using χ^2 or Fisher exact tests. Additionally, the Kruskal-Wallis test was used to analyze differences in years of experience between the regions or based on the reported answers. We used two samples as a reference for assessments of the category frequency depending on the relevance of the question: the total number of respondents (n = 181) and the total number of those who reported providing GC for any psychiatric disorder or NDD (n = 106). We also compared three professional groups focusing on (1) genetic counselors, (2) clinical geneticists, and (3) psychiatrists and psychologists as one professional psychiatry group.

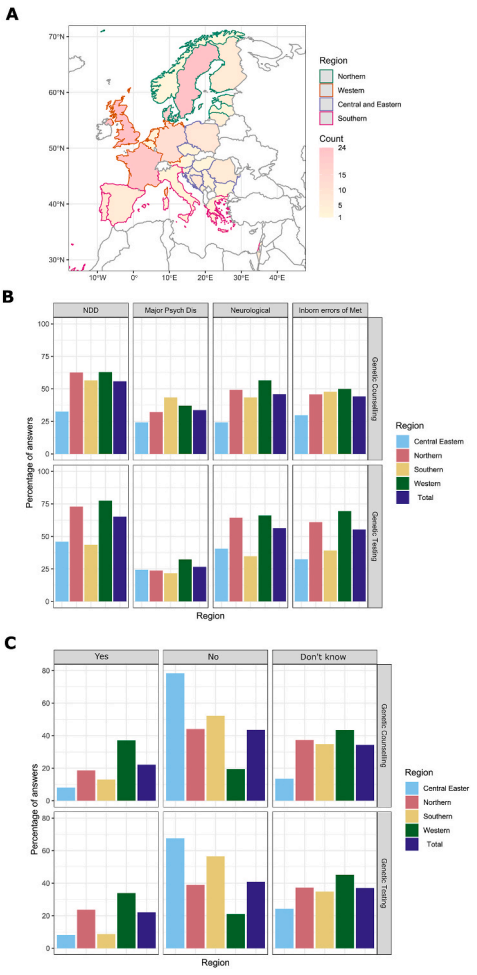

Fig. 1. General information on the status of psychiatric genetic counseling (PsychGC) and genetic testing (PsychGT) within Europe. (A) Distribution and the number of respondents across Europe, (B) Percentage of respondents indicating that themselves or within their institutions/clinic, GC and GT are offered to individuals with neurodevelopmental disorders (NDD), major psychiatric disorders (Major Psych Dis), neurological disorders, and inborn errors of metabolism (Inborn errors of Met) within each of the four regions and in total, (C) Percentage of respondents reporting whether guidelines for PsychGC and PsychGT exist as shown per region and in total.

Qualitative data from open questions for the major obstacles in implementing GC and GT for psychiatric disorders (Supplementary Table 1) were analyzed using thematic analysis (Braun and Clarke 2006). A group of 10 authors having experience from the different disciplines of GT, GC, and training evaluated the open-ended answers, generated initial codes, and finalized the consensus themes for the obstacles reported.

3. Results

3.1. Demographic information of the respondents

We received answers from 184 respondents, of which 181 were from a European country. Three responses outside Europe or EnGage participating countries were removed from the analysis. The main demographic characteristics of the respondents per European region are summarised in Table 1, and the response numbers per country are shown in Fig. 1A. Between 19 and 57% of respondents were already part of the EnGagE network, with significant differences across the four European regions ($p < 0.001$), with the highest percentage from Central and Eastern Europe (Table 1). We received more answers from females

Table 1
Demographic information of the respondents. Categories with less than five respondents are shown by < 5 if not 0.

	Central and Eastern Europe (n = 37)	Northern Europe (n = 59)	Southern Europe (n = 23)	Western Europe (n = 62)	Total (n = 181)	p-value
No of respondents from the EnGagE network (%)	21 (56.8)	11 (18.6)	9 (39.1)	13 (21.0)	54 (29.8)	<0.001
Gender						0.641
Female	29 (78.4)	42 (71.2)	14 (60.9)	44 (71.0)	129 (71.3)	
Male	8 (21.6)	16 (27.1)	9 (39.1)	18 (29.0)	51 (28.2)	
Other	0 (0.0)	<5	0 (0.0)	0 (0.0)	<5	
Level of education						
Bachelor	0 (0.0)	<5	0 (0.0)	10 (16.1)	13 (7.2)	0.006
Master	<5	7 (11.9)	7 (30.4)	26 (41.9)	43 (23.8)	<0.001
Ph.D.	29 (78.4)	42 (71.2)	13 (56.5)	19 (30.6)	103 (56.9)	<0.001
Medical Doctor	17 (45.9)	38 (64.4)	8 (34.8)	35 (56.5)	98 (54.1)	0.068
Years of work experience in GC and/or GT in clinical settings	n = 27	n = 49	n = 16	n = 53	n = 145	0.75
Mean years (SD, range)	15.22 (10.92, 1–40)	13.20 (9.35, 1–42)	14.47 (11.59, 3–44)	12.49 (9.27, 1–32)	13.5 (9.83, 1–44)	
Years of work experience in GC and/or GT in research settings	n = 28	n = 43	n = 13	n = 43	n = 127	0.27
Mean years (SD, range)	15.91 (10.53, 1–43)	14.16 (10.97, 2–52)	11.54 (11.86, 2–40)	11.92 (8.84, 0.5–33)	13.52 (10.30, 0.5–52)	
Occupation (several answers possible)						
Physician	6 (16.2)	16 (27.1)	1 (4.3)	11 (17.7)	34 (18.8)	0.110
Nurse	0 (0.0)	<5	0 (0.0)	<5	5 (2.8)	0.165
Clinical Geneticist	8 (21.6)	25 (42.4)	4 (17.4)	8 (12.9)	45 (24.9)	0.002
Adult Psychiatrist	8 (21.6)	6 (10.2)	4 (17.4)	16 (25.8)	34 (18.8)	0.165
Child Psychiatrist	2 (5.4)	5 (8.5)	0 (0.0)	5 (8.1)	12 (6.6)	0.522
Neurologist	<5	0 (0.0)	0 (0.0)	<5	<5	0.273
Paediatrician	<5	<5	0 (0.0)	<5	5 (2.8)	NA
Diagnostic Laboratory Scientist	7 (18.9)	6 (10.2)	<5	3 (4.8)	18 (9.9)	0.159
Genetic Counselor	<5	5 (8.5)	6 (26.1)	23 (37.1)	38 (21.0)	<0.001
Psychologist	<5	<5	6 (26.1)	<5	12 (6.6)	<0.001
Researcher	14 (37.8)	20 (33.9)	6 (26.1)	6 (9.7)	46 (25.4)	0.004
Other	5 (13.5)	<5	0 (0.0)	5 (8.1)	14 (7.7)	0.290
Organization profile						0.019
Public sector	28 (75.7)	53 (89.8)	19 (82.6)	59 (95.2)	159 (87.8)	
Private sector	<5	<5	<5	<5	8 (4.4)	
Combined	5 (13.5)	<5	<5	<5	11 (6.1)	
Non-profit organization	0 (0.0)	0 (0.0)	<5	<5	<5	
Part of activities related to GC and GT (several answers possible)						
Research	27 (73.0)	34 (57.6)	13 (56.5)	35 (56.5)	109 (60.2)	0.365
Education and training	19 (51.4)	29 (49.2)	9 (39.1)	32 (51.6)	89 (49.2)	0.766
Regulatory aspects	<5	8 (13.6)	<5	<5	18 (9.9)	0.400
Clinical Practice	26 (70.3)	51 (86.4)	14 (60.9)	56 (90.3)	147 (81.2)	0.004
Patient Advocacy	<5	6 (10.2)	<5	5 (8.1)	18 (9.9)	0.913
Other	2 (5.4)	3 (5.1)	3 (13.0)	3 (4.8)	11 (6.1)	0.522

