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Original Research

Use of the Adaptive Behaviour Dementia Questionnaire in a Down Syndrome Specialty Clinic

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Abstract

Objective: To study the use of a dementia screening tool in our clinic cohort of adults with Down syndrome. **Study Design**: A retrospective chart review of patients with Down syndrome was conducted to follow the use of the Adaptive Behaviour Dementia Questionnaire (ABDQ) in a dementia screening protocol. The ABDQ results for patients aged 40 years and older at a Down syndrome specialty clinic program were assessed. Based on caregiver feedback, an ABDQ with modified instructions was piloted and the impact assessed. **Results**: As part of our clinic's initiative to implement a new clinical protocol to screen for dementia, the ABDQ was completed by 47 caregivers of adults with Down syndrome, aged 39 years and above, from December, 2021 to April, 2023. Based on clinical impressions at the same timepoint, the ABDQ had a sensitivity of 0%, specificity of 97.4%, positive predictive value of 0%, and negative predictive value of 80.4%. Nine patients were deemed to have mild cognitive impairment and/or dementia by clinical impressions, but they did *not* identify as positive on the ABDQ. The Down syndrome clinic team modified the ABDQ in an effort to provide clearer language and increased sensitivity. The modified ABDQ showed a sensitivity of 0%, specificity of 93.8%, positive predictive value of 0% and negative predictive value of 75%. **Conclusion**: Neither the original ABDQ nor a modified version adequately identified patients with cognitive impairment and/or dementia within the Down syndrome clinical program. The inability to replicate findings from the initial ABDQ validation may be due to differences in setting and format.

Keywords: Dementia; Alzheimer's disease; Down syndrome; clinical screening

1. Introduction

Over 200,000 people with Down syndrome (DS) live in the United States [1]. Adults with DS have an increased risk for developing dementia, with a lifetime dementia risk in excess of 95%, and median age of onset of 55 years [2]. The increased risk for co-occurring Alzheimer's disease (AD) in adults with DS [3] is thought to result from the triplication of the amyloid precursor protein (*APP*) gene located on chromosome 21 [4], leading to an overabundance of amyloid plaque deposition in the brain, a main characteristic of AD, eventually leading to associated morbidity and mortality [5].

The diagnosis of AD in the general population is often made based on a combination of clinical history, symptoms, cognitive assessment, imaging, biomarker testing, and post-mortem brain tissue analysis. In people with DS, many of these approach have limitations. While biomarkers show utility, use of standardized rapid cognitive tools typically used in primary care for reliable in-office cognitive assessment are not appropriate and have limited value. Symptom profiles can vary from those in the general population. In certain population subsets of individuals with DS including those with severe intellectual disability, autism spectrum disorder, and sensitivity challenges, brain imaging can be challenging to obtain, and abnormal findings on imaging are often present prior to the onset of clinical symptomatology [2,3]. Comprehensive cognitive evaluation has been proposed as an alternative or complementary method to evaluate for co-occurring AD with tests such as a modified version of the Selective Reminding Test, the Modified Mini Mental Status Evaluation—Down Syndrome (MMMSE-DS), the Down Syndrome Mental Status Examination (DSMSE), or The Test for Severe Impairment (TSI), among others [6]. To triage those patients who should proceed to cognitive evaluation, imaging, and biomarker evaluation, a useful approach would be to screen adults with DS for signs and symptoms of memory changes associated with AD. While real-time, rapid screening for AD in DS would therefore offer important benefits, identifying a practical and useful screening tool in DS has many challenges [7,8]. Few instruments have been validated in DS, questions should focus on functional changes, and

questionnaires should be caregiver-reported as individuals with DS require lifelong caregivers who may have unique exposure to recollection bias not present in caregivers of elderly adults with AD in the general population who may be more recent in a caregiver role.

Acknowledging the importance of AD screening, the most recent evidence-based clinical practice guidelines for DS made a statement of good practice: a strong recommendation to screen for Alzheimer-type dementia annually starting at age 40 years [9]. The evidence-based clinical practice guidelines for DS specifically state that "Decline in 6 domains specified by the National Task Group–Early Detection Screen for Dementia (NTG-EDSD) should be used to identify early-stage age-related Alzheimer-type dementia." [9].

