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RESEARCH ARTICLE

Comparing research attitudes in Down syndrome and non-Down syndrome research decision-makers

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Abstract

INTRODUCTION: Recruitment challenges in people with and without Down syndrome (DS) can delay research progress and risk sample bias. This study identified and quantified differences in research attitudes across populations of research enrollment decision-makers for individuals with and without DS.

METHODS: We performed analyses using data from two registries: the University of California, Irvine Consent-to-Contact (C2C) Registry and DS-Connect. The former represented a sample of non-DS decision-makers ($N = 4818$), while for the latter, we excluded individuals with DS, leaving a population of DS family decision-makers ($N = 976$). We assessed scores on the Research Attitudes Questionnaire (RAQ) between DS and non-DS decision-makers. We compared total RAQ scores using linear regression and assessed item-level RAQ differences using proportional odds regression.

RESULTS: Mean total RAQ scores were not statistically different between decision-makers in the two registries, after adjusting for age, sex, race and ethnicity, education, and the coronavirus disease 2019 (COVID-19) time frame (Est. Diff = 0.11, 95% confidence interval [CI]: -0.22, 0.43; $p = 0.531$). However, in a pre-specified analysis, we did find evidence of differential attitudes on item-level RAQ scores. Specifically, decision-makers for participants with DS had increased odds of a more favorable response to the question of responsibility to help others (DS vs. non-DS: odds ratio [OR] = 1.26, 95% CI: 1.08, 1.48) and decreased odds of a more favorable response to the question regarding the belief that medical research would find cures for major diseases during their lifetime (DS vs. non-DS: OR = 0.77, 95% CI: 0.66, 0.90).

DISCUSSION: Our findings provide insights for researchers to develop strategies for recruiting individuals with and without DS into clinical research. The observed item-level differences warrant further investigation to instruct precise recruitment strategies.

KEYWORDS
clinical trials, Down syndrome, research attitudes, Research Attitudes Questionnaire, research registry

Highlights

- Research attitudes between decision-makers for individuals with Down syndrome (DS) and decision-makers without DS were observed to be similar on average.
- Item-level differences in research attitudes were observed to differ for DS and non-DS decision-makers.
- These results can help facilitate precise recruitment strategies for populations with DS.

1 | INTRODUCTION

Randomized controlled clinical trials (RCTs) provide an important standard for evaluating intervention effectiveness. A consistent barrier to RCTs, however, is the slow and inadequate recruitment of participants. This challenge contributes to delays in treatment advances and motivates the need for a "science of recruitment and retention," to establish evidence-based strategies that accelerate recruitment and therefore, research progress.[1]

Key to the science of recruitment is the need to better understand the attitudes, concerns, and interests of potential study enrollment decision-makers. In most cases, decision-makers are the participants themselves. However, in populations with developmental disabilities such as Down syndrome (DS), caregivers or family members may be mandated to serve as research enrollment decision-makers.

The past few decades have brought a welcome increase in lifespan for people with DS, who now can expect, on average, to live to 60 years old or beyond.[2] People with DS have a high prevalence of age-associated health conditions,[3] including a near 100% prevalence of Alzheimer's disease (AD) neuropathology and extremely high frequency of dementia.[4] Individuals with DS are likely to develop cognitive decline at earlier ages and at higher rates than the general population.[5,6] This susceptibility to AD and its impact on people with DS make clinical trials for the prevention and/or treatment of dementia imperative. Yet, there is a dearth of clinical trials in people with DS for AD[7] and a lack of empirical data about research attitudes that may affect clinical trial recruitment and retention.

