

RESEARCH ARTICLE

The association of dementia risk symptoms and functional activity in adults with Down syndrome

Selena E. Washington¹  | Amy E. Bodde² | Brian C. Helse³ | Rebecca M. Bollinger⁴ | Nora Smith¹ | Lauren T. Ptomey² | Beau Ances⁵ | Susan L. Stark⁴

¹Department of Occupational Science and Occupational Therapy, Saint Louis University, St. Louis, Missouri, USA

²Department of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas, USA

³Department of Neurology, University of Kansas Alzheimer's Disease Research Center, University of Kansas Medical Center, Kansas City, Kansas, USA

⁴Program in Occupational Therapy, Washington University School of Medicine in St. Louis, St. Louis, Missouri, USA

⁵Department of Neurology, Washington University School of Medicine in St. Louis, St. Louis, Missouri, USA

Correspondence

Selena E. Washington, Department of Occupational Science and Occupational Therapy, Saint Louis University, 3437 Caroline Mall, Suite 2020, St. Louis, MO 63104, USA.
Email: selena.washington@health.slu.edu

Funding information

U.S. National Institute on Aging; Promote Diversity in Health-Related Research, Grant/Award Number: R01AG057680-05S1; Preclinical Alzheimer's Disease; Mentored Research Scientist Development, Grant/Award Number: K01AG083130-01; Assessment of Physical Activity for Alzheimer's Disease Research, Grant/Award Number: R01AG063909-03; The Promotion of Physical; Paula and Rodger O. Riney Fund; the Daniel J Brennan MD Fund

Abstract

INTRODUCTION: Adults with Down syndrome (DS) have an increased risk of Alzheimer's disease (AD) dementia, often showing neuropathological indicators by age 40. Physical function and activities of daily living (ADLs) are understudied areas of function that may inform dementia risk. We investigated associations among age, physical function (gait/balance, grip strength, and lower extremity strength), ADLs, and dementia risk symptoms in adults with DS. We hypothesized that compromised physical function and lower independence with ADLs would be associated with an informant/caregiver-reported measure of dementia risk symptoms.

METHODS: A secondary analysis for this cross-sectional study was completed using data from two academic research centers with 43 adults with DS (age 30 ± 12 years). We examined the association of dementia risk symptoms, captured through the Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (DSQIID), with physical function (timed up and go [TUG], sit-to-stand [STS], grip strength) and ADLs (Waisman Activities of Daily Living Scale). A linear regression model for the continuous dementia risk measure in the DSQIID used a log transformation of $(1 + \log(Y + 1))$ to account for a high zero count. Wilcoxon rank-sum tests were used to assess differences in the physical function measures, DSQIID questionnaire, and Waisman ADL by dividing mean age categories.

RESULTS: Higher DSQIID scores were associated with lower independence with ADLs ($\beta = -0.103$, $p = 0.008$), slower gait times (TUG; $\beta = 0.112$, $p = 0.034$), and impaired lower extremity strength (STS; $\beta = 0.112$, $p = 0.017$) and grip strength ($\beta = -0.039$, $p = 0.034$). DSQIID scores differed significantly between the ≥ 30 and < 30 age groups. Participants ≥ 30 years of age scored 5 points higher on the DSQIID than participants < 30 , suggesting that age was associated with greater dementia risk.

DISCUSSION: Greater dementia risk symptoms were associated with age, lower physical function scores, and independence with ADLs, suggesting that declines in physical function and ADLs may be early indicators of subsequent dementia risk in adults with DS.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2024 The Author(s). Alzheimer's & Dementia: Translational Research & Clinical Interventions published by Wiley Periodicals LLC on behalf of Alzheimer's Association.

KEYWORDS

activities of daily living, cognition, dementia, Down syndrome, physical function

Highlights

- We explored the association of physical function and activities of daily living (ADLs) in aging adults with DS and their relationship with informant/caregiver report of dementia risk symptoms.
- Our findings demonstrated a significant relationship between a higher number of dementia risk symptoms observed and lower independence with ADLs, and impaired gait/balance, grip strength, and lower extremity strength.
- Further research with larger longitudinal studies is necessary to investigate any causative relationships among physical function, ADL function, and dementia risk symptoms.

