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ORIGINAL ARTICLE

Impact of a Genetic Diagnosis for a Child's Autism on Parental Perceptions

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Abstract

Genetic testing is recommended as part of an autism assessment, and most parents support genetic testing for their minor children. However, the impact on parents of receiving a monogenetic/ copy number variant diagnosis for autism in their child is not well understood. To explore this, we surveyed and interviewed parents of children in the SPARK study, a study of autism that includes genetic testing. Surveys were administered one month before and one and 12 months after parents received their child's genetic result. Interviews were conducted approximately one month after results disclosure. A genetic diagnosis (GD) for their child appeared to reduce parents' sense of self-blame and feelings of guilt, and this impact was relatively stable. The data also indicate a modest impact on parents' actions related to the condition, perceptions of themselves, and some aspects of life planning for their child, as measured by quantitative instruments at one month and 12 months after receipt of results. Other measures of parental identity and expectations for their child, in contrast, showed little change following receipt of genetic findings. Overall, parents who were told that no GD was identified showed minimal changes in their responses over time. These results suggest a discernable but relatively limited impact of genetic test results on parents of children with autism. These results should be reassuring to clinicians caring for children with autism and are consistent with studies in other areas of medicine that have suggested that genetic results tend to have fewer effects—negative or positive—than were anticipated.

Keywords Autism · Genetic testing · Genetic diagnosis · Impact of genetic testing

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Autism is a common neurodevelopmental condition. One in 44 children is diagnosed with autism by eight years of age, with a median age of diagnosis of 5.7 years and a four-fold higher prevalence in males (Shattuck et al., 2009). Individuals with autism often have co-occurring conditions such as congenital anomalies, intellectual disabilities, motor impairments, and seizures (Sanchack & Thomas, 2016). The heterogeneity of the condition also extends to the etiology. Autism has a complex genetic architecture including copy number variants (CNV), inherited or de novo rare sequence variants in over 100 genes, and common variants (Satterstrom et al., 2020; Zhou et al., 2022).

A genetic diagnosis (GD) is identified in 5–14% of individuals with autism who undergo chromosomal microarray testing and in 8–20% who undergo exome sequencing, with higher diagnostic yields in individuals with additional diagnoses (e.g., dysmorphic features, congenital anomalies, and/or intellectual disabilities). Genetic testing is now recommended as a routine part of assessment for autism and

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other neurodevelopmental disorders, and exome sequencing has been recommended as part of a first-tier evaluation for such individuals to inform individualized care (Hellquist & Tammimies, 2022; Srivastava et al., 2019). Based on these recommendations, GDs are likely to become more frequent and to be made at younger ages as access to genetic testing increases. Parents are impacted in a variety of ways by having a child with autism (Estes et al., 2013, 2021; Karst & van Hecke, 2012); however, the incremental impact of the addition of a GD is unclear.

A series of studies have found that a majority of parents support genetic testing for their child with autism, especially if it could identify a cause for the condition (Giarelli & Reiff, 2015; Johannessen et al., 2021; Reiff et al., 2015, 2017). Reiff et al. (2017) conducted interviews (n = 57) and surveys (n = 50) with parents whose children with autism had undergone chromosomal microarray testing. They reported that most parents found the results useful, especially if a pathogenic finding was reported. Parents who received diagnostic findings (n = 15) often appreciated the causal information, which reduced their sense of guilt and enhanced their acceptance of their child's condition, and found the results helpful in identifying educational, medical, and behavioral interventions and accessing services. Some used the results for reproductive planning or to join research studies. However, many parents were disappointed that the results were not more definitive in clarifying prognosis or guiding treatment. Smaller studies yielded similar findings (Hayeems et al., 2016; Trottier et al., 2013). However, not all reported experiences have been positive. Zhao et al. (2019) surveyed 124 parents of children with autism who had genetic testing; a third of these parents reported negative experiences related to lack of perceived benefits of the testing. Lucas et al. (2022) interviewed two different groups of parents of children with autism having genetic testing: 22 parents pre-test and 32 parents post-test and found both reported increased knowledge and coping as benefits of testing, but the pre-test group reported higher perceived benefits than were experienced by the post-test group. Although illustrative, the previous studies relied on relatively small samples of parents who received GDs and explored a limited number of outcome measures.

To explore the potential impact of a GD for autism on parents in greater depth, we surveyed parents in the largest study to date of autism (Zhou et al., 2022). We hypothesized that a GD for autism could impact parents in three ways. First, a GD may affect parents' perceptions of their *responsibility for* autism and their *responsibility to act* in response to autism (Leefmann et al., 2017). *Parental identity*, including internalized stigma (Urban, 2020), and *parental perceptions of the child's identity* could also be altered by genetic results. Finally, identification of a genetic cause of their child's autism may impact *parental life-planning* for themselves and their child's future. Labeling a condition as "genetic" can affect views of its prognosis and treatability, which in turn could change parental perceptions of their children's future lives and behaviors (Lebowitz et al., 2013), notwithstanding the inherent ambiguity of the implications of most GDs, potentially reflecting determinist views about the nature of genetic conditions (Harden, 2023). Because these issues have not been previously explored, we did not have specific hypotheses about the direction in which these variables could be affected.

Materials and Methods

Study Population

Participants were recruited from Spark, a U.S. study that currently includes over 100,000 people with autism and 175,000 of their family members (Zhou et al., 2022). Recruitment was limited to a sub-set of participants who elected to participate in the genetic research component of Spark and were scheduled to receive the genetic results during the recruitment window for this sub-study. Spark participants can choose to participate in genetic studies, complete online instruments, and pursue additional research opportunities through a research matching service. For the current study, a consent disclosure was presented to participants online prior to beginning the survey. Participants indicated their consent by clicking a link to continue. This research match study was approved by the New York State Psychiatric Institute Institutional Review Board.