The Research Attitudes Questionnaire (RAQ) is a brief, validated seven-question instrument designed to gauge a person's attitude toward biomedical research.[8] The RAQ was developed with the goal of measuring social and cultural factors that may influence research participation decisions, including enrollment in a clinical trial. RAQ scores have been previously shown to be associated with willingness to participate in research, compliance with study protocols, and study completion.[9–12] In a previous study, we showed the feasibility of using the RAQ in over 1000 family members for individuals with DS,[13] but we still do not understand how individual items on the RAQ compare to those in the general population. In the present report, we explored differences in RAQ scores between healthcare and research enrollment decision-makers for individuals with DS and those from a more general population, both of which come from research-friendly registries in the United States. We hypothesized that there would be differences in the RAQ, both in aggregate and at the item level, between DS and non-DS decision-makers.

2 | METHODS

2.1 | Data source and participants

The data we utilized for our analyses came from two registries: the University of California, Irvine (UCI) Consent-to-Contact (C2C) Registry and DS-Connect, representing the samples of non-DS and DS decision-makers, respectively.

The C2C (https://c2c.uci.edu/) is a local registry operated by the UCI Institute for Memory Impairments and Neurological Disorders.[14] Created in 2016, C2C provides a database of individuals mostly from Orange County, California, who are willing to consider participating in research, including prevention research for AD. Eligible C2C enrollees are routinely referred to clinical research studies, accelerating the recruitment process. When referred to a study, C2C participants themselves decide whether to participate in the study. At enrollment, registrants complete a survey that includes demographic information, medical history, and the RAQ. In this analysis, we utilized baseline data provided by individuals who enrolled in the C2C from June 1, 2016, to August 3, 2022, yielding a sample of 4818 non-DS decision-makers.

DS-Connect (https://dsconnect.nih.gov/) is a Web-based national registry created in 2007 and managed by the Eunice Shriver Kennedy National Institute for Child Health and Human Development of the National Institutes of Health.[15] Through DS-Connect, people with DS and their relatives/caregivers can learn about DS resources and research. At registration, 2100 participants agreed to be contacted about potential DS research and were contacted via email to complete a survey that assessed their demographic information, their relationship to the patient with DS, as wells as RAQ scores. From January 28, 2020, to October 29, 2020, 1048 family members of someone with DS and 22 individuals with DS responded to the survey. Because of the goals of our analyses, we focused on family members who were primary decision-makers for healthcare and research enrollment. Among the 1048 family members of individuals with DS, 996 indicated that they

were decision-makers. We excluded 20 responses out of 996 due to incomplete information on research attitudes. The DS-Connect sample therefore included 976 DS decision-makers.

2.2 | Primary outcome measure

The RAQ is a seven-item assessment that measures one's attitudes toward medical research. Each item in the RAQ is scored on a Likert scale ranging from (1) "strongly disagree" to (5) "strongly agree". The total RAQ score thus has a range from 7 to 35. Higher scores correspond to a more positive attitude toward medical research. The seven RAQ items include: "I have a positive view about medical research in general" (positive view), "Medical researchers can be trusted to protect the interests of people who take part in their research studies" (researcher trust), "We all have some responsibility to help others by volunteering for medical research" (help others), "Society needs to devote more resources to medical research" (devote resources), "Participating in medical research is generally safe" (research safety), "If I volunteer for medical research, I know my personal information will be kept private and confidential" (confidential), and "Medical research will find cures for many major diseases during my lifetime" (find cures). DS and non-DS decision-makers completed identical RAQ surveys.

2.3 | Available data and data harmonization

Beyond the RAQ, demographic, logistical, and clinical covariates were collected for both groups. Common covariates between C2C and DS-Connect included demographic characteristics such as age, years of education, sex, race, ethnicity, and a survey completion timestamp. The two registries elicited demographic information from participants through slightly different questions, which required that we harmonized covariates across the two samples.