1 | BACKGROUND

Adults with Down syndrome (DS) are at an increased risk of developing Alzheimer's disease (AD) dementia, with almost all individuals displaying neuropathological features (e.g., amyloid plaques and neurofibrillary tangles) by the age of 40 years¹⁻⁵; the risk of developing AD dementia in adults with DS increases with age.^{3,6} DS is a common chromosomal condition that is associated with numerous neurologic manifestations such as intellectual disability, sleep apnea, and dementia.^{7,8} With recent increases in the lifespan of individuals with DS (55–60 years of age), the number of aging adults with DS is growing quickly, necessitating the early identification of dementia risk factors.^{9,10} To address the prevalence of this diagnosis, the National Task Group on Intellectual Disabilities and Dementia Practices recommends a comprehensive assessment of risk factors and signs associated with dementia in adults with intellectual disabilities.⁷ Examples of dementia risk symptoms include cognitive function (e.g., loss of memory and/or confusion),^{11,12} behavior (e.g., aggression, sadness, fearfulness, or anxiety),^{13,14} sleep (disruption of),^{15,16} a decline in language skills,¹⁷ and social withdrawal.^{6,18} Dementia risk symptoms in relation to activities of daily living (ADLs) and physical function (gait/balance, grip strength, and lower extremity strength) in adults with DS have not been fully investigated prior to an AD dementia diagnosis. Given the risk of AD dementia in adults with DS, understanding connections among physical function, ADLs, and caregiver-reported dementia risk symptoms in this population could aid in early detection and assist caregivers and health care professionals in providing appropriate support and care.

Previous research has explored dementia risk symptoms in adults with DS, noting impairment in the areas of cognition,^{11,12} behavior,^{13,14} sleep,^{15,16} physical activity, and functional impairment,^{19,20} and the increased presence of dementia risk symptoms.^{12,18,21,22} However, the relationships among physical function, ADLs, and caregiver-reported dementia risk symptoms remain unclear. Before a formal clinical evaluation and diagnosis of AD dementia occur, caregivers and/or

health care professionals often report dementia risk symptoms using caregiver-reported screening assessments, such as the Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (DSQIID).^{18,21} These caregiver-reported dementia risk symptoms provide valuable insights into an individual's cognitive, behavioral, and functional changes that may precede a formal diagnosis; this information can guide early dementia identification efforts.²¹

Physical function, specifically within the gait-related brain regions, is among the earliest areas of function affected by amyloid beta ($A\beta$) plaque accumulation, affecting gait and balance performance.^{3,6,23,24} Recent studies have noted that age and gait dysfunction are early indicators of AD within adults with DS,^{20,23} and gait and balance impairment are associated with mild cognitive decline and dementia in adults with DS.²³ Other studies in non-DS populations have demonstrated associations between changes in gait (balance and speed) and the risk of dementia; they found that greater variability in stride length, swing time, and stance time was associated with dementia risk in both global- and domain-specific cognitive areas.²⁵ Similarly, previous studies have shown that lower grip strength is associated with functional status and cognitive decline in older adults without DS, concluding that lower grip strength is associated with a higher risk of the onset of cognitive decline and dementia.^{26,27} However, there is limited evidence that examines the specific association between measures of gait, balance, grip strength, and caregiver-reported dementia risk symptoms in adults with DS.²⁴

Although physical function measures reveal specific motor abilities, assessing of ADLs provides a comprehensive understanding of an individual's overall functional capacity and independence with daily activities. According to the National Task Group on Intellectual Disabilities and Dementia Practices (National Task Group), one of the hallmark features of dementia is a decline from the baseline level of function, including basic and instrumental ADLs.^{7,28} Basic ADLs are the self-care tasks (e.g., grooming, dressing, bathing) that individuals typically perform daily to live and maintain their well-being. Instrumental ADLs (e.g., work, managing a schedule) are more complex tasks

necessary for independent living within the home and community.^{29,30} The assessment of ADLs (basic and instrumental) in conjunction with an informant/caregiver-reported dementia risk questionnaire is recommended by the National Task Group to inform ADL baseline function and subsequent changes for individuals with intellectual and developmental disabilities.⁷ The literature has shown a significant relationship between a decline in cognitive function and the ability to perform ADLs.^{28,31,32} However, there is limited literature examining dementia risk symptoms and ADLs, which is needed to inform essential lifestyle adjustments and the level of care provided to adults aging with DS.³² Therefore, an examination of the relationship between ADLs, physical function (gait/balance, grip strength, and lower extremity strength), and caregiver assessment of dementia risk symptoms for individuals with DS is warranted to support the observation and reporting of functional changes over time.

Based on the current evidence, the goals of this study were to investigate the relationships between caregiver-reported dementia risk symptoms, as assessed by the DSQIID, and: (1) physical function (gait/balance, grip strength, and lower extremity strength) and (2) level of independence with ADLs among adults aging with DS. We hypothesized that compromised physical function and reduced independence in ADLs in adults with DS would be associated with DSQIID caregiver-reported dementia risk symptom assessment. Our findings intend to expand the knowledge regarding these areas of function and their association with dementia risk symptoms to inform clinicians, caregivers, and health care professionals about the importance of monitoring these specific changes within this population who are at risk of developing AD dementia.

