

## ORIGINAL ARTICLE

# Predictors of empowerment in parents of children with autism and related neurodevelopmental disorders who are undergoing genetic testing

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## Abstract

**Background:** There is limited empirical data quantifying the utility of genetic testing for families of children with autism spectrum disorder (ASD) or related neurodevelopmental disorders (NDD). We assessed the utility of clinical chromosomal microarray analysis (CMA), defined by diagnostic yield and parental empowerment, in population-based sample of parents of affected children; and explored child, family, and health services factors predictive of empowerment.

**Methods:** Participants were families of children undergoing diagnostic assessments, between 2016 and 2019. Diagnostic yield of CMA in affected children was determined. Parental empowerment was measured through adapted version of the Genetics Counseling Outcome Scale-24. Parents completed questionnaires to capture child, family, and health service factors.

**Results:** The diagnostic yield of CMA was 2.8% for pathogenic variants. Parental empowerment was significantly correlated with family functioning and aspects of perceived family-centeredness of care. The model accounted for 49.8% of the variation in parental empowerment,  $F(10,37) = 3.67, p = 0.002$ . After accounting for other predictors, parental perception of the provision of general information remained significantly associated with empowerment.

**Conclusion:** The informational needs of families play an important role in their empowerment during genetic testing. Meeting these needs and monitoring empowerment can aid genomic technologies integration in personalized healthcare for ASD/NDD.

## KEYWORDS

autism spectrum disorder, empowerment, genetic testing, neurodevelopmental disorders

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## 1 | INTRODUCTION

Clinical recommendations advocate for the use of genetic tests, namely chromosomal microarray analysis (CMA), and more recently exome sequencing (ES), in the clinical care of individuals with neurodevelopmental disorders (NDDs), like autism spectrum disorder (ASD), global developmental delay (GDD), and intellectual disability (ID) (Miller et al., 2010; Srivastava et al., 2019). Despite widespread use, there is still limited understanding of the impact of clinical genetic testing on families who have a child with an NDD. This impact has traditionally been evaluated based on *clinical utility*, defined as the extent to which tests are thought to be safe, effective, and/or improve health outcomes (Kohler et al., 2017).

However, such a narrow definition of utility has been insufficient to understand the full impact of genetic testing on families. Clinical utility has often been understood through the diagnostic yield of the test, that is, proportion of individuals who obtain a molecular genetic diagnosis as a result of testing. However, population estimates of the diagnostic yield of clinical genetic testing in NDDs are not available, because published reports are based on samples of children from single subspecialty clinics, resulting in wide variation of reported diagnostic yield (McGrew et al., 2012; Miller et al., 2010; Tammimies et al., 2015). Thus, diagnostic yield cannot be the sole measure of impact of genetic testing on families.

Other measures of clinical utility are defined based on changes in clinical management as a result of genetic testing (Malinowski et al., 2020). However, studies are showing that individuals and families undergoing genetic testing also experience a different outcome than typically measured in clinical services, namely personal utility (Bossuyt et al., 2012; Kohler et al., 2017). *Personal utility* encompasses a broad range of non-health related outcomes of genetic testing, including psychological outcomes (e.g., feelings of control), increased knowledge about oneself or one's family, and future planning (Bunnik et al., 2011; Kohler et al., 2017). Relative to the broader field of medical genetics and genetic counseling, there are few empirical studies on the personal utility of genetic testing for families affected by ASD/NDD (Kohler et al., 2017; Malinowski et al., 2020). Most of the available information comes from qualitative studies, which are small and have limited generalizability (Giarelli & Reiff, 2015; Hayeems et al., 2016; Kiedrowski et al., 2016; Mollison et al., 2020; Reiff et al., 2015). On the whole, the literature suggests that both positive and negative implications of genetic testing are possible for families.

One potential positive impact of clinical genetic testing is to provide an explanation for the child's challenges and offer direction to care (Hayeems et al., 2016). Establishing

an etiology may end the "diagnostic odyssey" (Chen et al., 2013; Kiedrowski et al., 2016). Some parents reported a sense of comfort in knowing the biologic cause of their child's condition and that knowledge may help clarify the child's profile (Giarelli & Reiff, 2015). In fact, many parents who did not report a direct medical benefit of the genetic result still expressed a benefit from feeling informed (Mollison et al., 2020; Reiff et al., 2015).

