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Caregivers' perception of adults with Down syndrome willingness to participate in research

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Abstract

Background Historically, individuals with Down syndrome have been excluded from clinical research. Our objective was to assess the degree of interest adults with Down syndrome have in participating in research from the perspective of the caregivers who care for them.

Methods We conducted an online survey of $N = 390$ caregivers of adults with Down syndrome and asked about interest in research participation and demographics.

Results Caregivers were mostly family members, older than 55 years, and White. Caregivers reported that the adult with Down syndrome that they cared for would be more comfortable participating in research that was physiological, such as research involving fit bits (70.2% would participate), exercise (63.3%) or diet apps (53.9%), whereas they would be less likely to participate in clinical trials involving more invasive procedures such as injections (10.9%) and laboratory exams like MRIs (32.0%). We found little difference by age or gender of the adult with Down syndrome or by caregiver education level.

Conclusions Our survey identified high interest for less invasive studies, illustrating acceptability of observational and lifestyle studies. More effort may be needed to understand fear and barriers to participation and to create tools and methods to increase interest in more invasive studies.

Keywords clinical trials, Down syndrome, research participation

Introduction

With recent advances in healthcare, individuals with Down syndrome are living longer and have an improved quality of life. Remarkably, life expectancy has increased from 12 years in 1949 to >60 years of age today, attributable to reduction in respiratory infections, de-institutionalisation and treatment for congenital heart defects (Bittles & Glasson 2004). Improved knowledge about Down syndrome has generated these major advances in healthcare, yet much more research is needed to ameliorate burdensome co-occurring conditions, such as Alzheimer's disease, that lower quality of life and lead to premature mortality. Individuals with Down syndrome are at a very high risk of developing Alzheimer's disease, which is the leading cause of death in the Down syndrome population (Fortea *et al.* 2021).

Currently, individuals with Down syndrome have less opportunities to be involved in impactful clinical research compared with peers. Although Down syndrome is the most common chromosomal abnormality, it is rare in the general population,

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affecting one in 400–1500 births in the USA (Kazemi *et al.*, 2016). Based on probabilistic sampling, it would be unlikely for an adequate sample of individuals with Down syndrome to be sampled in a general population study. A trial studying primarily individuals with Down syndrome would be very time intensive due to concentrated recruitment efforts and may ultimately not yield the statistical power needed to assess significant results. Through projects like INCLUDE, an NIH effort to increase Down syndrome research, there is a push to increase inclusion of individuals with Down syndrome in clinical trial research (National Institutes of Health 2022). Still, individuals with Down syndrome are often not included in the clinical trials most pertinent to their health, for example, Alzheimer's disease (Baumer *et al.* 2022). In a study analysing the exclusion of people with disabilities in clinical studies, DeCormier Plosky *et al.* (2022), found that 86% of dementia studies and 83% of depression-related studies, both of which are pertinent to individuals with Down syndrome, excluded those with cognitive disability. Brooker *et al.* (2015) conducted a systematic review of public health journals and found that cohort studies often passively excluded people with intellectual disabilities and randomised control trials actively exclude people with intellectual disability.

A major factor that often leads to the exclusion of individuals with Down syndrome from clinical trials is the popular belief that individuals with Down syndrome are incapable of providing consent (Horner-Johnson & Bailey, 2013). Many studies exclude individuals with Down syndrome on the basis that they could not understand the study description and disclosures presented in the consent process (Horner-Johnson & Bailey, 2013). Research has proven this notion to be false, as evidenced by Horner-Johnson and Bailey's (2013) study of 131 participants with intellectual disabilities, where 57% of participants were able to correctly answer questions aimed at assessing their understanding of key aspects of the study (Horner-Johnson & Bailey 2013). Further, even with individuals who are not able to provide legal consent, they can exercise choice. Assent is also possible for those with Down syndrome with a surrogate decision maker (Baumer *et al.* 2022). While obtaining consent or assent may not be as straightforward for people with Down syndrome compared with peers without Down syndrome, their inclusion in clinical trials is still feasible and important for scientific advancement. Other factors that contribute to the challenges of individuals with Down syndrome participating in research include the associated risks of the study to the individual, the level of transparency of the study, competing responsibilities, and time commitment (White *et al.* 2022).