Study Sample

Spark participants who are parents of minor and adult probands with autism for whom exome/genome sequencing was completed between March 2017 and February 2020 were invited via email to participate in this study before they were notified of their child's genetic results. Parents were unaware of their child's genetic test results when they were invited to the study but were aware that they would receive results in approximately 4–6 weeks. Both biological parents, when available, were invited to participate and were asked to invite their children with a diagnosis of autism from ages 12–22 to participate. Here we present only the data from parent participants. Following consent to the study, these participants completed a baseline survey online prior to the receipt of genetic results. They subsequently received either a diagnostic (pathogenic or likely pathogenic) genetic result associated with their child's autism via a written genetic test report, condition-specific clinical guide, and telephone call with a study geneticist or genetic counselor or their health care provider (GD group) or were notified via the Spark

participant portal or email that there were no diagnostic genetic findings at this time [no genetic diagnosis (NGD) group]. An invitation to complete a follow-up survey was sent one month and 12 months later. Participants who completed both baseline and at least one follow-up survey were included in the analysis. Participants were asked at the end of the one-month survey if they would be willing to be contacted for an interview. Surveys were completed between April 2019 and January 2023, and participants received a $20 gift card for each survey completed. Interviews with a sub-sample of GD parents were completed between April 2019 and April 2022, and participants received a $50 gift card. Participants were purposefully sampled for interview based on their demographics and genetic test results in an effort to have diverse perspectives represented.

Surveys

The surveys were developed by an interdisciplinary team with experience studying the impact of genetic results and autism. The team included two physician-bioethicists, a pediatric medical geneticist, and a genetic counselor. Survey drafts were reviewed by members of the Spark community advisory council group at several points and iterative changes made. The community advisory council is part of the Spark study and is composed of participants in the Spark study including parents of children participants. The community advisory counsel is available to review ancillary Spark studies. The survey included validated measures and questions developed for this study that explore changes to parents' perceptions of responsibility for their child's autism and responsibility to act, caregiver identity, and life-planning for their child's future (Table S1).

Interviews

Semi-structured interviews were conducted with parents of children who received a GD to explore, in depth, the impact of a genetic finding on the family, focusing on the themes included on the survey. The Principal Investigator (RLK) for the qualitative portion of the study, who has extensive experience conducting and analyzing qualitative interviews conducted the interviews (See Supplemental Material for details).

Data Analysis

Quantitative Data Analysis

Summary statistics for comparisons of socio-demographic variables between GD and NGD groups were used to compare group characteristics. All complete responses for each question or scale were included in the analysis, except for the questions about future expectations for which only responses from participants with children under 22 years were included because of the greater likelihood that the patterns of their adult lives were not yet obvious. The means and standard deviations for each scale were computed for baseline and follow up and grouped by result type received. Frequency and proportions were computed for the questions on the survey.

To compare the impact of receiving GDs against no identifiable genetic cause (NGD) on survey responses, we applied a bi-directional differences-in-differences approach. In separate analyses for one- and 12-month follow-ups: we first subtracted the baseline scores from the follow-up scores for each response variable, then regressed these differences on the GD group using generalized estimating equations with a linear link function, which allows us to report responses for both parents of each child while accounting for the non-independence of their responses. To focus the analysis on the impact of receipt of a GD, the models were adjusted for demographic variables that differ between the GD and NGD groups, which included: child age, child gender identity, parent gender identity, parents' educational attainment, and baseline parental perceptions of the child's functional status in daily living (Daily Living Score; WHO-DAS 2.0, 2008). Standardized differences in changes from baseline to follow up across groups are reported and p-values were adjusted for multiple comparisons using the Benjamini–Hochberg procedure (Benjamini & Hochberg, 1995). We also reported the adjusted means for changes from baseline to one-month follow-up and from baseline to 12-month follow-up within each group. Additional models included an interaction with parent gender identity to assess whether parental gender moderated the relationship between results and baseline to follow-up changes.

We tested the key assumption that Likert-scale variables could be treated as continuous outcomes by conducting sensitivity analyses using cumulative logistic regression, in which the variables were treated as ordinal and comparing the direction of effect and p-values between the model types (data not shown). All data analyses were performed using SAS software (SAS Institute Inc. SAS 9.4 [Computer Program], 2014).

Qualitative Data Analyses

The interviews were recorded, transcribed, and analyzed using adapted key elements from "grounded theory" (Corbin & Strauss, 2012), informed by techniques of "constant comparison," with data from different contexts compared for similarities and differences, to see if they suggest reasons for differences. This technique generates new analytic categories and questions and checks them for reasonableness (see Supplemental Material for additional details). In this paper, we present interview findings only from GD parents.

Results

Participants

Of the over 100,000 Spark participants, 3197 parent–participants were eligible for this study and invited to join, and 1174 (37%) completed a baseline survey. Only those who completed a baseline survey were invited to complete the follow-up 1 (one-month, FU1) and follow-up 2 (12-month, FU2) surveys, which had response rates of 89% and 75%, respectively (Figure S1). The 847 who completed both the baseline survey and at least one follow-up survey were included in this analysis. Of these, 148 participants were notified of a genetic diagnosis (GD) result and 699 were told there was no genetic diagnostic result for their child at this time (NGD); response rates were similar for the two groups. Parental and child demographics are summarized in Tables 1 and 2. Respondent parents were predominantly White, non-Latinx, female and college-educated. This is reflective of the demographics of the Spark study (Zhou et al., 2022). The mean parental age was 44 (range: 26–72) and the mean child age was 12 (range: 4–43). Analyses comparing the responses of the GD and NGD groups were corrected for parental race, age, gender, education, and Daily Living Score.

Notably, GD children were more likely to be female (GD 34% vs. NGD 15%, p value < 0.0001), and have a lower imputed full-scale IQ (GD 69, NGD 80, p value < 0.0001) and higher parental perceived impact of autism on their child's daily life (GD 19.5, NGD 17.6, p value < 0.0001). These differences reflect a higher frequency of identified genetic etiology in autism with co-occurring intellectual disabilities (ID). This also skews the male:female ratio in each group from the known 3–4:1 male:female across the autism spectrum, as the sex ratio in those with ID is closer to 1:1 (Posserud et al., 2021).

