Information and genetic counselling for psychiatric risks in children with rare disorders

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Abstract

Background: The diagnosis of developmental disorders is being transformed by advances in whole genome technologies. However, continuing uncertainties about the individual risks and potential severity of psychiatric impacts attributed to causal genomic variants limits the availability of comprehensive family-oriented information. In addition, there is insufficient evidence about how the parents of children with developmental disorders comprehend the facts and implications of their diagnosis through genetic counselling, nor how they gather developmental and mental health information to guide their understanding.

Methods: Parents of children (aged 0–17 years) referred to paediatric genetics services completed an anonymous online 46-item survey about: (i) the experience of attending services to receive their child's genetic diagnosis, and (ii) the availability, quality and helpfulness of information about psychiatric and neurodevelopmental conditions associated with genomic disorders.

Findings: Two-hundred and eighty-six families (199 UK and 87 USA) completed the survey. One-in-three UK and one-in-five US respondents were dissatisfied with how their child's genetic diagnosis was communicated. Satisfaction was predicted by face-to-face communication (odds ratio 2·91 [95% CI 1·43–5·94]; p=0·003); results being presented by genetics specialists (2·97 [1·41–6·26]; p=0·004); receiving clear explanations (5·14 [2·58–10·26]; p<0·001); receiving support (2·99 [1·21–7·36], p=0·017); and male gender of the tested child (2·56 [1·28–5·14]; p=0·008). Compared to health-related information on developmental delay or intellectual disability, parents were more likely to obtain information about psychiatric manifestations from non-professional lay sources than from clinical specialists (p<0·001). This was particularly evident for families in the UK compared to the USA (p<0·001). Parents considered information from rare disorder support groups to be more helpful than from genetics specialists (odds ratio 11·0 [95% CI 5·08–86·75]; p<0·001), or paediatricians (11·0 [1·42–85·20]; p=0·006), or internet sites (15·5 [3·71–

64·77]; $p<0·001$), which in turn proved more helpful than information provided by geneticists (2·5 [1·44–4·31]; $p=0·001$).

Interpretation: Psychiatric comorbidity is a common feature of rare genomic disorders, but the paucity of suitable information available from clinical specialists suggests families are not optimally informed about these challenges. Wider implementation of genomic testing in general medicine should include adequate training in genetic counselling to ensure best practice in communicating and explaining complex test results supported by comprehensive, family-oriented information.

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Introduction

Intellectual and developmental disabilities affect up to 1 in 25 children in high income countries.[1] Clinical evaluation includes molecular cytogenetic investigations to improve diagnostic accuracy, inform genetic counselling, care management and ongoing family support. Barriers to identifying causal genomic variants in severely disabled children have substantially diminished as technological advances have translated into clinical services. Since their introduction in the mid 2000s, genome-wide tests have substantially increased the diagnosis of intellectual and developmental disorders, largely through detecting genomic micro-deletions and micro-duplications called copy number variants (CNVs). First-line chromosomal microarray genotyping of children with intellectual and developmental disorders identifies pathogenic CNVs in approximately 10-15% of tests.[2] More recent developments in clinical exome and whole genome sequencing have allowed further advances with the diagnosis of previously unexplained cases, bringing opportunities to improve diagnostic precision and offer new insights into disease mechanisms.[3–5] These new developments, however, require major changes in service delivery and clinical practice,

including education and training for health professionals, service commissioning and patient engagement.[6]

CNVs in individuals diagnosed with developmental disorders are associated with increased risks of multiple psychiatric disorders, including autism spectrum disorder (ASD), ADHD, and psychotic and bipolar disorders.[7–9] For example, individuals with 22q11.2 Deletion Syndrome (22q11.2DS, formerly Velocardiofacial syndrome or DiGeorge syndrome) are at high risk of, ASD, ADHD, anxiety, oppositional defiant disorder and schizophrenia.[10–12] Emerging evidence concerning risks of neurodevelopmental, physical and psychiatric morbidity in diagnostic CNVs reported by clinical genetics services indicates a substantial variation in their penetrance and expressivity, which is susceptible to socioenvironmental modification.[13–15] Despite these uncertainties, which currently limit personalisation of risk, treatment, prognosis and information provision, genomic testing is widely recognised as a major advance in health and social care for developmental disorders.[16] Rapid increases in rates of genetic diagnosis and emergent knowledge concerning genotypic risk and phenotypic variability, impose significant challenges and considerations for genetic counsellors with responsibilities towards presenting accurate, comprehendible information while supporting patients and their families.[17–19]

In this study we explored parents' opinions and experiences concerning psychiatric, neurodevelopmental and physical manifestations associated with genomic variants diagnosed in children with developmental disorders. Specifically, we asked parents about (i) their satisfaction with receiving genetic test results through attending specialist paediatric services; and (ii) the availability and practicality of information obtained about clinical manifestations of genomic disorders subsequent to their child's diagnosis.

Methods

Survey respondents and procedures

We designed a 46-item online survey, using Bristol Online Surveys (https://www.onlinesurveys.ac.uk, Bristol, UK), for parents of children aged 0-17 years with developmental, intellectual and congenital disorders having a clinical genetic diagnosis. The survey comprised 4 main sections: (1) family demographics, child genotype, reported clinical diagnoses, family genetic history; (2) awareness of clinical disorders associated with the genetic diagnosis and sources of information used to understand them; (3) ratings of the quantity, content and helpfulness of information from each source; and (4) experiences of clinical services and receiving genetic test results. An introductory section included information about the research team, the purpose of the study, instructions for participating, participant confidentiality and data protection. Participants provided consent by agreeing with the statement, "I have read the information above and on the previous page, understand that my participation is voluntary and I am happy to complete the questionnaire". The study received ethical approval from Cardiff University School of Medicine Ethics Committee on 19 September 2014 (reference SMREC 14/34). Invitations to take part were distributed by advertisements in newsletters, websites and Facebook pages and by word-of-mouth at family support days sponsored by rare disorders support groups, including Unique – Understanding Rare Chromosome and Gene Disorders, Max Appeal and Microdeletion 16p11.2 Support and Information UK.

