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### Authors

Wallace, ER  
Harp, JP  
Van Pelt, KL  
[et al.](#)

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## Identifying Dementia in Down Syndrome with the Severe Impairment Battery, Brief Praxis Test, and Dementia Scale for People with Learning Disabilities

Elizabeth R. Wallace, M.S.<sup>1</sup>, Jordan P. Harp, Ph.D.<sup>2</sup>, Kathryn L. Van Pelt, Ph.D.<sup>3</sup>, Lisa M. Koehl, Ph.D.<sup>2</sup>, Allison M. Caban-Holt, Ph.D.<sup>3</sup>, Amelia J. Anderson-Mooney, Ph.D.<sup>2</sup>, Gregory A. Jicha, M.D., Ph.D.<sup>2,3</sup>, Donita D. Lightner, M.D.<sup>2</sup>, William C. Robertson, M.D.<sup>2</sup>, Elizabeth Head, Ph.D.<sup>4</sup>, Frederick A. Schmitt, Ph.D.<sup>2,3</sup>

<sup>1</sup>Department of Psychology, University of Kentucky

<sup>2</sup>Department of Neurology, University of Kentucky

<sup>3</sup>Sanders-Brown Center on Aging, University of Kentucky

<sup>4</sup>Department of Pathology & Laboratory Medicine, University of California—Irvine

### Abstract

**Background:** Individuals with Down syndrome (DS) are at high risk for dementia, specifically Alzheimer’s disease (AD). However, many measures regularly used for the detection of dementia in the general population are not suitable for individuals with DS due in part to floor effects. Some measures, including the Severe Impairment Battery (SIB), Brief Praxis Test (BPT), and Dementia Scale for People with Learning Disabilities (DLD), have been used in clinical trials and other research with this population. Validity research is limited, particularly regarding the use of such tools for detection of prodromal dementia in the DS population. The current project presents baseline cross-sectional SIB, BPT, and DLD performance in order to characterise their predictive utility in discriminating normal cognition, possible dementia, and probable dementia in adult DS.

**Method:** Baseline SIB, BPT, and DLD performances from 100 individuals (No Dementia = 68, Possible Dementia = 16, Probable Dementia = 16) were examined from a longitudinal cohort of aging individuals with DS. Receiver operating characteristic (ROC) curves investigated the accuracy of these measures in relation to consensus dementia diagnoses, diagnoses which demonstrated high percent agreement with the examining neurologist’s independent diagnostic impression.

**Results:** The SIB and BPT exhibited fair discrimination ability for differentiating no/possible vs. probable dementia (AUC = .61 and .66, respectively). The DLD exhibited good discrimination ability for differentiating no vs. possible/probable dementia (AUC = .75), and further demonstrated better performance of the DLD-Cognitive subscale compared to the DLD-Social subscale (AUC = .77 and .67, respectively).

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**Corresponding Author:** Frederick A. Schmitt, Ph.D., 800 S. Limestone St. Room 312, Lexington, KY 40536, Phone: 859-218-3850, fascom@uky.edu.

Conflicts of Interest:

No conflicts of interest have been declared.

**Conclusions:** Results suggest that the SIB, BPT, and DLD are able to reasonably discriminate consensus dementia diagnoses in individuals with DS, supporting their continued use in the clinical assessment of dementia in DS. The general performance of these measures suggests that further work in the area of test development is needed to improve on the AUCs for dementia status discrimination in this unique population. At present, however, the current findings suggest that the DLD may be the best option for reliable identification of prodromal dementia in this population, reinforcing the importance of including informant behaviour ratings in assessment of cognition for adults with DS.

### Keywords

dementia; Down syndrome; cognition

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### Background

Dementia affects older people with Down syndrome (DS) at high rates. Of individuals under age 40 with DS, 3–5% are diagnosed with dementia, with an exponential increase to 55–66% in individuals over age 55 (Rubenstein et al., 2020). Alzheimer’s disease (AD) is especially prevalent in the DS population, with AD neuropathology, including hallmark neurofibrillary tangles and amyloid plaques, present in the brains of most, if not all, individuals with DS by their mid 30s (Lott & Head, 2019; Head et al., 2016). Such an early and disproportionate accumulation of AD neuropathology is thought to result primarily from the triplication of chromosome 21 and subsequent overexpression of amyloid precursor protein (APP; Johnstone et al., 1991).