2 | METHODS

This secondary analysis involved cross-sectional data gathered from 43 adults (≥ 18 years of age) with a confirmed diagnosis of DS. These individuals participated in one completed and one ongoing study at one of two academic medical research centers located in the Midwest (USA).^{33,34} Common participant eligibility inclusion criteria between the two sites included: (1) DS diagnosis; (2) age ≥ 18 years; (3) lived at home with a parent/guardian, in a supported living environment with a caregiver who agreed to serve as a study partner or lived alone; (4) the ability to participate in physical activity, and (5) the ability to understand 1- to 2-step directions. Participants with a diagnosis of mild cognitive impairment (MCI) were not excluded from the study. Participants with DSQIID scores of ≥ 20 were excluded from one site due to the requirements of the parent trial. Standardized cognitive assessment was not included for this study, because there was not a common assessment obtained between sites. Common recruitment efforts employed between sites were as follows: (1) community outreach; (2) invitations to participants of previous studies; (3) health care provider outreach; (4) flyer distribution; and (5) social media outreach. Consent and assent were completed with the participant and caregiver before collecting study data. Questionnaires were completed by participants with DS and their caregiver(s), who were the partici-

RESEARCH IN CONTEXT

- 1. Systematic review:** Recent studies establish a strong relationship between age and dementia risk in aging adults with Down syndrome (DS). To expand upon this knowledge, we explored the association of physical function and ADLs in aging adults with DS and their relationship with Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (DSQIID) informant/caregiver report of dementia risk symptoms.
- 2. Interpretation:** Our findings showed a significant relationship between a greater number of observed dementia risk symptoms and decreased independence in activities of daily living (ADLs), along with impairments in gait, balance, hand grip strength, and lower extremity strength. This information can serve as a catalyst for the individuals, caregivers, and/or professionals working with individuals with DS to seek a formal cognitive assessment under the direction of a physician or health care professional.
- 3. Future directions:** Further research with larger longitudinal studies is necessary to investigate any causative relationships among physical function, ADL function, and dementia risk symptoms.

pants' proxies or study partners. All physical function measures were assessed or obtained by trained research personnel, and all study procedures were approved by each institution's institutional review board.

2.1 | Demographics and cognition/dementia risk

The demographic data collected from the participants included age (≥ 18 years), sex, race (i.e., Asian, Black, White), ethnicity (i.e., Hispanic/Latino), and residential status (i.e., living alone, living with parents, living with other family members, or a supported living facility). Informant/caregiver-reported dementia risk in adults with DS was assessed at each site with the DSQIID through an electronic or paper format.¹⁸ The DSQIID is a valid and reliable caregiver-reported dementia screening questionnaire consisting of 53 items that assess dementia risk symptoms in the areas of general physical and psychological function, sleep and speech abnormalities, loss of memory, confusion, and social withdrawal.^{18,35} The DSQIID is not a diagnostic instrument for the diagnosis of dementia; however, it is based on the actual symptoms of dementia.¹⁸ Forty-three of the questions are scored as 0 for "has always been the case" and "does not apply" or 1 for "always but worse" and "new symptom." Ten items suggesting comparative decline (e.g., "slower speech") are scored as 1 for "yes" or as 0 for "no." A total score ≥ 20 indicates possible dementia risk. This

scale was used as a continuous variable, with a greater score indicating more changes in behavior over time.³⁵

2.2 | Gait and balance

To assess physical function (gait/balance), we used the timed up and go (TUG), which has been administered previously and validated with adults with DS.^{36,37} It is administered by clinical or research personnel. From a sitting position in a standard armchair, participants are asked to stand up, walk to a line 10 feet away, turn around, return to the chair, and sit down. The score is the time in seconds it takes to complete the task, with the fastest of two trials determining the score. Higher scores (i.e., longer times) indicate greater impairment in gait and balance.

2.3 | Grip strength

Grip strength was assessed for the dominant hand using a Jamar digital hand grip dynamometer.³⁸ Participants were asked to hold their arm with their elbow bent at a 90-degree angle and to squeeze the dynamometer as hard as possible using a smooth motion. The procedure was repeated three times, with the average of the three readings used in the analysis with the dominant hand only.³⁹

2.4 | Lower extremity strength

Lower extremity strength was measured using the sit-to-stand (STS) test. This assessment has been used previously with adults with DS⁴⁰ and is useful for evaluating functional lower extremity strength, transitional movements, fall risk, and balance. Each institution used a different protocol for the STS test (i.e., time in seconds to complete five repetitions⁴¹ or the number of repetitions in 30 s⁴²). Thus, to harmonize the data between the institutions, we created an estimated time to complete five repetitions from the 30-s chair stand test (i.e., (30 s/number of reps)*5 reps) and an estimated number of completed repetitions in 30 s from the five-repetition chair stand test (i.e., (30 s/seconds for 5 reps)/5).