Statistical analysis

Response data was coded and downloaded from the survey website into the SPSS package (SPSS 23.0, IBM Inc., Chicago, ILL) for statistical analysis. To test association between categorical variables in survey questions covering information sources and experiences of attending genetic testing services, 2 x 2 contingency tables were used and Pearson Chi-square tests. McNemar's test was used to assess the significance of differences between correlated proportions in subjects assessed for pairs of binary

variables, specifically to compare responses to questions about lay or professional sources of clinical information and questions about information utility. Odds ratios and 95% confidence intervals were calculated with VassarStats at vassarstats.net/propcorr.html. Wilcoxon's signed-rank test was used to assess ordinal data for significance of differences between distributions of responses for non-independent samples. This was applied to Likert scale responses to questions concerning the amount and the content of information from multiple sources. Effect sizes (r) were derived from Z scores. Binary logistic regression was employed to test for association between demographic, genetic counselling and communication factors and satisfaction with genetics services. Specifically, the binary outcome variable was defined by parents expressing satisfaction (or dissatisfaction) with how their child's genetic test result was communicated. The initial regression model incorporated family and child specific covariate using method 'Enter'. Sequential hierarchical models incorporated genetic counselling specific and communication modality specific covariates. Where appropriate, ordinal variables with low responses for some categories were collapsed. Odds ratios correspond to the exponentiated unstandardized coefficients (beta weights) for each variable.

Role of the funding source

The funder had no role in the study design, data collection, analysis and interpretation of findings and made no contribution to writing the report. All authors had full access to all the data collected in the survey. The corresponding author had final responsibility for the decision to submit for publication.

Results

Child and family characteristics

Two-hundred and 86 survey responses were recorded between 12 December 2014 and 31 May 2016. Of these 199 (61·6%) were located in the UK, 87 (26·9%) in the USA. Table 1 shows details of the respondents and children they reported on. The most frequent reasons for referral to paediatric genetics services were developmental delay (29·7%), congenital malformations (8·0%) and dysmorphic features (7·3%). There was extensive co-morbidity among children in the study, the mean number of diagnoses per child was 5·7. This included early developmental disorders (mean 2·4 per child); congenital malformations (mean 2·2 per child) and neuropsychiatric disorders including ASD, ADHD and OCD (mean 0·8 per child). The most common genetic diagnoses were unique CNVs (44·4%) not reported by other respondents. Slightly fewer reported recurrently occurring CNVs (40·6%), the most common being the 22q11·2 micro-deletion (9·6%). A quarter of respondents (25·2%) reported other family members had CNVs, including 39 (13·6%) parent carriers (table 1).

Experiences of genetics services

For the majority of participants, genetic test results were communicated either by the child's paediatrician (130/286, 45·5%), geneticist (116/286, 40·6%) or genetic counsellor (28/286, 9·8%). Compared to parents in the US, parents in the UK were more likely to have test results communicated by paediatricians than genetics specialists, (107/199 vs 23/87; p <0·001) (figure 1). Eighty of the 274 respondents (29·2%) who received test results from paediatricians and genetic specialists were not satisfied with how they were communicated. Dissatisfaction was significantly more likely among parents who received results from paediatricians (52/130, 40·0%) than geneticists (28/144, 19·4%; p<0·001). When we compared communication of results between countries, parents in UK were more likely to be dissatisfied compared to the US (66/199, 33·2% vs 19/87, 21·8%; p=0·054). In addition, 101/286 (35·3%) parents said they were not satisfied with their practitioner's explanation of the result. Dissatisfaction was more prevalent among UK families than the

US (78/199, 39·2% vs 23/87, 26·4%; p=0·038) (figure 1). More than 70% of parents (208/286) reported not being offered support by their practitioner at the time of receiving test results and nearly 50% (142/286) were not offered follow-up appointments, of whom two-thirds (94/142) would have attended if made available.

To understand which factors predicted satisfaction with receiving genetic test results we did multi-level regression of 3 categories of variables, (i) child and family specific, (ii) genetic counselling, and (iii) modes of communication (table 2). Satisfaction was predicted by variables in all 3 categories, the most significant being satisfaction with the explanation of results (final model OR = 5·14, 95% CI 2·58–10·26). Receiving results from specialists in genetics as opposed to paediatrics was more likely to elicit satisfaction (OR = 2·97, CI 1·41–6·26). Communication in person as opposed to letters or telephone calls was also favoured (OR = 2·91, CI 1·41–6·26). Initially, satisfaction was more predictable among US families, but this lost significance when genetic counselling-specific variables were added to the model. Interestingly, parents with male children diagnosed were more likely to be satisfied than those with females (OR = 2·56, CI 1·28–5·14), with odds increasing as additional variables were added to the model (table 2). The final model accounted for 40·5% of the variance in the outcome variable.

Sources of information about genomic disorders

We asked parents where they first obtained information about clinical manifestations which they considered were associated with their child's genetic diagnosis. Initially we asked which of a series of manifestations they associated with their child's diagnosis. Table 3 shows the frequency of association for each manifestation. We combined responses for information sources across each of four groups of clinical manifestations: developmental, congenital, neuropsychiatric, and mood and psychotic disorders (table 4). Respondents were more likely to find out about neuropsychiatric, mood and psychotic disorders from information they initially obtained from non-professional (lay) sources, compared to developmental and congenital disorders, which they were more likely to hear about from their child's clinician. Nearly two-thirds (65·3%) of combined responses for all psychiatric

disorders indicated information was obtained from lay sources (mainly internet sites and rare disorder support organisations), compared to 34·7% from clinical specialists. When we combined responses across all developmental and congenital disorders that were surveyed, 59% indicated information first came from clinical specialists, compared to 41% from lay sources. The difference between reported sources for combined psychiatric manifestations and combined developmental-congenital manifestations was considerable (Pearson Chi-Square = 11·56, $p<0·001$). Parents' propensity for using lay sources of information for anxiety, depression and psychotic disorders (71·4% combined) was more pronounced than for ASD, ADHD, OCD and DCD (62·1% combined) (table 4).