To address this new recommendation on universal screening for AD in DS, our Down syndrome clinic began a quality improvement initiative to study the use of a newly instituted dementia screening protocol in patients with DS, 40 years and older. Although the evidence-based clinical practice guideline recommends utilizing the NTG-EDSD, we factored several additional considerations into the instrument selection process, given our experience working with caregivers of and individuals with DS, the clinical visit process and flow, and our team's collective prior experience in diagnosing and caring for DS patients with AD. Considerations included, questionnaire length and ease for families, caregiver accessibility, instrument validation and validation population, ability to repeat screening over time to assess for change, the ability to produce a score to guide clinical care by indicating the presence or absence of signs of dementia, available in English, and publicly available for use free of charge. After searching and reviewing existing instruments to screen for Alzheimer's disease dementia based on the above criteria [7,8,10–15], we ultimately identified four validated screening tools for AD in DS that generally met the above criteria, each with strengths, limitations, and varied published use in individuals in DS [16]. The four identified screens for dementia included, the Early Detection and Screen for Dementia (the NTG-EDSD), developed by The National Task Group on Intellectual Disabilities and Dementia Practices (NTG) [17], the Adaptive Behaviour Dementia Questionnaire (ABDQ) [18], the Dementia Questionnaire for People with Learning Disabilities (DLD) [19], and the American Association on Mental Deficiency Adaptive Behavior Scale, Part I [20].

With this paper, we present the results of our newly implemented clinical dementia screening protocol which included several aims: (1) to describe our experience selecting a screening instrument for AD in DS, (2) to summarize the scoring results, and (3) to describe our attempts to pilot a modified screening instrument. To our knowledge, no study has yet to assess the implementation process or implications of a universal dementia screening recommendation for adults with DS ages 40 and older. Given the screening recommendations, this report provides the first description and results of implementing a universal AD screening protocol in adults with DS utilizing a validated instrument, thereby offering useful guidance for clinicians caring for individuals with DS seeking to implement the recommended DS clinical care guideline.

2. Methods

2.1 Setting

The Down syndrome clinical program described in this report is a multidisciplinary specialty program for individuals with DS. Medical visits include a physician, a social worker, a nutritionist, a self-advocate with DS, and a program coordinator. In addition to the medical visit, patients may be referred for visits with the affiliated psychiatrist or neuropsychologists. Waiting periods often represent a significant barrier for neuropsychological evaluations, with visits currently being scheduled over 12 months out at our institution, underscoring the need for more rapid dementia screening options.

2.2 Selecting a Screening Instrument

As previously described, after reviewing available cognitive screener options, we considered four caregiver-completed screening instruments that met many of our predefined criteria (**Supplementary Table 1**):

(1) **The National Task Group on Intellectual Disabilities and Dementia Practices' Early Detection and Screen for Dementia (NTG-EDSD)**: The NTG-EDSD is an administrative screening tool used to record observed changes in function [17]. Although identified as a useful tool by Tsou *et al*. [9], it does not yield a raw score with established cut-off values, and has not been validated in adults with DS [17]. We were further concerned that the 6-page tool of over 60 items related to activities of daily living, language and communication, sleep-wake pattern changes, ambulation, memory, and behavior [17] would be impractical for completing during a clinic visit.

(2) **The Adaptive Behaviour Dementia Questionnaire (ABDQ)**: The ABDQ is a short 15-item questionnaire which yields a score with established values which indicate normal, mild dementia, moderate dementia or profound dementia [18]. The ABDQ was studied in 150 adults with DS in the United Kingdom age 16–76 of mild (18%), moderate (69%) and severe (13%) intellectual disability. The ABDQ is scored with weighting of certain items and uses a cut-score of 78 on the total weighted score (0–77 = dementia in Alzheimer's *not* present; 78–89 = mild dementia in Alzheimer's disease; 90–99 = moderate dementia in Alzheimer's disease; 100 or more = severe dementia in Alzheimer's disease). The ABDQ had the following properties when compared to a clinical diagnosis of Alzheimer's-type dementia on International Classification of Diseases (ICD)-10 criteria: the sensitivity was 89%, the specificity was 94%, the positive predictive value was 89%,

and the negative predictive value 94% [18]. The authors describe that the overall percentage correct identification (accuracy) of AD and non-AD cases was 92% [18].

(3) **Dementia Questionnaire for People with Learning Disabilities (DLD)**: The DLD is a 50-item instrument, subdivided into two subcategories and eight subscales. Each item has three response categories; points of each subcategory are summed up to scores. The diagnostic criterion for dementia is based on score changes over time; a difference of 7 or more points in the sum score for "cognitive subcategory" or a difference of 5 or more points for "social subcategory" is regarded as indicative for dementia. Differences below these cut-scores are interpreted as tendencies [19,21]. The DLD was studied in 78 adults with DS, ages 35 and older, with varied intellectual disability [10]. In a cohort with DS, using the lower cut-score of 4, the DLD was found to have a sensitivity of 100% and specificity of 69% [10]. Although identifying status change over time yields important information that can assist in diagnosing AD, a major limitation of the DLD is that it requires repeated use to track score changes over time and cannot be used as a single moment-in-time time diagnostic tool.