GC - genetic counseling, GT - genetic testing.

(71.3%). The majority of the respondents had either a Ph.D. (56.9%) and/or an MD degree (54.1%). The average years of work experience in GC and/or GT in clinical and research settings was 13 yrs. The three main occupational categories were genetic counselor (21.0%), clinical geneticist (24.9%), and researcher (25.4%). We had significantly more answers from clinical geneticists from Northern Europe and fewer genetic counselors from Central and Eastern Europe and Northern Europe.

3.2. Access and facilities for genetic counseling and testing within the European countries

First, we assessed the access and facilities for GT and GC within the countries and institutions of the respondents. In total, 61.3% of the respondents themselves offered GC, with no significant differences across the regions (Table 2). Different practices and healthcare structures exist across Europe; therefore, we also asked who is responsible for and allowed to order GC services. The majority reported that clinical geneticists (71.3%), clinical specialists (63.5%), or primary care physicians (63.0%) order GC for the patient (Supplementary Fig. 1A). The largest difference among the regions was in the differences in whether genetic counselors were responsible for or allowed to refer the patient to GC ($p < 0.001$). GC is covered mainly by a national healthcare system, with the highest coverage in Northern Europe (81.4%) and Western Europe (71%) (Supplementary Fig. 1B).

Genetic testing, in general, was offered in approximately 50% of the respondents' clinics, hospitals, or institutions (Table 2). Also, many reported that GT was outsourced to other hospitals or companies; thus, most respondents (85%) have access to GT. There were significant differences between the regions in the percentage of respondents stating if GT was available within their clinic or institution (Table 2), with the lowest rate within the Southern European respondents and the highest within Northern Europe. The majority reported that clinical geneticists (74.0%) or clinical specialists (72.4%) are responsible for and allowed to order GT (Supplementary Fig. 1A). The largest difference among the regions was in the differences in whether genetic counselors were responsible for or entitled to order GT, with almost 60% within Western Europe. Most respondents indicated that in their country, GT is fully covered by the national health care system (70.2%); however, with significant differences between the regions (Supplementary Fig. 1B).

3.3. Genetic counseling for brain-related conditions

Next, we focused on how many respondents provided PsychGC. Of all 181 respondents, 106 provide GC for any psychiatric disorder or NDD, corresponding to 58.6% of the whole group ranging from 43.2% in Central Eastern Europe to 66.1% in Western Europe. No significant

Table 2
Results of genetic testing, counseling, and pharmacogenetic testing questions.

	Central and Eastern Europe (n = 37)	Northern Europe (n = 59)	Southern Europe (n = 23)	Western Europe (n = 62)	Total (n = 181)	p-value
TESTING Availability of GT in institution (several answers possible)						
Yes, within the clinic	11 (29.7)	38 (64.4)	6 (26.1)	34 (54.8)	89 (49.2)	<0.001
Yes, within the institution	20 (54.1)	21 (35.6)	9 (39.1)	39 (62.9)	89 (49.2)	0.016
Yes, outsourced from the hospital	12 (32.4)	15 (25.4)	7 (30.4)	16 (25.8)	50 (27.6)	0.858
Yes, outsourced to a company abroad	7 (18.9)	13 (22.0)	6 (26.1)	<5	30 (16.6)	0.057
No	7 (18.9)	<5	4 (17.4)	<5	18 (9.9)	0.065
Don't know	<5	<5	<5	0 (0.0)	9 (5.0)	0.013
No of persons (%) performing pharmacogenetic testing for psychiatric and/or NDD	5 (13.5)	9 (15.3)	0 (0.0)	13 (21.0)	27 (14.9)	0.022
No of persons (%) participating in laboratory quality assurance schemes	13 (35.1)	25 (42.4)	7 (30.4)	17 (27.4)	62 (34.3)	0.071
COUNSELING						
No of persons (%) providing GC for any disorder	19 (51.4)	35 (59.3)	12 (52.2)	45 (72.6)	111 (61.3)	0.364
No of persons (%) providing GC for any type of psychiatric or NDD	16 (43.2)	36 (61.0)	13 (56.5)	41 (66.1)	106 (58.6)	0.435