In contrast, parents have expressed a sense of ambivalence about genetic testing and had concerns about the potential for psychological distress, insurance discrimination, making sense of ambiguous findings, and "managing the weight of inflicted insight" (Anderson et al., 2016). Some reported difficulty understanding genetic information and lack of family-centeredness (Chen et al., 2013). Interviews with mothers of autistic children who had clinical CMA showed that there were aspects that were "missing" from their experience of genetic testing that would have helped them understand the value of the test, such as information on genetics and genomics in general, the genetics of ASD, use of genetic results and their relevance to life-long care (Giarelli & Reiff, 2015; Reiff et al., 2015).

There are very few quantitative studies that have examined the potential impact of genetic testing on families. A survey exploring the genetic testing experiences of parents of autistic children showed that 37.6% were "unsatisfied" mainly due to lack of perceived testing benefits to their children and unpleasant testing experiences with health-care providers (Zhao et al., 2019a). In a large study of psychological outcomes related to exome sequencing (ES) and genome sequencing (GS) for a variety of conditions, parents of children had the greatest levels of uncertainty and distress, but also the highest degree of positive experiences (Robinson et al., 2019).

These differing impacts may be explained by the varied contexts in which each family experiences genetic testing. In the studies summarized above, families had exposure to genetic testing in different settings, such as large urban pediatric centers (Giarelli & Reiff, 2015; Reiff et al., 2015), private centers offering clinical services (Giarelli & Reiff, 2015; Reiff et al., 2015), clinical research projects where genetic information was offered by clinician-researchers or genetic counsellors (Anderson et al., 2016; Robinson et al., 2019), and through various unspecified healthcare providers (including non-genetic specialists; Chen et al., 2013; Zhao et al., 2019a). Assessing *personal utility* from genetic testing in ASD/NDDs relates to the child, family, and health service factors that may modify the impact of genetic testing. We recently reported a series of findings from a cohort study of families of children diagnosed with ASD/NDDs from routine clinical services, who underwent clinical genetic testing (Yusuf et al., 2019; Yusuf, Peltekova,

Savion-Lemieux, Frei, Bruno, et al., 2020). We found that parental distress and ASD knowledge correlated among families undergoing genetic testing (Yusuf et al., 2019). We showed that child and family functioning correlated with perceived utility for biological testing among these families (Yusuf, Peltekova, Savion-Lemieux, Frei, Bruno, et al., 2020). Family functioning and child factors may affect parental experience of genetic testing as interactions may be under greater strain in families who have a child with a chronic condition (Kelly et al., 2008) and family conflict may be intertwined with child symptomatology (Kelly et al., 2008). Health services experience may also play a role. While we did not find a significant correlation between level of family-centered care and perceived utility of biological testing (Yusuf, Peltekova, Savion-Lemieux, Frei, Bruno, et al., 2020), other studies have shown the frustration of affected families from encountering a care system that lacks a family-centered approach (Nicholas et al., 2016). Taken together, interactions between child, family, and health services factors may modify the impact of clinical genetic testing for individual families.

Personal utility of genetic testing in families affected by ASD and related NDDs has been challenging to measure due to lack of consensus on constructs and limited standardized tools (McAllister & Dearing, 2015). One outcome that has shown promise in capturing personal utility from genetic services is “empowerment” (McAllister, Dunn, et al., 2011). The World Health Organization defines empowerment as “a process through which people gain better understanding and control over their lives” (Baumann, 2010). More specific to genetic services, McAllister et al. defined empowerment as the belief that the individual receiving genetic services has “decisional”, “cognitive”, and “behavioral control”, “emotional regulation” and “hope”, and that the beneficial effects of genetic information are reflected in these five aspects (McAllister, Dunn, et al., 2011; McAllister et al., 2008). The construct of empowerment has been operationally defined and validly measured to describe the potential patient benefits from genetic information and services using a Patient Reported Outcome Measure (PROM) called the Genetic Counseling Outcome Scale (GCSO)-24 (McAllister, Dunn, et al., 2011; McAllister et al., 2008).