We then compared the responses for UK and US parents, illustrated in figure 2. Combined responses for all clinical disorders revealed that parents in UK were more likely than in the US to receive information from sources other than clinical specialists, primarily through internet searches and from rare disorder support organisations (UK 57·6% vs US 38·3%; $p=0·005$). The difference between UK and US parents concerning developmental and congenital disorders was smaller, but significantly fewer families on the UK received information on these conditions from their child's clinician (UK 54·3% vs 68·5%; $p=0·042$). The largest difference between countries concerned information about psychiatric disorders. For combined responses, 73·4% of UK parents reported information was first obtained from lay sources, compared to 47·9% of responses from US families ($p<0·001$). For anxiety, depressive and psychotic disorders, less than one fifth of UK parents received information from health professionals in the first instance, compared to approximately half in the US ($p<0·001$).

We evaluated the extent to which knowledge of individual psychiatric manifestations was more or less likely to originate from non-professional than professional sources, referenced against (i) intellectual disability (ID), (ii) cardiac anomalies, and (iii) autism spectrum disorder (ASD) as common indications for paediatric referral (figure 3). In comparison to ID, parents were significantly more likely to gain information about any psychiatric disorder queried from non-health professional sources, with odds ratios ranging from 2·7 (95% CI 1·5–4·8) for ASD to 18·0 (CI 2·4–134·8) for depression. Information about developmental delay was

significantly more likely to originate from health specialists (OR 13·0, CI 5·2–32·3). Comparisons with cardiac anomalies showed a similar pattern to ID, information concerning any psychiatric disorder being significantly more likely to be found through non-professional sources (OR range 3·6–31·0). In comparison to ASD, information about anxiety (OR 16·0, CI 2·1–120·6), depression (OR 7·0, CI 1·6–30·8) and OCD (OR 6·0, CI, 1·8–20·4) was more likely to originate from lay sources, whereas information concerning most physical and developmental disorders was more likely to originate from clinical specialists (figure 3).

Respondents were also asked to evaluate the quantity and content of information from each source they encountered (table 5). Parents rated the quantity of information available from support groups as optimal more often compared to that provided by paediatricians (r 0·48, $p<0·001$) and geneticists (r 0·47, $p<0·001$), or found on internet sites (r 0·39, $p<0·001$). Similarly, internet information was rated optimal more often compared to paediatricians (r 0·20, $p=0·006$) and geneticists (r 0·25, $p<0·001$). In terms of quality, parents reported the content of information from support groups was greater more often compared to internet sites (r 0·40, $p<0·001$), paediatricians (r 0·29, $p=0·002$) and geneticists (r 0·40, $p<0·001$), where content was more likely to be difficult to understand, too scientific, or not relevant (table 5). Comparisons between countries revealed that significantly more UK than US respondents rated the quality of information from support groups as clear and understandable ($p=0·015$). No other between country differences were observed.

Finally, respondents rated the utility of information (helpful or not helpful) from each information source (figure 4). Materials from support groups was more likely to be rated as helpful compared to internet content (OR 15·5 [95% CI 3·71–64·77]; $p<0·001$), paediatricians (OR 11·0 [1·42–85·2]; $p=0·006$) and geneticists (OR 21·0 [5·08–86·75]; $p<0·001$). Overall, respondents were more likely to say information from non-professional sources was helpful compared to information provided by clinical specialists (OR 2·2 [1·37–3·53]; $p=0·001$).

Discussion

This is the first quantitative survey of its kind to investigate how parents experience the communication of genomic tests for rare developmental disorders and their subsequent endeavours to gain knowledge about the psychiatric risk implications associated with their child's genetic diagnosis. This is an important topic; our survey indicates that parents had mixed experiences of attending genetics services; a large proportion in the UK reported dissatisfaction with genetic counselling for communication of results and the accompanying information which was less helpful than from other sources. In particular, parents rely extensively on non-professional sources for information about psychiatric risks. They often receive sub-optimal information from clinical specialists who deliver genomic tests who tend to focus on early developmental and physical disabilities typically present at diagnosis. Families in the UK were more reliant on internet and Third Sector groups for clinically relevant information than in the USA, particularly information concerning psychiatric problems their children may be susceptible to.

The findings extend previous evidence showing that families often have difficulties obtaining satisfactory information from clinical specialists to aid comprehension of genomic tests results.[20–22] We have revealed new evidence concerning a broad range of genomic disorders consistent with earlier findings concerning 22q11.2 deletion syndrome - one of the most frequently diagnosed genomic disorders - in which parents predominantly obtained psychiatric information from internet sites and support groups.[23,24] Consistent with rare disorders studies more generally, we have shown that the great majority of parents search the internet to help comprehend their child's diagnosis.[25] However, many families do not seek medical information online, particularly in more deprived socioeconomic groups.[26] Inadequate access to information is associated with increased stress and uncertainty for parents and negatively influences their engagement with services, potentially denying them the advantages of a precise diagnosis.[27] Our survey did not gather sufficient demographic data to determine whether

hard-pressed families were less likely to seek online content. However, we are concerned that socially disadvantaged families may not have the same degree of access to high quality information, support and access to services to which they are equally entitled.[28]

That paediatric and genetic specialists tended to focus on providing information about developmental and physical disabilities, suggests that suitable information about psychiatric risks may be relatively scanty, or that addressing emotional and behavioural challenges is a lower priority when providing diagnostic genetic counselling. Alternatively, genetic counsellors may lack the requisite knowledge and skills to address psychiatric concerns. In turn, this may hinder information provision or referral to support agencies. Concerns expressed about overloading parents with information in the aftermath of a genetic diagnosis need to be balanced against the best interests of children and their parents' trust in health services.[29,30] Consistent with earlier studies of rare chromosomal disorders, our findings also reveal that parents consider information from clinical specialists has lower practical value than online or support group resources and is often too complicated or irrelevant.[31]