A small fraction of individuals above 90 years of age in the non-DS sample ($N = 21$ of 4818 participants) had age recorded as "90+". We replaced those values with a numeric 90 and considered age as a continuous variable. We also defined categorical age groups (<45, 45–59, 60–70, and >70) with boundaries roughly equivalent to the age quartiles from the combined data. Years of education in both samples were recorded as numeric, with an exception for 25 individuals in the non-DS sample whose education was recorded as "greater than 26 years" with no specific numeric values. We assigned a numerical value of 26 for years of education for these individuals. We also grouped education years into four categories determined by conventional educational milestones: <12 years, 12 years (high school diploma), 12–16 years (bachelor's degree), and >16 years (graduate degree). The DS-Connect survey asked, "What is your gender?," and provided male and female response options. The C2C survey asked for "sex" and provided male, female, and other options. We combined these two variables into a single variable called "sex" with three categories (male, female, and other). Because the proportion of those who responded other as sex in the C2C sample was small (17 out of 4818 decision-makers responded other), it should have no influence on the estimates corresponding to sex categories in the regression models.

In both samples, ethnicity was categorized as Hispanic or Latino and Not Hispanic or Latino. Race in both samples was categorized as American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, and Other. Participants in the non-DS sample could select multiple race categories. We considered those with more than one race category indicated ($N = 146$) as Other. Due to sparseness in the data, we collapsed American Indian or Alaska Native ($N = 15$) and Native Hawaiian or Other Pacific Islander ($N = 9$) into the Other category. Also in the non-DS sample, participants were allowed to select "refuse to answer" to race and ethnicity. We considered those who responded with "refuse" solely to either race or ethnicity ($N = 135$) as missing. We combined race and ethnicity variables into a variable that encapsulated these constructs. We first assigned ethnicity (Hispanic or non-Hispanic) to the decision-makers and then assigned their corresponding race category (Asian, Black, White, or Other). Individuals with either ethnicity or Other race were categorized as Other race and ethnicity. Those who left either race, ethnicity, or both missing were considered missing. We collapsed Hispanic Asian ($N = 2$) and Hispanic Black ($N = 3$) into Other due to the sparsity of data. Thus, the final race and ethnicity categories were Hispanic White, non-Hispanic Asian, non-Hispanic Black, non-Hispanic White, and Other. Finally, we created a binary "COVID-19-time frame" variable that indicated whether a respondent completed their survey after March 13, 2020, which was the day the United States government declared a national emergency concerning COVID-19.

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed the literature using PubMed and other common databases. While there have been studies on research attitudes among family members of individuals with Down syndrome (DS) and research attitudes of research registry participants, to our knowledge, this is the first comparison of research attitudes of decision-makers for individuals with DS and decision-makers without DS.
2. **Interpretation**: DS and non-DS decision-makers were observed to have similar overall attitudes toward medical research. However, there were differences in research attitudes at the item level.
3. **Future directions**: Our findings may help instruct recruitment plans and designs for studies that may be reasonable in both groups such as Alzheimer's prevention treatments. The observed differences in particular research attitudes across the two groups may help facilitate precise recruitment strategies for populations with DS.

2.4 | Statistical analysis

Descriptive statistics for the decision-makers were reported as mean (standard deviation) for continuous variables and count (percent) for categorical variables and were stratified by non-DS and DS samples. In the primary analysis, we quantified the difference in mean total RAQ scores comparing DS to non-DS decision-makers. We used linear regression to model the mean total RAQ score. The predictor of interest was whether the decision-makers were from DS or non-DS sample. We adjusted for age, sex, race and ethnicity, years of education, and COVID-19-time frame as potential confounders. The covariates were a priori determined to potentially confound the relationship between RAQ and DS status based upon their likelihood of being predictive of RAQ scores and their potential imbalance between participants coming from the two registries. Sex, race and ethnicity, and COVID-19-time frame were adjusted for categorical variables. Age and education were adjusted for continuous variables. As subanalyses, we included age and education as categorical variables to estimate associations between each category and the total RAQ score. To guard against any potential violations of the homoscedasticity assumption employed by classical linear regression, we utilized a robust variance estimator to provide valid inference in the presence of heteroscedasticity.[16]