In this study, we extend our previous work (Yusuf et al., 2019; Yusuf, Peltekova, Savion-Lemieux, Frei, Bruno, et al., 2020) by examining both clinical and personal utility of clinical genetic testing in a cohort of families of children with ASD and related NDDs, in routine healthcare settings. First, we assessed diagnostic yield (clinical utility) in a population-based sample of families with an affected child, as they underwent diagnostic assessment. Second, we examined empowerment of parents (personal utility) around the time of clinical genetic testing for the child,

using a modified version of the GCOS-24 (mGCOS-24) that we recently adapted and validated for use in parents of children with NDDs (Yusuf, Peltekova, Savion-Lemieux, Frei, Joober, et al., 2020). Finally, we explored child, family, and health services factors proposed as potential predictors of empowerment in the context of genetic testing for ASD and related NDD (Kasparian et al., 2014).

## 2 | PARTICIPANTS AND METHODS

### 2.1 | Sample

Recruitment of participants relied on a clinically embedded protocol (i.e., families were recruited directly from clinical services as their child underwent diagnostic assessment for suspected NDD), as part of a longitudinal genetic study in Montreal, Canada, called Genome to Outcome. The Genome to Outcome study aimed to assess the standard of care in genetic testing for children with NDDs and contribute to understanding the genetic basis of NDDs. Inclusion criteria for this larger study were: families of a child or youth (age 0–18 years) referred for an evaluation of NDD for which genetic testing was recommended. Children with previously diagnosed genetic disorders were excluded.

### 2.2 | Ethical compliance

The study was approved by the Research Ethics Board of the Research-Institute of McGill University Health Centre.

Families were alerted about the Genome to Outcome study by clinicians in Child Development (developmental pediatricians, psychologists), Psychiatry (child and adolescent psychiatrists), and Genetic (genetic counselors and geneticists) clinics at a pediatric center (McGill University Health Center) and at a specialized mental health center (Douglas Mental Health University Institute), as well as by primary care providers (pediatricians and family doctors) in Community clinics. These clinicians were involved in the child's clinical care either through a diagnostic assessment that included information on genetic testing, or through pre-test genetic counseling that followed the diagnosis of NDD made by another clinician. The majority of pre-test genetic counseling was done by non-genetic clinicians and there was no standardized approach to the pre-test genetic counseling (i.e., each clinician relied on their own expertise and knowledge in deciding what information to provide). Interested families then spoke with a research assistant to learn more about the study. Families

that remained interested met with the research assistant, who carried out informed consent and enrollment.

During the study visit, the “parent most knowledgeable” (PMK) about the child was introduced to a set of online questionnaires, some of which were completed during the visit and the remainder at home. Typically, the blood-draw for the clinical genetic test (CMA) took place on the same day as the research study visit, but in some cases it took place before or after. In all cases, the questionnaires for the outcome measure (empowerment), for the family sociodemographic factors and for the health service factors (perception of family-centeredness of care) were completed before the family was aware of the clinical genetic result. As part of the broader Genome to Outcome study, the proband and first-degree family members also provided blood samples for research genetic testing.

For the purpose of the current study, data on empowerment was analyzed only from families whose child had no previous genetic testing, in order to capture the impact of undergoing clinical genetic testing for the first time (the inclusion criteria for the larger Genome to Outcome Study allowed for families with previous clinical genetic testing as long as no genetic condition had been diagnosed). A genetic result was available on average 10.9 weeks after the child's final diagnostic assessment visit. At this visit, the clinician typically discussed with the family the diagnosis of ASD/NDD and/or information on clinical genetic testing and determined if the family was interested in learning more about the research study. The sociodemographic data (Table 1) for the Genome to Outcome study cohort suggests that the participating families were representative of the general Montreal population, as compared to the 2016 Canadian Census (Statistics Canada, 2016).

## 2.3 | Measures

### 2.3.1 | Diagnostic yield

Diagnostic yield from clinical CMA was determined by performing a chart review for each child. Yield was calculated as the proportion of pathogenic results (as interpreted by the clinical analytic laboratory) from all reported results.