Our findings reveal patterns of information gathering that distinguish between UK and US families. In the USA, parents received a broader range of medical and mental health information from their clinician after diagnosis, whereas UK parents were less likely to receive psychiatric risk information from clinical specialists. More than half of families in the UK had their child's diagnosis communicated by paediatricians, compared to one-in-five in the US. However, this did not correlate with variation in information provision by health professionals. Potentially, paediatric specialists may be less familiar with available information concerning psychiatric risks, particularly for manifestations which generally develop towards adulthood, prioritising immediate health and developmental concerns instead. Our survey failed to identify any clear insights as to why psychiatric information is seldom offered by paediatric and genetics specialists in the UK, or why practitioners in the US appear to offer a more comprehensive range of information. Conceivably, service-driven factors such as limited clinic time, or differences in professional development and training may account for the differences revealed in our survey. A clearer understanding

of current limitations to providing comprehensive psychiatric genetic counselling when diagnosing developmental disorders would be welcomed and may reveal opportunities for resolving existing gaps in knowledge for concerned patients and families.

Opinions vary on the benefits and risks of online health information, ranging from concerns among health professionals over accuracy and regulation, to sociologists' endorsements, praising its contribution to client empowerment. Between these views exists evidence that the general public adopt contingent behaviours towards online content, discriminating between trustworthy and untrustworthy content pages to supplement rather than replace traditional media.[32] Importantly, near universal online search methods are increasingly concordant with the structure of internet health information and the hierarchical nature of results created by popular search engines. Therefore, we urge the development of new initiatives to explore how clinicians may improve access to information around the time of diagnosis, including signposting to high quality content beyond traditional media and assist Third Sector groups to innovate and procure new ways of supporting children with complex neurological disabilities.

The findings presented here are timely; paediatric genetics services strike a fine balance between delivering high quality services for escalating referrals and performing increasingly sophisticated tests with lengthy consent procedures. That a large proportion of families in our survey expressed dissatisfaction receiving genetic diagnoses, particularly in the UK, highlights the challenge facing long-established services. As the availability of genomic testing in mainstream clinical services increases, demands for relevant patient-oriented information concerning genetic influences on psychiatric risks are predicted to increase.[33,34] However, informing patients and families about complex and uncertain implications of genetic tests is challenging, requiring highly specialised skills in communication and psychosocial support. Personalizing psychiatric risk across the lifespan of affected children such that service users understand the true nature of their risks, is likely to become a priority for psychiatrists and allied professionals working in the realm of rare disorders.[35,36] We recommend that additional education and training and in brain disorders is prioritised for all clinical specialties offering genetic tests. Curriculum

content for skills training should be developed accordingly, ensuring genetic counselling includes meaningful conversations about the full spectrum of medical and mental health risks and is accompanied by contemporary, relevant information.

Our study has limitations. Recruitment was biased in favour of parents who engage with support groups who promoted the survey, potentially limiting the generalizability of our findings. The survey was designed with broad accessibility in mind. However, online surveys require significant internet literacy and time for participation, which may be difficult for some families. Parents who readily access the internet are, conceivably, more likely to use it for seeking information related to that which the current survey investigated. The survey was overwhelmingly completed by mothers. However, families with severely disabled children are rare and unrepresentative of the general population. This may be a reflection of the socio-domestic influences on caregiving in the context of disability.[37] Also, we were unable to independently verify health information provided by parents. Self-report surveys have recognised shortcomings which may have been exacerbated by respondents recalling facts and experiences potentially several years after the event. Despite these limitations, the views and experiences expressed by a large number of families provides a timely insight into the current state of medical health information, clinical services and lay support for the developmental disorders community.

In summary, our findings reveal that parents are inadequately informed by their clinical specialists about potential neurodevelopmental and psychiatric challenges in the context of paediatric genetic testing. Parents search extensively for information about their child's genetic diagnosis, retrieving neuropsychiatric information primarily from internet sites and lay support groups, where its accuracy and validity is unregulated and potentially less reliable. We believe the current results are important in informing service development and training in both clinical genetics and psychiatry. In particular, they point to the need for closer integration of medical genetics and psychiatry to address the needs of those receiving a genetic diagnosis. Future initiatives should focus on identifying measures to promote the inclusion of psychiatric risk information and support in genetic counselling

clinics and to ensure education and training for practitioners encompasses the full spectrum of neuropsychiatric challenges for children with rare genomic disorders.

Contributors

ACh, MvdB, JH and conceived of the research question and designed the study. ACh developed the study ethics application. ACu and ACh and oversaw participant recruitment and data acquisition. ACu oversaw and conducted the data analysis. ACu, JH and MvdB interpreted and discussed the data. ACu drafted the report. All authors provided critical revisions to the report, important intellectual content and final approval.

Declaration of interests

We declare no competing interests.

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Table 1. Characteristics of the study sample and children diagnosed with genetic disorders.

Respondents			Children with genomic disorder				
Location	**N**	**%**	**Gender**	**N (UK)**	**%**	**N (US)**	**%**
UK	199	69·6	Female	81	40·7	44	50·6
USA	87	30·4	Male	118	59·3	43	49·4
Gender	**N**	**%**	**Age of child (years)**	**Mean**		**Median**	**Range**
Female	270	94·4	At time of survey	8·5		7	0-42
Male	16	5·6	Age at genetic diagnosis	3·7		3	0-17
Relationship	**N**	**%**	**Reason for referral**	**N**		**%**	
Biological Parent	267	93·3	Developmental delay	85		29·7	
Adoptive Parent	10	3·5	Congenital anomaly	23		8·0	
Guardian	2	0·7	Dysmorphic features	21		7·3	
Other	7	2·4	Growth or stature	16		5·6	
			Neurological	16		5·6	
Occupation	**N**	**%**	Multiple concerns	13		4·5	
Paid employment	141	49·3	Speech and language delay	13		4·5	
Full time carer	78	27·3	Cardiac defect	12		4·2	
Home maker	58	20·3	Learning disability	11		3·8	
Other	9	3·1	Family history	10		3·5	
			Neurodevelopmental disorder	10		3·5	
			Neonatal indication	9		3·1	
			Foetal anomaly	7		2·4	
			Metabolic disorder	2		0·7	
			Unspecified	38		13·3	
			Clinical disorder diagnoses§	N		per child	
			Developmental α	695		2·4	
			Congenital β	638		2·2	
			Neuropsychiatric χ	230		0·8	
			Mood and Psychotic δ	80		0·3	
			Total	1643		5·7	
			Genetic diagnosis	N		%	
			Unique CNV	127		44·4	
			Recurrent CNV †	116		40·6	
			Multiple CNVs	16		5·6	
			Single gene disorder	17		5·9	
			Named syndrome	5		1·7	
			Uncertain or unspecified	5		1·7	
			Family genetic history	N		%	
			Parent CNV carrier	39		13·6	
			Sibling(s) CNV carrier	20		7·0	
			Other relatives	13		4·5	

