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Down Syndrome Cures: Perspectives of People with Down Syndrome and Their Parents

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Down Syndrome Cures: Perspectives of People with Down Syndrome and Their Parents

ABSTRACT

Down syndrome (DS) research is advancing rapidly, yet efforts have raised ethical questions. This mixed methods study describes views of people with DS (self-advocates) and their parents regarding medical interventions for DS. Responses from 35/171 (20.5%) self-advocates and 430/867 (49.6%) parents showed majority of self-advocates were glad they have DS (27/35; 77.1%) and liked who they are (33/35; 94.3%), but did want to learn faster (23/35; 65.7%). Parents much more commonly agreed with a willingness to give medications to prevent Alzheimer's disease (427/429; 99.5%) or blood cancer (428/430; 99.5%) as compared with a medicine to cure DS (225/425; 52.9%).Qualitative comments intertwined DS with identity yet indicated desire for improved quality of life and opportunities. Responses decoupled DS itself from the complications of DS with treatment of complications being more acceptable.

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INTRODUCTION

Down syndrome (DS) is the most common genetic cause of intellectual disability (de Graaf, Buckley and Skotko, 2017). As a common target of prenatal diagnosis and preimplantation genetic diagnosis technology, the DS community has become an archetypal subject of ethical discussions on quality of life, normative functioning and biomedical advancement (Kaposy, 2013; Boardman, 2014; Harmon, 2005). The focus of these ethical discussions has recently expanded to include gene editing and cognitive enhancement with increasing push for the development of these technologies for DS (Laidman, 2014). While clinical trials targeting various receptors for improved cognition have not shown efficacy to date (Hart et al., 2017), advancements in gene editing technology like CRISPR, have increased optimism in future treatments for DS that may include both genetic and pharmacologic interventions (Halliday & Mallucci, 2019).

Responding to research developments, headlines like “Could there be a cure? Breakthrough prompts Down syndrome soul searching” (Aleccia, 2013) grace the media and highlight the controversy over DS treatments. In an attempt to understand parents’ views on hypothetical treatments for DS, one anonymous online study found that while the majority of parents supported using hypothetical interventions for DS, a wide variance of support existed depending on the target of the intervention and its potential impact on the person (Michie & Allyse, 2019). This online study was unable to evaluate the association of demographic and socioeconomic characteristics with responses. Further qualitative analysis of the parental responses from the same study indicated that the principal concern of parents were the theoretical risks of treatment (Riggan et al., 2020). Additionally, the views of people with DS themselves on such treatments have yet to be explored, which is a key gap in this area of study.

To address limitations in prior research, our study aimed to describe the views of the DS community towards the development of treatments to cure DS or improve cognitive function in absence of risk and describe factors that may be associated with such views on treatment. We report the results from two mixed method online surveys, one for people with DS (herein termed self-advocates) and one for parents and/or guardians of people with DS (herein termed parents) on their views of treatments to cure DS or improve cognitive function.

METHODS

Ethics Statement

This study was approved by the XXX Institutional Review Board (IRB) (ID 14-003036) as a minimal risk study. Protocol-approved passive consent was obtained from all study participants.

Survey development

Two separate surveys, one for parents and one for self-advocates, were developed with input from academic experts in DS and informed by previous DS surveys (Skotko, Levine, and Goldstein, 2011, p. 2360; Skotko, Levine, Macklin, and Goldstein, 2011). Surveys included components of demographics/characteristics, DS self-concept, and parental level of agreement on willingness to use hypothetical treatments for DS or conditions commonly associated with DS. Four independent focus groups of 18 adults with DS and 45 parents, organized through the DS Association of Minnesota, informed iterative survey development and edits. Surveys were designed to be low-burden and focus groups confirmed acceptability.

Validity and Reliability Testing

Recruitment for survey validation occurred through emails sent out by DS Associations of Minnesota and Greater Charlotte, North Carolina with a link that assessed eligibility and forwarded eligible email addresses to the Survey Research Center (SRC) at our institution. To

evaluate reliability, those who responded to the initial survey received identical surveys 4 weeks later. A total of 13 self-advocates and 74 parents responded to both test and retest surveys. All data were de-identified by the SRC prior to being released to investigators.

Reliability was evaluated by associating test-retest responses for each of 34 individual questions for parents, each with a 7-point Likert scale, and 9 questions for self-advocates, each with a 5-point Likert scale. Reliability for a given question was defined a priori as >80% of participants responding with ≤ 1 point difference on the test and retest surveys. Only one question required editing, a parental survey question regarding prenatal interventions for DS and cognitive functioning. The question was edited and a subsequent focus group of 10 parents confirmed improved clarity of the question. The final survey for self-advocates had a Flesh-Kincaid grade level of 3 and an Automated Readability Index of grade 1-2. The final survey for parents had a Flesh-Kincaid grade level of 10 and an Automated Readability Index of grade 8-9. The responses from our pilot test-retest study were not included in the final analysis.

Data Collection

Survey participants were recruited from the National Institutes of Health (NIH) DS Registry, DS-Connect (https://dsconnect.nih.gov). DS-Connect sent emails to 2772 email addresses registered to parents and/or guardians of someone with DS and 11 email addresses of self-advocates with a link that assessed eligibility and enabled them to provide their email address to the SRC in order to send the survey. DS-Connect also included the recruitment link in their annual newsletter. The recruitment link allowed parents to provide their child's email address for participation. In total, the SRC received 171 email addresses for self-advocates and 867 email addresses for parents. Survey was open for response between November 2016 and December 2017 as surveys were incrementally sent. Participants who completed the survey were entered into a drawing for a prize of a miniature electronic tablet.

Participants

Participants were eligible for study inclusion if they were a parent and/or guardian of someone with DS (herein referred to as parents) or a person of DS of at least 12 years of age. The age cutoff for self-advocates was consistent with prior studies (Skotko, Levine and Goldstein, 2011) and based on literature of DS and developmental ability to make complex social comparisons (Grieco et al., 2015). Self-advocate survey instructions indicated that a trusted person could help write answers but all answers must be in the person's own words.