### 2.3.2 | Empowerment

Work on the concept of empowerment has led to the creation of a validated PROM, consisting of 24 questions, called the GCOS-24 (McAllister, Wood, et al., 2011). It is designed for use in genetic services and measures

**TABLE 1** Descriptive data for families enrolled in the Genome to Outcome cohort ( $n = 113$ )

Characteristics of the child	
Mean child age in years at time of study referral ( <i>SD</i> )	6.7 (3.7)
ASD	97 (85.8%)
GDD or ID	16 (14.2%)
Male	84 (74.3%)
Female	29 (25.7%)
Characteristics of the PMK	
Biological mother	98 (86.7%)
Biological father	11 (9.7%)
Adoptive mother	4 (3.5%)
Marital status <i>N</i> (%)	
Married/common law	96 (85%)
Divorced/Separated/Single	17 (15%)
Education <i>N</i> (%)	
High school or College	53 (46.9%)
University or Post-secondary	60 (53.1%)
Annual household income <i>N</i> (%)	
Less than \$40,000	34 (30.1%)
Between \$40,000 and \$80,000	35 (30.1%)
More than \$80,000	43 (39.1%)
Missing	1 (0.9%)

Abbreviations: *N*, total Number; *SD*, standard deviation.

empowerment from the receipt of genetic information (Barr et al., 2015). Psychometric analysis of the GCOS-24, in a population of individuals with genetic conditions, revealed good internal consistency, test–retest reliability, sensitivity to change, and evidence of construct validity (McAllister, Wood, et al., 2011). For the purpose of our study, we utilized an adapted version of the GCOS-24, the mGCOS-24, as previously described (Yusuf, Peltekova, Savion-Lemieux, Frei, Joobar, et al., 2020). Higher scores indicate greater degree of empowerment.

## 2.4 | Sociodemographic and clinical variables of interest

Family annual income, age, and education level of the PMK were assessed using a structured interview during the study visit, the Family Background Information Questionnaire (FBIQ) (Statistics Canada. *The National Longitudinal Survey of Children and Youth (NLSCY) - Survey Overview for the 2008/2009 Data Collection Cycle 8.*, 2010). Diagnostic and medical information on the child was obtained through chart review.

## 2.5 | Child's emotional and behavioral problems

Emotional and behavioral problems in the child were assessed using the Child Behavior Checklist-2 (CBCL-2) (Achenbach and Rescorla, 2001). The CBCL obtains parent ratings on 99 to 113 items of their child's emotional, behavioral, and social problems. The CBCL has been developed for use in children aged from 1½ to 5 years and from 6 to 18 years. T-scores were used to summarize scores across both age groups. Higher total scores indicate greater problems in child emotional and behavioral functioning.

## 2.6 | Family functioning

Parental (PMK) perception of their function within the family was evaluated through a parent self-report tool, Brief form of the Family Assessment Measure, third edition, Self-rating scale, (Brief FAM-III SR) (Skinner et al., 2000). The Brief FAM-III SR has 14 items that allow a person to rate their own functioning within the family. The Brief FAM-III SR is a module of the Brief FAM-III measure, which is based on the Process Model of Family Functioning. This model suggests that that relationships within the family change along with an individual's perception of their own functioning (Skinner et al., 2000). The Brief FAM-III has been used in families of children with chronic conditions and developmental disabilities (Skinner et al., 2000) and is reported to have good internal reliability and test-retest reliability (Skinner et al., 2000). Higher scores denote lower sense of functioning.

## 2.7 | Parental perception of family-centeredness of care

Family-centeredness of care, as perceived by the PMK, was assessed using a 20-item questionnaire, the Measure of Processes of Care (MPOC-20). The MPOC-20 was developed to assess parents' perceptions of the extent to which health services they and their child received over the past year were family-centered (King et al., 2004). The MPOC-20 captures five dimensions of care (1) Enabling and partnership; (2) Providing general information; (3) Providing specific information about the child; (4) Coordinated and comprehensive care for the child and family; and (5) Respectful and supportive care. The MPOC-20 has been validated in parents of children with NDDs and was reported to have good internal reliability and test-retest reliability (King et al., 2004). Higher scores reflect parental perception of greater family-centered care.