Life expectancy for those with DS has continued to improve in recent decades due to advances in medical care, such as treatment of congenital heart defects and respiratory infections, and improved social integration for people with intellectual disabilities (ID; Coppus, 2013; Presson et al., 2013). Mean life expectancy has increased to above 50 years (Coppus, 2013; De Graaf et al., 2017), with about 14% of U.S. individuals with DS currently over 50 years of age (De Graaf et al., 2017). Longer life expectancy, in combination with the preexisting risk factors and early accumulation of AD neuropathology, results in higher dementia prevalence, with dementia likely the main cause of mortality in elderly DS persons (Coppus, 2013; Landes et al., 2020). Thus, the accurate assessment for and detection of dementia in people with DS is essential for early diagnosis to inform clinical intervention for reducing dementia-related mortality (Hithersay et al., 2019).

Identification of incipient dementia is difficult in the adult DS population as the order of which domains of cognition are affected earliest remains unclear. Frontal lobe functions, such as personality and affective changes, may be observed before memory impairments (Ball et al., 2006a), in contrast to the temporal evolution of deficits in AD that notably begins with early episodic memory impairments followed later by personality and affective changes (Salardini, 2019). However, declining memory has also been identified in individuals with DS years before dementia diagnosis (Devenny, Zimmerli, Kittler, & Krinsky-McHale, 2002). Thus standard neurocognitive measures that focus on early memory impairment, used to assess AD in the general population, may lack the sensitivity to detect

the earliest dementia symptoms in individuals with DS. Another challenge in the assessment of persons with DS includes the inherent difficulty of testing those with differing degrees of baseline intellectual disability (ID), resulting in confounding floor effects frequently seen on measures not designed for use with these individuals. Thus, longitudinal assessments remain essential for the detection of prodromal dementia in DS (Burt & Aylward, 2000), but lack of appropriate neurocognitive tests with established cut scores for adults with DS exacerbates the challenges of assessment in this population (Nieuwenhuis-Mark, 2009).

Neurocognitive screens and measures have been previously utilised in the aging DS population with varying success. These measures include both informant reports and direct assessment of the individual. Commonly used informant reports include the Dementia Scale for Down Syndrome (Gedye, 1995), which was designed for use with severe to profound ID in DS; the Early Signs of Dementia Checklist (Visser et al., 1997), which has demonstrated poor agreement with other measures of cognitive function; and the Short Informant Questionnaire on Cognitive Decline in the Elderly (Jorm, 1994) that has demonstrated questionable reliability (Strydom & Hassiotis, 2003). Direct assessments include the Mini Mental State Exam (MMSE; Folstein et al., 1975), which has been found to be unreliable with increasing ID severity levels; and delayed match-to-sample and Fuld object memory tasks (Dalton, 1995; Burt & Aylward, 2000), which to date have limited empirical evidence supporting their validity for the detection of prodromal dementia in adult DS (Strydom & Hassiotis, 2003). Other direct measures, such as the Test for Severe Impairment (Albert & Cohen, 1992) and The Rapid Assessment for Developmental Disabilities (Walsh et al., 2015), have demonstrated promising results in assessing cognitive function in DS but require further validation. Additionally, the Cambridge Examination for Mental Disorders of Older People with Down's Syndrome and Others with Intellectual Disabilities (CAMDEX-DS; Ball, Holland, Huppert, Treppner, & Dodd, 2006) combines informant/patient interview and patient cognitive assessments. The CAMDEX-DS has demonstrated strong interrater reliability and high sensitivity and specificity for AD in DS, although the lengthy administration time limits the use of this tool in routine clinical research practice (Ball et al., 2004; O'Caoimh, Clune & Molloy, 2013).

Three other neurocognitive measures that have been used in a diagnostic setting for the assessment of dementia in DS include the Brief Praxis Test (BPT; Dalton, 2008), Severe Impairment Battery (SIB; Panisset et al., 1994), and the Dementia Scale for People with Learning Disabilities (DLD; Evenhuis, 1996). The DLD was developed for use with individuals with DS (Strydom & Hassiotis, 2003), demonstrating good specificity and acceptable sensitivity at modified cut scores (Prasher, 1997). Similarly, the SIB has exhibited high test-retest reliability and alignment with measures of adaptive functioning, as well as minimal floor effects in this population (Witts & Elders, 1998). The BPT is sensitive both to baseline cognitive impairment and cognitive change over time in a longitudinal investigation by Sano and colleagues (2005). The SIB, BPT, and DLD have demonstrated moderate to good reliability after one year in individuals with DS and borderline to moderate ID (Koehl et al., 2020). These assessments have also served as outcome measures in clinical trials investigating interventions for dementia in DS, including use singly or in combination across 6-month (Prasher et al., 2002), 2-year (Lott et al., 2011), 3-year (Sano et al., 2016), and 14-year (McCarron et al., 2014) time periods. McCarron and colleagues (2014)

demonstrated particular sensitivity of the DLD to baseline impairment and change over time. These assessments have continued to be used as indicators of cognition in ad hoc analyses investigating associations of related conditions with DS and dementia (e.g., seizures; Lott et al., 2012) and in validating new combinations of test items to create DS-appropriate assessments (Rapid Assessment for Developmental Disabilities; Walsh et al., 2015).