Of the electronic surveys sent, 35/171 (20.5%) self-advocates and 430/867 (49.6%) parents completed the survey (Consort diagram, Figure). Characteristics of self-advocates and parents are displayed in Table 1. Parent and self-advocate respondents were mostly non-Hispanic (400/430; 93.0% and 31/35; 88.6% respectively) and white (387/430; 90.0% and 30/35; 85.7% respectively) and were well-distributed geographically across the United States. The majority of parent respondents were highly educated (378/430; 87.9% with college degree or higher) and nearly all participants (400/430; 93.0%) indicated that the person with DS resided with the parent.

Data Analysis

Qualitative Analysis

Four survey questions (2 self-advocate and 2 parental) allowed opportunity for respondents to give detail as to the rationale for their responses to quantitative questions (self-advocate question on self-perception and on intelligence or parental questions on utilizing medicine for a cure for DS and on increasing intelligence). Qualitative analysis of these responses was performed to add depth of understanding to the responses. All qualitative responses were grouped by the respondent's level of agreement to the corresponding question (agree, neutral, disagree). Qualitative responses were analyzed using a worldview of pragmatism and a

framework of social constructivism, acknowledging that reality is socially defined through the experiences of self-advocates and their parents (Creswell and Plano Clark, 2017; Evans, Coon, and Ume, 2011). Two authors, one (XX) a former board member of DS Association of Minnesota and sibling of a person with DS and another (XX) a primary care physician with clinical and research expertise in family-centered care, independently reviewed all qualitative responses, coded responses inductively, identified key themes independently, compared themes and developed codebook of final themes and representative quotes by consensus.

Quantitative Analysis

A composite functional activity score (range 11 to 77), developed by Skotko et al. (2011), was calculated for each person with DS whose parent provided responses to all 11 functional activities by summing the 7-point Likert responses of each activity (e.g., walking, preparing meals, and going on dates). Any response of ‘‘not applicable’’ was assigned a score of ‘‘1’’. To derive a score that is not correlated with age, we calculated the “developmental quotient of functional abilities”, as described by de Graaf et al. (2019), by dividing the fore-mentioned composite score by an age-related expected score, multiplied by 100. The expected scores were obtained by fitting a cubic regression model to predict the composite functional activity score as a function of age (age >30 years truncated at age 30). The R^2 of our model (0.57) was comparable to those reported for two cohorts in the prior paper (R^2 = 0.63 for the United States and R^2 = 0.58 for the Netherlands). As stated by de Graaf et al. (2019), a higher score implies relatively well-developed functional abilities, as perceived by parents.

The survey responses were summarized using standard descriptive statistics. Characteristics were evaluated for an association with agreement (response of 5-7 vs 1-4 on the 7-point Likert scale) with willingness to give a hypothetical side-effect free medication to their child a) causing them to no longer have DS and b) increasing their intelligence significantly, respectively.

Associations were evaluated using the chi-square test for categorical variables, two-sample t-test for continuous variables, and Wilcoxon rank sum test for ordinal variables. A multivariable logistic regression model was fit to identify characteristics significantly associated with agreeing with each statement above (a and b, respectively) by including all variables with a p-value less than 0.20 based on univariate analysis. Prior to fitting the multivariable model an additional category was created for each variable with missing data and the median value was imputed for continuous or ordinal data with missing data. All calculated p-values were two-sided and p-values less than 0.05 were considered statistically significant. Analysis was performed using the SAS version 9.4 software package (SAS Institute, Inc.; Cary, NC).

RESULTS

Self-advocate opinions on DS

Self-advocates' opinions of DS are detailed in Table 2, with a majority indicating a 'Yes' or 'Most of the time' response that they are glad they have DS (27/35; 77.1%), like who they are (33/35; 94.3%), like how they look (33/35; 94.3%), and are healthy (33/35; 94.3%). The majority of respondents (30/35; 85.7%) gave a qualitative response as to why they gave the response they did to the question, "Are you glad you have DS?" There were three main themes of responses: 1) Identity/personality 2) Quality-of-life considerations and 3) Social/societal statements. Many respondents regarded DS as either a negative or positive part of their identity.

"It's part of me and I like who I am"

"I don't want to be special needs."

Statements about quality of life included comments on happiness, independence, and challenges.

"I would like to change being able to do more things on my own."

"Because I make everyone happy and smile. I am happy and love my family."

"Down syndrome is good. I have many opportunities."

Statements geared towards the social and societal aspects of DS included comments related to stigma, friends, and pop culture.

"I do not like DS people make fun of that word."

"2 of my friends who have it too. Plus the show I've been watching Born This Way is about DS too."

"I really want to be like my sister."

Self-advocate opinions on increasing intelligence

Most self-advocates, 23/35 (65.7%), wished they could learn faster. The majority (32/35; 91.4%) provided a comment regarding their response to the question "Do you wish you could learn faster?" Respondents made quality-of-life statements, specifically wanting learning to be easier.

"I went to college to get an associate degree but the math and English are too hard. That makes me sad."

"I like to read and study things but can't explain what I mean and other things like money skills are hard."

"Sometimes learning is frustrating."

Other comments described social concerns, e.g. being behind their peers.

"So I could be a better worker."

"I wish it was easier to do some things like my brother."

In contrast to responses regarding their opinions of having DS, there were no comments on identity.

Parental Responses

The range of agreement to parents willingness to give a hypothetical side-effect free medication to their child to no longer have DS, improve language abilities, improve memory, change appearance, change personality, increase intelligence slightly, increase intelligence significantly, prevent Alzheimer's disease, or prevent blood cancer are detailed in Table 3. Parents much more commonly agreed with giving medications to prevent Alzheimer's disease (427/429; 99.5%) or blood cancer (428/430; 99.5%) as compared with a medicine to cure DS (225/425; 52.9%).