Because our target population included French-speaking individuals, we followed established guidelines (Wild et al., 2005) to translate all measures into French, if no validated translation already existed.

## 2.8 | Statistical analyses

Bivariate associations between parental empowerment (mGCOS-24 scores), sociodemographic variables, and child, parent (PMK) and health services factors, were explored using correlation analyses: continuous variables were analyzed using Spearman's  $\rho$  test while group comparisons were performed using independent  $t$ -test. In order to minimize Type I error due to multiple comparisons, the Bonferroni correction was applied, yielding a more stringent  $p$ -value of 0.005. For the purpose of all statistical analyses, square root transformation of the Brief FAM-III SR data was used, to ensure a normal distribution. To examine the combined impact of different covariates and factors on parental empowerment, we used a general linear model analysis with a significance level of  $\alpha = 0.05$  (two-sided). All statistical analyses were done using the statistical software Statistical Package for the Social Sciences (SPSS) 26.0 for Mac (SPSS Inc.).

# 3 | RESULTS

## 3.1 | Participants

A total of 257 eligible families were referred to the Genome to Outcome study between 2016 and 2019. Forty three percent of families agreed to participate ( $n = 113$ ). The most common reason for not participating was that families were too busy. Further details on the cohort were previously reported by Yusuf et al. (Yusuf et al., 2019; Yusuf, Peltekova, Savion-Lemieux, Frei, Bruno, et al., 2020).

## 3.2 | Diagnostic yield

Of all enrolled families ( $n = 113$ ), 105 (93%) had a CMA result available from clinical genetic testing done either before or after study enrollment; this information was missing for seven families. Of these, 94 (89.5%) had a negative CMA result; 6 (5.7%) had a "variant of unclear significance" (VUS); 3 (2.8%) had a pathogenic variant; and 2 (1.9%) had a variant classified as "benign". Therefore, the overall diagnostic yield for pathogenic results identified by clinical CMA in our population-based cohort of children with NDDs was 2.8%.

### 3.3 | Descriptive information on predictors and outcome measure

Of the complete sample ( $n = 113$ ), 70 families had a child diagnosed with an NDD, who did not have previous genetic testing (36 had previous testing and 7 were missing that information). One family was excluded because study enrollment and genetic testing occurred over 1 year from the time of the diagnostic assessment. Parents' experience of health care services beyond 1 year cannot be reliably measured using the MPOC-20. Thus, all subsequent analyses were done on a sample of  $n = 69$ . Out of these families, the majority (75.4%,  $n = 52$ ) had been referred to our study by a developmental pediatrician/child and adolescent psychiatrist, and the remainder by a community pediatrician/family doctor (15.9%,  $n = 11$ ) or a geneticist/genetic counsellor (8.7%,  $n = 6$ ). Table 2 presents descriptive statistics for the outcome measure and predictors.

### 3.4 | Exploratory analyses

We first assessed the extent to which child and parent (PMK) sociodemographic variables were independently associated with parental empowerment. After correcting for multiple comparisons, there was no statistically significant association (defined as  $p < 0.005$ ) between any of the sociodemographic factors and parental empowerment around the time of genetic testing (Table 3). Due to the uneven split in sample size for child's diagnosis and the

**TABLE 2** Descriptive statistics for the outcome measure and predictors ( $n = 69$ )

Measure	Mean (SD)
Outcome	
mGCOS-24 total score ( $n = 68$ )	118.9 (19.2)
Predictors	
CBCL-2 total <i>T</i> score ( $n = 50$ )	62.6 (10.7)
Brief-FAM-III SR total score ( $n = 54$ )	12.2 (5.9)
MPOC-20 subscales score ( $n = 62$ )	
Enabling and partnership	4.2 (2.0)
Providing general info	3.9 (1.9)
Providing specific info	4.4 (1.8)
Coordinated and comprehensive care	4.4 (1.7)
Respectful and supportive care	4.8 (1.6)

Abbreviations: Brief-FAM-III SR, Brief form of the Family Assessment Measure, third edition, Self-rating scale; CBCL-2, Child Behavioral Checklist; mGCOS-24, modified Genetic Counselling Outcome Scale - 24; MPOC-20, Measure of Processes of Care - 20; SD, standard deviation.