	Central Eastern Europe (n = 16)	**Northern Europe (n = 36)**	**Southern Europe (n = 13)**	**Western Europe (n = 41)**	**Total (n = 106)**	**p-value**	**Genetic counselor (n = 21)**	**Clinical geneticist (n = 43)**	**Psychiatry (n = 32)**
Methods of GC[a]									
Family history based	13 (81.2)	33 (91.7)	13 (100.0)	38 (92.7)	97 (91.5)	0.222	20 (95.2, 0.664)	41 (93.5, 0.318)	29 (90.6, 0.008)
Genetic testing based	11 (68.8)	31 (86.1)	9 (69.2)	33 (80.5)	84 (79.2)	0.317	16 (76.2, 0.528)	43 (100, <0.001)	15 (46.9, <0.001)
No of persons providing remote GC[a]	8 (50.0)	28 (77.8)	5 (38.5)	21 (51.2)	62 (58.5)	0.125	20 (95.2, 0.002)	33 (76.7, 0.008)	4 (12.5, <0.001)
No of members of quality assurance scheme[a]	<5	15 (41.7)	<5	21 (51.2)	41 (38.7)	0.066	14 (66.7, 0.021)	15 (34.9, 0.291)	7 (21.9, 0.058)

GT - genetic testing, GC - genetic counseling, NDD - neurodevelopmental disorder.
[a] By region [number, %] and by profession [number, %, p-value (group vs two other groups combined)], n = 106 - number of persons providing genetic counseling for any type of psychiatric or NDD.

differences between regions were seen (p = 0.435) (Table 2). Among the 106 counseling respondents, the most common disorders to provide GC for are NDDs (82.1%), followed by neurological disorders (67.9%) and inborn errors of metabolism and endocrine disorders (63.2%), with no significant differences between regions (Table 2 and Fig. 1B).

When we analyzed differences between professions, more than three out of four clinical geneticists and genetic counselors provide counseling for NDDs (100 and 76.2%, respectively), inborn errors of metabolism and endocrine disorders (90.7 and 81%, respectively), and neurological disorders (90.7 and 85.7%, respectively) (Table 2). In contrast, less than half provide PsychGT (48.8 and 33.3%, respectively). Most psychiatrists and psychologists, coded as one psychiatry group, state that they provide GC for psychiatric disorders (68.8%), followed by NDDs (56.2%) (Table 2).

Of all 181 respondents, only 22.1% stated that their countries have existing guidelines or regulations regarding PsychGC (Fig. 1C), with significant differences between regions (p < 0.001). The collected guidelines are presented in Supplementary Table 3. Most respondents within Western Europe stated that there are guidelines or recommendations regarding PsychGC (37.1%). However, it is also the region with the highest rate of not knowing about the policies (43.5%). When analyzing specific countries reporting the guidelines, a similar trend can be seen; many of the respondents from the country were not sure or aware of the existing guidelines. For instance, in France, 40.9% (n = 9) indicated that there are guidelines, 22.7% (n = 5) indicated that there are no guidelines, and 36.4% (n = 8) were not sure or did not know about guidelines. In Central Eastern Europe, only 8.1% indicated that there are guidelines or recommendations, and almost four out of five (78.4%) answered that there are no guidelines in that region.

When comparing the healthcare professional groups regarding their awareness of guidelines, there is a significant difference where only 7.9% of the genetic counselors state there are national guidelines compared with 24.4% and 28.1% of the clinical geneticists and psychiatry group, respectively. As many as 50% of the genetic counselors do not know that there are national guidelines, compared to 17.8% and 31.6% of the clinical geneticists and psychiatry group, respectively.

The vast majority of respondents who provide PsychGC (n = 106) use family history-based risk assessment (91.5%), and 79.2% use genetic testing-based risk assessment and interpretation in GC. In each professional group, more than 90% use family-based risk assessment as one model of providing GC. In addition, all clinical geneticists (100%) reported using a genetic test-based risk assessment as an additional model for risk assessment. In contrast, only 76.2% of genetic counselors use a genetic test-based assessment (Table 2). There was no significant difference between the regions regarding which model was used.

Of those providing GC for any psychiatric disorder, 58.5% also provide remote GC via telephone or video. Remote GC is provided most in Northern Europe (77.8%), followed by Western Europe (51.2%), Central Eastern Europe (50%), and Southern Europe (38.5%) (Table 2).

About half of the respondents from Northern (41.7%) and Western

Europe (51.2%) are members of some formal or informal quality assurance scheme, clinical supervision, or other peer networks for their GC methods. In contrast, 18.8% and 15.4% of the respondents from Central Eastern Europe and Southern Europe are members of such a quality assurance scheme, respectively. By comparing the professional groups, it is clear that it is more common among genetic counselors to be part of such a scheme than for clinical geneticists and least common within the psychiatry group (66.7%, 34.9%, and 21.9%, respectively) (Table 2).

3.4. Genetic testing for brain-related conditions

We asked whether the respondents or their clinic/institution offered GT for the following four conditions also contrasted within the GC questions: NDDs, neurological disorders, inborn errors of metabolism and endocrine diseases, and major psychiatric disorders. Overall, 65.2% reported that GT is offered to individuals with NDDs, 55.2% that it is provided for individuals with inborn errors of metabolism and endocrine diseases, 56.4% reported that it is available for neurological disorders, and 26.5% reported that GT is offered for individuals affected by major psychiatric disorders (Fig. 1B). Significant differences were seen between the regions for the other conditions but not major psychiatric disorders (p-values <0.001, 0.001, 0.007, and 0.649, respectively).

The respondents from the following countries reported that GT is offered for individuals with major psychiatric disorders: Germany, Denmark, Slovenia, Malta, Poland, France, Israel, Sweden, Austria, France, Lithuania, the United Kingdom, Denmark, Netherlands, Estonia, Finland, and Portugal. There seem to be differences or discrepancies in information across these countries that offer PsychGT. For instance, in Denmark, seven respondents reported that GT is provided to individuals with major psychiatric disorders, while 12 reported that it was not. Similarly, in France, 14 reported that they or their clinic offer GT for this category of conditions, and eight reported that they do not. Interestingly, 22.1% of the respondents indicated their country has guidelines for offering GT for major psychiatric disorders in their countries (Fig. 1C). The collected guidelines are presented in Supplementary Table 3. Similar to GC guidelines, the answers within regions and countries were mixed with disagreement among the respondents. For instance, in Sweden, 20.8% (n = 5) reported guidelines for PsychGT, 37.5% (n = 9) reported no guidelines, and 41.7% (n = 10) were not sure or unaware.