In a pre-specified secondary analysis, we quantified the relative difference in the odds of having a more positive attitude toward research with respect to each RAQ item between the DS and non-DS decision-makers. In this analysis, we made use of the ordered nature of itemized RAQ score and employed a proportional odds model to estimate the odds ratio (OR) of having a "high" RAQ score comparing DS to non-DS decision-makers. In this model, the cutoff value for a "high" RAQ score is arbitrary in that all possible cut points for a high response are modeled simultaneously. More simply, the estimated OR obtained from the proportional odds model can be thought of as a weighted average of the estimated ORs obtained from four separate logistic regression models in which "success" is defined as a RAQ score >1, >2, >3, and >4, respectively. As such, proportional odds models assume that the relative odds of a "high" response comparing DS to non-DS is roughly constant, regardless of where the cutoff for "high" versus "low" is made. In each of the seven proportional odds models corresponding to each RAQ item, we adjusted for age, sex, race and ethnicity, education, and COVID-19-time frame. We performed a sensitivity analysis to assess the validity of the proportional odds assumption. Specifically, we fit four logistic regression models per RAQ item and compared the estimated ORs across each to the proportional odds model estimate. Substantial deviation of the estimates from the proportional odds model from the other four logistic regression estimates would have indicated a violation of the proportional odds assumption. We did not observe strong departures from the proportional odds assumption.

To account for multiplicity in the item-level analyses, we utilized a Holm-Bonferroni correction to control the familywise type I error rate in our analysis.[17] We stated the determination of statistical significance, after application of the Holm-Bonferroni correction, throughout the presented results.

Finally, in a descriptive analysis, we fit linear regression models with the same adjustment covariates as described in the primary analysis for each RAQ item score (ranges from 1 to 5). The purpose of this analysis was to quantify absolute differences in mean item level scores on the original scale of the questions being asked.

3 | RESULTS

3.1 | Descriptive statistics

Demographics for decision-makers in the DS and non-DS groups are displayed in Table 1. Of the 5794 decision-makers, 976 (16.8%) came from the DS group and 4818 (83.2%) were from the non-DS group. Table 1 also highlights that the demographics of the DS and non-DS decision-makers were similar. For the most part, the decision-makers from these registries had at least 12 years of education, were non-Hispanic White individuals, female, and older than 50 years. Due to the homogeneity of these two groups, we did not pursue any covariate balancing techniques, such as propensity score matching. The primary discrepancy between the two groups was the time frame in which the survey was completed. The majority (67.3%) of DS decision-makers completed the survey after March 13, 2020, compared to only 14.6% of the non-DS decision-makers.

3.2 | Total RAQ scores comparison

The mean (standard deviation) of the total RAQ score was 28.66 (4.41) for non-DS decision-makers and 29.20 (3.75) for DS decision-makers. The results from our primary analysis are summarized in Table 2. We estimated that the mean composite RAQ score was 0.55 (95% CI: 0.28, 0.81; $p < 0.001$) higher in the population of DS decision-makers compared to that in the population of non-DS decision-makers without accounting for any potential confounding factors. After adjustment for age, sex, race and ethnicity, education, and COVID-19-time frame, the expected difference in composite RAQ scores was estimated to be 0.11 (95% CI: -0.22, 0.43; $p = 0.531$) comparing DS to non-DS decision-makers. Also from the adjusted model, we found that an increase in age or years of education was associated with a higher mean RAQ score. We also observed that decision-makers completing the survey after March 13, 2020, had slightly higher RAQ compared to those completing the survey prior to then.

3.3 | Itemized RAQ scores comparison

Figure 1A illustrates our descriptive analysis of the estimated difference in mean RAQ score per item comparing DS and non-DS decision-makers adjusted for age, sex, race and ethnicity, education, and COVID-19-time frame. We observed that the DS decision-makers had higher mean RAQ scores for helping others and research safety, whereas non-DS decision-makers had higher mean RAQ scores for

TABLE 1 Characteristics of decision-makers stratified by non-DS and DS sample.