**TABLE 3** Correlation of sociodemographic variables with parental empowerment around the time of genetic testing ( $n = 69$ )

Sociodemographic Factors	Parental Empowerment (mGCOS-24 Score)
Child's age	$r(68) = 0.088$ $p = 0.475$
Child's sex Male vs. female	$t(66) = -0.583$ $p = 0.562$
Parental age	$r(68) = 0.082$ $p = 0.508$
Parental education High school/Vocational/College University/Professional	$t(66) = 2.58$ $p = 0.012$
Family income < \$70,000 > \$70,000	$t(64) = -1.13$ $p = 0.261$

Abbreviation: mGCOS-24, modified Genetic Counselling Outcome Scale - 24

PMK's marital status (Table 1), the correlation between these factors and empowerment were not analyzed.

We then assessed the extent to which child (child's emotional and behavioral problems), family (family functioning), and health services factors (perception of family-centeredness of care) were independently associated with parental empowerment around the time of genetic testing (Table 4). After correcting for multiple comparisons, there was no correlation between the child's degree of emotional and behavioral problems and parental empowerment. There was a significant negative correlation between family functioning and empowerment (i.e., lower perception of function in the family was associated with lower empowerment). There was a significant positive correlation between several aspects of perceived family-centeredness of care and parental empowerment, namely, provision of general information, coordinated and comprehensive care, and respectful and supportive care.

### 3.5 | Predictors of empowerment

To explore predictors of parental empowerment around the time of genetic testing for the affected child, we used a general linear model with mGCOS-24 total scores as the dependent variable; family income and parental education level as fixed factors; and child's age, extent of child's emotional and behavioral problems (CBCL-2 total *T*-scores), family functioning (Brief FAM-III SR scores), and parentally perceived family-centeredness of care (MPOC-20 subscale scores) as covariates ( $R^2_{\text{corr}} = 0.362$ ). The model explains 49.8% of the variation in parental empowerment around the time of genetic testing,  $F(10, 37) = 3.67$ ,  $p = 0.002$ ,  $R^2 = 0.498$  (Table 5). Parental

**TABLE 4** Correlation between child, family, and health service factors, and parental empowerment around the time of genetic testing ( $n = 69$ )

Additional factors	Parental empowerment (mGCOS-24 Scores)
<b>Child</b>	
CBCL-2 total <i>T</i> -score	$r(50) = -0.127$ $p = 0.379$
<b>Family</b>	
Brief FAM-III SR total score	$r(55) = -0.391^*$ $p = 0.003$
<b>Health services</b>	
MPOC-20 subscales score for:	
Enabling and partnership	$r(62) = 0.295$ $p = 0.02$
Providing general info	$r(62) = 0.411^*$ $p = 0.001$
Providing specific info	$r(62) = 0.301$ $p = 0.017$
Coordinated and comprehensive care	$r(62) = 0.440^*$ $p < 0.0005$
Respectful and supportive care	$r(63) = 0.451^*$ $p < 0.0005$

Abbreviations: Brief-FAM-III SR, Brief form of the Family Assessment Measure, third edition, Self-rating scale; CBCL-2, Child Behavioral Checklist; mGCOS-24, modified Genetic Counselling Outcome Scale – 24; MPOC-20, Measure of Processes of Care – 20.

\*Denotes  $p < 0.005$ .

perception of provision of general information makes a significant contribution to the model and accounts for significant amount of the variation in parental empowerment,  $F(1,37) = 6.74$ ,  $p = 0.013$  (Table 5). There is a trend toward significance for parental education level,  $F(1, 37) = 3.72$ ,  $p = 0.061$  and parental perception of function in the family  $F(1, 37) = 3.24$ ,  $p = 0.080$ , as contributors to the model (Table 5). No other factors are predictive of parental empowerment.