Parental opinions on a cure for DS

Agreement to wanting to give a medication to cure DS was given by 225 of 425 (52.9%) parents, including 35.5% who strongly agreed with this statement. Factors that were univariately significantly associated with agreeing with this statement include parental male gender (p=0.002), being the biological parent (p=0.016), religious affiliation other than Christianity or Judaism (p=0.02), and the person with DS having higher extent of educational/learning difficulties (p<0.001) (Table 4). In addition, the mean developmental quotient of functional abilities score was significantly lower for children of parents who did versus did not agree with this statement (mean (SD), 97.1 (21.1) vs. 103.0 (20.9); p=0.005). In the multivariable analysis including all of the variables with a p-value less than 0.20 based on

univariate analysis, only parental male gender and the extent of educational/learning difficulties retained statistical significance ($p<0.05$).

The majority of parents (404/430; 94.0%) included a qualitative response regarding their response about using a side-effect free medication to cure DS. Four themes emerged from the responses and are detailed in Table 5: 1) Identity/personality 2) Social barriers/contributions to society 3) Quality-of-life considerations and 4) Uncertainty about what a cure would look like.

Those that indicated they would not give their child a side-effect free medication to no longer have DS responded chiefly with themes of identity/personality. Participants also commented on a desire to improve quality of life, but not by removing the DS. Those that agreed with giving a hypothetical medication often gave responses within the theme of quality-of-life considerations. Social comments focused on the stigma and social challenges associated with DS. Comments on identity/personality and uncertainty were sparse.

Parental opinions on increasing intelligence

Agreement to willingness to give a medicine to increase intelligence significantly was endorsed by 369 of 429 (86.0%) parents, including 59.4% who strongly agreed with this statement. Based on the univariate analysis, parents who rated their child as having a higher extent of educational/learning difficulties ($p=0.006$) or significant behavior problems ($p=0.013$) were more likely to agree with this statement (Table 4). In the multivariable analysis including all of the variables with a p-value less than 0.20 based on univariate analysis, only extent of educational/learning difficulties retained statistical significance ($p<0.05$).

The majority of respondents (407/430; 94.7%) included a qualitative comment about their response toward increasing intelligence. Responses were coded into 6 categories as detailed in Table 5 : 1) Identity/personality 2) Social barriers/contributions to society 3) Quality-of-life

considerations 4) Uncertainty about what “increased intelligence” means 5) Life values and 6) Everyone wants increased intelligence

Those that responded that they would not want to increase their child’s intelligence offered responses with themes on the life values and identity/personality of their child. Parents who responded that they were neutral about increasing intelligence offered responses on life values and identity/personality, similar to those that responded negatively. Additional responses corresponded to the themes of quality-of-life considerations and uncertainty. Parents who responded positively to giving a medication to increase intelligence in their child made comments within the theme of quality of life. In addition, comments on increased intelligence being a universal value were offered by this group of parental responses. Illustrative quotes are detailed in Table 5.

DISCUSSION

This study on views of potential interventions for DS includes the valuable and needed opinions of self-advocates. Similar to another study (Skotko, Levine and Goldstein, 2011, p. 2360), our study confirms that people with DS report high self-esteem and quality of life. Our study additionally found that self-advocates were comfortable with having DS, perceiving it as part of their identity. They did indicate a desire, however, to increase intelligence and learn more easily.

The responses of parents decoupled intelligence or medical/social complications of DS from DS itself, indicating more willingness to give medication to treat a complication (like Alzheimer’s disease or cancer), or even increase intelligence rather than removing DS. These findings are similar to a 2014 study from a different healthcare system (Canada) where the majority (61%) of parents would reverse intellectual disability but only 41% would 'cure' DS if it were possible (Inglis et al., 2014). While the Inglis et al. (2014) study analyzed responses relative to the severity of DS for the participants’ children, our study further explored how preferences toward

treatments for DS were associated with other respondent characteristics, such as gender, race/ethnicity, geography, and religion.

Many qualitative comments viewed DS as a key part of the fabric of their child and feared that changing that would also take away positive qualities of their child. Parents, did, however, indicate a general desire to help reduce the frustrations of their child. Therefore, while many indicated that increasing intelligence may help reduce frustration and improve independence and opportunities for their child, there was also a tension noted with differing views of the universal desire of higher intelligence vs. the lack of society's acceptance of intellectual diversity.

Our findings are similar to a previous study where roughly half of parents indicated that they would give a medication that would prenatally silence the genes associated with DS (Michie & Allyse, 2019). While qualitative analysis of parental responses to that study (Riggan et al., 2020) indicated that parents were concerned about the risks associated with the intervention, our study indicates a similar rate of hesitancy toward elimination of DS even absent of risks. While parents indicate much more positive acceptance of treatments that may reduce the risk of diseases associated with DS or even of improving cognitive abilities, there continues to be hesitancy to remove DS itself.

Our study investigated respondent characteristics associated with agreement toward willingness to give a medication to cure DS and increasing intelligence significantly. Agreement with willingness to give a medication to cure DS was significantly associated with both parental male gender and the extent of educational/learning difficulties based on multivariable analysis. Agreement with willingness to give a medicine to increase intelligence significantly was significantly associated with the extent of learning difficulties and behavior problems, on univariate analysis, but not functional abilities or health problems. This finding may reflect that

parents who see their child's quality of life impacted by loss of function or other health problems may perceive more benefit to be gained from a medicine that would cure DS due to its impact on more than intelligence. The age of the child with DS was not significantly associated with willingness to give a medication to cure DS or increase intelligence significantly, so acceptance of the person or reluctance to cure DS may not be a factor of age. Another study (Skotko, Levine, and Goldstein 2017, p. 2340) similarly did not find an association between the age of the child and parental regret of having their child with DS. Respondents of Judeo-Christian religion were less likely to agree with giving a medicine to cure DS. Certainly, religious paradigms may have influenced opinions towards treating DS similar to some members of the Christian faith previously expressing concerns with some genetic technologies (Sullivan & Salladay, 2007). It is interesting, however, that many identifying as nonreligious also object to curing DS; so religion alone is not influencing the decision. Since these quantitative analyses are exploratory, these concepts require further investigation. While male and biological parents were more likely to agree with willingness to give a medication to cure DS, these findings need to be interpreted with caution and further validated given the limited number of male and non-biological parent respondents.