§ Parent-reported developmental, physical and psychiatric diagnoses:
α Developmental Delay, Learning Disability, Speech and Language Delay,
β Palatal, Cardiac, Respiratory, Musculoskeletal, Growth, Seizures/epilepsy, Sight, Hearing, Skin
χ Attention deficit hyperactivity disorder, ADHD (N= 47), autism spectrum disorder, ASD (N= 86), obsessional compulsive disorder, OCD (N = 48), developmental coordination disorder, DCD (N = 49), dyslexia (N = 19)
δ Anxiety, Depression, Schizophrenia or Psychosis
† Recurrent neurodevelopmental susceptibility CNVs: 1q21.1 deletion, 1q21.1 duplication, 2p16.3 deletion (NRXN1), 9q34.3 deletion, 15q11.2 deletion, 15q11.2 duplication, 15q11.2 (NOS), 15q13.3 deletion, 15q13.3 duplication, 15q13.3 (NOS), 16p11.2 deletion, 16p11.2 duplication, 16p11.2 (NOS), 16p12.2 deletion, 16p13.11 deletion, 16p13.11 duplication, 16p13.11 (NOS), 17q12 deletion, 22q11.2 deletion, 22q11.2 distal deletion, 22q11.2 duplication.

Table 2. Multilevel logistic regression of variables predicting satisfaction with receiving genetic test results.

	Model 1†		Model 2‡		Model 3§	
Variables	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Level 1 (child and family)						
Family Location (vs UK)	**2·30 (1·17 – 4·53)**	**0·016**	1·62 (0·77 – 3·38)	0·201	1·27 (0·57 – 2·87	0·564
Child's gender (vs female)	**2·18 (1·21 – 3·93)**	**0·009**	**2·54 (1·31 – 4·91)**	**0·006**	**2·56 (1·28 – 5·14)**	**0·008**
Age at genetic diagnosis (years)	0·93 (0·83 – 1·03)	0·159	0·91 (0·80 – 1·02)	0·114	0·90 (0·79 – 1·02)	0·094
Respondent's gender (vs female)	0·0	0·998	0·0	0·998	0·0	0·998
Home maker/carer (vs paid employment)	0·60 (0·33 – 1·07)	0·083	0·68 (0·36 – 1·31)	0·251	0·57 (0·29 – 1·13)	0·107
Level 2 (genetic counselling)						
Satisfied with explanation (vs not satisfied)			**5·47 (2·82 – 10·58)**	**<0·001**	**5·14 (2·58 – 10·26)**	**<0·001**
Offered additional information (vs not offered)			1·22 (0·62 – 2·43)	0·563	1·05 (0·51 – 2·16)	0·896
Offered support (vs not offered)			**2·83 (1·22 – 6·56)**	**0·015**	**2·99 (1·21 – 7·36)**	**0·017**
Offered follow-up at diagnosis (vs not offered)			1·05 (0·55 – 2·01)	0·889	1·15 (0·59 – 2·27)	0·68
Level 3 (mode of communication)						
Communicated by geneticist (vs paediatrician)					**2·97 (1·41 – 6·26)**	**0·004**
Communicated in person (vs letter/telephone)					**2·91 (1·43 – 5·94)**	**0·003**
Model Summary						
Nagelkerke R-square	0·145		0·335		0·405	

† Binomial regression with family specific variables only; ‡ Hierarchical model with added genetic counselling specific variables; § Hierarchical model with added communication modality variables.

Table 3. Parent reported associations between their child's genetic diagnosis and clinical manifestations.

Clinical manifestations	Frequency (%)	
Referral criteria manifestations		
Developmental delay (DD)	274	(95·8)
Intellectual disability (ID)	267	(93·4)
Speech and language delay (SLD)	257	(89·9)
Seizures or epilepsy	166	(58·0)
Cardiac defects	153	(53·5)
Palatal defects	97	(33·9)
Co-occurring manifestations		
Autism spectrum disorder (ASD)	203	(71·0)
Obsessive compulsive disorder (OCD)	140	(49·0)
Attention deficit hyperactivity disorder (ADHD)	130	(45·5)
Developmental coordination disorder (DCD)	115	(40·2)
Anxiety disorder	154	(53·8)
Depressive disorder	85	(29·7)
Psychotic disorder (schizophrenia or psychosis)	73	(25·5)

Table 4. Frequency of sources used by respondents to obtain information on developmental, congenital, neuropsychiatric, mood and psychotic manifestations after receiving their child's genetic diagnosis.