	Overall (*N* = 5794)	Non-DS (*N* = 4818)	DS (*N* = 976)
Age (years) (mean (SD))	56.36 (16.22)	56.98 (16.92)	53.36 (11.86)
<45 (*n* (%))	1385 (23.9)	1122 (23.3)	263 (26.9)
45–59 (*n* (%))	1587 (27.4)	1177 (24.4)	410 (42.0)
60–70 (*n* (%))	1559 (26.9)	1327 (27.5)	232 (23.8)
>70 (*n* (%))	1179 (20.3)	1109 (23.0)	70 (7.2)
Missing (*n* (%))	84 (1.4)	83 (1.7)	1 (0.1)
Sex			
Female (*n* (%))	3970 (68.5)	3111 (64.6)	859 (88.0)
Male (*n* (%))	1807 (31.2)	1690 (35.1)	117 (12.0)
Other (*n* (%))	17 (0.3)	17 (0.4)	0 (0.0)
Race and ethnicity			
Non-Hispanic White (*n* (%))	4209 (72.6)	3408 (70.7)	801 (82.1)
Non-Hispanic Asian (*n* (%))	375 (6.5)	364 (7.6)	11 (1.1)
Non-Hispanic Black (*n* (%))	79 (1.4)	66 (1.4)	13 (1.3)
Hispanic White (*n* (%))	265 (4.6)	239 (5.0)	26 (2.7)
Other (*n* (%))	332 (5.7)	316 (6.6)	16 (1.6)
Missing (*n* (%))	534 (9.2)	425 (8.8)	109 (11.2)
Education (years) (mean (SD))	16.87 (5.49)	16.68 (5.81)	17.80 (3.32)
12 (*n* (%))	400 (6.9)	366 (7.6)	34 (3.5)
<12 (*n* (%))	44 (0.8)	37 (0.8)	7 (0.7)
12–16 (*n* (%))	2853 (49.2)	2525 (52.4)	328 (33.6)
>16 (*n* (%))	2429 (41.9)	1835 (38.1)	594 (60.9)
Missing (*n* (%))	68 (1.2)	55 (1.1)	13 (1.3)
COVID-19-time frame[a]			
Up to March 13, 2020 (*n* (%))	4433 (76.5)	4114 (85.4)	319 (32.7)
After March 13, 2020 (*n* (%))	1361 (23.5)	704 (14.6)	657 (67.3)

Note: Continuous variables were reported as mean (standard deviation) and categorical variables were reported as count (percent).
Abbreviation: COVID-19, coronavirus disease 2019; DS, Down syndrome; SD, standard deviation.
[a]On March 13, 2020, the US government declared a nationwide emergency and issued an additional travel ban on non-US citizens traveling from 26 European countries due to COVID-19.

finding cures. The differential direction in the item-level responses coincided with the lack of difference in the total RAQ score after collapsing across all items.

The results of our secondary analysis are summarized in Figure 1B. Adjusting for age, sex, race and ethnicity, education, and COVID-19-time frame, we estimated that DS decision-makers had 26% (OR = 1.26, 95% CI: 1.08, 1.48) higher odds of having a more positive attitude toward the belief of the responsibility to help others and 23% (OR = 0.77, 95% CI: 0.66, 0.90) lower odds of having a more positive attitude toward the belief that medical research will find cures for many major diseases during their lifetimes. Adjusting for multiple comparisons, these estimates remained statistically significant. From our sensitivity analysis (see Figure S1), the proportional odds assumption appeared to hold for each of the seven-question models we fit.

4 | DISCUSSION

The results of our primary analyses show similarities in overall research attitudes between decision-makers for individuals with DS and those decision-makers in a registry primarily tailored to AD research within the general population without DS. Research attitudes based on RAQ were positive among both DS and non-DS decision-makers. The mean RAQ score was slightly higher in the DS decision-makers, but this difference attenuated after adjusting for potential confounding factors. The findings suggest that some aspects of recruitment science may be shared between decision-makers for individuals with and without DS. Mean RAQ scores were also higher with the increasing age of the respondents. This may reflect the awareness of older decision-makers to many of the comorbidities that define the process of aging.[18]

TABLE 2 Estimated difference in total RAQ scores from robust linear regression models.