Although frequently used in investigations of dementia in people with DS, validity research on the SIB, BPT, and DLD as a relatively brief and multimethod neurocognitive battery is limited. Research is particularly needed on the measures' ability to identify prodromal dementia symptoms in the DS population given the utility of accurate early detection. Validity evidence for this battery in the assessment of cognition in people with DS with dementia, as well as early detection, would augment the extant literature by extending previous work and supporting their use in future studies and in clinical settings. Given the challenges of early detection of prodromal dementia in the DS population, this study investigated the validity of a brief SIB, BPT, and DLD battery for detecting incipient dementia in DS at baseline. We hypothesised that group SIB, BPT, and DLD mean scores will differ across "no dementia," "possible dementia," and "probable dementia" diagnostic groups, as well as demonstrate acceptable sensitivity, specificity, and overall accuracy in distinguishing these groups in the Aging and Down syndrome (ADS) cohort.

## Methods

### Participants

The SIB, BPT, and DLD were acquired in a longitudinal cohort of aging individuals with DS, the Aging and Down Syndrome (ADS) study at the University of Kentucky. The ADS baseline cohort in the present study includes a wide range of ages (25 – 64 years) of individuals with DS, making this group appropriate for the detection of early cognitive changes. Inclusion criteria for this cohort include the following: 1) Existing diagnosis of DS; 2) over the age of 25; 3) medically stable; 4) completion of annual visits with MRI and blood samples; 5) English speaking; 6) absence of neurological disease other than DS; 7) toleration of MRI. Exclusion criteria include the following: 1) no diagnosis of DS; 2) under the age of 25; 3) not medically stable and have changed medications in the last three months with the exception of anxiolytic use as needed for medical procedures; 4) unable to complete annual visits with MRI and blood samples; 5) non-English speaking; 6) neurological disease other than DS. Research procedures were independently reviewed and approved by the University of Kentucky Institutional Review Board. Participants completed approved protocols for informed consent or assent with guardian approval. Participants were community residing men and women with DS recruited through local DS support groups and residential facilities in Kentucky, southern Indiana, and southern Ohio.

All participants who completed a baseline study visit, including the BPT, SIB, and DLD, through January 2020 were available for inclusion in the analyses. These participants totaled 117. Of those participants, individuals with any missing assessment data (n=8) and whose dementia status was unknown (n=9) were excluded, leaving 100 participants for inclusion.

## Assessments

The BPT (Dalton, 2008) is a 20-item measure of dyspraxia that minimises verbal demands in favour of simple behavioural output. Low scores on the BPT indicate severe dyspraxia, an indicator of functional deterioration closely linked to cognitive decline in individuals with DS (Anderson-Mooney, Schmitt, Head, Lott, & Heilman, 2016; Sano et al., 2005). The SIB (Panisset et al., 1994) utilises one-step commands and gestural cues and allows for non-verbal responses and partially correct responses in order to assess cognition in individuals with severe dementia. The SIB yields a total score along with six major subscales, including attention, orientation, language, memory, visuospatial ability, and construction. Lower scores indicate more severe deficits. The DLD (Evenhuis, 1996) is a 50-item informant questionnaire measuring behavioural and cognitive dysfunction. The DLD results in the following scores: sum of cognitive scores (SCS), including short-term memory, long-term memory, and spatial/temporal orientation; sum of social scores (SOS), including speech, practical skills, mood, activity/interest, and behavioural disturbance; and a total score consisting of the combined SCS and SOS, with higher scores on the DLD indicating greater difficulties. DLD raters for the current study were caregivers and/or legal guardians who were responsible for daily care of the participants either in the home or an assisted living facility.

## Consensus Diagnosis

Dementia diagnoses were based on NINCDS-ADRDA criteria (McKhann et al., 1984; McKhann et al., 2011; Table 1) and determined through consensus review of the independent diagnostic impressions of the neurologist who examined the participant and the neuropsychologist or psychologist who tested the participant. These initial impressions were discussed along with SIB, BPT, and DLD test data in consensus diagnosis decisions. Consensus diagnostic discussions incorporated single completion DLD cut points by level of intellectual disability, as reported by Prasher (1997) for care provider SCS and SOS ratings. Agreement between the neurologist's independent diagnostic impression and eventual consensus diagnosis was 96%. Baseline levels of ID were determined by caregiver report of prior evaluation results and by review of records when available. ID severity was determined according to DSM-IV-TR criteria (American Psychiatric Association, 2000).