(4) **American Association on Mental Deficiency (AAMD) Adaptive Behavior Scale**: The AAMD behavior scales have been published in two versions, the Adaptive Behavior Scales-Residential and Community, 2nd edition (ABS-RC) and the Adaptive Behavior Scales-School, 2nd edition (ABS-S) and includes 65 items covering ten domains [20]. The ABS-S shows internal consistency (0.79 to 0.98), stability (0.82 to 0.97), and interscorer reliability (0.95 to 0.98). The ABS-RC has an internal consistency ranging from 0.81 to 0.97 [20]. The ABS-S has been used to effectively identify dementia in patients with Down syndrome in prior studies [22,23]. Yet, given the number of items, the AAMD was deemed too lengthy for use as a clinical screening tool by the Down syndrome clinic team.

After reviewing available screening instrument options and in re-considering our *a priori* criteria, our clinical team refined our criteria for a clinical screening tool for use as an annual AD screener as follows: that it (1) be a validated instrument for assessing AD in DS, (2) be able to be completed independently by caregivers or families, (3) be able to be completed quickly (<10–15 minutes) during a clinic visit, (4) yield an actionable result (e.g., a score with established criteria) to guide clinical management, and (5) yield an outcome that can provide immediate clinical care decision support (i.e., completion in a single assessment that does not require longitudinal data or serial assessments over time). Based on the number of items and need for repeated assessments, we eliminated the NTG-EDSD, DLD and AAMD scales, and identified the ABDQ as the instrument we chose to evaluate first for our AD screening protocol in DS. Universal annual dementia screening using the ABDQ in all patients ages 40 years and older began in December 2021.

2.3 ABDQ Screening

The ABDQ was administered electronically through Research Electronic Data Capture (REDCap) [24] and delivered to families via email prior to the patient's scheduled Down syndrome clinic team visit. REDCap (https://projectredcap.org/resources/citations/) is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources [24,25]. If the ABDQ was not completed prior to the visit, a paper version of the ABDQ was completed by caregivers upon arrival on the visit day prior to the scheduled visit.

2.4 ABDQ Scoring

This 15-question assessment was designed to assess dementia in AD through comparison of a patient's behavior at the time of assessment to a "normal" baseline. "Normal" is defined as a patient's behavior prior to the onset of any signs of dementia. The survey is completed by a caregiver and/or parent who knows the patient well or an interviewer who has experience working with people with intellectual disabilities (our clinic only had caregivers and/or parents complete the survey). The ABDQ is scored with weighting of specific items, and a score is positive if the total weighted score is 78 or more. Scores of 78 and above are broken down by severity: 78–89 screen as mild dementia, 90–99 as moderate dementia, and 100 or more as severe dementia [18]. We grouped ABDQ scores as: "+ ABDQ" for screening positive for dementia in Alzheimer's disease (score 78 or above) or "– ABDQ" for screening negative for dementia in Alzheimer's disease.

2.5 Modified ABDQ Screening

After reviewing results data from 47 patients using the original ABDQ, we found that our clinical impressions differed from ABDQ screening scores. ABDQ scores did not correlate (i.e., scores were not within positive range) with clinical impressions of patients with symptoms of mild cognitive impairment and/or dementia. Guided by an iterative process based on feedback from caregivers and clinicians assessing face validity, we modified the ABDQ to clarify the survey instructions to more clearly emphasize the survey's aim of capturing change in the individual's status over time. We changed the category language from "normal" to "usual" in the instrument instructions and item responses to more accurately communicate what the baseline status in the ABDQ is intended to capture. We piloted our modified ABDQ both in clinic and online via REDCap. For a subset of patients, we provided both the original ABDQ along with the modified ABDQ for comparison and col-