We also examined whether offering GT for the four categories of conditions was associated with the testing being fully covered by national health insurance. Indeed, those respondents that reported genetic testing is fully covered by national health insurance also more often offered GT for individuals with NDDs (74.8% vs. 42.6%) ($p < 0.001$), inborn errors of metabolism 63.8% vs. 35.2% ($p < 0.001$), neurological disorders 63.0% vs. 40.7% ($p = 0.006$). However, we did not see this association between full coverage from the national health insurance and offering GT for individuals with major psychiatric disorders 28.3% vs. 22.2% ($p = 0.393$).

All the types of GT methods that we surveyed were offered to the four groups of disorders with significant differences among the regions for (a) targeted gene or genetic loci tests using, for instance, MLPA, FISH, and Sanger sequencing and (b) exome/genome sequencing (Supplementary Fig. 2). All the methods were offered in similar percentages for the other groups of conditions but less for major psychiatric disorders. We also asked if the respondents performed pharmacogenetic testing for NDDs and psychiatric disorders. However, only 15% of the respondents answered that they did (Table 2). Of those, 68% indicated ordering less than 50 genetic tests for the conditions in the last 12 months. The only difference between countries was that the respondents from Southern Europe did not offer pharmacogenetic testing. Participation in external laboratory quality assurance or intra-laboratory quality networks for GT methods was indicated by 34.3% of the respondents (Table 2).

3.5. Major obstacles and need for guidelines for implementing PsychGC and PsychGT

Thematic analyses of open question answers of all respondents for describing the major obstacles in implementing PsychGC and PsychGT resulted in seven large themes (Fig. 2A). When analyzing the frequency of each of the seven themes of barriers for PsychGC and PsychGT, the lack of guidelines and knowledge on how to utilize and use genetic tests, as well as education and training, were reported most often (Fig. 2B).

We also asked whether the respondents thought pan-European professional guidelines for PsychGC and PsychGT would be relevant and improve their daily practice in the area. For PsychGC, 106 respondents replied to the question, and the majority thought it was either essential (21.7%) or highly relevant (48.1%) (Fig. 2C). For guidelines related to PsychGT, 134 respondents answered the question, and also the majority thought it was either essential (24.6%) or highly relevant (50.0%) (Fig. 2C). The years of experience in GC or GT in either clinical or research setting did not influence the responses to the question on "relevance of professional guidelines to daily practice" ($p = 0.739$ and $p = 0.155$, respectively). Similarly, the attitude of two categories of professionals towards "relevance of training and education on daily practice" was not affected by years of experience ($p = 0.128$ and $p = 0.421$, respectively).

3.6. Education and training within PsychGC and PsychGT

As PsychGC and PsychGT are emerging fields, it is important to know whether specific training exists within European universities. For general GC, formal education and training programs were confirmed in most respondents' institutions (53%), with no significant difference between European regions (Table 3). The availability of education and training programs in general GT was similar, with 57.5% of affirmative answers (Table 3). An opposite situation was found for education and training specifically for PsychGC and PsychGT, as only 11.6% reported that training courses were available (Table 3). We found no statistical differences in the profile of professionals responding to the survey or respondents' country/region of origin.

Not surprisingly, the majority of the respondents highlight that up-to-date education and training in PsychGC/GT are essential (24.9%) or highly relevant (45.9%) for their everyday practice within the field (Fig. 3A), but with significant differences between the four regions ($p = 0.023$) (Fig. 3A). Respondents from Northern Europe had the most diverse attitude towards the significance of education in improving everyday practice in the PsychGT/GC, with 18% unaware or not believing it necessary. When analyzing the need for special training between different professional groups, there was no statistically significant difference between geneticists, counselors, and psychiatry groups ($p = 0.824$, 0.613, and 0.1888, respectively).

Integrating PsychGC/GT into the postgraduate academic programs in the form of specialized curricula was regarded as beneficial across all respondents. The highest values of affirmation were among participants from Southern Europe (82.6%), followed by Western (72.6%) and Central-Eastern Europe (70.3%), and more than half of the respondents within Northern Europe (57.6%). The psychiatry group had the highest number of respondents (80.7%) in favor of a specialized curriculum, followed by genetic counselors (73.7%) and clinical geneticists (60%), with statistically significant differences among the professional groups ($p = 0.048$, 0.625, and 0.366, respectively) (Fig. 3B).

4. Discussion

Here, we present the first attempt to provide information on the current state of implementing PsychGC and PsychGT within European countries participating in the ongoing EnGagE COST action network. We contrast the implementation of PsychGC/GT to NDDs, neurological disorders, and inborn errors of metabolism, conditions for which the