	Unadjusted		Adjusted	
	Est. (95% CI)	*p*	Est. (95% CI)	*p*-Value
Decision-maker				
Non-DS	Reference		Reference	
DS	0.545 (0.279, 0.812)	<0.001	0.105 (−0.224, 0.434)	0.531
Age (per 10 years)	0.141 (0.070, 0.211)	<0.001	0.100 (0.021, 0.179)	0.013
<45	Reference		Reference	
45–59	0.123 (−0.197, 0.443)	0.450	−0.088 (−0.422, 0.246)	0.606
60- 70	0.448 (0.124, 0.773)	0.007	0.341 (−0.006, 0.688)	0.054
>70	0.625 (0.290, 0.961)	<0.001	0.446 (0.073, 0.819)	0.019
Sex		0.158[a]		0.077[a]
Female	Reference		Reference	
Male	−0.190 (−0.433, 0.054)	0.127	−0.267 (−0.528, −0.005)	0.046
Other	−1.166 (−3.037, 0.705)	0.222	−1.094 (−3.011, 0.822)	0.263
Race and ethnicity		0.003[a]		0.197
Non-Hispanic White	Reference		Reference	
Non-Hispanic Asian	−0.846 (−1.318, −0.374)	<0.001	−0.598 (−1.080, −0.117)	0.015
Non-Hispanic Black	−0.355 (−1.290, 0.580)	0.457	−0.201 (−1.118, 0.716)	0.668
Hispanic White	−0.412 (−1.038, 0.214)	0.197	−0.082 (−0.712, 0.547)	0.798
Other	−0.483 (−1.019, 0.052)	0.077	−0.140 (−0.697, 0.416)	0.622
Education (per 5 years)	0.688 (0.503, 0.873)	<0.001	0.679 (0.483, 0.875)	<0.001
<12	Reference		Reference	
12	−1.221 (−2.415, −0.027)	0.045	−1.054 (−2.330, 0.222)	0.106
12–16	−0.911 (−2.029, 0.207)	0.110	−0.792 (−1.992, 0.408)	0.196
>16	−0.206 (−1.324, 0.912)	0.718	−0.160 (−1.360, 1.040)	0.794
COVID-19-time frame				
Up to March 13, 2020	Reference		Reference	
After March 13, 2020	0.390 (0.141, 0.638)	0.002	0.269 (−0.025, 0.563)	0.073

Abbreviation: CI, confidence interval; COVID-19, coronavirus disease 2019; DS, Down syndrome; RAQ, Research Attitudes Questionnaire.
[a]Multivariate Wald test-based *p*-values were calculated for the construct of variables with more than two categories to test whether their corresponding coefficients were simultaneously equal to 0.

Besides age, we observed an association between education and RAQ scores controlling for covariates. Potential cohort effects related to the COVID-19 pandemic were not statistically associated with RAQ scores in the adjusted analysis though the COVID-19 pandemic had a differential impact on the community with DS.[19–22]

Our secondary analyses of the RAQ data did reveal some differences between the two populations. In item-level analyses, DS decision-makers were more favorably disposed toward "responsibility for helping others through volunteering for medical research." In our previous study, favorable attitudes toward research participation were also noted.[13] In children with DS under the age of 18 years, 72% of their parents expressed willingness to participate in research, although only 36% had actually enrolled in a clinical trial. Barriers to research participation for people with DS have been reviewed and include benefit-risk assessment, time commitment, access to results, and the "power distance" between the researchers and families. Here, decision-makers for individuals with DS were less favorably disposed toward the belief that "cures would be found for many major diseases during their lifetime". Though this question was not specific as to what cures were meant, families who have a relative with DS do not show unanimity in hoping for a cure for DS.[23] Parental attitudes toward a cure for DS are complex and reflect ethical issues, perceived societal values, and other pragmatic considerations. These differences in RAQ items between the two groups may facilitate development of precise recruitment strategies for populations with DS.