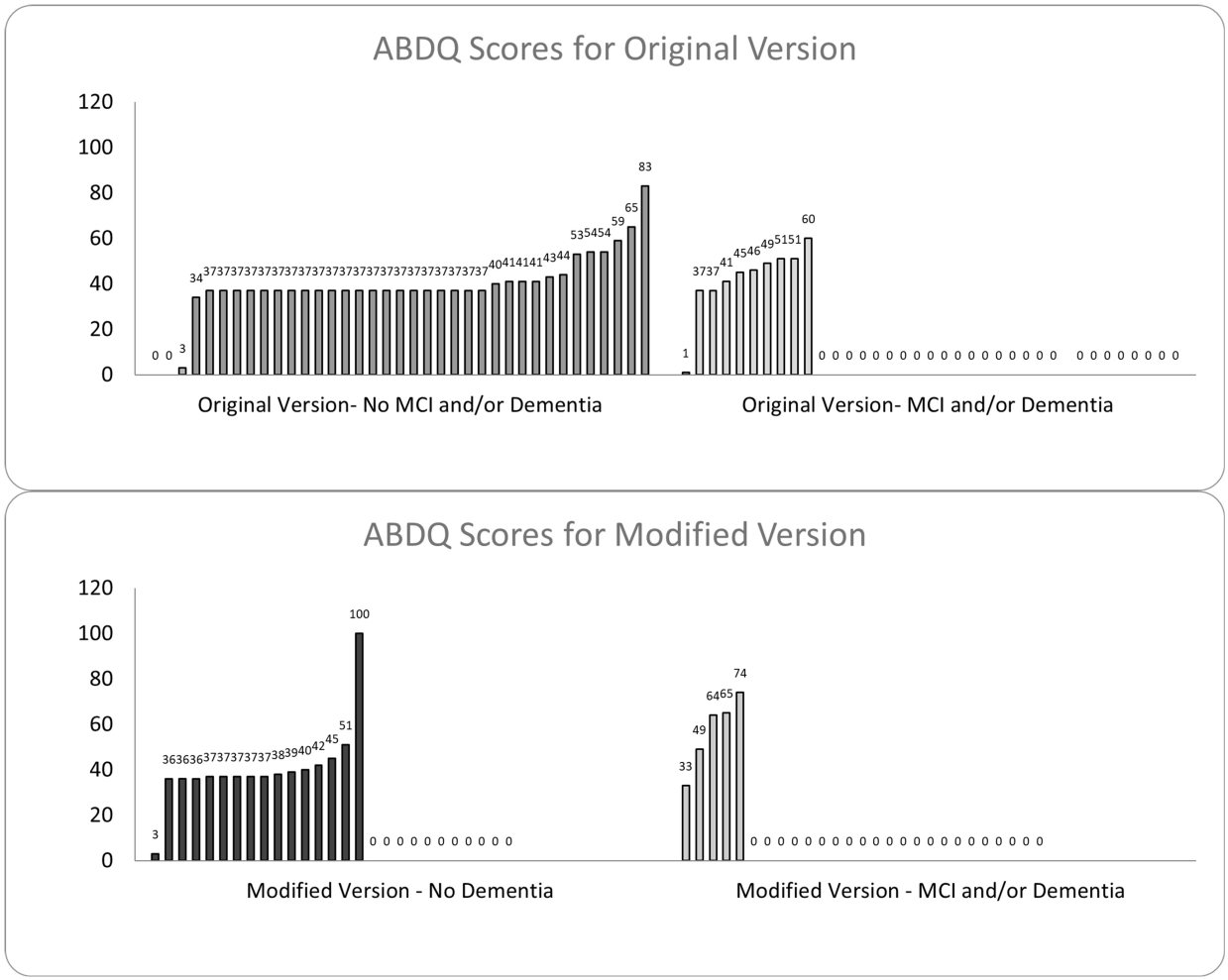

Fig. 1. Caregiver-reported Adaptive Behaviour Dementia Questionnaire (ABDQ) Scores: original version (December 2021–April 2023) & modified version (May 2023–Mid August 2023) compared to clinical impression of symptoms of Alzheimer's Disease. Each bar represents an individual score reported by the caregiver of an adult with Down syndrome. MCI, Mild Cognitive Impairment.

lected face value feedback from caregivers. We used the original ABDQ scoring protocol when scoring the modified ABDQ results.

2.6 Chart Review Procedure

Through retrospective analyses of electronic health records, we obtained the clinical impression on presence of dementia for each patient with DS. Clinical impression on presence of dementia was ascertained from clinic visit notes by the treating physicians and/or social workers from the Down syndrome clinic team. Clinical determinations of dementia were based on past medical and behavioral history documented in clinical notes, the clinical team's longitudinal knowledge of the patient caring for the patient over time, expanded caregiver report—beyond responses offered in the ABDQ, and clinical assessment during the study visit. Patients were grouped as "Clinical dementia present" if cognitive impairment (with or without formal diagnosis of dementia) was directly indicated in the signed Down syndrome clinic team visit notes from board-certified physicians or licensed social workers, and "No clinical dementia" if cognitive impairment was not indicated. Patients with mild cognitive impairment were categorized as "Clinical dementia present". For any cases without clear clinical impression of dementia documented in the clinic visit notes, the primary physician and social worker reviewed the electronic health record to provide a clinical impression. Clinicians assessing dementia status were not blinded to dementia screening results. Demographic information, including age, race, ethnicity, sex and history of neuropsychological testing were obtained from the electronic health record.