Our objective was to assess what types of research individuals with Down syndrome would be more or less likely to participate in, as reported by their caregivers in an online survey. Caregivers often are the ones that share information about opportunities and facilitate participation in research, so though the voice of individuals with Down syndrome is crucial, the caregiver's report provides critical information. We examined differences by age and gender of the individual with Down syndrome and the education level of the caregiver. We hypothesised that non-invasive studies would be preferred and age of the individual with Down syndrome and caregiver education would be associated with increased interest in participating in research.

Methods

Caregiver survey

Data were collected from an internet-based survey of caregivers of individuals with Down syndrome co-led by researchers at Boston University and LuMind IDSC. The goal of the survey was to characterise the health and employment status of the individual with Down syndrome while describing and understanding the challenges and barriers for caregivers and individuals with Down syndrome. Survey design began in January 2021 with guidance from researchers, caregivers, Down syndrome non-profit executives, advocates, and other stakeholders. The final survey, which took each respondent approximately 1 h to complete, was created through Qualtrics and consisted of 115 questions with various response options (fill-in, yes/no, open-ended and Likert scale). The survey consisted of six sections: caregiver demographics, individual with Down syndrome demographics, Down syndrome employment history, Down syndrome healthcare, caregiver stress and clinical trial participation. The

Table 1 Demographic characteristics of adults with Down syndrome and their caregivers who participated in a caregiver survey

Characteristics of adults with Down syndrome *N* = 390	***N***	**%**	**Caregiver characteristics *N* = 390**	***N***	**%**
Age (years)			Caregiver age (years)		
18–39	292	74.9	18–44	17	4.5
40–54	73	18.7	45–54	64	17.1
55+	25	6.4	55–64	158	42.1
Mean (SD)	32.9	11.3	65–74	111	29.6
Median (range)	30	18–62	75+	25	6.7
			Missing	15	
Gender					
Male	193	49.6	Caregiver type		
Female	196	50.4	Primary caregiver	252	64.6
Missing	1		Equally share responsibilities	83	21.3
			Other	55	14.1
Race					
White	349	92.3	Caregiver relationship[†]		
Black/African American	12	3.2	Mother	303	77.7
Mixed race/American Indian	19	5.0	Father	15	3.8
Missing/prefer not to say	12		Sister	52	13.3
			Other family member	14	3.6
Ethnic group			Paid caregiver	15	3.8
Hispanic	20	5.1			
Non-Hispanic	370	94.9	Caregiver education		
			High school graduate or less	63	17.0
Physical health conditions[†]			Some college/associates degree	45	12.0
Attention deficit hyperactivity disorder	32	8.2	Bachelor's degree	138	37.0
Autism	44	11.3	Graduate degree	127	34.0
Alzheimer's disease	39	10.0	Missing	17	
Epilepsy	22	5.6			
Cardiovascular conditions	149	38.2	Income (USD)		
Obesity/overweight	187	47.9	<20 000	76	22.0
Sleep apnoea	163	41.8	50 000–79 999	69	20.0
Thyroid conditions	226	57.9	80 000–99 000	49	14.0
			100 0000–149 999	76	22.0
Mental health conditions[†]			>150 000	70	21.0
Anxiety disorders	105	26.9	Missing	50	
Behavioural challenges	100	25.6			
Depression/depressive disorders	64	16.4			
Obsessive compulsive disorder	17	4.4			
Country					
USA	373	95.6			
Other	17	4.4			
Living situation					
In a group home	16	4.1			
In caregiver's home with paid support	89	22.8			
In caregiver's home with unpaid family support	213	54.6			
Independent/alone	8	2.1			
Other	64	16.4			

[†]Non-exclusive categories.

Boston University Institutional Review Board approved the survey and recruitment materials.

Recruitment

In April 2021, the survey was opened. Participants were eligible if they identified as a caregiver of an adult with Down syndrome ≥18 years of age, they could read and comprehend the survey in English and they themselves were ≥18 years of age. Caregivers were recruited through LuMind IDSC and National Down Syndrome Society post-card mailers, email listservs and social media pages. When caregivers enrolled, they were eligible for a raffle for three $50 Amazon gift cards. When the recruitment goal of n = 500 consented to the survey in September 2021, the survey was closed.