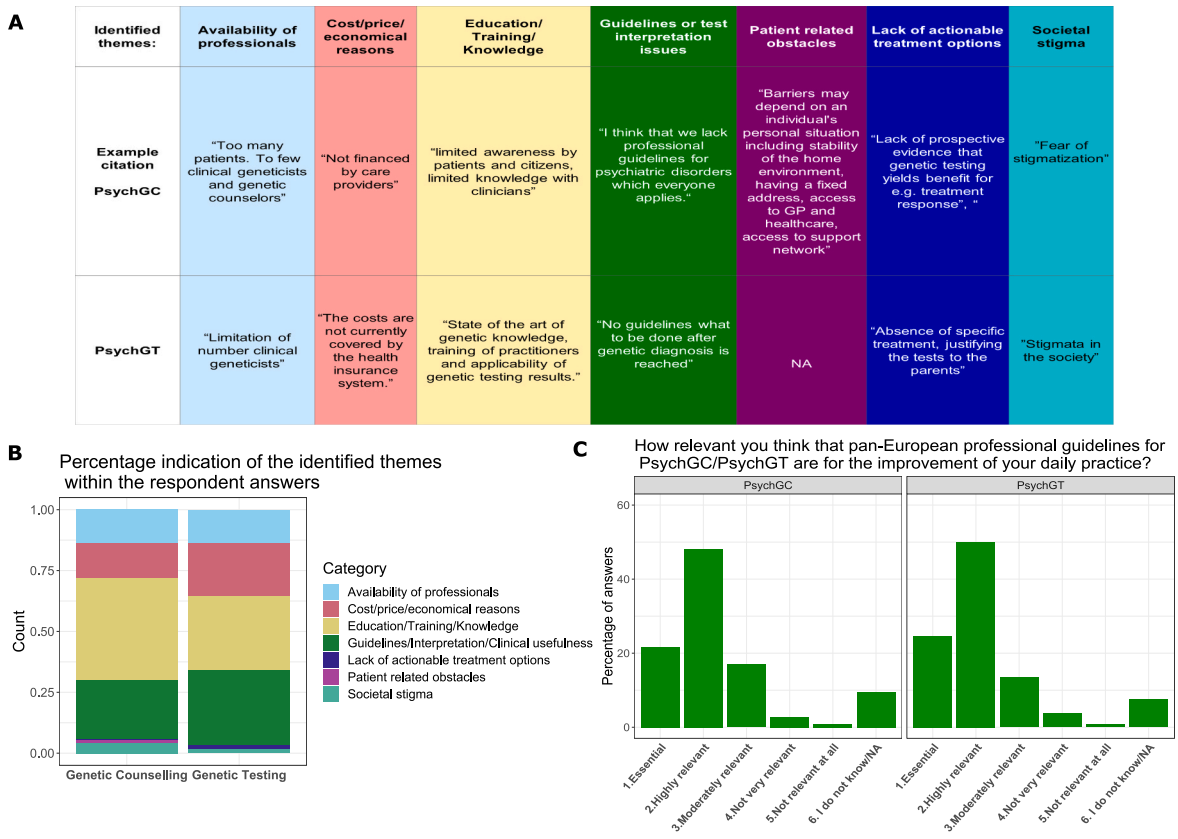

Fig. 2. Obstacles in implementing Psychiatryc genetic counseling and testing in clinical settings and the need of guidelines. (A) Thematic themes identified from the open-ended questions on the opinions on the major obstacles in implementing psychiatric genetic counseling and genetic testing, (B) Quantification of the number of respondents indicating each thematic theme from the qualitative analyses presented in A. (C) Option percentage for the need for guidelines of GC and GT.

Table 3
Distribution of answers to main questions on education and training.

Opinion on …	"Yes" (%)	"No" (%)	"Do not know" (%)	p-value
Availability of general GC training	53	35.9	11	0.218
Availability of general GT training	57.5	30.4	12.2	0.605
Availability of education/ training on PsychGC	11.6	68	20.4	0.175
Availability of education/ training on PsychGT	11.6	66.9	21.5	0.150

GC - genetic counseling, GT - genetic testing, Psych - psychiatric.

implementation of GC and GT has been ongoing longer. However, most respondents indicated that there are no available guidelines for the clinical implementation of PsychGC/GT; 58.6% and 26.5% of the respondents already provide PsychGC and PsychGT, respectively, either themselves or within their clinics/institutions. We also show significant differences between the regions in our study for the implementation and access to the facilities. Interestingly, but not surprisingly, we show discrepancies if PsychGC and PsychGT are also offered within a country. Overall, our data shows that there is very heterogeneous knowledge and implementation throughout Europe of available techniques, guidelines, and sources of information in general for GC and GT, but also reflecting the early implementation of these for major psychiatric disorders.

We aimed to capture a large variety of professions across Europe to gather the practices and opinions regarding the topic. Indeed, we had more than 11 professions among the respondents. Therefore, we could capture some of the heterogeneity of tools and implementation from different professional backgrounds. For instance, we show that psychiatrists and psychologists provide more GC based on family history than genetic testing-based risk assessments. In contrast, all clinical geneticists state that they provide GC with genetic testing-based risk assessment (mostly in addition to family history). This can further explain why providing PsychGC is less common among clinical geneticists than among the psychiatry group, as no clear risk assessment can be provided given the complexity of multifactorial disorders, which major psychiatric disorders are. The lack of PsycGC could also be explained because, in this study, most respondents stated that clinical geneticists refer to GC. They might not always be aware of the positive outcome of GC when no test results are available (Inglis et al., 2015; Hippman et al., 2016).

Many obstacles to the implementation were identified within the responses. Most respondents pointed towards a lack of guidelines and knowledge followed by a lack of appropriate training within the field. As different profession groups provide GC in this area, and as different approaches for risk assessment are used, it is of great importance to create clear definitions of GC and genetic counselors' role (Skirton et al., 2015; Ingvoldstad et al., 2016) and develop guidelines and educational activities to give the caregiver the skills and tools to provide PsychGC in a way to enhance patient safety. The good clinical practice in producing medically relevant genetic information and its effective communication within interdisciplinary medical teams is evident in many European healthcare centres (Middleton et al., 2017), with many substantial non-administrative and administrative barriers associated with its translation into everyday practice still ongoing (Becker et al., 2011). The quality of general GT services in Europe is coordinated by the European Society of Human Genetics (ESHG) and its integrated committee (Eurogentest) through the harmonization of professional requirements criteria and continuous education of healthcare professionals engaged with GT and GC (Liehr et al., 2019).