2.7 Analysis

Dementia clinical impression was compared to ABDQ scores in 2 $\times$ 2 tables and sensitivity, specificity, positive predictive value and negative predictive value were calculated. Descriptive data including means, standard deviations, frequencies and ranges were calculated.

This quality improvement study was approved by the institutional review board at Massachusetts General Hospi-

Table 1. Demographic traits of 59 individuals with Down syndrome who had the caregiver-administered Adaptive Behaviour Dementia Questionnaire (ABDQ) completed.

	Original ABDQ Cohort from Dec 2021 to April 2023 (N = 47)	Modified ABDQ cohort from May 2023 to Aug 2023 (N = 21)
	N (%)	N (%)
Sex		
Male	27 (57.4)	9 (42.9)
Female	20 (42.6)	12 (57.1)
Race		
White	44 (93.6)	20 (95.2)
Black or African American	1 (2.1)	0 (0)
Other	1 (2.1)	0 (0)
Unavailable	1 (2.1)	1 (4.8)
Ethnicity		
Hispanic	17 (36.2)	0 (0)
Not Hispanic	30 (63.8)	21 (100)
Age		
35–39	2 (4.3)	0 (0)
40–44	14 (29.8)	6 (28.6)
45–49	14 (29.8)	5 (23.8)
50–54	11 (23.4)	5 (23.8)
55–59	4 (8.5)	3 (14.3)
60–65	2 (4.3)	2 (9.5)
Neuropsychological Testing Performed		
Yes	31 (66)	11 (52.4)
Not yet, but referred for testing	15 (31.9)	9 (42.9)
No	1 (2.1)	1 (4.8)
Intellectual Disability Level		
Mild	10 (21.3)	4 (19.0)
Moderate	24 (51.1)	8 (38.1)
Severe	3 (6.4)	2 (9.5)
Profound	1 (2.1)	0 (0)
Unknown	9 (19.1)	7 (33.3)
Clinical MCI or Dementia		
Yes	10 (21.3)	5 (23.8)
No	37 (78.7)	10 (47.6)

6 participants did the original twice (we have only counted these participants once in the table below, with time point of their most recent ABDQ). 9 did both original and modified (these are included in both columns). MCI, Mild Cognitive Impairment.

tal. Consent is given through completion of the clinic survey. Data are presented in an aggregate, de-identified manner and were collected to study this quality improvement protocol.

3. Results

3.1 Original ABDQ Results

Fifty total ABDQ responses were collected from caregivers and/or parents between December 2021 to April 2023, 47 of which were included in our analyses (3 caregivers completed the ABDQ twice over this time frame, with only the most recent timepoints analyzed). Among the 47 responses (mean age 47.7 years old (SD = 5.8), range 39 to 63 years old), 45 were for adults ages 40 and older, and 2 were 39 years old. Demographic traits show a slight male predominance (57.4%) with participants mostly white (93.6%) and mostly not Hispanic (63.8%). Most participants had neuropsychological testing performed (66%); several patients were referred and still awaiting appointments at the time of data analysis (Table 1). All patients followed in the clinical Down Syndrome Program are recommended to have and referred for baseline neuropsychological assessments prior to or by age 40 years, and for repeat testing as indicated based on clinical findings or memory concerns.

Among the 47 respondents on the original ABDQ, the mean ABDQ score was 39.4, with a range of 0 to 83 (Fig. 1). Nearly all (46/47) adults with DS had negative

Table 2. Comparing results on the Adaptive Behaviour Dementia Questionnaire (ABDQ) and clinical interpretation for N = 47 patients December 2021 to April 2023.

	Dementia and/or Cognitive Impairment (Clinical Interpretation) Present	No Dementia and/or Cognitive Impairment (Clinical Interpretation)	Total
Positive ABDQ screening $\geq$78	0	1	1
Negative ABDQ screening $<$78	9	37	46
Total; [median ABDQ score]	9 [45.5]	38 [37]	47 [37]

ABDQ scores (score $<$78), with only 1 adult having a positive ABDQ score of 83. The ABDQ had a corresponding sensitivity of 0%, specificity of 97.4%, positive predictive value of 0% and negative predictive value of 80.4% (Table 2). Of the 47 patients screened, 38 were documented as not having dementia or early signs of dementia (mild cognitive impairment) and 9 were categorized as having dementia or mild cognitive impairment based on the clinical impression of their Down Syndrome Program (DSP) clinicians (**Supplementary Table 2**).