Among the 148 GD parents, they had 129 children with a GD identified. When inheritance status was known, most (97%) GD variants were de novo, i.e., not inherited from either parent. For de novo cases, the incremental recurrence risk of autism in subsequent pregnancies for parents is approximately 1% above base rate due to the small chance of gonadal mosaicism in a parent. The inheritance status was unknown for 27% of the individuals with a GD. However, based on published high frequencies of de novo origin associated with these genes in individuals with autism and neurodevelopmental disorders, these families were counseled about the likely de novo inheritance and offered parental testing to confirm inheritance (Zhou et al., 2022). It is unknown how many pursued follow up parental testing. There were two participants with inherited genetic variants who were excluded from the analysis of perceived recurrence risk; this analysis only included those with known or suspected de novo genetic diagnoses.

Seventeen mothers and 15 fathers from the GD group were interviewed. Of these 75% identified as White and 9% as Latino, and the race and ethnicity of 16% were not available. These 32 parents included seven couples.

Impact of Genetic Results on Perceived Responsibilities

Surveys

Parents were queried about what they thought might have contributed to cause their child's autism to explore perceptions of responsibility for the child's condition. At baseline, findings were similar for GD and NGD groups. The strongest endorsement for both groups was genetic or hereditary causes (offered as a single choice) (Table S2). At one month and remaining at 12 months, parents in the GD group increased their endorsement of chance or luck, but there was a significantly lower endorsement of hereditary/genetic (offered as a single response) at 12 months. Both an increase in chance/luck responses and a decrease in perceived hereditary causes probably represents the de novo occurrence of the vast majority of GDs (Table S2, Fig. 1a, b). One month after receipt of results, the GD group decreased endorsement of causes that might implicate their own actions or accidents, including exposures during pregnancy, physical accidents, and complications of pregnancy and childbirth; most of these remained lower than baseline at 12 months (Table 3). These changes likely reflect the genetic counseling that accompanied return of GD results, which emphasized the chance nature of de novo variants and the lack of a relationship to parental behavior. Overall, the NGD group's views on whether the cause was genetic or hereditary were relatively stable over time, perhaps reflecting a nuanced understanding that the lack of results at this time did not eliminate the possibility of a genetic cause. While neither group strongly endorsed vaccines as a cause, the GD group had a modest decrease at 1 month, which remained at 12 months (Table 3).

Parents also were asked to estimate the risk of having another child with autism with the choices of no risk, 1-in-100, 1-in-20, 1-in-10, 1-in-4, and 1-in-2. Recurrence risk estimates were similar at baseline, with many parents likely overestimating recurrence risk; 26% and 32% in the GD group and NGD group, respectively, identified a 1-in-2 risk, the highest risk option (Fig. 2a, b). Parents in the GD group who received de novo results (the three parents of children with inherited variants were excluded from this analysis) more frequently identified a lower recurrence risk at one-month compared to the risk they selected at baseline, illustrating their understanding of the low recurrence

Table 1 Demographics of full sample with baseline and follow-up survey data, stratified by those with and without results

Variables	Total sample (n = 847)			Genetic diagnosis (n = 148)			No genetic diagnosis (n = 699)		Range	p value
	N	% or Mean (SD)	Range	N	% or Mean (SD)	Range	N	% or Mean (SD)		
Parent gender[a]										0.008
Female	628	74.1%		121	81.8%		507	72.5%		
Male	218	25.7%		27	18.2%		191	27.3%		
Transgender	1	0.1%		0	0.0%		1	0.1%		
Age at baseline[a]	847	44.1 (8.1)	27–73	148	44.61 (9.01)	28–70	699	44.0 (7.9)	27–73	0.5
Race[a]										0.06[b]
Native American	7	0.8%		0	0.0%		7	1.0%		
Asian	24	2.8%		1	0.7%		23	3.3%		
Black	22	2.6%		3	2.0%		19	2.7%		
Pacific Islander/Hawaiian	2	0.2%		0	0.0%		2	0.3%		
White	708	83.6%		131	88.5%		577	82.5%		
Middle Eastern/Mediterranean	5	0.6%		0	0.0%		5	0.7%		
Unknown	55	6.5%		11	7.4%		44	6.3%		
Multiple	24	2.8%		2	1.4%		22	3.1%		
Hispanic										0.3
Not-Hispanic/Latino	779	92.0%		139	93.9%		640	91.6%		
Hispanic/Latino	68	8.0%		9	6.1%		59	8.4%		
Household Income										0.9[c]
Less than $20,000	21	2.5%		4	2.8%		17	2.5%		
$21,000–$35,000	60	7.3%		12	8.5%		48	7.0%		
$36,000–$50,000	61	7.4%		17	12.0%		44	6.4%		
$51,000–$65,000	68	8.2%		13	9.2%		55	8.1%		
$66,000–$80,000	91	11.0%		12	8.5%		79	11.6%		
81,000–$100,000	125	15.2%		22	15.5%		103	15.1%		
101,000–$130,000	150	18.2%		29	20.4%		121	17.7%		
$131,000–$160,000	78	9.5%		9	6.3%		69	10.1%		
Over $161,000	171	20.7%		24	16.9%		147	21.5%		
Education[a]										0.03
Didn't graduate college	295	35.0%		57	39.0%		238	34.1%		
Graduated college	549	65.0%		89	61.0%		460	65.9%		
Job										
Full time caregiver	237	28.0%		40	27.0%		197	28.2%		
Employed	559	66.1%		100	67.6%		459	65.8%		
Not Employed	50	5.9%		8	5.4%		42	6.0%		
Impact of child's autism (Daily Living Score)[a]	843	17.9 (3.9)	5–25	148	19.53 (3.74)	7–25	695	17.6 (3.9)	5–25	< 0.0001

[a]Demographic factors adjusted for in the analysis comparing GD to NGD

[b]White compared to non-White

[c] < 160,000 compared to > 161,000

risk. In contrast, the estimated recurrence risk of the parents in the NGD group remained stable over time. Reflective of the genetic counseling they received, the largest shift at one-month follow up for the GD group was to the 1-in-100 risk response, which was 16% of the responses of the GD group at baseline and 45% at one month. However, by 12 months responses shifted back towards baseline with 28% identifying a 1-in-100 risk. The reported recurrence risk was relatively stable in the NGD group.