Participants

Of 500 caregivers, we excluded 30 who completed <20% of the survey and 56 who did not answer the questions related to trial participation. We excluded 32 responses where the individual with Down syndrome was <18 years of age, resulting in an analytic sample of N = 390. Over half of caregivers were ≥55 years of age (Table 1), most caregivers were mothers of the adult with Down syndrome, and

Table 2 Interest in participating in research studies for adults with Down syndrome, stratified by age, as reported by caregivers

	Total		**Age 18–39**		**Age 40–54**		**Age ≥55**			
	N = 390		***N* = 292**		***N* = 73**		***N* = 25**			
	N	**%**	***N***	**%**	***N***	**%**	***N***	**%**	**X^2**	***P***
Adult with DS previously participated in a clinical trial										
Yes	63	16.2	47	16.1	13	17.8	3	12.0	15.0	0.005
No	326	83.6	245	83.9	60	82.2	21	84.0		
I do not know	1	0.26	0	0	0	0	1	4.0		
Interest in learning about future studies for adult with DS										
Yes	187	48.0	147	50.3	29	39.7	11	44.0	6.7	0.16
Interested in natural history study	71	18.2	56	19.2	12	16.4	3	12.0	1.0	0.61
Interested in drug or medical device trial	74	19.0	62	21.2	10	13.7	2	8.0	4.2	0.12
Interested in other trials	35	9.0	23	7.9	7	9.6	5	20.0	4.2	0.12
No	53	13.6	33	11.3	14	19.2	6	24.0		
Maybe	17	38.5	112	38.4	30	41.1	8	32.0		
The adult with DS would participate in the following studies										
A survey on medical care with no medical tests or experimental drug or device	250	64.1	205	70.2	36	49.3	9	36.0	20.2	<0.001
An observational study with medical tests (such as memory test) but not with an experimental drug or device	256	65.6	207	70.9	36	49.3	13	52.0	14.3	<0.001
An observational study with medical tests (including blood draws or MRI, etc.) but not with an experimental drug or device	155	39.7	124	42.5	25	34.3	6	24.0	4.4	0.11
A clinical trial to test the safety and efficacy of a drug of device that is safe and FDA approved for the general population but not yet approved for people with Down syndrome	99	25.4	81	27.7	14	19.2	4	16.0	3.5	0.17
A clinical trial of an experimental drug or device that might treat a disease or condition common in people with Down syndrome	73	18.7	51	17.5	16	21.9	6	24.0	1.3	0.54
I would not ask the adult with DS to participate in a trial	55	14.1	35	12.0	16	21.9	4	16.0	4.8	0.09
I do not trust the researcher's ethics	2	3.6	2	5.7	0	0	0	0	1.2	0.55
My loved one has no interest in participating	49	57.7	34	58.6	12	60.0	3	42.9	0.7	0.71
My loved one has never been eligible	24	31.2	22	40.0	1	5.9	1	20.0	7.4	0.03
Other	41	53.3	20	45.5	14	63.6	7	63.6	2.5	0.29

X^2 compares differences across the three ages.

caregivers were highly educated (64.1% completed college or graduate education). Of the individuals with Down syndrome, most were white, were non-Hispanic and lived in the USA. The average age of individuals with Down syndrome was 32.9 years. The most prevalent health conditions among individuals with Down syndrome were thyroid conditions (57.9%) and obesity (47.9%).

Clinical trial and research participation questions

The clinical trial questions were geared towards asking about current interest in clinical trials and whether caregivers were willing to learn more about upcoming trials and research studies. If caregivers expressed that the individual with Down syndrome that they care for would be interested in participating in clinical trials, we asked them, 'What type of research study would you consider asking your loved one if they wanted to participate in?', to determine different potential clinical trial and research topics. Caregivers were given a list of options that they could select (see Table 2). Following these questions, we asked caregivers to rate how likely it was that the adult with Down syndrome they care for would comply with different experimental treatments, including diets, injections, exercise apps and clinical tests of the adult with Down syndrome that they care for.

Other variables

Caregivers reported the demographics for the adult with Down syndrome. For several variables, we collapsed categories to prevent sparse data (e.g. for ethnic groups, collapsing categories in 'Hispanic' and 'non-Hispanic'). We categorised the age of the individual with Down syndrome as 18–39, 40–54 and ≥55. We chose this parameterisation to align with dementia studies, especially because dementia is a major age-related change particularly relevant to individuals with Down syndrome that could impact our findings. Dementia impacts individuals with Down syndrome with little incidence before 40 years of age and high incidence after 55 (Rubenstein *et al.*, 2020).