3.2 Feedback Data Collection

With changes to the ABDQ instructions and response categories (Table 3), 11 caregivers were shown both the new and old versions of the ABDQ and asked to provide feedback. Each caregiver or parent described their conceptualization of the phrase "usual self" and described the age this was "bringing to mind". Caregivers and parents described a wide range of answers as the 'age' for their individual with DS's "usual self", ranging from being only a few months up to a few years prior to their adult "prime" (e.g., their early 20s/shortly after completing high school). As caregivers described adults with DS age 39 and older, it became apparent that the difference between the current time and the "usual self" time caregivers were recalling could range from a few months prior to decades ago.

Clarifying questions during feedback collection were answered by a study team member. For example, one parent asked what the word "persistent" meant—whether it referred to repeated and/or resilient behavior(s). In all cases, we asked the caregiver to complete the survey to the best of their ability based on their own interpretation, although these clarifying questions signaled possible ongoing areas of respondent confusion and questionable face validity of the instrument. Overall, feedback from caregivers indicated a preference for the updated set of instructions, along with a preference for the nomenclature "usual" rather than "normal."

3.3 Piloting the Modified ABDQ

From May 2023 to mid-August 2023, 29 adults with DS age 40 and older in the Down syndrome clinic program were eligible for the modified ABDQ; 21 modified ABDQ surveys were completed (mean age 49.6 years old (SD = 6.8), range 40 to 66 with 57% female; Table 1). Out of those 21 individuals with DS, 9 were in the original ABDQ cohort. Eleven surveys were administered face-to-face in clinic and/or on video conferencing, enabling caregivers to provide feedback on the comparison between the old and new versions, with 10 completed via REDCap before clinic without assistance or feedback.

Scores on the modified ABDQ showed a mean of 44.6 with a range of 3 to 100 (Fig. 1). Of the 21 adults with DS screened, 20 screened negative on modified ABDQ (scores $<$78) and 1 adult screened positive (score = 100). Results comparing the modified ABDQ screening results and clinical impression showed a sensitivity of 0%, specificity of 93.8%, positive predictive value of 0% and a negative predictive value of 75% (Table 4). Of the 21 screened, 16 did not have dementia or early signs of dementia (mild cognitive impairment) and 5 were categorized as having dementia or mild cognitive impairment present based on clinical notes.

4. Discussion

Based on recent evidence-based care guidance [9], we prospectively implemented a new clinical protocol to screen for AD in adults with DS. We selected the ABDQ screening tool, comparing ABDQ scores to the contemporaneous clinical impression of AD, and found the original ABDQ to have high specificity, but low sensitivity, and with a high negative predictive value for identifying dementia in adults with DS. Based on these properties and feedback from caregivers, we piloted a modified ABDQ with minor modifications to the instructions and response options, which did not result in significant improvements in psychometric properties.

In our clinic cohort, neither the original nor the modified ABDQ survey functioned well as a screening tool. For one patient with an original ABDQ score indicative of dementia, this did not correlate with the clinical impressions

Table 3. Comparison of directions from original Adaptive Behaviour Dementia Questionnaire (ABDQ) and updated ABDQ for MGH DSP.

Original	Modified
Instructions	
The questionnaire sets out to collect information on how the observed person **compares** *now* to their previous normal (usual) level of social functioning. By "normal" we mean when the person was in good health and BEFORE the onset of any recent problems suggestive of dementia. The term "normal" is used in each question. If never been able to perform question mark as "same as normal". **The ABDQ is designed to detect CHANGE in clinical status over time.**	We want to know how '*first name*' is doing now compared to when '*first name*' was in usual health. We are viewing **usual health as** '*first name's*' **health baseline BEFORE the onset of recent changes (if any).** The questions will ask about any changes that '*first name*' has had in his/her daily activities and any changes from '*first name's*' baseline functioning. This questionnaire is designed to detect **CHANGE** over time. If you feel there has been no change over time, please mark the question as "same as usual self". If the person with Down syndrome has never been able to perform the question, please mark the question as "same as usual self". **Please answer ALL questions by selecting the answer which you think most closely applies to the question.**
Response Categories	
Better than normal	Better than usual self
Same as normal	Same as usual self
Worse than normal	Worse than usual self
Much worse than normal	Much worse than usual self

Bolded sections indicate wording in the ABDQ that was modified. MGH DSP, Massachusetts General Hospital Down Syndrome Program.

Table 4. Comparing results on the Modified Adaptive Behaviour Dementia Questionnaire (ABDQ) and clinical interpretation for N = 21 patients from May 2023 to mid-August 2023.