## 4 | DISCUSSION

We assessed the utility of undergoing clinical genetic testing in a population-based cohort of parents of children with ASD/NDD, recruited from routine clinical services. We assessed utility using two complementary measures: diagnostic yield, which is a measure of clinical utility, and parental empowerment, which is a measure of personal utility for individual families. We assessed child, family, and health service factors that may predict parental empowerment. Diagnostic yield of clinical CMA in our sample was 2.8% for pathogenic results. Parental perception of provision of general information was the only predictor of

**TABLE 5** Impact of child, family, and health service factors on parental empowerment

Predictors	F (df)	p-value
Corrected model	3.67 (10)	0.002
Child's age	0.56 (1)	0.461
Child's emotional and behavioral functioning (CBCL-2)	0.05 (1)	0.818
Family income	2.55 (1)	0.119
Parental education	3.72 (1)	0.061
Family function (Brief FAM-III SR)	3.24 (1)	0.080
Family-centeredness of care (MPOC-20)		
Enabling and partnership	0.01 (1)	0.939
Providing general info	6.74 (1)	0.013*
Providing specific info	0.10 (1)	0.754
Coordinated and comprehensive care	0.01 (1)	0.943
Respectful and supportive care	0.02 (1)	0.897

Abbreviations: Brief-FAM-III SR, Brief form of the Family Assessment Measure, third edition, Self-rating scale; CBCL-2, Child Behavioral Checklist; MPOC-20, Measure of Processes of Care – 20.

\* $p < 0.05$ .

their empowerment at the time of genetic testing. There was also a significant negative correlation between family function and parental empowerment, although family function was not a significant predictor of empowerment in our model.

Data drawn from a population-based cohort representative of clinical services, such as ours, is likely to offer information that has greater applicability to understanding and improving the use of genomics in healthcare for NDDs. The diagnostic yield in our sample was lower than those typically reported in other studies (Miller et al., 2010; Tammimies et al., 2015). The recommendation for clinical use of CMA in the investigation of ASD and related NDDs was based on a review of 33 studies and reported an average diagnostic yield of 12.2% (Miller et al., 2010). The reviewed studies were in populations from clinical genetics services, which generally have more clinical findings (e.g., congenital anomalies, dysmorphic features) and symptomatology (e.g., intellectual disability, seizures), leading to higher likelihood of detecting a large pathogenic variant by CMA.

Clinical genetic testing is recommended for ASD/NDDs as a first-tier test, independent of a referral to clinical genetics services. ASD and related NDDs present with heterogeneous phenotypes, with many autistic individuals showing at least average cognitive abilities, and no recognizable dysmorphic features (McGrew et al., 2012). Studies in cohorts external to clinical genetic services show a CMA yield closer to 9% (McGrew et al., 2012; Tammimies

et al., 2015). Our cohort may be more representative of the heterogeneous ASD/NDD population than other studies and of the clinical care pathways, in which CMA is implemented. Therefore, the diagnostic yield in our cohort may be reflective of CMA testing outcomes in the broader ASD/NDD phenotype across clinical services in general.

We used a PROM, the mGCOS-24, to measure another aspect of clinical utility, namely parental empowerment. This measure allowed us to quantify the personal utility experienced by each parent in the sample around the time of clinical genetic testing for their affected child. Interestingly, empowerment was not predicted by sociodemographic or child-specific factors. Rather, there is some specificity of the effects on empowerment by factors unrelated to parental or child characteristics, namely quality of care and family dynamics. An interesting finding in the context of ASD/NDD is that empowerment was linked to parental experience of healthcare services, that is, the extent to which parents thought they were provided with relevant information about the child's condition and services (King et al., 2004). A positive experience with information provision may increase a parent's sense of empowerment around genetic testing because this may align with the constructs inherent in the concept of empowerment, such as "decisional control", "cognitive control", and "behavioral control" (McAllister, Dunn, et al., 2011).

Studies have shown the importance parents place on information about genetic testing (Li et al., 2016; Zhao et al., 2019b). Zhao et al. (2019) demonstrated that most parents (73.7%) of a child with ASD, who was undergoing genetic testing, were interested in receiving health education on genetic testing (Zhao et al., 2019b). The most desired topics for health education were accuracy of genetic testing, cost, relevant benefits of testing, testing procedure, eligibility to undergo genetic testing, potential harms, previous use and experience among individuals affected by ASD, and confidentiality issues (Zhao et al., 2019b). Studies have shown that, when the informational needs of parents were not met, this resulted in negative experiences during genetic testing, such as difficulty understanding genetic concepts and terminology, and difficulty understanding the "value" of the test (Chen et al., 2013; Giarelli & Reiff, 2015).