	Developmental and physical manifestations						Psychiatric manifestations					
Information source	**Developmental**		**Physical**		**Combined**		**Neuropsychiatric**		**Mood + psychotic**		**Combined**	
	N	%*	N	%*	N	%*	N	%*	N	%*	N	%*
Clinical specialist												
With diagnosis	318	39·8	149	35·2	467	38·2	121	20·6	45	14·2	166	18·3
At follow-up	70	8·8	38	9·0	108	8·8	38	6·5	12	3·8	50	5·5
Other	96	12·0	49	11·6	145	11·9	64	10·9	34	10·7	98	10·8
Total	484	60·7	236	55·8	720	59·0	223	37·9	91	28·6	314	34·7
Non-professional												
Internet sites	167	20·9	103	24·3	270	22·1	163	27·7	106	33·3	269	29·7
Support groups	74	9·3	40	9·5	114	9·3	100	17·0	66	20·8	166	18·3
Other sources	73	9·1	44	10·4	117	9·6	102	17·3	55	17·3	157	17·3
Total	314	39·3	187	44·2	501	41·0	365	62·1	227	71·4	592	65·3
Total (all)	798		423		1221		588		318		906	

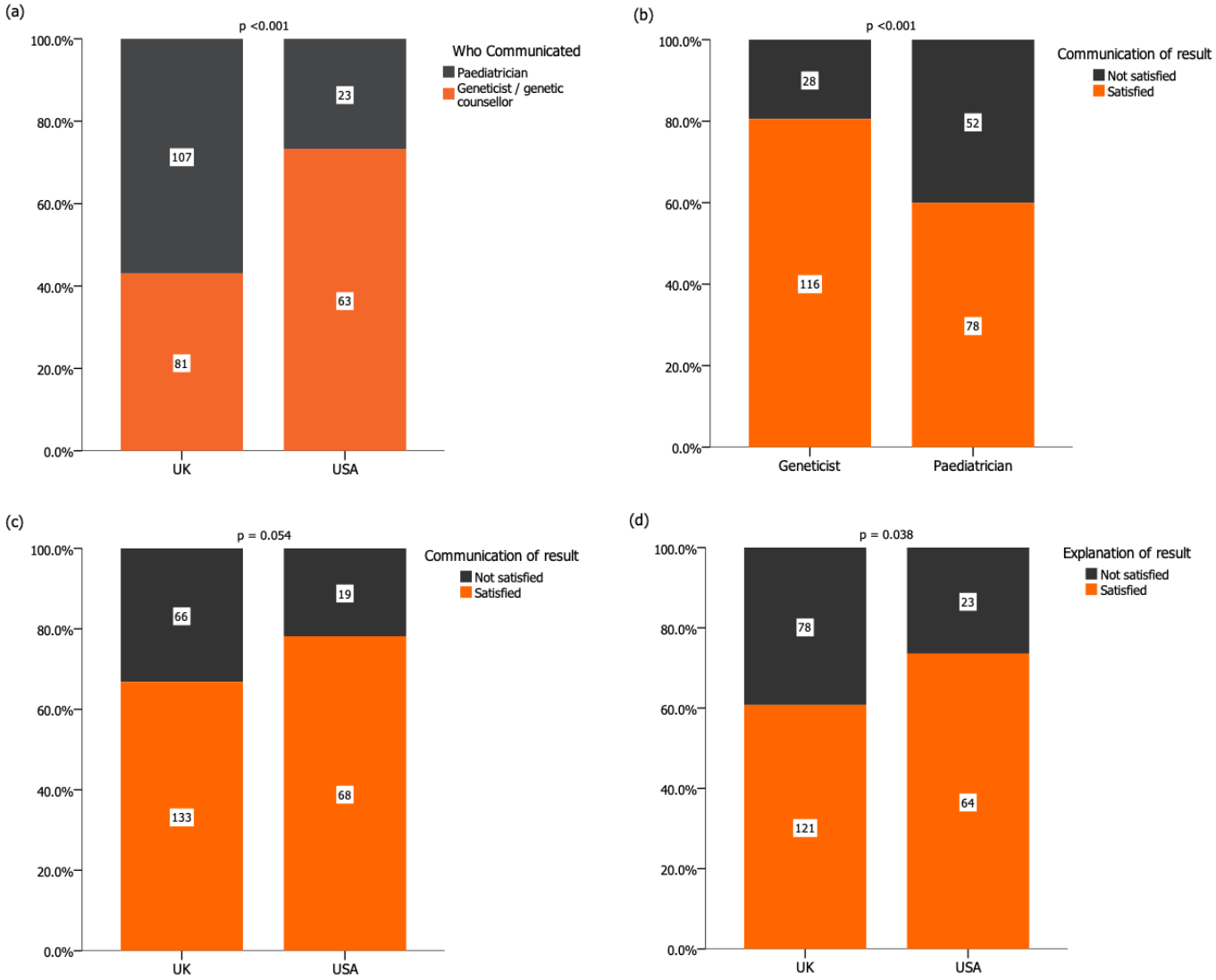
Disorder groups: Developmental = global developmental delay, intellectual disability, speech and language delay; Physical = cardiac defects, palatal defects; seizures/epilepsy; Neuropsychiatric = autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), developmental co-ordination disorder (DCD); Mood and psychotic = anxiety, depression, schizophrenia or other psychosis.
* percentages are for combined responses for each clinical disorder queried.

Table 5. Comparisons of information obtained from clinical professionals and non-professional sources following diagnosis of a genomic disorder.

Comparison groups	Observations	Effect size (r)	*P* value
(a) Amount of information			
Geneticists <> Paediatricians	142	0·05	0·513
Internet sites > Paediatricians	182	0·20	0·006
Support groups ≫ Paediatricians	120	0·48	< 0·001
Internet sites > Geneticists	360	0·25	< 0·001
Support groups ≫ Geneticists	252	0·47	< 0·001
Support groups ≫ Internet sites	330	0·39	< 0·001
(b) Content of information			
Geneticists <> Paediatricians	142	0·11	0·18
Paediatricians <> Internet sites	182	0·10	0·157
Support groups > Paediatricians	120	0·29	0·002
Internet sites <> Geneticists	360	0·07	0·159
Support groups ≫ Geneticists	252	0·40	< 0·001
Support groups ≫ Internet sites	330	0·40	< 0·001