	Dementia and/or Cognitive Impairment (Clinical Interpretation)	No Dementia and/or Cognitive Impairment (Clinical Interpretation)	Total
Positive ABDQ screening $\geq$78	0	1	1
Negative ABDQ screening $<$78	5	15	20
Total	5	16	21

of the treating physicians or the social workers. In 9 patients in whom AD was suspected clinically, the original ABDQ was negative: giving low sensitivity and low positive predictive value. Our findings are in conflict with the strong psychometric properties published in the original validation of the ABDQ [18]. Prasher *et al*. [18] found the ABDQ to have "good reliability and validity, with an overall accuracy of 92%" in a cohort of caregivers of individuals with DS. However, many notable differences between our study and the original validation study by Prasher *et al*. [18] exist. Our study used the ABDQ in clinical practice as a clinical screener while Prasher *et al*. [18] studied the ABDQ in research validation. Although we obtained ABDQ results on most of our eligible patients, our cohort is smaller than the original validation sample of 150 adults. Additionally, for ease of administration prior to a clinic visit, we distributed the ABDQ by e-mail link with the questionnaire administered in web-based format through REDCap while the original validation used paper-and-pencil surveys.

To assess the 9 false negatives, and better understand the reasoning behind caregiver answers, the clinical team piloted the use of a modified ABDQ, understanding that a modified instrument would not yield validated scores. In the modified ABDQ, we changed some of the wording and then shared both the original and modified ABDQ text with caregivers. After modifications, based on caregiver feedback, we found the modified questionnaire to again have high specificity, but still have low sensitivity and low positive predictive value, suggesting that our modifications did not substantially improve the ability of the questionnaire to screen for AD in adults with DS. This lack of improvement might result from our modifications not having successfully

addressed the discordance between clinical and family perspectives. Additionally, many caregivers in the modified ABDQ group were the same caregivers who had previously completed the original ABDQ, resulting in potential recall bias and memory effects – where respondents learn from completing a survey twice within a short window of time.

While the ABDQ questions focuses on adaptive function, we found in the 9 false negative patients that in addition to changes in activities of daily living, many of the early signs of dementia presented as change in sleep, memory problems, irritability, and objects misplacement. As the ABQD does not include questions assessing changes in memory or behavior, it may be of limited utility for clinical dementia screening in DS. We also found that scores differed between patients with and without clinical findings of dementia, with median scores higher, though still not reaching the recommended cut-off value, when clinical dementia was present, suggesting that establishing a lower cut-off value may be of clinical benefit.

Our study has several limitations worth highlighting which may explain the study's negative findings. The study's small sample size and generalizability may impact external validity, while potential for bias including social desirability, recall bias, and scoring bias may impact internal validity. Our initial sample was small, in line with our goal of piloting the ABDQ as a screening tool. In the future, we could re-study the ABDQ, or other screeners for AD, in a larger, multi-site study of adults with DS based on a larger sample size determined by pre-study power requirement calculations. We utilized the ABDQ as a one-time screening tool as originally validated in patients with DS, however, the instrument may provide greater ability to detect AD with longitudinal use, such as repeated annual screenings, which could be tested as an alternate approach to AD screening in DS. Our results are from one clinic population; the patient cohort in the Down syndrome clinic team may not generalize to all adults with DS, and our clinic protocols may not generalize to all specialty clinics for DS. Caregivers completing the instrument were familiar with the clinical team treating the individual with DS with the possibility of bias in providing socially desirable answers. Conversely, clinicians were aware of the results of the ABDQ prior to the visit (not blinded) as we were using the ABDQ as a clinical screening tool; this could have impacted the clinician's impression of dementia. All data were collected during the COVID-19 pandemic, with potential implications on behavior changes related to social isolation and on caregiver-reported change ascertainment bias related to increased time for direct observation by caregivers.