Analysis

First, we removed participants who completed <20% of the survey. We selected the 20% threshold because it indicates completion of at least one of the six survey sections. After this, we excluded responses where the individual with Down syndrome was <18 years of age. We calculated the descriptive statistics for demographic variables and compared responses for clinical trial questions by age group, caregiver education and gender using chi-square tests. We then ran log-binomial regression models to estimate risk ratios assessing whether interest in participation in clinical trials was associated with age group (re-parameterised as <40 or ≥40 to account for small sample sizes in the ≥55 group) and ran a regression model adjusted for caregiver education (re-parametrised as <college degree or ≥college degree) and the gender of the adult with Down syndrome, in consideration of possible confounding due to those factors.

Results

We saw that most adults with Down syndrome had not previously participated in a clinical trial (83.6%; Table 2). Many caregivers were interested in learning about future studies for adults with Down syndrome (86% reported 'yes' or 'maybe'). Caregivers indicated surveys on medical history with no medical test or experimental drugs (64.1%), and observational study with medical tests (like a memory test; 65.6%) would be of most interest for adults with Down syndrome. Only 14.1% of caregivers would not ask the individual they care for with Down syndrome to participate in a research study. Among those that would not ask, 57.7% reported that the primary reason was that the individual with Down syndrome they cared for would have no interest in participating.

We stratified results by the age of the individual with Down syndrome (Table 2), gender of the individual with Down syndrome (Table S1) and caregiver education (Table S2). Older adults with Down syndrome were less likely to have participated in trials in the past and were reported to be less likely to participate in survey or observational research. We saw little difference between genders and caregiver education.

Caregivers believed that the adult they care for with Down syndrome would be more likely to participate in trials that were non-invasive and could be conducted at home. The most liked trial was one that included the use of a tablet or phone, with 46.4% of

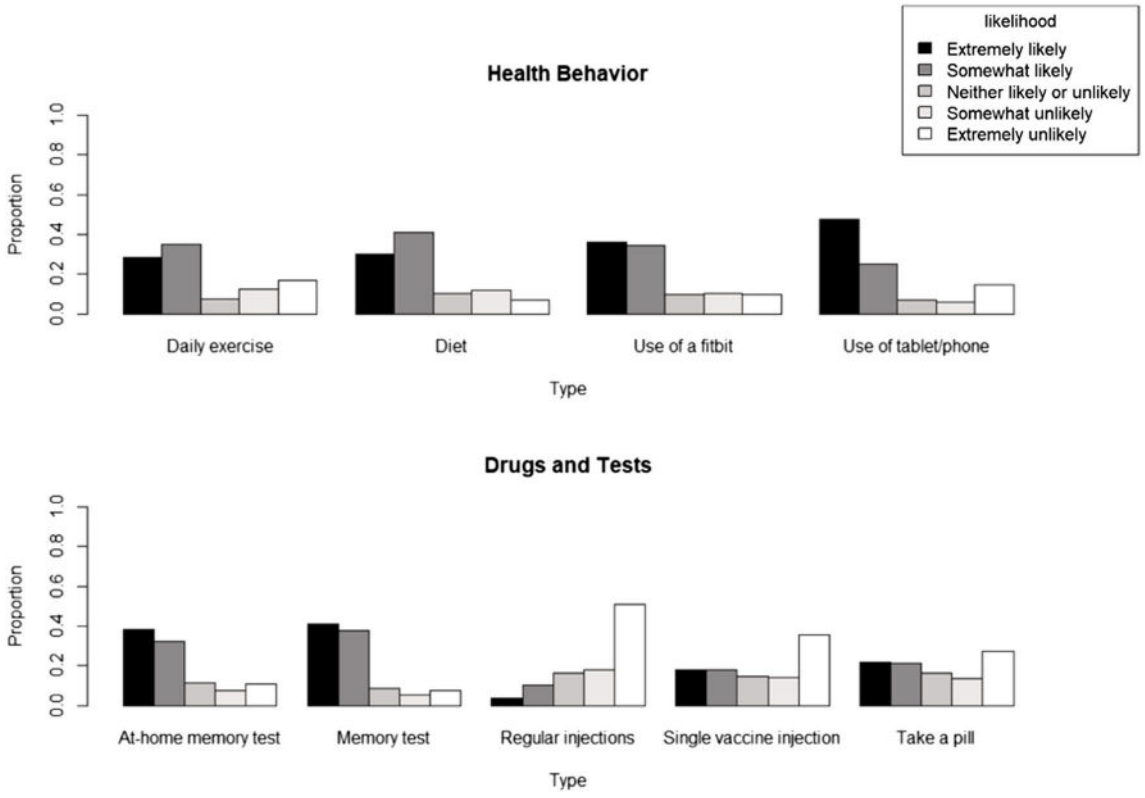

Figure 1. Interest in participating in clinical trial types for adults with Down syndrome as reported by caregivers.