Of those who reported their child was receiving an educational or behavioral intervention, endorsement of the effectiveness of treatment was relatively stable over time, regardless of GD group (Tables 4, S2, S3). Demonstrating the complexity of parental responses, parents of children in the

Table 2 Demographics of child of parents who completed the survey

	Total sample (n = 700)			Genetic diagnosis (n = 129)			No genetic diagnosis (n = 571)			p value
	N	Mean (SD) or %	Range	N	Mean (SD) or %	Range	N	Mean (SD) or %	Range	
Child's gender[a]										< 0.0001
Female	130	18.6%		44	34.1%		86	15.1%		
Male	569	81.3%		85	65.9%		484	84.8%		
Transgender	1	0.1%		0	0.0%		1	0.2%		
Child's age at baseline[a]	697	13.0 (6.5)	3–43	128	14.2 (7.7)	4–43	569	12.8 (6.2)	3–42	0.0224
Child's age at autism diagnosis	696	4.1 (2.9)	1–33	127	4.7 (3)	1–33	569	4 (2.8)	1–18	0.0098
Child's full scale IQ-imputed	602	77.8 (18.1)	35–122	101	69.1 (16.2)	35–108	501	79.5 (18)	34–122	< 0.0001
Does child have health insurance										
No	43	6.2%		7	5.5%		36	6.3%		0.772
Yes	656	93.8%		121	94.5%		535	93.7%		

[a]Demographic factors adjusted for in the analysis comparing GD to no GD

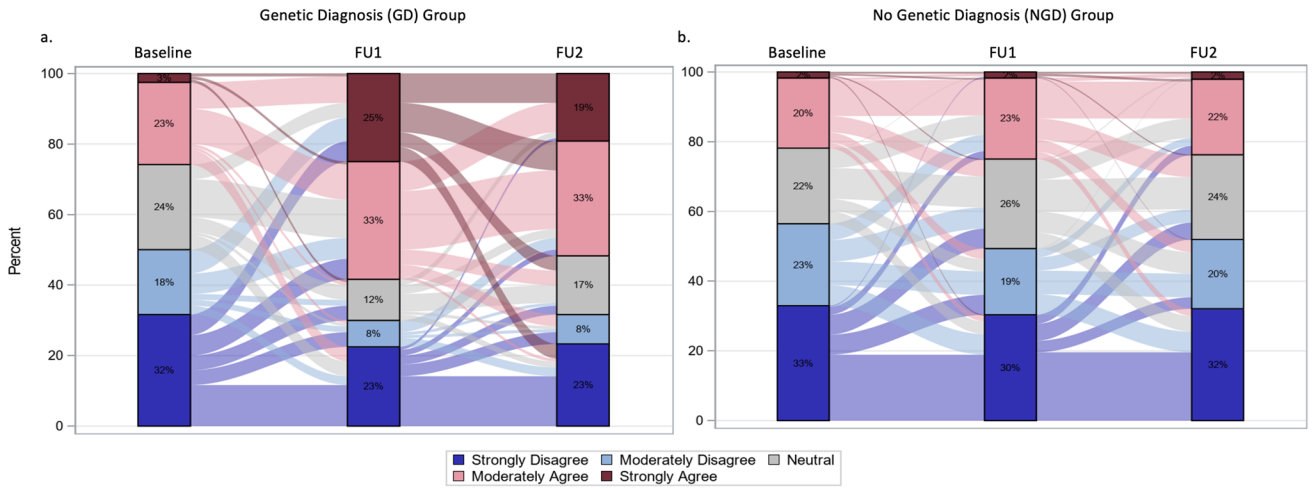

Fig. 1 Sankey plots of participant responses at baseline, one-month follow up (FU1), and 12-months follow up (FU2) to the question of how much they agreed that Chance or Luck was a cause of their child's autism. The plots show the proportion of participants responding at each level and movement of responses from before (baseline) to after (FU1 and FU2) they were notified of their child's results. **a** Parents whose children received a genetic diagnosis (GD). **b** Parents whose children were not identified as having a genetic diagnosis (NGD)

GD group had decreased endorsement of the effectiveness of medication at one month, but endorsement had returned to baseline at 12 months (Table 4). The GD parents all shared the results with at least one person, most commonly family members, and over half also shared with a co-worker or boss; the majority of the sharing happened by one month but sharing continued over the year after receiving results especially sharing with non-family members (Figure S2). Perceived responsibilities to act, including joining an online support group and volunteering for research, were modestly greater in the GD group. However, looking for alternative treatment and medical treatment were slightly higher in the NGD, perhaps reflective of not having a specific diagnosis on which to focus care (Figure S2a). The GD group was asked about actions specific to their child's GD. Most families reported searching for other research and less frequently connecting with families or becoming an advocate, which may reflect the relative rarity of the specific GDs (Fig. S2b).

Interviews

Parents in the GD group tended to blame themselves less for their child's autism after receiving results. As one father said,

> It was a relief, actually, because neither my wife nor I carry the mutation, so it kind of took a little pressure off the thinking that we have contributed to his

Table 3 Change in parent perceived cause of autism from baseline to FU1 and baseline to FU2 for those with no genetic diagnosis (NGD) and with a genetic diagnosis (GD)

Domain	Individual Scale or Question		BL -> FU1	BL -> FU2
Parent Perceived Cause of Child's Autism (scale 1- 5)	Chance/Luck	No Genetic Diagnosis	↑	-
		Genetic Diagnosis	↑	↑
		B-H p-value	<.0001	<.0001
	Childbirth Complication	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	<.0001	0.0008
	Germ/Pollution in Pregnancy	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	<.0001	0.01
	Germ/Pollution after Birth	No Genetic Diagnosis	↑	-
		Genetic Diagnosis	↓	↓
		B-H p-value	<.0001	0.01
	Parents' Age	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	0.002	0.01
	Physical Accident	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	0.0004	0.01
	Vaccination	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	<.0001	0.04
	Pregnancy Complication	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	<.0001	NS
	My Lifestyle	No Genetic Diagnosis	↓	↓
		Genetic Diagnosis	↓	-
		B-H p-value	0.03	NS
	Hereditary/Genetic	No Genetic Diagnosis	-	-
		Genetic Diagnosis	-	↓
		B-H p-value	NS	0.002
	Child's Behavior/Personality	No Genetic Diagnosis	-	-
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS
	My emotions/attitude	No Genetic Diagnosis	↓	↓
		Genetic Diagnosis	↓	↓
		B-H p-value	NS	NS
	Emotional/Psych. Trauma	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	-
		B-H p-value	NS	NS
	No cause	No Genetic Diagnosis	-	-
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS

A within-group significant change is indicated with an arrow (up increase, down decrease) and no significant change is indicated with a dash. If both groups had a significant change in the same direction, the group with the larger change is indicated with a thicker arrow. The Benjamini-Hochberg (BH) procedure corrected p values for the difference in the change between the NGD and GD groups. No significant change is indicated with NS. The specific p value is shown when significant (<0.05)

autism. Because in the general population, the occurrence of autism is higher in the scientist and medical population. [Father 4]

Yet ambiguities about what caused the de novo pathogenic variants also left room for continuing self-blame:

I took an antibiotic early in my pregnancy before I knew I was pregnant. Just those niggling fears: 'Did that cause it?' I might have had a glass of wine before I knew I was pregnant…Could *that* have caused it? [Mother 1]

Genetic test results may affect views of parental responsibility not only among parents, but others, particularly the child's grandparents and other extended family members.

My parents are a lot older, so still kind [of] have the mentality of, 'It's because you spoil him...' But I can now say, 'Hey, it's not just because of my mothering.' So, the genetic test has helped with that…[My parents' views are] still hard to deal with sometimes, but at least they have a better understanding. [Mother 1]

Parents also expressed an increased sense of responsibility to participate in research to help others and/or facilitate scientific progress. They noted that the genetic results helped to steer them to studies involving genetic variants similar to their child's. Such contributions to research could be either formal (e.g., enrolling in a specific study) or informal.

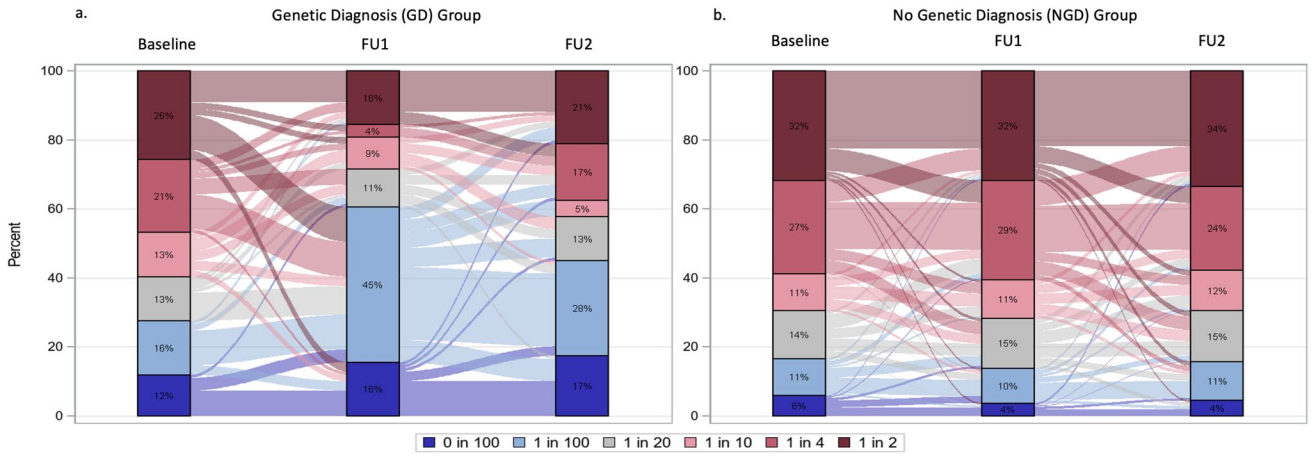

Fig. 2 Sankey plots of participant responses at baseline, one-month follow up (FU1) and 12-months follow up (FU2) to the question asking them to estimate the chance of having another child affected with autism. The plots show the proportion of participants responding to each risk response choice and movement of responses from before (baseline) to after (FU1 and FU2) they were notified of their child's results. **a** Parents whose children received a genetic diagnosis (GD). **b** Parents whose children were not identified as having a genetic diagnosis (NGD)

Table 4 Change in parent perception of helpfulness of intervention and expectations for the future (children < 22 years) from baseline to FU1 and baseline to FU2 for those with no genetic diagnosis (NGD) and with a genetic diagnosis (GD)

Domain	Individual Scale or Question		BL -> FU1	BL -> FU2
Intervention Helpfulness (scale 0- 3)	Helpfulness Medication	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	-
		B-H p-value	0.03	NS
	Helpfulness Educational Intervention	No Genetic Diagnosis	↓	↓
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS
	Helpfulness Behavioral Intervention	No Genetic Diagnosis	-	-
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS
Future Expectations* (scale 0-3)	Romantic Relationships	No Genetic Diagnosis	↑	-
		Genetic Diagnosis	-	↓
		B-H p-value	0.0006	0.03
	Have Children	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	0.03	0.002
	Support Themself Financially	No Genetic Diagnosis	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	0.03	0.0008
	College Degree	No Genetic Diagnosis	-	↑
		Genetic Diagnosis	-	↓
		B-H p-value	NS	<.0001
	Master/Doctorate	No Genetic Diagnosis	-	-
		Genetic Diagnosis	-	↓
		B-H p-value	NS	0.003
	Meaningful Friendships	No Genetic Diagnosis	↑	-
		Genetic Diagnosis	↑	-
		B-H p-value	NS	NS
	Live Independently	No Genetic Diagnosis	-	-
		Genetic Diagnosis	-	↓
		B-H p-value	NS	NS
	Graduate High School	No Genetic Diagnosis	↑	↑
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS