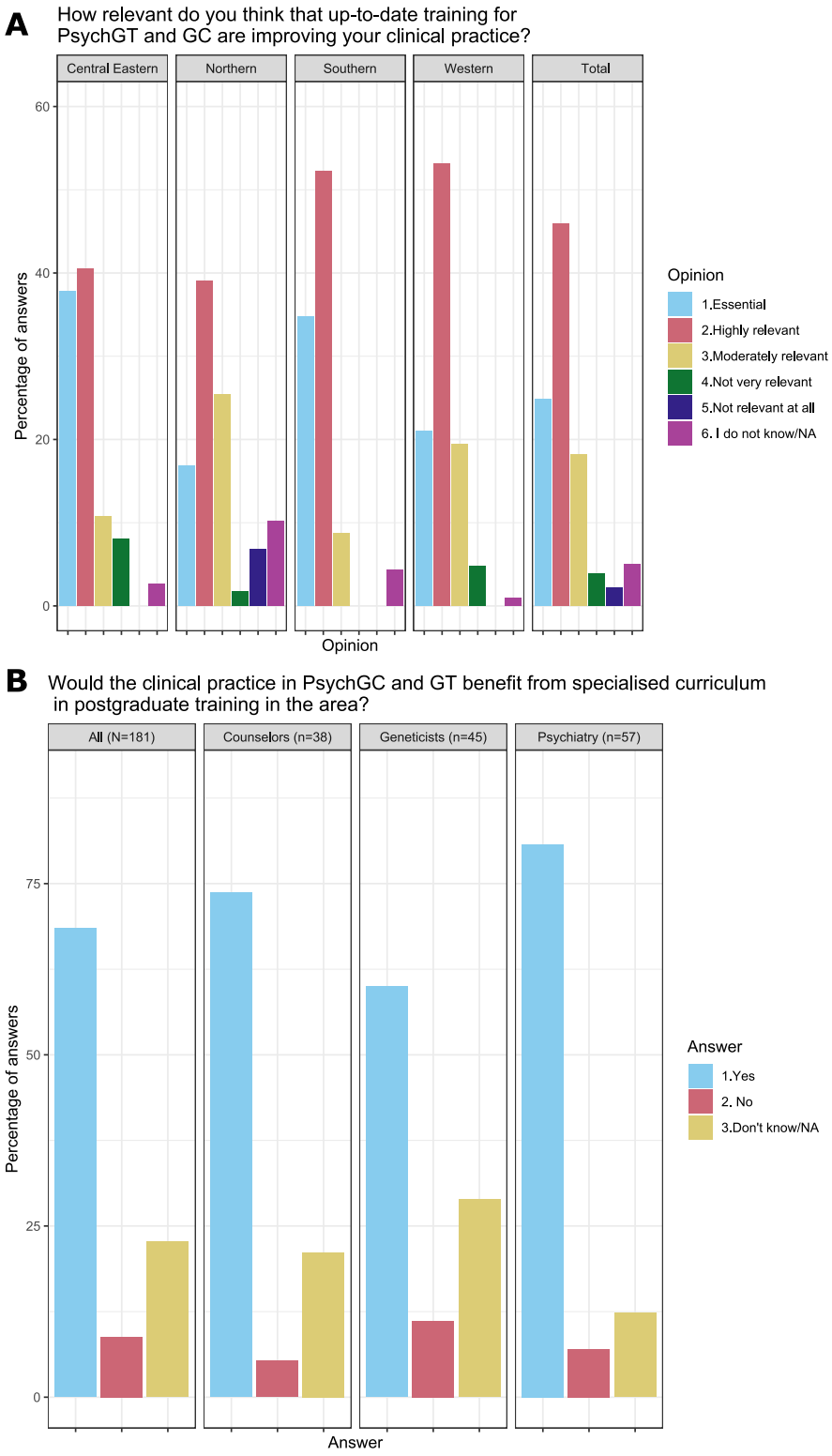

Fig. 3. Relevance of training in psychiatric genetic counseling and testing for clinical practice. (A) Relevance of PsychGC/GT training for daily clinical practice by regions, (B) Benefit from the specialized curriculum on PsychGC/GT training for clinical practice by professional groups.

Furthermore, the most common major hindrances identified were economic considerations and patient-related obstacles. Based on the identified themes of major obstacles, many could be resolved with clear and comprehensive guidelines. Therefore, we clearly show that guidelines and recommendations on implementing PsychGC/GT are needed within Europe to ensure knowledge transfer from research to the clinics and equal access to services for individuals with psychiatric disorders. We acknowledge differences in legislation and regulations related to GC and GT and in the usage of national and international guidelines between countries. However, in this relatively new area of practice, new common European guidelines could create more equality in the availability and capacity of PsychGT and PsychGC all around Europe.

In this study, we provide information about the current state of GC and GT in psychiatry as an inextricably linked process in the scientifically grounded and ethically justified application of genetic information in precision diagnostics, prognostics, and therapeutic targeting. The evaluated capacities in PsychGC and PsychGT share common obstacles that should be addressed simultaneously through harmonizing professional guidelines and education programs. The role of genetic counselors within both clinical genetics and psychiatry should be more established in the health care system.

There is a progressive trend in the validation and integration of genetic and genomic testing and counseling services as a part of future precision medicine strategies in Europe and worldwide (Horgan et al. 2017; Pastorino et al., 2019). This fact is also reflected in our survey results, with formal education and training programs in (general) GC confirmed in most of the respondents' institutions.

The limitation of this current study should be considered for future work. As there seems to be high variability even within countries for access and implementation, a larger study with more specific questions that could separate local and national practices is needed. Furthermore, as PsychGC and PsychGT are still in their infancy, better explanations and instructions are also required to capture the actual implementation rate of these within clinics. We also acknowledge that the questionnaire was not distributed similarly in all the countries, thus leading to a potential sampling bias. We also had a significant number of respondents already from the EnGagE network with better knowledge of the topic, which provides good feedback from knowledgeable people.

Despite the limitations, the results provided through this multiprofessional pan-European survey support the aims of EnGagE action and provide a platform for future discussions for the clinical implementation of PsychGC and PsychGT. Larger communication between disciplines and over the whole of Europe and potentially developing professional guidelines should be the top priority for the coming years.

Role of the funding sources

This publication is based upon work from COST Action Enhancing Psychiatric Genetic Counseling, Testing, and Training in Europe (EnGagE), CA17130, supported by COST (European Cooperation in Science and Technology). Other funding sources have contributed to this work: The Swedish Foundation of Strategic Research (K. Tammimies) The Fondation Bettencourt Schuller (B. Chaumette), UEFISCDI, Romania (M. Grigoroiu-Serbanescu), Ministry of Civil Affairs of Bosnia and Herzegovina (L. Pojskic).

Declaration of competing interest

The authors have no conflict of interest to declare in relation to this work.