The survey respondents for both populations were drawn from registries, representing both a strength and limitation of the current study. Recruitment registries in the general population have been shown to enhance recruitment in preclinical AD trials[24] and to improve engagement of underserved populations.[25] Understanding attitudes among

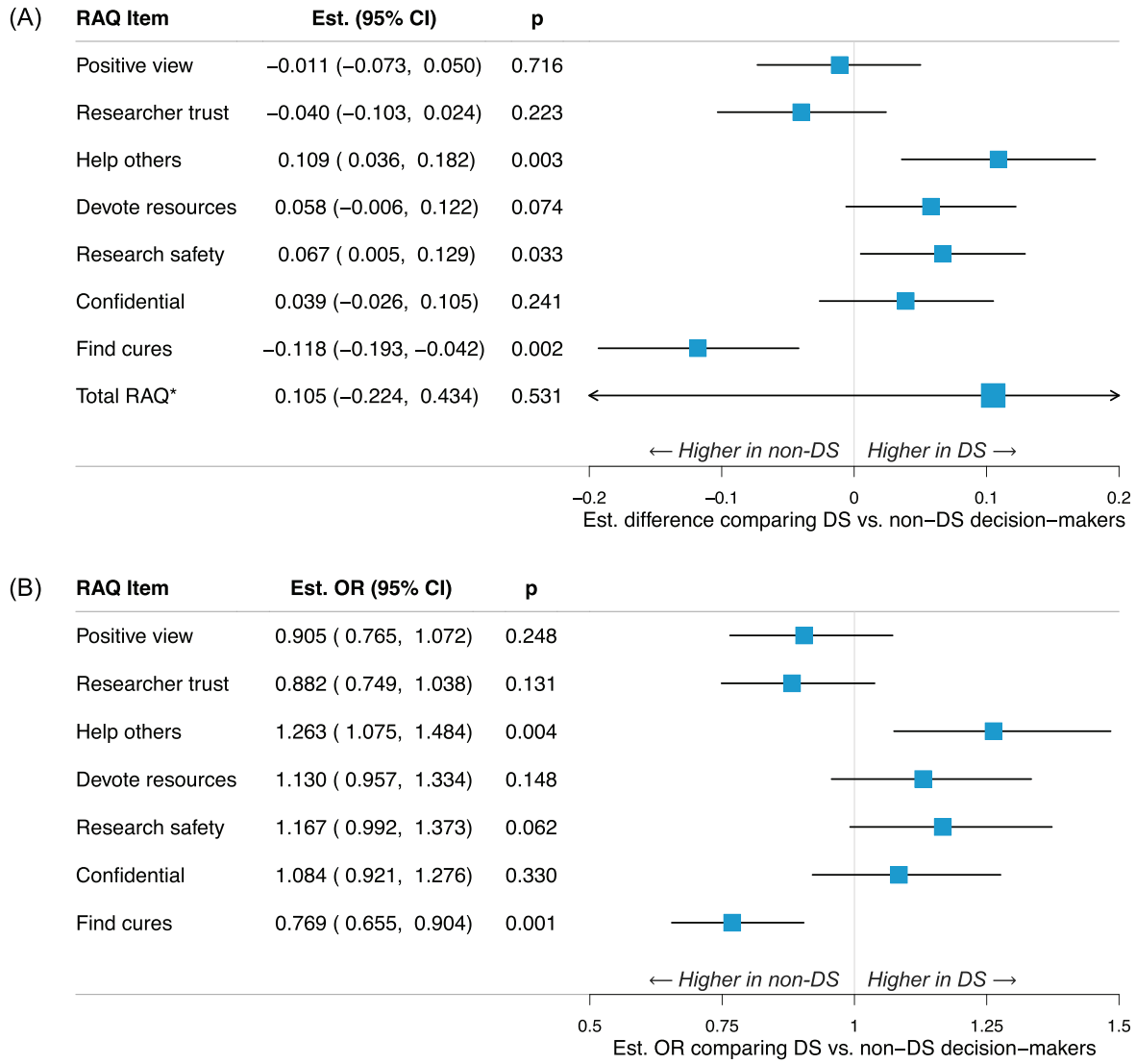

FIGURE 1 (A) Estimated difference in RAQ scores comparing DS to non-DS decision-makers adjusting for age, sex, race and ethnicity, education, and COVID-19-time frame (linear regression models); *Note*: * Total RAQ row presented the estimate corresponding to DS decision-makers from Table 2. Total RAQ score ranged from 7 to 35 whereas itemized RAQ score ranged from 1 to 5. Estimates *to the right* of the vertical bar at 0 indicate that *DS decision-makers have higher* mean itemized RAQ scores compared to non-DS decision-makers. Estimates *to the left* of the vertical bar at 0 indicate that *non-DS decision-makers have higher* mean itemized RAQ scores compared to DS decision-makers. (B) Estimated ORs of having "higher" RAQ scores comparing DS to non-DS decision-makers adjusting for age, sex, race and ethnicity, education, and COVID-19-time frame (proportional odds models); *Note*: Estimates *to the right* of the vertical bar at 1 indicate that *DS decision-makers have higher* odds of having a more positive attitude toward the RAQ item compared to non-DS decision-makers. Estimates *to the left* of the vertical bar at 1 indicate that *non-DS decision-makers have higher* odds of having a more positive attitude toward the RAQ item compared to DS decision-makers. Abbreviation: DS, Down syndrome; OR, odds ratio; RAQ, Research Attitudes Questionnaire.

those in a registry is applicable to future recruitment efforts. It is worth noting that registries are biased samples, in which participants generally have positive attitudes toward research. Not all registry participants agree to participate in research, however. In the present study, out of 2100 DS-Connect participants contacted, 1048 family members actually completed the survey. In addition, registry participants rarely represent the population at large, particularly historically underrepresented groups such as individuals of minority races and ethnicities. Methods to improve representation of these groups are critically needed.[26] Unfortunately, the current results do not shed further light on this need, nor the potential for intersectionality between key factors, such as the role of race, ethnicity, and culture in families with DS. These will be essential areas for future research.[27]