A within-group significant change is indicated with an arrow (up increase, down decrease) and no significant change is indicated with a dash. If both groups had a significant change in the same direction, the group with the larger change is indicated with a thicker arrow. The Benjamini-Hochberg (BH) procedure corrected p values for the difference in the change between the NGD and GD groups. No significant change is indicated with NS. The specific p value is shown when significant (< 0.05)

*Responses for parents of children under 22 years were included in analysis

> We both feel that we have a little more responsibility now to the…autism community and the [name of gene] community, in really keeping an eye on his health and his development, to be able to relay to you folks what we're seeing, what's changing with him just to further the science…we have a larger group of autism in general, but now we have a smaller…group we can focus with and work within. [Father 1]

Implications of Genetic Results for Life Planning

Surveys

Analysis of the data on anticipated life trajectories was limited to parents of children under 22 years, the group for whom life trajectories, such as educational attainments, friendships, romantic relationships, and independence, may be less certain. At baseline, parents in the GD group ranked their children significantly lower in their potential to have meaningful friendships, romantic relationships, or children; live independently; support themselves financially; and graduate from high school, college, or an advanced degree program than parents in the NGD group (Table S2).

There was a modest increase in the NGD parents' perceptions of their child's potential for a romantic relationship and decrease in the GD parents' perceptions resulting in a significant difference in change both at one month and 12 months (Table 4). At both timepoints, the GD parents decreased their endorsement of their child's ability to support themselves financially and have children in the future, while the NGD parents' endorsement remained stable. Similarly, the belief that their child will graduate from college decreased at 12 months in the GD group, while it modestly increased in the NGD group (Tables 4, S3).

Interviews

Parents' views of life planning were complicated by ambiguities concerning the child's life trajectory in several areas, including future symptoms, treatment, social functioning, and social services. Receiving genetic results sometimes increased the possibility of potential health problems and thus ambiguity concerning whether, when, and which symptoms may occur in the future.

> The gene typically might present seizures or epileptic issues…Will that be a future problem? We haven't seen it yet…It could happen. So, we wonder and worry about that. Is she more likely to have that? Is that going to be an adult issue for her? I don't know. [Father 7]

Several parents were concerned because they also did not know what unanticipated health problems to predict.

> It would be nice, looking at a bigger group of these children, knowing if there's any particularly identified comorbidities/coexisting conditions that we could expect down the road, things we should be looking for, screening for in her life." [Mother 12]

Ambiguities arose as well concerning future social functioning and independence.

> How far will she develop before she stops? What are we going to end up with for the rest of our lives?... What does our daughter end up achieving? That's the uncertainty. [Father 6]

Issues surfaced concerning not only perceived ambiguities, but *feelings* about these uncertainties, which could generate anxieties and/or senses of preparedness and acceptance. On one hand, these vagaries heightened worries and uncertainties: "We started to get more frightened about wanting to make sure that we're keeping our eyes open for all these things." [Father 12]

Yet genetic diagnoses could also help prepare parents and make them feel less helpless in the face of possible future problems.

> It may give you worries…It made us think – consider things that may be an issue that we had never thought about, but at least we *know that now*!...The fact that we have this information gives us a head start on being able to identify any issue. [Mother 3]

Impact of Genetic Results on Parental Identity and Perceptions of the Child's Identity

Surveys

At baseline, parents in both groups had measures of personal optimism (i.e., belief that circumstances will work out for the best; Scheier et al., 1994) and self-esteem (i.e., confidence in one's own worth; Rosenberg, 1965) at or slightly above reported median scores for the general population (Table S2). For the measures without a reference value, at baseline parents in the GD group had higher perceived autism stigma (i.e., how their child's autism is perceived by others; Boyd et al., 2014) and genetic stigma (i.e., how partners, employers and insurance companies view individuals with genetic conditions; Sabatello et al., 2015) compared to NGD parents.

Parental genetic stigma and optimism measures were relatively stable for both groups from baseline to one month and 12 months. At one-month follow-up, optimism, self-esteem, self-efficacy (i.e., confidence in one's own ability; Kupst et al., 2015) and autism stigma were not significantly different from baseline for either group (Table S3). Recognizing that parental experience of having a child with autism has

been shown to be different for mothers and fathers (Grebe et al., 2022; Vernhet et al., 2022), parental gender was analyzed as an interacting variable and was not found to interact with any measures. Genetic stigma decreased at one month and remained decreased, though not as much, at 12 months in the GD group and was relatively stable in the NGD group, resulting in a significant difference in change scores between the two groups from baseline to one-month (Tables 5, S3). This may reflect the impact of knowing that one's child has a genetic condition. There was a modest increase from baseline to follow up in genetic optimism (i.e., genetic research is over all good, Parrott & Smith, 2014) for both groups and no difference in the increase between groups. Genetic optimism increased similarly in both the GD and NGD groups and remained stable at 12 months (Tables 5, S3).

Interviews

The genetic results did not appear to alter parents' expressions of characteristics associated with their identity. Prior to receiving genetic results, parents frequently had already altered their perceived identity to accommodate the issues associated with raising a child with autism. Nor did most parents who received GD results markedly change their views of their child's identity: "…it doesn't change the way that I view him, or the way that we've been trying to help [or] support him." [Mother 3] "It doesn't really change how I look at him…He's my baby boy." [Father 1]

At times, however, parents' perceptions of the child's behavior were altered, especially during difficult behavioral periods (i.e., "meltdowns"), seeing the child now as less in control of symptoms, and therefore blaming the child less. Several parents suggested that at such stressful junctures, they now had more patience:

> It definitely solidified granting her a little more *grace*. So, when she drops her milk four times, she really doesn't mean to. She just has horrible fine and gross motor skills." [Mother 12]

Yet such lowered expectations of the child's future self could also reduce hope and generate a sense of sadness.