The qualitative responses give further insight into the perspective of parents. Parents that reported wanting to cure their child's DS commented on a desire for improved quality of life. However, parental concerns concomitantly pointed to societal issues that impact their child, for example, opportunities for education and employment. While treating DS may improve the quality of their child's life, many noted that further investment in societal considerations, like increased funding for education, would be beneficial. Similarly, parents recognized a need for societal change, specifically a need to embrace diversity, as an important aspect of helping their child thrive.

Our study has many implications for DS research. While most medical diseases, like diabetes, are unwanted, that sentiment is not uniformly embraced by those impacted by DS. In fact, most self-advocates reported being glad they have DS and slightly more than half of parents would agree to a medicine to cure DS despite a treatment not having any side effects. This suggests that while DS presents many challenges, DS likely provides advantages as well (Skotko, Levine, Macklin and Goldstein, 2016; Armstrong, 2015). For example, behavioral research has described a social advantage, as children with DS seek out social interactions more frequently and display positive facial expressions more frequently than typical children (Grieco et al., 2015). As medical research is advanced, it will be important to recognize that those impacted by DS find the complications of DS, rather than DS itself, to be most troublesome.

Strengths and Limitations

Our study utilized a national NIH DS registry to identify participants. The use of the registry allowed for control of survey access by sending one survey to each email address. The DS registry is the best tool currently available to researchers as a population-representative database for DS does not currently exist. While this registry is a reliable source for identifying members of the DS community, its use may bias responses toward views of those more interested in research efforts. While parental respondents were geographically diverse, the respondents were generally non-Hispanic white with a high level of education, which may have limited the power to detect significant differences in views related to other demographic characteristics. As our study utilized a convenience sample that does not fully represent the full community, caution should be maintained prior to generalizing the findings to the entire DS community.

Survey questions were designed to target opinions on the benefits of theoretical treatments for DS absent of risk, which is not necessarily realistic. If treatments for DS were developed, actual

clinical decision-making would be much more nuanced. This design, however, was intentional to focus on the views of the DS community towards the value of treatments themselves decoupled from worries about risk. Quantitative analyses were exploratory in nature and should be used as starting points for further investigation.

The self-advocate survey limited participation to those able to respond themselves thereby excluding those most impacted by DS. This is an inherent limitation in seeking their personal views. The views of self-advocates, as the people most impacted by DS, is critical and should continue to be investigated as ongoing treatments directed toward DS are pursued.

Conclusions

Our study finds that self-advocates are overwhelmingly glad they have DS, while parents exhibit a wide spectrum of opinions regarding interventions for DS and intelligence. Overall, there is a decoupling of the perceptions of DS itself from the perceptions of the complications of DS, such as intelligence, medical complications like Alzheimer's disease, or societal stigma. Both self-advocates and parents were more likely to be interested in treatments for the sequelae rather than DS itself. In addition to continuing research toward medical treatments for DS, simultaneous efforts to improve societal opportunities and attitudes towards DS will be important to help improve quality of life for people with DS and their families.

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FIGURE LEGEND

Consort diagram for survey data included in analysis.