We relied on medical record review and input from our Down syndrome clinic team to determine if patients clinically were likely to have cognitive changes or not. Additionally, it is possible that the 9 false negatives (negative ABDQ score, but positive clinical suspicion) could reflect differences in clinical and caregiver perspective: for example, there may be early subtle signs that raise clinical suspicion for AD before caregivers become concerned for AD. In our clinical practice, we did not send all adults with DS for repeat neuropsychological testing if they had past baseline evaluation. As such, some of those who screened negative on the ABDQ – those with low clinical impression of dementia, were not referred for neuropsychological evaluation—a commonly used optimal approach for diagnosing dementia in DS, especially when repeated over time, nor were additional screening modalities including biomarker of imaging tests performed. It is therefore not possible to entirely exclude dementia in individuals with a negative ABDQ screen and low clinical impression as they were not referred for further testing. Without formal additional testing such as neuropsychological testing, in a process that relies primarily on screening, it is possible that dementia may have been missed in a patient who scored negative on ABDQ with low clinical suspicion, resulting in the potential for missed or delayed diagnosis, especially given possible ascertainment bias as treating clinicians were not blinded to ABDQ scores. Although we feel the likelihood of missed dementia diagnoses are low given the clinicians and caregivers knowledge of and longitudinal relationships with the patients included in the study, the quality improvement initiative highlights the perils of adopting a screening protocol where suitable screening instruments may not be available. Although there is much research on the use of AD measures in the research setting, more research is needed to understand the best practical clinical screening approach to detect AD in adults with DS in clinical setting. The NTG-EDSD, DLD and AAMD could all be piloted using a similar clinical validation approach at our clinic or other clinics caring for individuals with DS.

Despite these limitations, this study has several important findings worth noting. Most importantly, our study found that one-time use of a previously validated population specific dementia screening tool did not improve the process for diagnosing dementia in adults with DS in a clinical setting. Making caregiver-informed face value modifications to the screening process did not improve our program's ability to identify dementia. Clinical assessment along with caregiver report remained more helpful in guiding the dementia screening process than reliance on a one-time ABDQ score.

Beyond the importance of following evidence-based care guidelines [9], it is important to screen adults with DS for AD given the high frequency of AD co-occurrence in DS and the disease burden for individuals with DS diagnosed with AD and their caregivers. If screening for AD can identify those with the highest clinical suspicion, screening could be used to triage referrals to the services necessary for obtaining a diagnosis, such as neuropsychiatric evaluation. Although limited successful treatments are available at this time, an earlier clinical diagnosis could potentially result in

earlier access to treatment if recent trials showing success [26] (e.g., amyloid-lowering immunotherapies) show similar efficacy in adults with DS. Researchers may wish to conduct additional studies to compare and contrast the use of the ABDQ, NTG-EDSD, DLD, and AAMD in clinical practice, assess the benefits of using a dementia screening questionnaire over time, or directly compare the capacity of screening questionnaires and neuropsychological testing for diagnosing dementia. Additionally, we present our results for other clinicians in DS clinics who may plan to implement similar screening protocols for AD based on the published evidence-based care guideline.

5. Conclusion

Despite strong psychometrics in original validation, the ABDQ did not function well as a clinical screener for dementia in a clinical care setting. Changing terminology in the modified ABDQ did not improve screener performance. Ongoing studies to determine the clinical utility of dementia screening tools for adults with DS are essential to achieve earlier detection, earlier diagnosis, and earlier treatment.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

NMO, MP, BGS, and SLS designed the research study, NMO, AH, CC, CB, MP, BGS, AT, AGS, and SLS performed the research, NMO, AH, AGS, and SLS analyzed the data. All authors contributed to the editorial changes in the manuscript, read and approved the final manuscript, and have participated sufficiently in the work and have agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This questionnaire and retrospective study were approved by the Massachusetts General Hospital institutional review board (IRB protocol: 2020P003890). The study was carried out in accordance with the guidelines of the Declaration of Helsinki and all patients or their families/legal guardians are informed consent.

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Conflict of Interest

The authors declare no conflict of interest. Dr. Skotko occasionally consults on the topic of Down syndrome through Gerson Lehrman Group. He receives remuneration from Down syndrome non-profit organizations for speaking engagements and associated travel expenses. In the past two years, Dr. Skotko received annual royalties from Woodbine House, Inc., for the publication of his book, Fasten Your Seatbelt: A Crash Course on Down Syndrome for Brothers and Sisters. Within the past two years, he has received research funding from AC Immune, and LuMind IDSC Down Syndrome Foundation to conduct clinical trials for people with Down syndrome. Dr. Skotko is occasionally asked to serve as an expert witness for legal cases where Down syndrome is discussed. Dr. Skotko serves in a non-paid capacity on the Honorary Board of Directors for the Massachusetts Down Syndrome Congress and the Professional Advisory Committee for the National Center for Prenatal and Postnatal Down Syndrome Resources. Dr. Skotko has a sister with Down syndrome. Dr. Santoro has received research funding from LuMind IDSC Down Syndrome Foundation to conduct clinical trials for people with Down syndrome (DS) within the past 2 years. She serves in a nonpaid capacity on the Board of Directors of the Massachusetts Down Syndrome Congress, the Board of Directors of the Down Syndrome Medical Interest Group (DSMIG-USA), and the Executive Committee of the American Academy of Pediatrics Council on Genetics.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/JIN25713.

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