participants indicating that the adult they care for with Down syndrome would be extremely likely to participate (Figure 1). Other popular trials included daily exercise of at least 30 min and the use of wearable technology such as a Fitbit. The least popular trials were the ones that were the most time consuming and the most invasive. Only 4.8% of participants perceived the adult they care for with Down syndrome would be interested in trials with regular injections, and only 2.2% participants thought the adult they care for with Down syndrome would be interested in trials focusing on lumbar punctures.

In regression models assessing the association between caregiver education and current trial interest and different types of studies participants may be interested in, older adults with Down syndrome were less likely to have been reported to be interested in participating in an observational study (RR 0.81, 95% CI 0.7, 0.9) or a survey (RR 0.79, 95% CI 0.7, 0.9; Table 3). The result was slightly attenuated after adjusted for gender and caregiver education. Caregivers were 7.9% less likely to ask older adults to participate in clinical trials compared to younger adults, but after adjustment for gender and caregiver education, the confidence interval crossed the null.

Discussion

Currently, it is rare for studies to include individuals with Down syndrome in clinical trials, even though many of these clinical trials study conditions and diseases that disproportionately affect individuals with Down syndrome. This issue is due to the challenges and misconceptions regarding consent and assent for individuals with developmental disorders and statistical power for subgroup analyses. Our study found that many caregivers, most of whom were family members, perceive that adults with Down syndrome would be interested in participating in clinical research studies, especially observational and behavioural studies.

Table 3 Risk ratios comparing likelihood of participating in a particular type of research study comparing younger and older adults with Down syndrome, as reported by caregivers

	Unadjusted model			Adjusted model		
Study type	**RR**	**95% CI**		**RR**	**95% CI**	
Ever trial participation	1.00	0.9	1.1	1.00	0.9	1.1
Survey on medical care	**0.79**	0.7	0.9	**0.80**	0.7	0.9
An observational study with medical tests (such as memory test) but not with an experimental drug or device	**0.81**	0.7	0.9	**0.83**	0.7	0.9
An observational study with medical tests (including blood draws or MRI, etc.) but not with an experimental drug or device	0.90	0.8	1.0	0.98	0.8	1.1
A clinical trial to test the safety and efficacy of a drug of device that is safe, and FDA approved for the general population but not yet approved for people with Down syndrome	0.91	0.8	1.0	0.91	0.8	1.0
A clinical trial of an experimental drug or device that might treat a disease or condition common in people with Down syndrome	1.05	1.0	1.2	1.07	1.0	1.2
I would not ask the adult with Down syndrome to participate in a trial	1.08	1.00	1.2	1.09	1.0	1.2

RR, risk ratio.
Referent group is younger adults (18–39 years) with Down syndrome.
Log binomial models.
Bold indicates statistical significance at an alpha = 0.05 level.
Adjusted for gender of adult with Down syndrome and caregiver education.

White *et al.* (2022) conducted a similar study of 228 parents of mostly children with Down syndrome to understand their perceptions and their views on enrolling the individuals with Down syndrome they care for in research. Some of the findings of this study are similar to our results. Many parents rated their likelihood of enrolling their child with Down syndrome in non-invasive research procedures much higher than in a research study, which involved invasive procedures and in general were interested in research (White *et al.* 2022). Ninety-two per cent of respondents reported wanting more treatment options related to drugs, therapies and interventions. Some of the differences between White *et al.* (2022) and our study can be seen in the barriers that parents and caregivers face when enrolling their individuals with Down syndrome they care for in research. The authors noted that the most common barriers that parents cite are risk/benefits to the child, adequate study compensation and time commitment (White *et al.* 2022). Parents were concerned about whether research studies would directly benefit the individuals with Down syndrome, and the majority (57.5%) were willing to travel within 50 mi. of their home. In comparison, our study found that the most common barriers caregivers cited include that the adults they care for with Down syndrome were not interested in participating. These differences in barriers may be attributed to the age difference of the individual with Down syndrome. We saw that in adults, age is important in our data, as older individuals are not as interested in clinical research as younger individuals. This may be why our study reflects that it is less likely for older adults to want to participate in research compared with younger adults. Further exploration as to research participation desires for older adults with Down syndrome is needed to understand how to improve research interest.