Figure

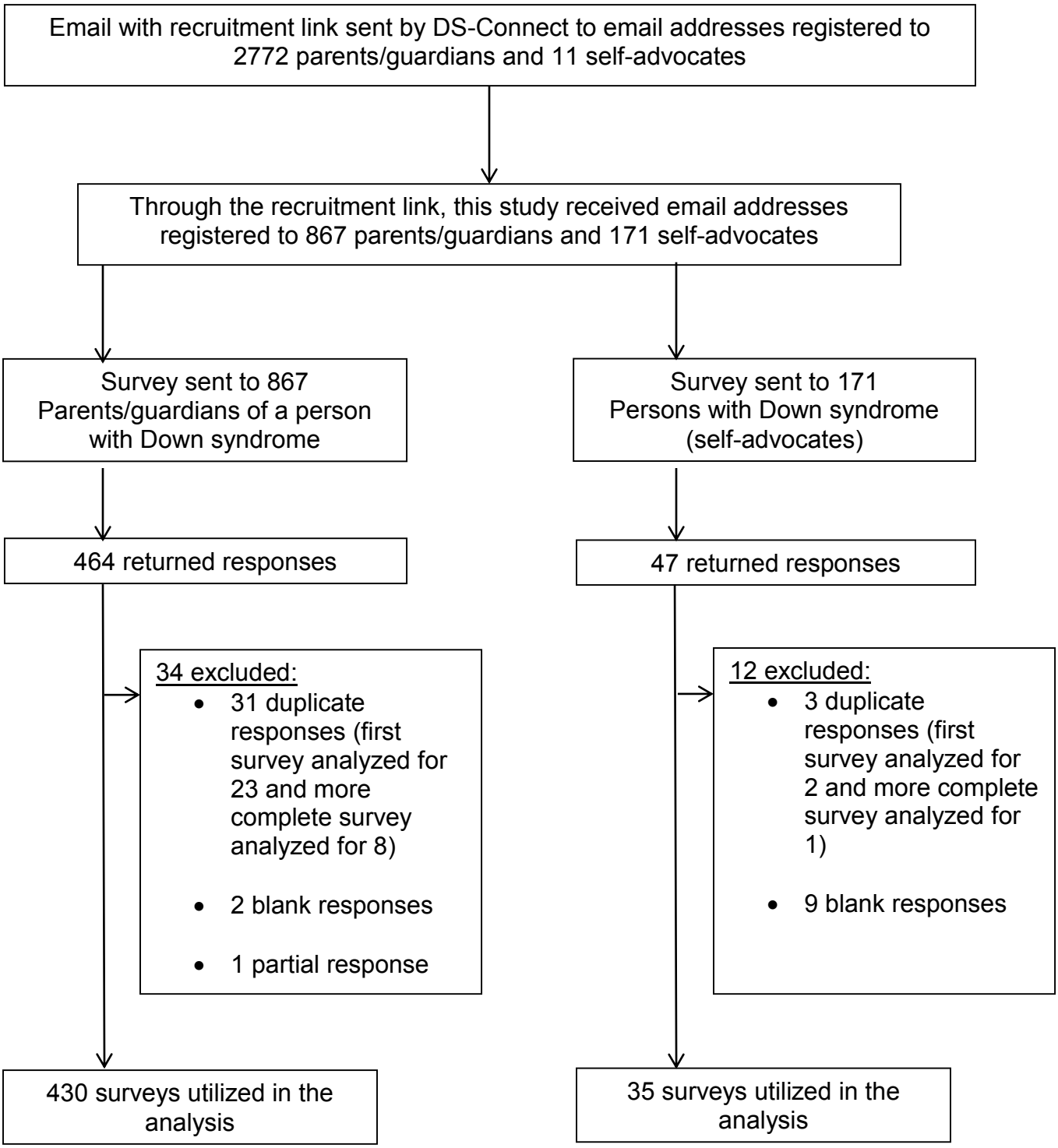

Table 1. Characteristics of Survey Participants including Self-Advocates (People with Down Syndrome) and Parents/Guardians of People with Down Syndrome

Characteristic	Self-Advocates (N=35)	Parents/Guardians (N=430)
Age (years)		
Respondent, Mean (SD; range)	24.1 (8.6; 13-48)	47.8 (10.8; 22-88)
Person with DS, Mean (SD; range)		13.4 (11.5;1-58)
Gender of person with DS, n (%)		
Female	19 (54.3%)	197 (45.8%)
Male	16 (45.7%)	231 (53.7%)
Not reported	0 (0.0%)	2 (0.5%)
Gender of respondent, n (%)		
Female	19 (54.3%)	359 (83.5%)
Male	16 (45.7%)	69 (16.0%)
Not reported	0 (0.0%)	2 (0.5%)
Respondent is biological parent, n (%)	Not applicable	
Yes		413 (96.0%)
No		14 (3.3%)
Not reported		3 (0.7%)
Marital status of respondent, n (%)	Not asked	
Married		379 (88.1%)
Single		6 (1.4%)
Divorced		24 (5.6%)
Widowed		10 (2.3%)
Unmarried, but with partner		11 (2.6%)
Race of respondent, n (%)		
White	30 (85.7%)	387 (90.0%)
Black or African American	0 (0.0%)	6 (1.4%)
Asian	0 (0.0%)	12 (2.8%)
American Indian or Alaskan native	1 (2.9%)	1 (0.2%)
Multi-racial	1 (2.9%)	10 (2.3%)
Other	0 (0.0%)	4 (0.9%)
Prefer not to disclose or not reported	3 (8.6%)	10 (2.3%)
Ethnicity of respondent, n (%)		
Hispanic	3 (8.6%)	20 (4.7%)
Not Hispanic	31 (88.6%)	400 (93.0%)
Prefer not to disclose or not reported	1 (2.9%)	10 (2.3%)
Religious affiliation of respondent, n (%)		
Christianity	29 (82.9%)	300 (69.8%)
Judaism	1 (2.9%)	17 (4.0%)
Islam	0 (0.0%)	1 (0.2%)
Hindu	0 (0.0%)	4 (0.9%)
Buddhism	0 (0.0%)	2 (0.5%)
Secular/Nonreligious/Agnostic/Atheist	3 (8.6%)	71 (16.5%)
Prefer not to disclose	1 (2.9%)	21 (4.9%)
Other	0 (0.0%)	7 (1.6%)
Not answered	1 (2.9%)	7 (1.6%)

Table 1. Characteristics of Survey Participants including Self-Advocates (People with Down Syndrome) and Parents/Guardians of People with Down Syndrome

Characteristic	Self-Advocates (N=35)	Parents/Guardians (N=430)
Residency of respondent, n (%)		
Northeast U.S.	4 (11.4%)	72 (16.7%)
Midwest U.S.	5 (14.3%)	99 (23.0%)
Southern U.S.	16 (45.7%)	143 (33.3%)
West U.S.	8 (22.9%)	89 (20.7%)
Non-U.S.	1 (2.9%)	19 (4.4%)
Not reported	1 (2.9%)	8 (1.9%)
Highest educational status of respondent, n (%)		
1st-8th grade	3 (8.6%)	0 (0.0%)
In high school	11 (31.4%)	0 (0.0%)
Completed high school	17 (48.6%)	43 (10.0%)
In college	2 (5.7%)	0 (0.0%)
College/University degree	1 (2.9%)	196 (45.6%)
Master's degree	0 (0.0%)	130 (30.2%)
Doctorate level degree	0 (0.0%)	52 (12.1%)
Prefer not to disclose or Not reported	1 (2.9%)	9 (2.1%)
Living place of person with DS, n (%)		
With parent/guardian	32 (91.4%)	400 (93.0%)
Lives elsewhere	2 (5.7%)	24 (5.6%)
Not reported	1 (2.9%)	6 (1.4%)

Abbreviations: DS, Down Syndrome; SD, Standard Deviation; IQR, Interquartile Range

Table 2. Self-advocate answers to quantitative questions about their experience with Down syndrome