2.5 | Activities of daily living (ADLs)

The performance of basic and instrumental ADLs was assessed using the Waisman Activities of Daily Living Scale (W-ADL), which was designed and validated for individuals with intellectual disabilities.⁴³ Caregivers completed the W-ADL on behalf of the participant with DS. The W-ADL includes 17 activities: six basic ADLs (e.g., washing/bathing, grooming, hygiene, dressing) and eleven instrumental ADLs (e.g., doing household tasks, food preparation, shopping, banking). Caregivers rate how the person with DS performs each task of

daily living using a 3-point Likert scale from 0 “does not do at all,” 1 “does with help,” to 2 “independent or does on own.” The responses are summed to yield a total W-ADL score, with higher scores indicating greater independence in ADLs.

2.6 | Analysis

We used continuous data reported as mean \pm SD and categorical measures are represented as frequency (%). Histograms, Q-Q plots, and Shapiro–Wilk tests were used to assess the normality of the W-ADL and physical function measures (i.e., gait/balance, grip strength, and lower extremity strength). We used non-parametric Wilcoxon rank sum tests to explore differences in the physical function measures, dementia risk, and ADLs by research site and mean age of participants (<30 years vs \geq 30 years). The DSQIID dementia risk score was right skewed, with 17 participants (40%) in our sample having no indications of probable dementia risk and scoring 0 on the DSQIID and three participants scoring \geq 20. Thus we performed a logarithmic transformation with a constant offset ($1 + \log(Y + 1)$) of the dementia risk score before regressing dementia risk on the physical function measures and ADLs in age- and sex-adjusted linear regressions. All models were checked for the independence of residuals, homoscedasticity, multicollinearity, and influential data points, and statistical significance was set at $P < 0.05$. The analysis was completed using R version 4.3.2 for statistical computing.⁴⁴

3 | RESULTS

Forty-three adults with DS (mean age \pm SD: 30 \pm 12 years, 53% female, 81% White) were included in this analysis. Approximately half (58%) of the participants lived at home with their parents, and others lived alone (21%) or in supported living (14%). The average score on the DSQIID dementia risk questionnaire was 5.8 \pm 8.7 of a possible score of 53 (Table 1). Three participants had a DSQIID dementia risk screening score \geq 20, indicating a possible risk of dementia and a recommendation for clinical assessment.¹⁸ Differences in informant/caregiver-reported dementia risk in adults with DS, physical function measures, and ADLs between individuals with DS who were <30 years and \geq 30 years of age are presented in Table 2. We statistically compared outcomes by site and added this information to Table 2. On average, we found that individuals with DS \geq 30 years of age had a slower time on the TUG test (<30 years: 6.5 \pm 1.9 s, \geq 30 years: 11.5 \pm 5.4 s, $P < 0.001$) and had reduced performance on the STS test by completing four fewer repetitions in 30 s ($p = 0.005$) and taking 3 s longer to complete five repetitions ($p = 0.003$). However, adults with DS \geq 30 years of age produced 11.1 kg more force on the dominant grip strength test when compared to individuals with DS who were <30 years of age ($P = 0.004$). In addition, individuals \geq 30 years of age had a higher score on the DSQIID screening; however, the differences were not statistically significant (<30 years: 3.7 \pm 4.9, \geq 30 years: 8.3 \pm 11.3, $p = 0.481$).

TABLE 1 Sample characteristics by site.

	Overall N = 43 ^a	Site 1 N = 24 ^a	Site 2 N = 19 ^a
Age	30.2 ± 11.5	23.0 ± 7.5	39.4 ± 8.9
Sex			
Female	23 (53%)	14 (58%)	9 (47%)
Male	20 (47%)	10 (42%)	10 (53%)
Race			
Asian	2 (4.7%)	2 (8.3%)	0 (0%)
Black	4 (9.3%)	3 (13%)	1 (5.3%)
Mixed race	2 (4.7%)	2 (8.3%)	0 (0%)
White	35 (81%)	17 (71%)	18 (95%)
Ethnicity			
Hispanic or Latino	1 (2.3%)	1 (4.2%)	0 (0%)
Not Hispanic or Latino	42 (98%)	23 (96%)	19 (100%)
Living situation			
Living alone	9 (21%)	2 (8.3%)	7 (37%)
Living with other family	3 (7.0%)	0 (0%)	3 (16%)
Living with parents	25 (58%)	18 (75%)	7 (37%)
Other living situation	6 (14%)	4 (17%)	2 (11%)
Dementia screening questionnaire	5.8 ± 8.7	3.0 ± 3.8	9.5 ± 11.5
Timed up and go (s)	8.8 ± 4.7	6.3 ± 1.6	12.0 ± 5.3
Sit-to-stand (reps in 30 s)	13 ± 5	15 ± 5	11 ± 3
Sit-to-stand (seconds to complete 5 reps)	12.9 ± 4.6	10.9 ± 3.6	15.4 ± 4.6
Grip strength: Dominant hand	27.6 ± 12.4	21.5 ± 7.7	35.3 ± 13.0
Waisman Activities of Daily Living Scale	24.3 ± 4.7	24.3 ± 3.8	24.3 ± 5.8
Asthma	5 (12%)	4 (17%)	1 (5.3%)
Diabetes	2 (4.7%)	0 (0%)	2 (11%)

Abbreviation: ADLs, activities of daily living.