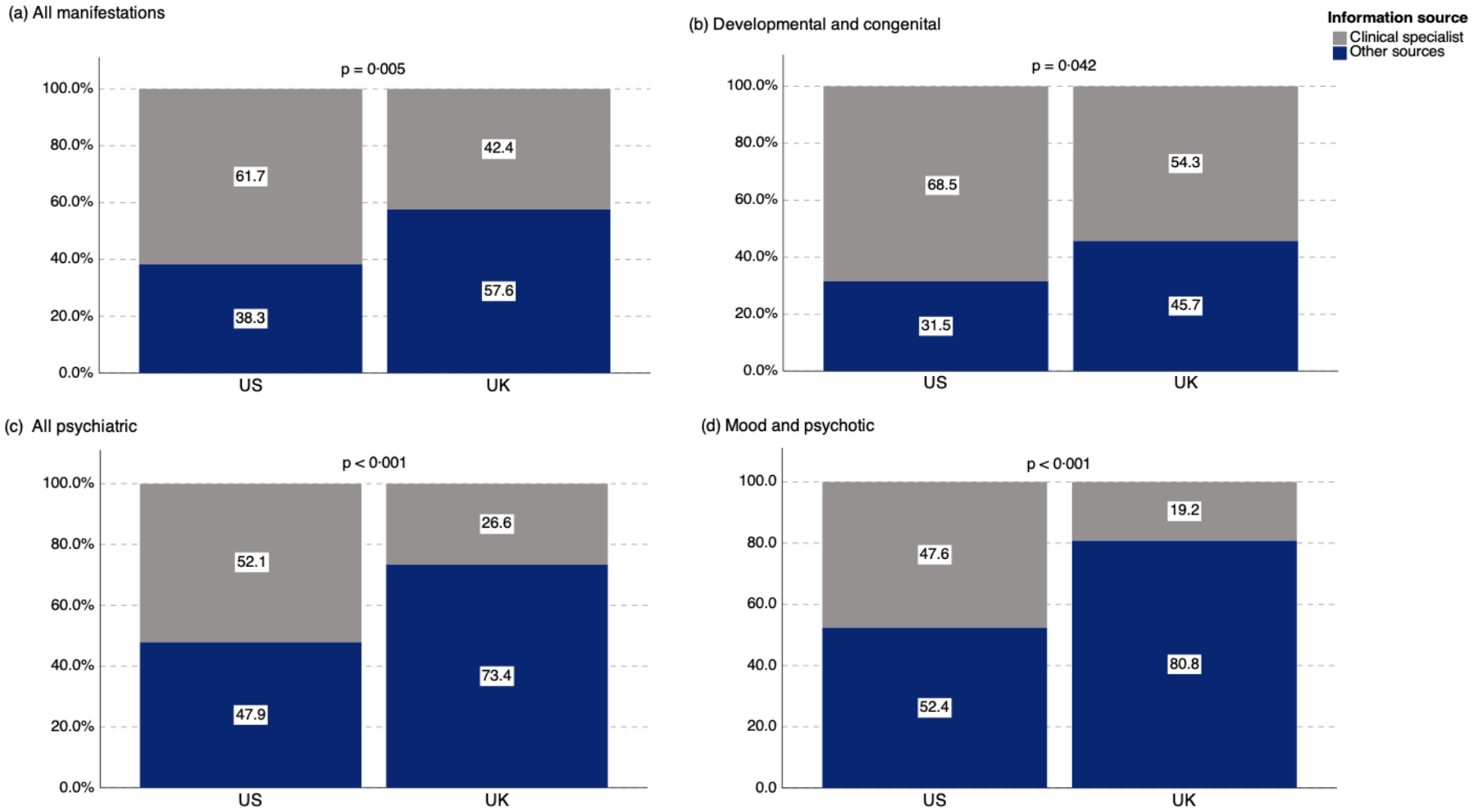
(a) Amount of information: optimal *vs* too much or not enough; (b) Content of information: easily understood *vs* complicated or irrelevant. P-values and effect sizes were derived from Wilcoxon signed-rank analyses.

Figure 1. Characteristics of communicating of genetic test results.



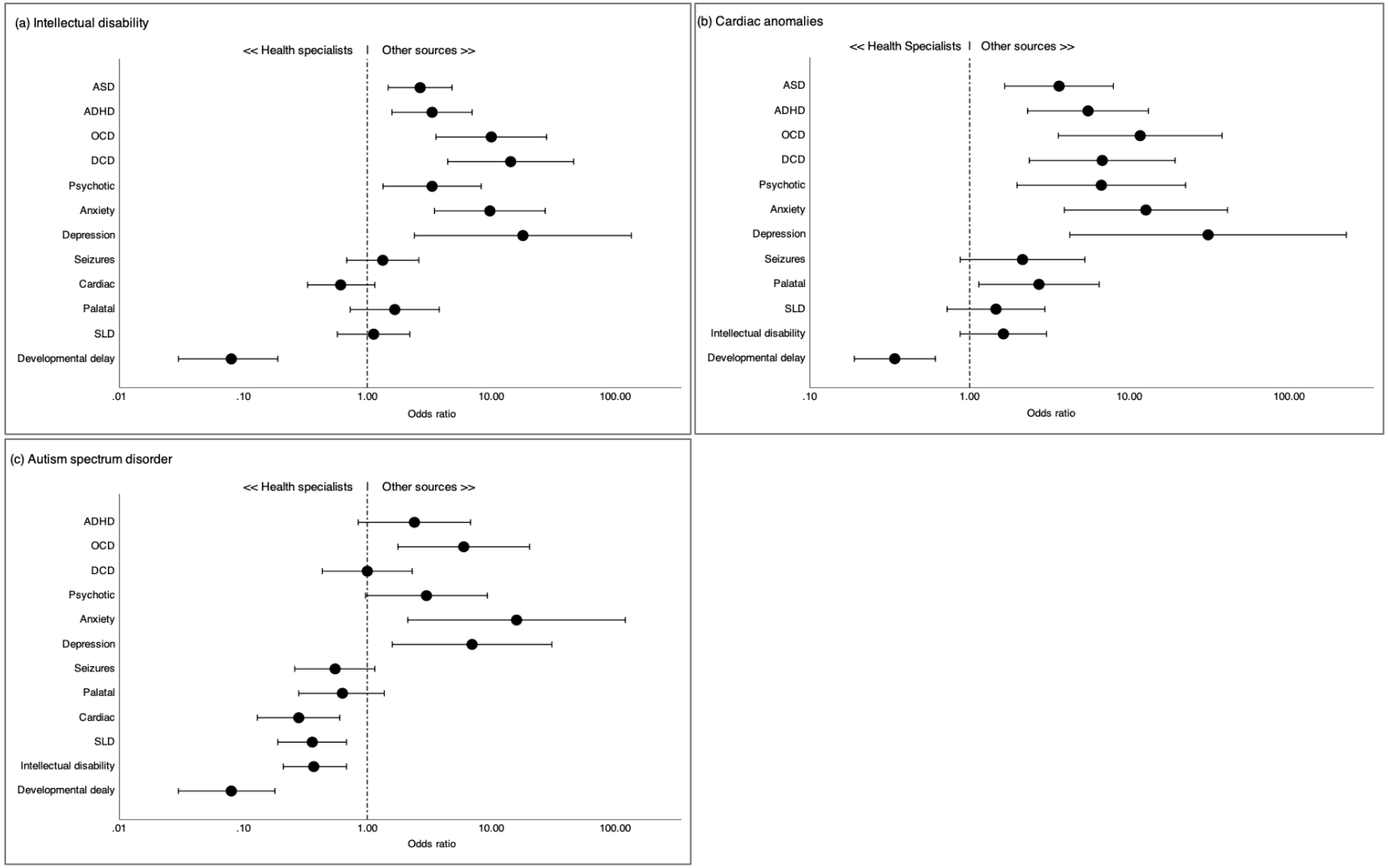
(a) Distribution of clinicians delivering results to families in the UK (199) and USA (87); (b) Comparison of parents' satisfaction with the communication of genetic test results; (c) Comparison of satisfaction with communication of results by country of residence; (d) Comparison of satisfaction with explanation of results by country of residence.