	Self-Advocates (N=35)
Are you glad you have DS?	
Yes	19 (54.3%)
Most of the time	8(22.9%)
Once in a while	3 (8.6%)
No	5 (14.3%)
Are you sad about your life?	
Yes	1 (2.9%)
Most of the time	1 (2.9%)
Once in a while	6 (17.1%)
No	27 (77.1%)
Is it easy to make friends?	
Yes	22 (62.9%)
Most of the time	8 (22.9%)
Once in a while	3 (8.6%)
No	1 (2.9%)
Not answered	1 (2.9%)
Do you like who you are?	
Yes	29 (82.9%)
Most of the time	4 (11.4%)
Once in a while	1 (2.9%)
No	1 (2.9%)
Do you wish you did not have DS?	
Yes	9 (25.7%)
Once in a while	10 (28.6%)
No	16 (45.7%)
Do you like how you look?	
Yes	29 (82.9%)
Most of the time	4 (11.4%)
Once in a while	1 (2.9%)
Not answered	1 (2.9%)
Do you wish you could learn faster?	
Yes	19 (54.3%)
Most of the time	4 (11.4%)
Once in a while	9 (25.7%)
No	3 (8.6%)
Do you think you are healthy?	
Yes	30 (85.7%)
Most of the time	3 (8.6%)
No	2 (5.7%)
Do you wish it was easier to speak?	
Yes	18 (51.4%)
Most of the time	6 (17.1%)
Once in a while	4 (11.4%)
No	7 (20.0%)

Abbreviations: DS, Down Syndrome

Table 3. Responses of parents/guardians to a 9-part question regarding willingness to give a hypothetical side-effect free medication to their child

	Assuming such a medication exists and has NO side effects, I would want to give my son or daughter a medication that has the sole purpose of:								
7-point response scale	Causing them to no longer have Down syndrome	Improving their language abilities	Improving their memory	Changing their appearance so that they do not look like they have Down syndrome	Changing their personality	Increasing their intelligence slightly	Increasing their intelligence significantly	Preventing Alzheimer's disease, keeping in mind that people with Down syndrome are more likely to develop Alzheimer's disease	Preventing blood cancer, keeping in mind that people with Down syndrome are more likely to develop blood cancers (i.e. leukemia)
1=Strongly disagree	54 (12.7%)	3 (0.7%)	3 (0.7%)	152 (35.5%)	278 (64.8%)	6 (1.4%)	7 (1.6%)	0 (0.0%)	0 (0.0%)
2	24 (5.6%)	1 (0.2%)	1 (0.2%)	46 (10.7%)	55 (12.8%)	7 (1.6%)	5 (1.2%)	0 (0.0%)	0 (0.0%)
3	27 (6.4%)	2 (0.5%)	1 (0.2%)	35 (8.2%)	35 (8.2%)	7 (1.6%)	8 (1.9%)	0 (0.0%)	0 (0.0%)
4=Neutral	95 (22.4%)	6 (1.4%)	29 (6.8%)	109 (25.5%)	37 (8.6%)	44 (10.3%)	40 (9.3%)	2 (0.5%)	2 (0.5%)
5	41 (9.6%)	21 (4.9%)	23 (5.4%)	30 (7.0%)	16 (3.7%)	72 (16.9%)	59 (13.8%)	5 (1.2%)	16 (3.7%)
6	33 (7.8%)	36 (8.4%)	40 (9.3%)	15 (3.5%)	5 (1.2%)	56 (13.1%)	55 (12.8%)	26 (6.1%)	31 (7.2%)
7=Strongly agree	151 (35.5%)	359 (83.9%)	332 (77.4%)	41 (9.6%)	3 (0.7%)	235 (55.0%)	255 (59.4%)	396 (92.3%)	381 (88.6%)
Not answered	5	2	1	2	1	3	1	1	0

Table 4. Characteristics evaluated for an association with agreeing to give a hypothetical side-effect free medication to their child (A) causing them to no longer have DS or (B) increasing their intelligence significantly.

	A.		B.	
Characteristic	**N (%) who endorsed agreement**	**p value†**	**N (%) who endorsed agreement**	**p value†**
Respondent characteristic				
Age quartiles (years)‡		0.89		0.56
Q1: ≤40	56/104 (53.8%)		90/106 (84.9%)	
Q2: 40-46	46/93 (49.5%)		85/94 (90.4%)	
Q3: 47-55	63/116 (54.3%)		102/118 (86.4%)	
Q4: ≥55	58/109 (53.2%)		90/108 (83.3%)	
Not reported	2/3 (66.7%)		2/3 (66.7%)	
Gender		0.002		0.18
Male	47/67 (70.1%)		63/69 (91.3%)	
Female	177/356 (49.7%)		305/358 (85.2%)	
Not reported	1/2 (50.0%)		1/2 (50.0%)	
Respondent is biological parent		0.016		0.10
Yes	221/409 (54.0%)		357/412 (86.7%)	
No	3/14 (21.4%)		10/14 (71.4%)	
Not reported	1/2 (50.0%)		2/3 (66.7%)	
Married		0.76		0.42
Yes	199/374 (53.2%)		327/378 (86.5%)	
No	26/51 (51.0%)		42/51 (82.4%)	
Race		0.36		0.85
White	200/382 (52.4%)		332/388 (86.0%)	
Not white	20/33 (60.6%)		28/33 (84.8%)	
Not reported	5/10 (50.0%)		9/10 (90.0%)	
Ethnicity		0.17		0.59
Hispanic	13/19 (68.4%)		18/20 (90.0%)	
Not hispanic	207/396 (52.3%)		342/399 (85.7%)	
Not reported	5/10 (50.0%)		9/10 (90.0%)	
Residency		0.17		0.24
Northeast U.S.	41/71 (57.7%)		58/71 (81.7%)	
Midwest U.S.	52/99 (52.5%)		81/99 (81.8%)	
Southern U.S.	77/141 (54.6%)		123/143 (86.0%)	
West U.S.	37/87 (42.5%)		81//89 (91.0%)	
Non-U.S.	13/19 (68.4%)		19/19 (94.7%)	
Not reported	5/8 (62.5%)		8/8 (100%)	
Highest education status		0.06		0.62
Completed high school	17/42 (40.5%)		34/43 (79.1%)	
College/university degree	101/194 (52.1%)		171/195 (87.7%)	
Master's degree	72/129 (55.8%)		112/130 (86.2%)	
Doctorate level degree	31/51 (60.8%)		45/52 (86.5%)	
Not reported	4/9 (44.4%)		7/9 (77.7%)	