^aMean ± SD; n (%).

In linear regressions adjusted for age, sex, and research site, we found that the time to complete five STS repetitions, W-ADL scores, hand grip strength, and TUG time were all significantly associated with dementia risk (DSQIID) (see Table 3). Individuals with a slower time on the TUG ($\beta = 0.112, p = 0.034$), a slower time completing five STS repetitions ($\beta = 0.112, p = 0.017$), and lower hand grip strength ($\beta = -0.039, p = 0.034$) had higher dementia risk scores (DSQIID). Conversely, individuals with a higher score on the W-ADL ($\beta = -0.103, p = 0.008$) had a lower dementia risk score (DSQIID; Table 3). We calculated Cohen's f^2 (eta-squared) effect size for all predictor variables in a non-adjusted linear regression and found a medium effect >0.20 for the TUG ($f^2 = 0.221$), time to complete five STS repetitions ($f^2 = 0.201$), and the W-ADL ($f^2 = 0.206$).

4 | DISCUSSION

We investigated whether physical function and independence in ADLs were associated with dementia risk symptoms as assessed by an informant/caregiver-reported dementia screening questionnaire in adults with DS across two study sites. Our findings suggest that compromised physical function (i.e., a slower time on the TUG test and five-repetition STS and lower hand grip strength) was associated with higher dementia risk symptoms. Greater independence in ADLs was associated with lower dementia risk symptoms in 43 adults with DS, which is consistent with our hypothesis.

Although the association of TUG with DSQIID in adults with DS has not been evaluated previously, studies in adults with DS have evaluated associations using other tests of dementia and/or gait and mobility. In contrast to our findings, Conceição et al.²³ found TUG to have no association with clinical assessments of dementia in 52 adults with DS. However, they did find a significant positive correlation between cognition and the Performance-Oriented Mobility Assessment gait subscale, a method of assessing balance and gait in older adults.²³ The participants in our study had a TUG score of 8.8 ± 4.7 s. Although normative values have been established for children with DS,⁴⁵ they have not been established for adults with DS. Our values were in the range of general population norms for older adults 60–69 years of age (8.1 s) and 70–79 years of age (9.2 s).³⁷

A longer duration in completing the STS task was associated with a higher score (indicating impairment) on the DSQIID. We are not aware of previous assessments of STS tests that were associated with any dementia risk measures in adults with DS. However, Annweiler et al.⁴⁶ found that the five-repetition STS was associated with cognitive performance in community-dwelling older women without DS. Our participants averaged 12.9 ± 4.6 s to complete five repetitions. Although no normative values have been published for those with DS, this does exceed Bohannon's estimated norms for community-dwelling older adults 60–69 (11.4 s) and 70–79 (12.6 s) years of age.⁴⁷ Lower hand grip strength in our sample was associated with higher DSQIID scores. Hand grip strength as a component of physical function is commonly found in the literature and warrants future study in the DS population.^{48,49}

The findings also demonstrated a correlation between ADLs and DSQIID. A higher score on the W-ADL assessment, indicating greater independence in ADLs ($\beta = -0.096, p = 0.012$), was linked to a lower DSQIID dementia screening score. This confirms findings from previous studies in the DS population. For example, in a cross-sectional study of 216 individuals with DS >15 years of age, the DSQIID had a significant inverse correlation with ADLs.²⁸ Further evidence indicates that decreased independence in ADLs can indicate dementia risk and should be monitored for changes.^{28,32,50}

Overall, the significant correlations between the physical function measures, TUG, STS, and grip strength, and the DSQIID assessment, demonstrated that impaired physical function is associated with higher scores on a dementia risk assessment for individuals with DS. Time to complete measures of physical function, lower grip strength, and

TABLE 2 Dementia screening, functional fitness, and Waisman Activities of Daily Living Scale (W-ADL) by age category and site.

	By age			By site		
	<30 years N = 23 ^a	≥30 years N = 20 ¹	p-value ^b	Site 1 N = 24 ^a	Site 2 N = 19 ^a	p-value ^b
Dementia screening Questionnaire	3.7 ± 4.9	8.3 ± 11.3	0.481	3.0 ± 3.8	9.5 ± 11.5	0.157
Timed up and go (s)	6.5 ± 1.9	11.5 ± 5.4	<0.001	6.3 ± 1.6	12.0 ± 5.3	<0.001
Sit-to-stand (reps in 30 s)	15 ± 5	11 ± 3	0.005	15 ± 5	11 ± 3	0.002
Sit-to-stand (seconds to complete 5 reps)	11.1 ± 4.1	14.9 ± 4.4	0.003	10.9 ± 3.6	15.4 ± 4.6	<0.001
Grip strength: Dominant hand	22.5 ± 8.7	33.6 ± 13.5	0.004	21.5 ± 7.7	35.3 ± 13.0	<0.001
W-ADL	24.9 ± 3.8	23.7 ± 5.6	0.608	24.3 ± 3.8	24.3 ± 5.8	0.573

Abbreviation: ADLs, activities of daily living.