We found a lack of interest to be a barrier, but we generally found high trust in researcher ethics from caregivers. In a qualitative study focused on older adults with Down syndrome and their motivations to participate in research, Fiordelli *et al.* (2021) found that obstacles included not being interested in the study results and distrust towards the researchers or the study itself. Differences between our findings about trust and Fiordelli *et al.* (2021) may be due to the specificity of Fiordelli's proposed research (dementia studies), caregiver- compared with self-

report, and the study population (Switzerland compared with mostly the USA).

We see from our survey analysis, that the interest in a clinical trial involving injecting a vaccine is very low. This may stem from injections being inconvenient, burdensome, and painful and be driven by a culture with high vaccine hesitancy (Shen & Dubey 2019). Whereas vaccines remain one of the most successful public health interventions to date, vaccine hesitancy is prevalent in the general population (Shen & Dubey 2019). Promisingly, COVID-19 vaccination rates have been high in the Down syndrome population (Huls *et al.* 2022), which may signal more trust in vaccines and eagerness to participate in vaccine research. However, based on our findings and the general hesitancy around vaccines, it is likely that increased clinical participation of individuals with Down syndrome in studies involving vaccinations will remain a challenge.

Research thus far, including the present study, indicates a discrepancy between what caregivers want and low willingness among individuals with Down syndrome to participate in interventional clinical trials. We found caregivers expressed high interest in knowing about future research studies, and White *et al.* (2022) found 92% of caregivers wanted new drugs and interventions for children with Down syndrome. It will be pivotal to bridge this major gap between interest and intent of participation in order to bring forth new treatment options. Possible areas where research advocacy organisations, researchers and regulators can work to improve research participation include improvement of the direct study benefits and how they are presented to adults with Down syndrome and their caregivers, making research participation easier (i.e. reducing reliance on transportation) and making the consent process more inclusive and equitable for adults with Down syndrome.

Some of the limitations of this study are a lack of racial diversity of caregivers and adults with Down syndrome. It is important to note the racial disparities because this impacts the health and life expectancy of individuals with Down syndrome (Kucik *et al.* 2013; Santoro *et al.* 2016). Because this survey consisted of mostly White people, our convenience sampling, English only survey, the findings associated with this survey may not be applicable to all individuals with Down syndrome. We also did not have data for those that did not make it to the clinical trial section of the survey, and if there was differential attrition, we further limit generalisability. Because we did not have a non-Down syndrome intellectual disability comparison group, we cannot be sure whether responses are unique to Down syndrome or are generally applicable to those with intellectual disabilities.

We had a small number of caregivers reporting on older adults, limiting our statistical power. The study should be replicated in more non-English-speaking and low-resource settings to understand trial readiness in these populations. We also primarily surveyed caregivers who were family members of the individual with Down syndrome; the experiences of paid non-family caregivers may be different. One avenue of recruitment was from a scientific advocacy organisation, which may have made it more likely that our source population would be more interested in research. We were not able to determine whether respondents were brought in by the LuMind IDSC or the National Down Syndrome Society.

It is also important to acknowledge that our analysis of the survey is based on the caregivers' perception of their loved ones' attitudes and beliefs as caregivers are the individuals who completed the survey. Though caregivers have a very deep knowledge and understanding of the individuals with Down syndrome they care for, the survey responses reflect what caregivers think that individuals with Down syndrome would answer rather than direct answers from those individuals themselves. Because the survey asked about a range of topics pertinent to caregivers, asking individuals with Down syndrome themselves was out of the scope of this project, and we intend to conduct surveys of adults with Down syndrome in the future.

Conclusion

In a survey of caregivers, we found that many individuals with Down syndrome would be interested in participating in research, especially observational or survey-based research. Furthermore, we see that individuals are more likely to participate in studies involving diet, exercise apps and memory tests rather than injections and blood infusions. Though caregiver education and gender does not seem to affect the responses of caregivers, the age of the individual with Down syndrome matters. These findings indicate that

though very few studies include individuals with Down syndrome, many individuals with Down syndrome are interested and willing to participate in clinical research.

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Conflict of interest

The authors have no conflicts of interest to disclose.

Data availability statement

Data are available upon request.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Table S1. Research study outcomes for adults with Down syndrome, by caregiver education, 2021
Table S2. Research study outcomes for adults with Down syndrome, by gender, 2021