The perception of provision of general health information by the families in our study may be related to the pre-test counseling they received from the healthcare provider, during the clinical visit for their affected child that preceded the study visit. This in turn may suggest that pre-test counseling plays an important role in the empowerment (i.e., personal utility) that parents derive from genetic testing for their child. One limitation of our study is that there was no standardization on how pre-test genetic counseling was done for each family, since information about clinical genetic testing was provided by a

variety of clinicians, most of whom were non-genetic specialists. This may have impacted the family's perception of quality of health information provided. An area for future study is to examine what quantifiable factors play a role in meeting the information needs of families faced with genetic testing (e.g., receiving pre-test genetic counseling by a genetic vs. non-genetic specialist). It will be helpful to study how the content and process of pre-test counseling can be optimized for what parents find helpful and relevant around the time of genetic testing. Development of informational tools for parents may increase effectiveness and impact of pre-test counseling. This may include provision of comprehensive information that is relevant to the child's diagnosis and encompasses health, services, and community resources (Catalano et al., 2018); novel delivery models (e.g., through telehealth, online modules, etc.) (Li et al., 2016); information to family members who may play an important family role (e.g., grandparents, siblings, other first-degree relatives, etc.) (Zakirova Engstrand et al., 2020); and information on peer-support groups (Catalano et al., 2018). It may also be important to develop and validate tools to assist non-genetic healthcare providers in pre-test genetic counseling, and foster collaboration with genetic specialists.

Our results suggest that parental perception of their function within the family may also potentially impact their empowerment around the time of genetic testing for their affected child. Another limitation of our study is that the number of families whose data were analyzed was still relatively small ( $n = 69$ ). Although almost all parents completed the outcome measure for empowerment (mGCOS-24), some did not complete the questionnaires related to other measurable factors (e.g., family function, child's emotional and behavioral problems). This may have led to a less powered analysis, which potentially may explain why family function was not a significant predictor of empowerment in our model. An analysis in a larger sample may offer greater insight into the relationship between family function and empowerment around the time of genetic testing. Overall family function may be impacted by the presence of an NDD in a child. For example, parents of autistic children report lower family cohesion and adaptability than parents of unaffected children (Higgins et al., 2005). Future studies can also shed light on the intersection between genetic and mental health services to support families undergoing genetic testing.

Our work lays the foundation for using PROMs to optimize and personalize the process of genetic testing, especially as novel genomic technologies, like ES and GS, become clinically integrated in NDDs, where PROMs have been scarcely utilized. Use of outcome measures, like empowerment, in families faced with advanced genetic tests, may prove particularly useful in their clinical integration



and in meeting the informational needs of families faced with complex genetic information.

Our study provides insight into the informational needs of families whose child with ASD/NDD is undergoing genetic testing. This knowledge may help to optimize the process of genetic testing for families, such as offering relevant and individualized pre-test counseling and support to parents. Furthermore, we demonstrate that a PROM assessing empowerment (GCOS-24) can capture an aspect of utility from genetic testing, namely personal utility. This tool can be used to guide the process of genomic technologies integration in the healthcare for families affected by ASD and related NDDs.

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## CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

## ETHICS DECLARATION

The study was reviewed and approved by the Research Ethics Board of the Research-Institute of McGill University Health Centre. Informed consent was obtained from all participants as required by the IRB.

## AUTHOR CONTRIBUTIONS

IP, AY and ME conceptualized the study. IP carried out implementation, data gathering, analyses, initial manuscript preparation and subsequent revisions; AY carried out data gathering, provided advice on methodology and analysis, and revised the manuscript. ME provided advice on methodology and analyses, and revised the manuscript. JF helped with implementation and data collection. TSL helped with advice on study conceptualization and methodology. RJ, JH and SWS provided advice on conceptualization and revised the manuscript.

## DATA AVAILABILITY STATEMENT

Access to data is available upon request to the corresponding author.

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