^aMean ± SD.

^bWilcoxon rank sum test.

TABLE 3 The linear effect of fitness or ADLs on DSQIID.

Predictor	Beta	SE	p-value	R squared	Adjusted R squared
Timed up and go	0.112	0.051	0.034	0.216	0.133
Sit-to-stand (reps)	-0.076	0.045	0.101	0.177	0.091
Sit-to-stand (s)	0.112	0.045	0.017	0.242	0.162
Dominant grip strength (kg)	-0.039	0.018	0.034	0.216	0.133
Waisman Activities of Daily Living Scale	-0.103	0.037	0.008	0.266	0.189

Note: Linear regressions adjusted for age, sex, and site.

Abbreviation: ADLs, activities of daily living; DSQIID, Dementia Screening Questionnaire for Individuals with Intellectual Disabilities.

independence in ADLs may be sensitive estimates of dementia risk in adults with DS, with medium effect sizes ranging from 0.20 to 0.22. Our findings suggest that physical function measures like TUG, STS, and grip strength alongside DSQIID scores, could serve as valuable indicators for assessing dementia risk in adults with DS. Given the absence of DS-specific physical function and ADL norms for adults, it is recommended that the assessments be conducted over time to monitor changes.⁷

5 | LIMITATIONS

Our study includes some limitations. One site included in our sample (N = 24) reducing the generalizability of the sample used the DSQIID in eligibility screening criteria for participation in a physical activity randomized controlled trial; those with high DSQIID scores (≥20) were excluded from the trial, possibly reducing the variability of dementia risk scores in our small sample. We employed DSQIID scores as a continuous measure due to the small number of persons within our sample. In addition, this cross-sectional study did not assess physical function and ADL change over time in relation to the DSQIID dementia risk assessment. Furthermore, age served as a limitation due to the young average age of this sample, potentially resulting in undetectable dementia risk symptoms. Causal inference and direction of associations cannot be determined due to the cross-sectional nature of the

study. We did not include any neuropsychological tests of cognition due to the restrictions of the available data and the focus of this study. Further research with larger longitudinal samples is necessary to investigate any causative relationships among physical function, ADLs, and dementia risk.

6 | CONCLUSION

Compromised physical function, as gauged by assessments such as the TUG and STS test, coupled with decreased independence in ADL performance, could suggest an increased dementia risk. In individuals with DS, these manifestations of dementia risk symptoms and compromised function may occur several years earlier than in the non-DS population.^{3,4,6} These user-friendly assessments of physical function and ADLs, along with dementia risk screening questionnaires, are useful tools for practitioners when assessing potential functional changes in adults with DS at risk for dementia over time. Remaining alert to functional changes and recognizing the necessity for early dementia assessments in adults with DS is vital.

ACKNOWLEDGMENTS

This study was funded by the U.S. National Institute on Aging: (1) Research Supplement to Promote Diversity in Health-Related Research, R01AG057680-05S1, Evaluation of Falls as a Behavioral

Biomarker for Preclinical Alzheimer's Disease in Adults Aging with Down syndrome (DS). (2) Mentored Research Scientist Development Award, K01AG083130-01, Assessment of Physical Activity for Alzheimer's Disease Research in Down Syndrome. (3) Research Project Grant, R01AG063909-03, The Promotion of Physical Activity for the Prevention of Alzheimer's Disease in Adults with Down Syndrome. (4) Paula and Rodger O. Riney Fund and the Daniel J Brennan MD Fund.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. All authors have seen and agreed with the contents of the article, and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication. Author disclosures are available in the [Supporting information](#).

CONSENT STATEMENT

Informed consent was obtained from all individual participants included in the studies.