> I always felt as though she had the potential to be some kind of 'normal' as they say. And the test results just wiped out that little inkling and hope that I had always held on to…And that's sad. [Mother 13]

Discussion

Given the increasing use of genetic testing for autism, understanding the impact of genetic information is important to inform pre- and post-test counseling and care for the family. The present findings suggest that identification of a genetic basis for autism impacts parents in several ways. Consistent with other studies, genetic diagnosis for their child appeared to reduce parents' sense of self-blame and feelings of guilt, and this impact was relatively stable (Lucas et al., 2022; Reiff et al., 2015). In addition, the degree to which parents shared results with family members, co-workers and even

Table 5 Change in parent identity measures from baseline to FU1 and baseline to FU2 for those with no genetic diagnosis (NGD) and with a genetic diagnosis (GD)

Domain	Individual Scale or Question		BL -> FU1	BL -> FU2
Parental Identity	**Genetic Stigma Change** scale 7-28	**No Genetic Diagnosis**	-	-
		Genetic Diagnosis	↓	↓
		B-H p-value	0.02	NS
	Genetic Optimism Change scale 4-16	**No Genetic Diagnosis**	↑	↑
		Genetic Diagnosis	↑	↑
		B-H p-value	NS	NS
	Genetic Essential Change Scale 4-20	**No Genetic Diagnosis**	↑	-
		Genetic Diagnosis	↑	↓
		B-H p-value	NS	NS
	Optimism Change scale 10-50	**No Genetic Diagnosis**	↑	-
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS
	Self Efficacy Change scale 9-36	**No Genetic Diagnosis**	-	-
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS
	Self Esteem Change scale 10-40	**No Genetic Diagnosis**	-	-
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS
	Autism Stigma Change scale 9-36	**No Genetic Diagnosis**	-	-
		Genetic Diagnosis	-	-
		B-H p-value	NS	NS

A within-group significant change is indicated with an arrow (up increase, down decrease) and no significant change is indicated with a dash. If both groups had a significant change in the same direction, the group with the larger change is indicated with a thicker arrow. The Benjamini-Hochberg (BH) procedure corrected p values for the difference in the change between the NGD and GD groups. No significant change is indicated with NS. The specific p value is shown when significant (<0.05)

employers suggests they see value in others having the information. The data also indicate a discernible though more modest impact on parents' actions related to the condition, perceptions of themselves, and some aspects of life planning for their child, as measured by quantitative instruments at one month and 12 months after receipt of results. Importantly, understanding of reproductive recurrence risk was modest and decreased over time, although this may not have been a priority for these parents given their age and reproductive status. Other measures of parental identity and expectations for their child, in contrast, showed little change following receipt of genetic findings. Taken as a whole, these results should be reassuring to practitioners who order genetic tests for autism.

Parents' perceptions of their responsibilities were examined in two respects: responsibility for the child's condition and responsibility to act in response to that condition. Many of the changes observed in the GD group are likely reflective of effective post-test genetic counseling and the de novo nature of the genetic diagnoses (Govaerts et al., 2017; Hayeems et al., 2021; Reiff et al., 2015). After receipt of results, parents appeared to feel less responsibility for causing their child's autism. They were more likely to see their child's condition as the result of chance and less likely to blame inherited factors (given that most variants were de novo). Interpretation of the decrease in the response of genetic/hereditary causes is limited because of the double-barrel response. Genetic refers to a variant in a gene but it may or may not be inherited from a parent. Therefore, parents may have responded in agreement to this cause because they believed there was a genetic variant in their child that contributed to their autism diagnosis and because they believed it was inherited from a parent, or responded in agreement because they agreed with one of these statements and not both. Evidence of reduced self-blame is seen in the reduction of endorsement of events for which they may have felt responsible, such as a physical accident or exposures during pregnancy. However, some residual sense of potential responsibility remained for whatever it was that caused the de novo mutation. Blame on the part of other family members, especially grandparents, was also reported to be diminished by a de novo genetic diagnosis, which may account for the widespread sharing of results by the parents.

Parents of children with a de novo genetic condition are counseled about an approximately 1% recurrence risk over population baseline (Bernkopf et al., 2022). Therefore, in this study, the parents of children with confirmed or likely de novo genetic diagnosis (98% of the sample) were counseled about the 1% recurrence risk for the same genetic cause of autism in addition to the general population risk for autism of 2% (Johannessen et al., 2021). The impact of the genetic diagnosis and counseling is demonstrated in the responses of the parents who received a de novo genetic diagnosis for their child at one-month, almost half of whom (45%) responded there was a 1-in-100 risk for a future child to be affected (the available response that was closest to the correct number). However, there were both parents who underestimated and overestimated the recurrence risk, reflecting the challenges of risk communication and the impact of personal beliefs and experiences, phenomena that have been documented in other genetic conditions (Emery et al., 1998; Mikkelsen et al., 2007; Zaccaro & Freda, 2014). Furthermore, the potentially transient nature of a more accurate understanding of recurrence risk is illustrated by the fact that only 26% of the GD group identified a 1-in-100 risk at 12 months. This underscores the importance for providers to discuss recurrence risk again at the time of a reproductive decision to enhance parental understanding and ensure parents are making fully informed reproductive choices. It is important to note that the de novo inheritance status of the genetic diagnosis was not confirmed for 27% of families at the time of results disclosure. If they did not elect to pursue parental testing to confirm inheritance status, this may have impacted their perception of recurrence risk.

The finding that a large proportion of parents shared results with their supervisors and co-workers may be linked to a perception that the findings would reduce blame and enhance understanding of the special demands of their parental roles. The increased sharing over time with the child's caregivers might indicate feelings about sharing changed over time or perhaps that opportunities to share arose over time (e.g., the start of a school year). Other studies have demonstrated that genetic test results are often shared among family members and motivations for sharing include both a sense of obligation to share information to inform family planning as well as general desire to share (Blase et al., 2007; Hunter et al., 2023; Studwell et al., 2021; Wynn et al., 2022). However, few studies have examined sharing results outside of family members, and therefore less is known about the motivations.

Respondents in the group that received a GD also reported becoming involved to a greater extent in seeking new treatments based on the genetic finding, joining research, or advocating on behalf of people with autism. Parents' interviews described the value of GD in helping to focus their involvement on a specific gene or condition rather than autism as a whole.