CRediT authorship contribution statement

Kati Koido: Conceptualization, Investigation, Methodology, Supervision, Writing – original draft. **Charlotta Ingvoldstad Malmgren:** Conceptualization, Investigation, Methodology, Supervision, Writing – original draft. **Lejla Pojskic:** Conceptualization, Investigation, Methodology, Supervision, Writing – original draft. **Peter Z. Almos:** Conceptualization, Investigation, Revision of final draft. **Sarah E. Bergen:** Conceptualization, Investigation, Analysis of data, Participation in writing including revision of the final draft. **Isabella Borg:** Conceptualization, Investigation, Analysis of data, Revision of final draft. **Nada Božina:** Investigation, Analysis of data, Revision of final draft. **Domenico A. Coviello:** Analysis of data, Revision of final draft. **Franziska Degenhardt:** Conceptualization, Funding acquisition. **Lana Ganoci:** Investigation, Analysis of data, Revision of final draft. **Uffe B. Jensen:** Conceptualization, Investigation, Methodology, Writing – original draft. **Louise Durand-Lennad:** Formal analysis, Writing. **Claudine Laurent-Levinson:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Andrew McQuillin:** Conceptualization, Participation in writing including revision of the final draft. **Alvydas Navickas:** Conceptualization, Investigation, Writing – original draft. **Nikolai P. Pace:** Conceptualization, Investigation. **Milena Paneque:** Conceptualization, Investigation, Analysis of data, Revision of final draft. **Marcella Rietschel:** Conceptualization, Participation in writing including revision of the final draft. **Maria Grigoroiu-Serbanescu:** Data collection, Formal analysis, Conceptualization, Participation in writing including revision of the final draft. **Maria Johansson Soller:** Data collection, Conceptualization, Participation in writing including revision of the final draft. **Jaana Suvisaari:** Conceptualization, Investigation. **Algirdas Utkus:** Conceptualization, Investigation, Writing – original draft. **Evelien Van Assche:** Conceptualization, Writing – original draft. **Lily Vissouze:** Formal analysis. **Shachar Zuckerman:** Data collection, Participation in writing. **Boris Chaumette:** Conceptualization, Data collection, Analyses, Supervision, Writing. **Kristiina Tammimies:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, and revision of final draft.

Data availability

Data will be made available on request.

Acknowledgments

We want to thank all the respondents for answering the survey. Our greatest gratitude goes to the collaborators from the monitoring tool task force of the EnGagE network (European Union COST Action CA17130 Enhancing Psychiatric Genetic Counseling, Testing, and Training in Europe (EnGagE)) – Dr. Laima Ambrozaitytė, Dr. Andrew Cuthbert, Dr. Piotr M. Czerski, Dr. Eliza Ivanova, Dr. Janos Kalman, Prof. Marie-Odile Krebs, Dr. Danijela Krgovic, Dr. Blazej Misiak, Prof. Ramona Moldovan, Dr. Nayia Nicolaou, Dr. Joanna Pawlak, Prof. Marija Raleva, Dr. Martina Rojnic, Prof. Silke Schicktanz, Mag. Monika Schlögelhofer, Dr. Monika Dmitrzak-Węglarz, Dr. Katrine Verena Wirgenes. We also thank Dr. Anna Hellquist for her technical assistance with the survey and other members of the EnGagE network – Mario Amore, Harald Aschauer, Visnja Banjac Baljak, Virginia Bizzarri, Anders Børglum, Sara Carneiro, Alper Han Cebi, Sven Cichon, Catalina-Angela Crisan, Goran Cuturilo, Vassiliki Daskalou, Markéta Havlovicová, William Hennah, Per Hoffmann, Katerina Popovska-Jankovic, Clara Serra-Juhé, Paweł Kapelski, Hojka Gregorič Kumperščak, Lorna Lopez, Milan Macek, Fermín Mayoral, Kevin McGhee, Andia Meksi, Signe Mezinska, Marina Mihaljevic, Milena Petrović, Alexandra Philipsen, Bart Rutten, Vidar M. Steen, Lidija Stevovic, Efthymia Sygkollitou, George Tanteles, Irina Todorova, Eero Vasar, Nadja Kokalj Vokač.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejmg.2023.104805.

References

Brainstorm Consortium, Anttila, Verneri, Bulik-Sullivan, Brendan, Finucane, Hilary K., Walters, Raymond K., Bras, Jose, Duncan, Laramie, et al., 2018. Analysis of shared heritability in common disorders of the brain. Science 360 (6395), eaap8757.

Austin, Jehannine C., 2020. Evidence-based genetic counseling for psychiatric disorders: a road map. Cold Spring Harbor Perspect. Med. 10 (6), a036608.

Becker, Frauke, Carla van El, G., Ibarreta, Dolores, Zika, Eleni, Hogarth, Stuart, Pascal, Borry, Cambon-Thomsen, Anne, et al., 2011. Genetic testing and common disorders in a public health framework: how to assess relevance and possibilities. Eur. J. Hum. Genet. 19 (1), S6–S44.

Braun, Virginia, Clarke, Victoria, 2006. Using thematic analysis in psychology. Qual. Res. Psychol. 3 (2), 77–101.

Brownstein, Catherine A., Douard, Elise, Mollon, Josephine, Smith, Richard, Hojlo, Margaret A., Das, Ananth, Goldman, Maria, et al., 2022. Similar rates of