ORCID

Selena E. Washington  <https://orcid.org/0000-0002-1686-4802>

REFERENCES

- Hendrix JA, Amon A, Abbeduto L, et al. Opportunities, barriers, and recommendations in Down syndrome research. *Transl Sci Rare Dis*. 2020;5(3-4):99-129.
- Wisniewski KE, Wisniewski HM, Wen GY. Occurrence of neuropathological changes and dementia of Alzheimer's disease in Down's syndrome. *Ann Neurol*. 1985;17(3):278-282.
- Lott IT, Head E. Dementia in Down syndrome: unique insights for Alzheimer disease research. *Nat Rev Neurol*. 2019;15(3):135-147.
- Head E, Powell D, Gold BT, Schmitt FA. Alzheimer's disease in Down syndrome. *Eur J Neurodegener Dis*. 2012;1(3):353.
- Hartley SL, Handen BL, Tudorascu D, et al. Role of tau deposition in early cognitive decline in Down syndrome. *Alzheimers Dement*. 2022;14(1):e12256.
- Handen BL, Lott IT, Christian BT, et al. The Alzheimer's biomarker consortium-Down syndrome: rationale and methodology. *Alzheimers Dement*. 2020;12(1):e12065.
- Bishop KM, Hogan M, Janicki MP, et al. Guidelines for dementia-related health advocacy for adults with intellectual disability and dementia: National Task Group on Intellectual Disabilities and Dementia Practices. *Intellect Dev Disabil*. 2015;53(1):2-29.
- Rafii MS, Kleschevnikov AM, Sawa M, Mobley WC. Chapter 17 - Down syndrome, in *Handbook of Clinical Neurology*. In: Dekosky ST, Asthana S, eds. Elsevier; 2019:321-336.
- De Graaf G, Buckley F, Skotko BG. Estimation of the number of people with Down syndrome in the United States. *Genet Med*. 2017;19(4):439-447.
- Hartley D, Blumenthal T, Carrillo M, et al. Down syndrome and Alzheimer's disease: common pathways, common goals. *Alzheimers Dement*. 2015;11(6):700-709.
- Krinsky-McHale SJ, Hartley S, Hom C, et al. A modified Cued Recall Test for detecting prodromal AD in adults with Down syndrome. *Alzheimers Dement*. 2022;14(1):e12361.
- Lautarescu BA, Holl AJ, Zaman SH. The early presentation of dementia in people with Down syndrome: a systematic review of longitudinal studies. *Neuropsychol Rev*. 2017;27:31-45.
- Prasher V, Farooq A, Holder R. The Adaptive Behaviour Dementia Questionnaire (ABDQ): screening questionnaire for dementia in Alzheimer's disease in adults with Down syndrome. *Res Dev Disabil*. 2004;25(4):385-397.
- Dekker AD, Ulgiati AM, Groen H, et al. The Behavioral and Psychological Symptoms of Dementia in Down Syndrome Scale (BPSD-DS II): optimization and further validation. *Journal of Alzheimer's Disease*. 2021;81(4):1505-1527.
- Fleming V, Piro-Gambetti B, Patrick A, et al. Physical activity and cognitive and imaging biomarkers of Alzheimer's disease in Down syndrome. *Neurobiol Aging*. 2021;107:118-127.
- Cody KA, Piro-Gambetti B, Zammit MD, et al. Association of sleep with cognition and beta amyloid accumulation in adults with Down syndrome. *Neurobiol Aging*. 2020;93:44-51.
- Pulsifer MB, Evans CL, Hom C, et al. Language skills as a predictor of cognitive decline in adults with Down syndrome. *Alzheimers Dement*. 2020;12(1):e12080.
- Deb S, Hare M, Prior L, Bhaumik S. Dementia screening questionnaire for individuals with intellectual disabilities. *Br J Psychiatry*. 2007;190:440-444.
- Pape SE, Baksh RA, Startin C, Hamburg S, Hithersay R, Strydom A. The association between physical activity and CAMDEX-DS changes prior to the onset of Alzheimer's disease in Down syndrome. *J Clin Med*. 2021;10(9):1882.
- Van Pelt KL, Koehl L, Caban-Holt A, Anderson-Mooney A, Head E, Schmitt FA. Feasibility of dual-task gait to estimate Alzheimer's related cognitive decline in Down syndrome. *Alzheimers Dement (Amst)*. 2020;12(1):e12092.
- Deb SS, Strydom A, Hithersay R, et al. Dementia in people with intellectual disabilities. *Textbook of Psychiatry for Intellectual Disability and Autism Spectrum Disorder*. Springer; 2022:719-756.
- Zeilinger EL, Novakovic IZ, Komenda S, et al. Informant-based assessment instruments for dementia in people with intellectual disability: a systematic review and standardised evaluation. *Res Dev Disabil*. 2022;121:104148.
- Conceição AS, Sant LF, Mattar GP, et al. Balance and gait: associations with cognitive impairment and dementia in individuals with Down syndrome. *Alzheimer Dis Assoc Disord*. 2023;37(4):349-356.
- Washington SE, Cler E, Lowery C, Stark SL. Down syndrome and Alzheimer's disease: a scoping review of functional performance and fall risk. *Alzheimers Dement*. 2023;9(2):e12393.
- Savica R, Wennberg AM, Hagen C, et al. Comparison of gait parameters for predicting cognitive decline: the mayo clinic study of aging. *J Alzheimers Dis*. 2017;55(2):559-567.
- McGrath R, Vincent BM, Hackney KJ, et al. Weakness and cognitive impairment are independently and jointly associated with functional decline in aging Americans. *Aging Clin Exp Res*. 2020;32:1723-1730.
- Cui M, Zhang S, Liu Y, Gang X, Wang G. Grip strength and the risk of cognitive decline and dementia: a systematic review and meta-analysis of longitudinal cohort studies. *Front Aging Neurosci*. 2021;13:625551.
- Lin J-D, Lin L-P, Hsu S-W, et al. Are early onset aging conditions correlated to daily activity functions in youth and adults with Down syndrome? *Res Dev Disabil*. 2015;36:532-536.
- Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc*. 1983;31(12):721-727.
- Lawton M, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Nurs Res*. 1970;19(3):278.
- Lifshitz HB, Bustan N, Shnitzer-Meirovich S. Intelligence trajectories in adolescents and adults with Down syndrome: cognitively stimulating leisure activities mitigate health and ADL problems. *J Appl Res Intellect Disabil*. 2021;34(2):491-506.
- Listwan TA, Krinsky-McHale SJ, Kovacs CM, et al. Prodromal Alzheimer's disease can affect activities of daily living for adults with Down syndrome. *Alzheimers Dement*. 2024;16(1):e12562.