We acknowledge other limitations in our study. We did not have complete information on some covariates that could have helped better estimate differences in RAQ between the two populations of decision-makers. Examples include decision-makers' occupations, comorbidities, and previous research participation. Previous participation in research has shown to be a strong predictor of research attitudes.[13] This information was not readily available for non-DS

decision-makers, required additional investigation to obtain and, thus, was not part of this analysis.

Our results suggest some directions for future research. The cost-effectiveness of utilizing registries in DS must be determined. Registries have been shown to enhance clinical trials in AD, particularly those that are local.[14,28] Further, the effectiveness of registries in aiding recruitment of traditionally underrepresented groups remains an area of study.[29,30] For people with DS, an additional understanding of research attitudes for decision-makers will be necessary to enhance these aspects of recruitment science.

In conclusion, the current results are a novel assessment, comparing research attitudes among key enrollment decision-makers in populations with and without DS. Studies such as this one may be key to instructing recruitment plans as well as trial designs for interventional studies that aim to test therapies, particularly therapies that may be reasonable in both groups such as Alzheimer's prevention treatments. Recruitment science research should be continued to better understand the unique barriers and facilitators of participation, particularly among more granular subgroups of DS and non-DS decision-makers.

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CONFLICT OF INTEREST STATEMENT

J.D.G. reports research support from NIA, the Alzheimer's Association, BrightFocus Foundation, Eli Lilly, Genentech, Biogen, and Eisai. The remaining authors declare no conflicting interests. Author disclosures are available in the supporting information.

CONSENT STATEMENT

All data used in these analyses were non-identifiable.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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