Parental perceptions of their identity did not reflect the findings of previous studies of genetic testing for other indications that suggested we would see lower levels of optimism, self-esteem, and self-efficacy (e.g., "There's nothing I can do about it—I have a child with a genetic disorder") (Michie et al., 2001; Oliveri et al., 2015). We found little impact on these measures. The stigma that parents thought was associated with someone who had a genetic condition associated with autism decreased in the group that received

a GD, perhaps motivated by the knowledge that their child's autism had a genetic cause. However, this impact was less stable; genetic stigma increased, though not to baseline levels, by 12 months. Although the interviews confirm relatively limited effects on parental identity, there were changes in how parents viewed and reacted to their child and their child's behavior. Several parents indicated that they saw their child with a GD result as less in control of their behavior and hence less to blame for it, leading to greater patience and understanding on the part of the parent.

Projection of future life plans by parents for their children showed some, but limited impact of genetic results, even when restricted to children under the age of 22. To the extent that an impact was detected, for parents of children in the GD group, it was associated with somewhat reduced optimism about their child having children of their own or being able to support themselves financially, perhaps due to a sense that a GD implied less amenability to treatment or continued limitations for independence. Among the parents of children in the GD group there was also a modest decrease from one to 12 months in the expectation that their child would achieve a college degree or advanced education, have romantic relationships, or have children that could be related to their observations of their child's development over the year following genetic diagnosis. Parental expectations were relatively stable for children in the NGD group, though there was a modest increase in the expectation for their child to have romantic relationships. Overall, the modest impact of a genetic diagnosis on expectations might be because parental expectations had already been shaped by their child's diagnosis and development. The average age of the children in the study was 13 years and even at baseline most parents responded that their children were unlikely or very unlikely to achieve these milestones. However, in interviews some parents indicated that the genetic results had increased their uncertainty about the future, specifically regarding co-morbidities (e.g., seizures or psychosis) associated with their child's genetic condition.

Despite its large sample size, the limitations of this study include a sample that was largely White, well-educated, and already engaged in autism research, hence not representative of all parents of children with autism. As noted, the children in this study were, on average, early adolescents and parents had completed childbearing; it is possible that testing earlier in life or predictive testing prior to the appearance of autism would have different impacts on parents. Similarly, given that most results reported back to parents were de novo variants, which are expected to account for 90% of monogenic forms of autism, with great enough statistical certainty to return as American College of Medical Genetics and Genomics (ACMG) pathogenic/likely pathogenic findings (Zhou et al., 2022), parental reactions to inherited variants might be quite different, especially regarding issues of identity and responsibility. Our data reflect parental responses at baseline and at one and 12 months after return of results; longer-term follow-up might yield different findings. Additionally, while parental responses varied little from baseline to follow up on average, there were parents whose responses were outliers for some questions, although no pattern could be identified to characterize them. Finally, this paper focuses on parental experiences; opinions about and experiences of genetic testing for people with autism may be different and should continue to be explored (Byres et al., 2023).

In the current study, there was, on average, nearly a decade between the child's diagnosis of autism and the identification of a genetic diagnosis. This elapsed time may have facilitated parental acceptance of the autism diagnosis and therefore tempered the experience of receiving a genetic diagnosis. However, prior studies of parental acceptance have not clearly demonstrated elapsed time to be associated with acceptance of the diagnosis (Milshtein et al., 2009; Yirmiya et al., 2015). One study found increased acceptance by mothers after a span of three years but did not see this same change for fathers (Milshtein et al., 2009). Another study found that the time elapsed since diagnosis was not associated with parental acceptance and fewer than half of all parents had resolved their ambivalence after a period of four years; the only trait associated with resolution was fewer negative associations of having a child with autism (Yirmiya et al., 2015) These studies do not clearly suggest that parents who have had a shorter period of time since diagnosis will have a different experience receiving a genetic diagnosis.

Taken as a whole, the results from this study suggest a discernable but relatively limited impact of a GD on parents of children with autism. These results should be reassuring to clinicians caring for children with autism who are considering ordering genetic testing as part of their overall evaluation and are consistent with other studies related to autism and in other areas of medicine that have suggested that genetic findings tend to have fewer effects—negative or positive—than often were anticipated, and most individuals do not regret the decision to have the test (Giarelli & Reiff, 2015; Hayeems et al., 2021; Hellquist & Tammimies, 2022; Lumish et al., 2017; Reed-Weston et al., 2020; Wiesner et al., 2020; Wou et al., 2018; Wynn et al., 2018a, 2018b; Zhao et al., 2019). One factor that likely influenced these findings, including reduction in feelings of responsibility for a child's condition found in this and other studies, is genetic education (Kleinendorst et al., 2020; Lucas et al., 2022; Reiff et al., 2015). Post-test genetic education may have helped parents process and understand the results and the de novo nature of most of the pathogenic variants. In this study, most participants received telephonic genetic counseling, which increasingly has been demonstrated to be an effective mode

of education that can help increase access to this service (Bradbury et al., 2011; Christensen et al., 2018; O'Reilly et al., 2007; Zierhut et al., 2018).

Finally, it should be noted that while the aggregate impact on parents was small, for each of the domains evaluated there were outliers. This may be related to pre-existing psychological conditions that have been noted to impact the experience of receiving genetic information in other studies (Wynn et al., 2018a) or other unmeasured variables. The existence of outliers underscores the importance of individualized assessment of the impact of genetic information and the availability of appropriate counseling.

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Data Availability A de-identified data set that enables the user to replicate the analysis is available upon request from the author.

Declarations

Community Engagement SPARK parent advisory board reviewed and provided comments for preliminary drafts of the survey and the final version used in the study. The Community Advisory Board for this study, comprising autistic people, parents of autistic children, and SPARK investigators, reviewed relevant portions of the qualitative data and analyses prior to submission for peer review.

Ethical Approval Julia Wynn is an employee at BillionToOne Inc. and owns options in the company. She was an employee of Columbia University Irving Medical Center at the time this study was conducted. This study was approved by the New York Psychiatric Institute IRB.

Informed Consent Informed consent was obtained for all participants prior to the survey or interview completion.

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