33. Ptomey LT, Szabo-Reed AN, Martin LE, et al. The promotion of physical activity for the prevention of Alzheimer's disease in adults with Down Syndrome: rationale and design for a 12 month randomized trial. *Contemp Clin Trials Commun*. 2020;19:100607.
34. Washington SE, Bollinger RM, Ances B, Stark SL. Falls and cognition in adults aging with Down syndrome. *Alzheimers Dement*. 2023;19:e082501.
35. Parmenter TR. The dementia screening questionnaire for individuals with intellectual disabilities has high sensitivity and specificity in adults with Down's syndrome. *Evid Based Ment Health*. 2008;11(1):11-11.
36. Boer PH, Moss SJ. Test-retest reliability and minimal detectable change scores of twelve functional fitness tests in adults with Down syndrome. *Res Dev Disabil*. 2016;48:176-185.
37. Bohannon RW. Reference values for the timed up and go test: a descriptive meta-analysis. *J Geriatr Phys Ther*. 2006;29(2):64-68.
38. Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: normative data for adults. *Arch Phys Med Rehabil*. 1985;66(2):69-74.
39. Cabeza-Ruiz R, Alcántara-Cordero FJ, Ruiz-Gavilán I, Sánchez-López AM. Feasibility and reliability of a physical fitness test battery in individuals with Down syndrome. *Int J Environ Res Public Health*. 2019;16(15):2685.
40. Shields N, Taylor NF, Wee E, Wollersheim D, O'Shea SD, Fernhall B. A community-based strength training programme increases muscle strength and physical activity in young people with Down syndrome: a randomised controlled trial. *Res Dev Disabil*. 2013;34(12):4385-4394.
41. Csuka M, McCarty DJ. Simple method for measurement of lower extremity muscle strength. *Am J Med*. 1985;78(1):77-81.
42. Rikli R, Jones C. Development and validation of a functional fitness test for community-residing older adults. *J Aging Phys Act*. 1999;7(2):129-161.
43. Maenner MJ, Smith LE, Hong J, Makuch R, Greenberg JS, Mailick MR. Evaluation of an activities of daily living scale for adolescents and adults with developmental disabilities. *Disabil Health J*. 2013;6(1): 8-17.
44. R Core team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria. 2021. <http://www.R-project.org>
45. Nicolini-Panisson RD, Donadio MV. Normative values for the Timed 'Up and Go' test in children and adolescents and validation for individuals with Down syndrome. *Dev Med Child Neurol*. 2014;56(5):490-497.
46. Annweiler C, Schott A-M, Abellan van Kan G, Rolland Y, Blain H, Fantino B, et al. The five-times-sit-to-stand test, a marker of global cognitive functioning among community-dwelling older women. *J Nutr Health Aging*. 2011;15:271-276.
47. Bohannon RW. Reference values for the five-repetition sit-to-stand test: a descriptive meta-analysis of data from elders. *Percept Mot Skills*. 2006;103(1):215-222.
48. Temple VA, Rintala P, Zeitz S, Lloyd M, Foley JT. Age and sex-based differences in functional strength of adults participating in Special Olympics. *Eur J Adapt Phys Act*. 2022;15.
49. Cleveringa M, Pitchford EA. Low muscle strength, low bone mineral density, and high body mass index among adult special Olympics athletes: a cross-sectional examination. *Adapt Phys Activ Q*. 2022;40(1):19-37.
50. Aschenbrenner AJ, Baksh RA, Benejam B, et al. Markers of early changes in cognition across cohorts of adults with Down syndrome at risk of Alzheimer's disease. *Alzheimers Dement*. 2021;13(1):e12184.

SUPPORTING INFORMATION

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

How to cite this article: Washington SE, Bodde AE, Helsel BC, et al. The association of dementia risk symptoms and functional activity in adults with Down syndrome. *Alzheimer's Dement*. 2024;e70007. <https://doi.org/10.1002/trc2.70007>