Figure 2. Comparisons of sources reported by UK and US respondents to obtain information about clinical manifestations of genomic disorders, grouped by developmental, congenital, neuropsychiatric, mood and psychotic disorders.



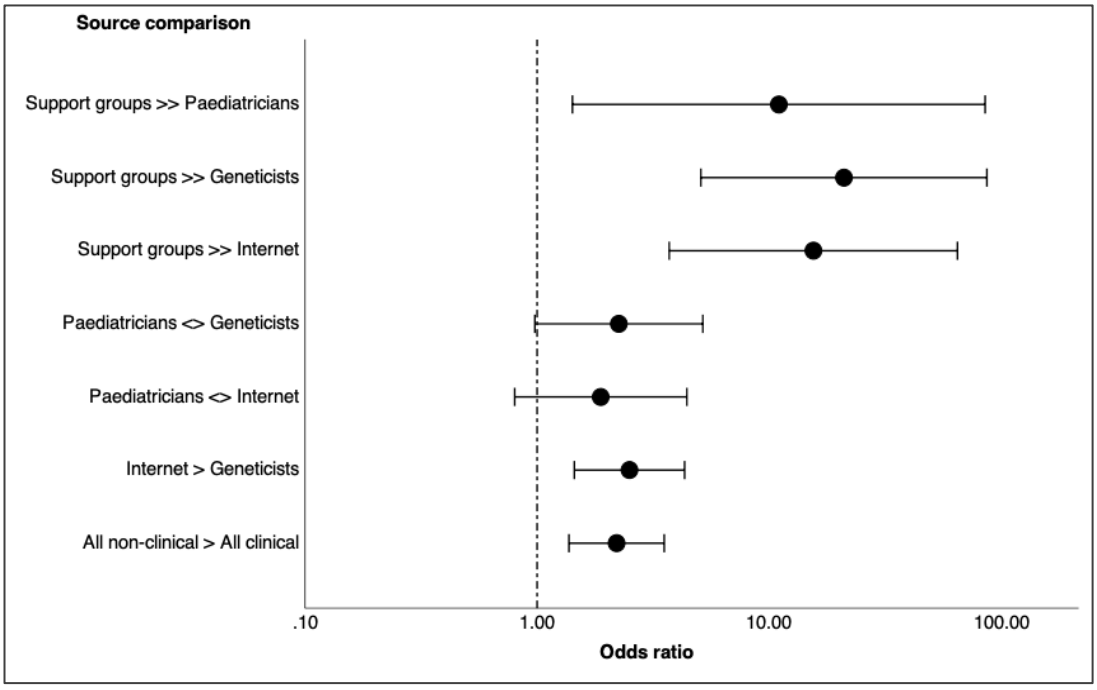
Information sources: (i) clinical specialist (at time of diagnosis, at follow-up, other health professional); (ii) other sources (internet sites, support groups including Facebook, friends and family, books and leaflets). Grouped manifestations: (i) developmental disorders = developmental delay, intellectual disability, speech and language delay; (ii) congenital disorders = cardiac anomalies, palatal anomalies, seizures/epilepsy; (iii) neurodevelopmental disorders = autism spectrum, attention deficit hyperactivity, obsessive compulsive, developmental coordination; (iv) mood and psychotic disorders = anxiety, depression, schizophrenia/other psychosis.

Figure 3. Variation in information sources for individual manifestations.



Dot plots depict odds ratios for pairwise comparisons between sources first used for information about recurrent CNV-associated manifestations compared with sources representative of three major classes of disorder: (a) developmental disorders (intellectual disability); (b) congenital disorders (cardiac anomalies); (c) neuropsychiatric disorders (autism spectrum disorder). Sources: (i) health specialists = clinician at time of genetic diagnosis; clinician at follow-up appointment; other health professional, (ii) other sources = internet sites; voluntary support groups (including Facebook groups); friends and family; books and leaflets). Bars represent 95% confidence intervals.

Figure 4. Variation in parent reported helpfulness of information from clinical specialists, rare disorder support groups and internet sites.



Dot plots depict odds ratios for pairwise comparison of information utility (helpful versus not helpful. Bars represent 95% confidence intervals. Y axis symbols reflect scale of difference between paired sources: ≫, much greater than; >, greater than, <>, not significant.