Characteristic	A. N (%) who endorsed agreement	A. p value†	B. N (%) who endorsed agreement	B. p value†
Religious affiliation		0.020		0.36
Christianity or Judaism	158/314 (50.3%)		269/316 (85.1%)	
Islam, Hindu, Buddhism, Other	12/14 (85.7%)		12/14 (85.7%)	
Secular/Non-religious/Agnostic/Atheist	42/71 (59.2%)		65/71 (91.5%)	
Not reported	13/26 (50.0%)		23/28 (81.2%)	
Person with DS characteristic				
Living arrangement		0.89		0.87
With parent/guardian	208/395 (52.7%)		343/400 (85.8%)	
Lives elsewhere	13/24 (54.2%)		20/23 (87.0%)	
Not reported	4/6 (66.7%)		6/6 (100%)	
Gender		0.26		0.85
Male	127/229 (55.5%)		197/230 (85.7%)	
Female	97/194 (50.0%)		170/197 (86.3%)	
Not reported	1/2 (50.0%)		2/2 (100%)	
Age quartiles (years)‡		0.78		0.19
Q1: ≤4	58/105 (55.2%)		91/107 (85.0%)	
Q2: 5-10	44/91 (48.4%)		84/94 (89.4%)	
Q3: 10-19	61/113 (54.0%)		102/113 (90.3%)	
Q4: ≥20	54/105 (51.4%)		81/104 (77.9%)	
Not reported	8/11 (72.7%)		11/11 (100%)	
Developmental quotient of functional abilities quartiles^		0.003		0.15
Q1: ≤86.1	62/99 (62.6%)		90/100 (90.0%)	
Q2: 86.2-99.4	59/101 (58.4%)		86/101 (85.1%)	
Q3: 99.5-115.9	41/99 (41.4%)		85/102 (83.3%)	
Q4:≥ 116.0	46/100 (46.0%)		83/100 (83.0%)	
Not reported	17/26 (65.4%)		25/26 (96.2%)	
Extent of significant health problems		0.08		0.60
1=Not at all	36/81 (44.4%)		69/80 (86.3%)	
2	64/114 (56.1%)		99/115 (86.1%)	
3	19/52 (36.5%)		48/54 (88.9%)	
4=Somewhat	41/74 (55.4%)		64/75 (85.3%)	
5	32/48 (66.7%)		41/48 (85.4%)	
6	19/30 (63.3%)		27/31 (87.1%)	
7=Very much	10/21 (47.6%)		16/21 (76.2%)	
Not reported	4/5 (80.0%)		5/5 (100%)	
Extent of significant educational/ learning difficulties		<0.001		0.006
1=Not at all	1/4 (25.0%)		4/4 (100%)	
2	7/16 (43.8%)		12/16 (75.0%)	
3	14/30 (46.7%)		24/29 (82.8%)	
4=Somewhat	39/89 (43.8%)		72/92 (78.3%)	
5	42/92 (45.7%)		79/92 (85.9%)	
6	61/99 (61.6%)		89/100 (89.0%)	

Characteristic	A. N (%) who endorsed agreement	A. p value†	B. N (%) who endorsed agreement	B. p value†
7=Very much	56/89 (62.9%)		83/90 (92.2%)	
Not reported	5/6 (83.3%)		6/6 (100%)	
Extent of significant behavior problems		0.19		0.013
1=Not at all	56/103 (54.4%)		81/102 (79.4%)	
2	38/88 (43.2%)		75/90 (83.3%)	
3	26/53 (49.1%)		47/55 (85.5%)	
4=Somewhat	48/90 (53.3%)		82/90 (91.1%)	
5	30/46 (65.2%)		45/46 (97.8%)	
6	16/29 (59.3%)		23/28 (82.1%)	
7=Very much	7/12 (58.3%)		10/12 (83.3%)	
Not reported	4/6 (66.7%)		6/6 (100%)	

†Associations were evaluated using the chi-square test for categorical variables and the Wilcoxon rank sum test for ordinal variables (higher education status, variables reported as quartiles, and variables with a 7-point Likert scale), and the two-sample t-test for continuous variables reported in the additional footnotes (age and developmental quotient of functional abilities score). The results for the "Not reported" category were ignored when evaluating each association.

‡There was no significant difference in the mean age of the parents (mean (SD), 48.0 (10.5) vs 47.6 (11.1) years; p=0.76) or age of the persons with DS (13.0 (10.8) vs. 14.1 (12.3) years; p=0.31) between those parents who did vs did not agree with statement A. Likewise, there was no significant difference in the mean age of the parents (mean (SD), 47.5 (10.4) vs 49.0 (12.7) years; p=0.40) or age of the persons with DS (12.9 (11.0) vs. 16.2 (13.4) years; p=0.08) between those parents who did vs did not agree with statement B.

^The mean developmental quotient of functional abilities score was significantly lower for children of parents who did vs did not agree with statement A (mean (SD), 97.1 (21.1) vs. 103.0 (20.9); p=0.005). There was no significant difference in this mean score between those parents who did vs did not agree with statement B (mean (SD), 99.3 (21.1) vs. 103.4 (21.2); p=0.17).