deleterious copy number variants in early-onset psychosis and autism spectrum disorder. Am. J. Psychiatr. 179 (11), 853–861.
Chaumette, B., Laurent-Levinson, C., Almos, P., Degenhardt, F., 2021. How genetics can help diagnosis and treatment in psychiatric conditions. Eur. Psychiatr. 64 (S1), S49. –S49.
Coleman, Jonathan R.I., Gaspar, Héléna A., Bryois, Julien, Bipolar Disorder Working Group of the Psychiatric Genomics Consortium, Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium, and Gerome Breen, 2020. The genetics of the mood disorder spectrum: genome-wide association analyses of more than 185,000 cases and 439,000 controls. Biol. Psychiatr. 88 (2), 169–184.
Ditte, D.G., Bragi, Walters, Georgios, Athanasiadis, Raymond, Walters, Karen, Therrien, Leila, Farajzadeh, Georgios, Voloudakis, et al., 2022. Genome-wide analyses of ADHD identify 27 risk loci, refine the genetic architecture and implicate several cognitive domains. medRxiv.
Finucane, Brenda M., Ledbetter, David H., As Vorstman, Jacob, 2021. Diagnostic genetic testing for neurodevelopmental psychiatric disorders: closing the gap between recommendation and clinical implementation. Curr. Opin. Genet. Dev. 68 (June), 1–8.
Foley, Claire, Heron, Elizabeth A., Harold, Denise, Walters, James, Owen, Michael, O'Donovan, Michael, Sebat, Jonathan, et al., 2020. Identifying schizophrenia patients who carry pathogenic genetic copy number variants using standard clinical assessment: retrospective cohort study. Br. J. Psychiatr.: J. Ment. Sci. 216 (5), 275–279.
Grove, Jakob, Ripke, Stephan, Als, Thomas D., Mattheisen, Manuel, Walters, Raymond K., Won, Hyejung, Pallesen, Jonatan, et al., 2019. Identification of common genetic risk variants for autism spectrum disorder. Nat. Genet. 51 (3), 431–444.
Hippman, Catriona, Ringrose, Andrea, Inglis, Angela, Cheek, Joanna, Arianne, Y., Albert, K., Remick, Ronald, Honer, William G., C Austin, Jehannine, 2016. A pilot randomized clinical trial evaluating the impact of genetic counseling for serious mental illnesses. J. Clin. Psychiatry 77 (2), e190–e198.
Horgan, Denis, Romao, Mario, Hastings, Rob, 2017. Pulling the strands together: MEGA steps to drive European genomics and personalised medicine. Biomed. Hub 2 (Suppl. 1), 1–11.
Inglis, Angela, Koehn, David, McGillivray, Barbara, Evelyn Stewart, S., Austin, Jehannine, 2015. Evaluating a unique, specialist psychiatric genetic counseling clinic: uptake and impact. Clin. Genet. 87 (3), 218–224.
Ingvoldstad, C., Seven, M., Taris, N., Cordier, C., Paneque, M., Skirton, H., 2016. Components of genetic counsellor education: a systematic review of the peer-reviewed literature. J. Community Genet. 7 (2), 107–118.
International Society of Psychiatric Genetics, 2019. Genetic Testing Statement, 2019. https://ispg.net/genetic-testing-statement/.
Jacquemont, Sébastien, Huguet, Guillaume, Klein, Marieke, Samuel, J., Chawner, R.A., Donald, Kirsten A., Marianne van den Bree, B.M., Sebat, Jonathan, et al., 2022. Genes to mental health (G2MH): a framework to map the combined effects of rare and common variants on dimensions of cognition and psychopathology. Am. J. Psychiatr. 179 (3), 189–203.
Lewis, Cathryn M., Vassos, Evangelos, 2022. Polygenic scores in psychiatry: on the road from discovery to implementation. Am. J. Psychiatr. 179 (11), 800–806.
Liehr, Thomas, Carreira, Isabel M., Balogh, Zsofia, Dominguez Garrido, Elena, Verdorfer, Irmgard, Coviello, Domenico A., Florentin, Lina, Scheffer, Hans, Rincic, Martina, Heather, E., Williams, 2019. Regarding the rights and duties of clinical laboratory geneticists in genetic healthcare systems; results of a survey in over 50 countries. Eur. J. Hum. Genet. 27 (8), 1168–1174.
Middleton, Anna, Marks, Peter, Bruce, Anita, Liwsi, K., Protheroe-Davies, King, Cath, Claber, Oonagh, Houghton, Catherine, et al., 2017. The role of genetic counsellors in genomic healthcare in the United Kingdom: a statement by the association of genetic nurses and counsellors. Eur. J. Hum. Genet. 25 (6), 659–661.
Palmer, Duncan S., Howrigan, Daniel P., Chapman, Sinéad B., Rolf, Adolfsson, Bass, Nick, Douglas, Blackwood, Marco, P., Boks, M., et al., 2022. Exome sequencing in bipolar disorder identifies AKAP11 as a risk gene shared with schizophrenia. Nat. Genet. 54 (5), 541–547.
Pastorino, Roberta, De Vito, Corrado, Migliara, Giuseppe, Glocker, Katrin, Binenbaum, Ilona, Ricciardi, Walter, Boccia, Stefania, 2019. Benefits and challenges of big data in healthcare: an overview of the European initiatives. Eur. J. Publ. Health 29 (Suppl. 3), 23–27.
Resta, Robert, Bowles Biesecker, Barbara, Bennett, Robin L., Blum, Sandra, Hahn, Susan Estabrooks, Strecker, Michelle N., Williams, Janet L., 2006. A new definition of genetic counseling: national society of genetic counselors' task force Report. J. Genet. Counsel. 15 (2), 77–83.
Satterstrom, F. Kyle, Walters, Raymond K., Tarjinder, Singh, Wigdor, Emilie M., Lescai, Francesco, Demontis, Ditte, Kosmicki, Jack A., et al., 2019. Autism spectrum disorder and attention deficit hyperactivity disorder have a similar burden of rare protein-truncating variants. Nat. Neurosci. 22 (12), 1961–1965.
Semaka, Alicia, Austin, Jehannine, 2019. Patient perspectives on the process and outcomes of psychiatric genetic counseling: an 'empowering encounter. J. Genet. Counsel. 28 (4), 856–868.
Singh, Tarjinder, Poterba, Timothy, Curtis, David, Akil, Huda, Eissa, Mariam Al, Barchas, Jack D., Bass, Nicholas, et al., 2022. Rare coding variants in ten genes confer substantial risk for schizophrenia. Nature 604 (7906), 509–516.
Skirton, Heather, Cordier, Christophe, Ingvoldstad, Charlotta, Taris, Nicolas, Benjamin, Caroline, 2015. The role of the genetic counsellor: a systematic review of research evidence. Eur. J. Hum. Genet. 23 (4), 452–458.
Trost, Brett, Thiruvahindrapuram, Bhooma, Ada, J., Chan, S., Engchuan, Worrawat, Higginbotham, Edward J., Howe, Jennifer L., Loureiro, Livia O., et al., 2022. Genomic architecture of autism from comprehensive whole-genome sequence annotation. Cell 185 (23), 4409–4427.e18.
Trubetskoy, Vassily, Pardiñas, Antonio F., Qi, Ting, Georgia, Panagiotaropoulou, Swapnil, Awasthi, Tim, B.Bigdeli, Julien, Bryois, et al., 2022. Mapping genomic loci implicates genes and synaptic biology in schizophrenia. Nature 604 (7906), 502–508.
Vorstman, Jacob, Scherer, Stephen W., 2021. What a finding of gene copy number variation can add to the diagnosis of developmental neuropsychiatric disorders. Curr. Opin. Genet. Dev. 68 (June), 18–25.
Zoghbi, Anthony W., Dhindsa, Ryan S., Goldberg, Terry E., Mehralizade, Aydan, Motelow, Joshua E., Wang, Xinchen, Anna, Alkelai, et al., 2021. High-impact rare genetic variants in severe schizophrenia. Proc. Natl. Acad. Sci. U.S.A. 118 (51), e2112560118.