Abbreviation: DS, Down Syndrome

Table 5. Parental Qualitative Responses to Reasons for Answering with Agree, Disagree, or Neutral to Giving a Side-Effect Free Medication

Opinions on Medicine to No Longer Have Down Syndrome		
Disagree with Medicine		
You indicated that you would not want to give your son or daughter a drug so that they no longer have Down syndrome. In the space below, please give any reasons you have for this response		
	Theme	**Representative Quotes**
	Identity/ Personality	Down syndrome does not define my son, but it is part of who he is. It would be the same as you asking me if I want to take a medication to make my eyes a different color or make me more social.
	Quality of life	I don't want to change her, just make things a little easier for her. It isn't the DS that's the problem. It's the side-effects of DS such as congenital heart disease, Alzheimer's, delayed speech.
	Social and societal considerations	I believe my daughter has a full life and has much to teach others. I believe the world would be a poorer place without people with Down syndrome Society needs a pill that allows them to love and embrace differences.
Neutral to Medicine		
You indicated that you are neutral about giving your son or daughter a drug so that they no longer have Down syndrome. In the space below, please give any reasons you have for this response.		
	Theme	**Representative Quotes**
	Identity/ Personality	I think it's part of who she is and what makes her unique, including some of her personality traits. I hate how other people make assumptions about my daughter because of her DS without even knowing her but on the other hand DS is part of who she is.
	Quality of life	I don't know. I love him just the way he is, and he wouldn't be the same if he didn't have Down syndrome. But would his life be easier without DS? Probably.

Table 5. Parental Qualitative Responses to Reasons for Answering with Agree, Disagree, or Neutral to Giving a Side-Effect Free Medication

	Social and societal considerations	Our world is enriched by people with Down syndrome, and yet I know there have been times where my daughter wished she could be more like her typical peers, especially within school and extra-curricular activities. I hate to see her struggle, and yet her way of being in the world has made us a stronger family and given me a richer life.
	Uncertainty	Would not having DS make our life easier? Sure. But I don't know that it would make us happier or life noticeably better. It's impossible to imagine what this would mean and what it would look like.
Agree with Medicine		
You indicated that you would want to give your son or daughter a drug so that they no longer have Down syndrome. In the space below, please give any reasons you have for this response.		
	Theme	**Representative Quotes**
	Quality of life	Down syndrome is a condition that puts a surcharge on my daughter's life. She has to make double the effort to achieve have the success. My son has numerous medical issues and significant developmental delays largely due to the fact that he has Down syndrome. If we could eliminate these from his life I would do it in a heartbeat.
	Social and societal considerations	Our society is utterly racist and is not made for people with disabilities. Because of cuts in school funding. Because of cuts in Medicaid. Due to lack of employment opportunities.
Opinions on Medicine to Increase Intelligence Significantly		
Disagree with Medicine		
You indicated that you would not want to give your son or daughter a drug that increases their intelligence significantly. In the space below, please give any reasons you have for this response.		
	Theme	**Representative Quotes**
	Identity/ Personality	How intelligent is a matter of what you want. He is very happy being the person he is.
	Social barriers/ contributions to society	He is already very intelligent... just not necessarily in the ways society defines "intelligence". He sheds a unique and important perspective on the world. I don't want to change that.
	Quality of life	She is happy and feels like her life is meaningful.

Table 5. Parental Qualitative Responses to Reasons for Answering with Agree, Disagree, or Neutral to Giving a Side-Effect Free Medication

	Uncertainty	It's hard to say what increasing intelligence significantly might do in terms of affecting the other qualities that are associated with Down syndrome.
	Life values	Intelligence is not the most important quality in a person.
	Everyone wants increased intelligence	Being too intelligent can be just as much of a handicap as not being as intelligent as others.
Neutral to Medicine		
You indicated that you are neutral about giving your son or daughter a drug that increases their intelligence significantly. In the space below, please give any reasons you have for this response.		
	Theme	**Representative Quotes**
	Identity/ Personality	Making him more intelligent would change the essence of who he is and we love him the way he is.
	Social barriers/ contributions to society	With proper support, I believe my son is intelligent.
	Quality of life	How would increasing her other areas of intelligence- emotional, social, spiritual- be affected by increasing her intellect? On the other hand, this would have a huge impact on her independent function in the world."
	Uncertainty	How would increasing her other areas of intelligence- emotional, social, spiritual- be affected by increasing her intellect? On the other hand, this would have a huge impact on her independent function in the world
	Life values	Not all intelligence can be measured by an IQ test
	Everyone wants increased intelligence	She's perfect the way she is. Would parents of 'typical' kids give their child a medication to increase their intelligence? I don't think so. Don't we all wish that we could improve our intelligence?
Agree with Medicine		
You indicated that you would want to give your son or daughter a drug that increases intelligence significantly. In the space below, please give any reasons you have for this response.		
	Theme	**Representative Quotes**
	Identity/ Personality	I want [name], or others with Down syndrome, to be the best they can be

Table 5. Parental Qualitative Responses to Reasons for Answering with Agree, Disagree, or Neutral to Giving a Side-Effect Free Medication

	Social barriers/ contributions to society	I think this would make her life easier in school, but more importantly it would allow her to function more independently as an adult. Based on my experience, schools are not very well prepared to exploit all the cognitive potential that people with Down Syndrome
	Quality of life	If I could make her struggle/frustration less I would. My daughter is low functioning and she is unhappy with that. She is very frustrated
	Uncertainty	It gives me anxiety to realize one day she will be without us to look out for her!!
	Life values	It would help him be more successful in life. To achieve or surpass what is considered normal for a regular person
	Everyone wants increased intelligence	If there was something out there to change a person's intelligence significantly, I would want that for everyone. I probably would give such a medication to my typical child and would take it myself too. As for my daughter with Down syndrome, she is already very smart, but it would help her. I would take it myself too. It isn't that she has a problem with intelligence, improving intelligence could be great for every person