## Analyses

Chi-squared tests and Kruskal-Wallis rank sum tests evaluated group differences on participant characteristics. Follow-up Wilcoxon rank-sum tests evaluated pairwise differences for continuous variables.

A separate linear regression model was fit for each clinical outcome score (SIB, BPT, DLD, DLD Cognitive, and DLD Social) and diagnosis. Because all clinical outcome scores are highly skewed, they were transformed using formulas reported in Supplementary Table 1. Transformed clinical scores are indicated with the subscript *trans*. All figures back transform each clinical outcome score to its original units to facilitate interpretation. All models controlled for the covariates of age, gender, and ID. All assumption checks were completed for each model. Post-hoc pairwise comparisons used a Tukey correction.

Receiver operating characteristic (ROC) curves were constructed to examine the ability of the BPT, SIB, and DLD to differentiate participants based on dementia status. ROC curves plot the proportion of participants correctly identified with dementia (sensitivity) against the proportion of those incorrectly identified (1-specificity). Accuracy of the measures is represented in the area under the curve (AUC). Data were analysed using *R 4.0.2*.

## Results

Demographic and clinical characteristics of the participants are shown in Table 2. Descriptive statistics for the BPT, SIB, and DLD can be found in Table 3. Regarding possible floor effects for the performance-based measures, no participants scored at floor (raw score = 0) on the SIB or BPT. Only 5% (n=5) and 4% (n=4) of the total sample scored below 40 on the SIB and BPT, respectively.

Linear regression model results indicated no significant association between gender and  $SIB_{trans}$  [ $F^{(1,98)} = 0.25, p = 0.62$ ],  $BPT_{trans}$  [ $F^{(1,98)} = 3.02, p = 0.09$ ],  $DLD\ Total_{trans}$  [ $F^{(1,98)} = 0.02, p = 0.88$ ],  $DLD\ Cognitive_{trans}$  [ $F^{(1,98)} = 0.04, p = 0.84$ ], or  $DLD\ Social_{trans}$  [ $F^{(1,98)} = 0.26, p = 0.61$ ]. However, there was a trend between gender and  $BPT_{trans}$ . ID was significantly associated with  $SIB_{trans}$  [ $F^{(1,98)} = 16.46, p < 0.001$ ],  $BPT_{trans}$  [ $F^{(1,98)} = 13.62, p < 0.001$ ],  $DLD\ Total_{trans}$  [ $F^{(1,98)} = 13.00, p < 0.001$ ],  $DLD\ Cognitive_{trans}$  [ $F^{(1,98)} = 12.84, p < 0.001$ ], and  $DLD\ Social_{trans}$  [ $F^{(1,98)} = 7.43, p = 0.008$ ]. Age was significantly associated with  $SIB_{trans}$  [ $F^{(1,98)} = 8.22, p = 0.005$ ],  $BPT_{trans}$  [ $F^{(1,98)} = 4.56, p = 0.035$ ],  $DLD\ Total_{trans}$  [ $F^{(1,98)} = 10.01, p = 0.002$ ],  $DLD\ Cognitive_{trans}$  [ $F^{(1,98)} = 16.68, p < 0.001$ ], and  $DLD\ Social_{trans}$  [ $F^{(1,98)} = 4.64, p = 0.034$ ]. Because of the significant associations between ID, age, and clinical outcome scores, ID and age were included in additional models as covariates. Gender was also included as a covariate because of the trend observed with BPT.

Full model results are provided in Supplementary Table 2. Predicted test scores and associated 95% confidence intervals by dementia status are graphed in Figure 1. For all test instruments there was a significant association with dementia status (all  $p < 0.05$ ). On the  $SIB_{trans}$  the no dementia groups had significantly higher scores than the probable group ( $t = -2.83; p = 0.016$ ), and there was a trend for the possible group to have higher scores than the probable group ( $t = -2.40; p = 0.05$ ). On the  $BPT_{trans}$ , the no dementia ( $t = -4.47; p < 0.001$ ) and possible ( $t = -3.80; p < 0.001$ ) groups had significantly higher scores than the probable group. On the SIB and BPT the scores appeared to distinguish the possible from probable group, but could not distinguish between no and possible dementia (Figure 1A–B).

$DLD\ Total_{trans}$  was significantly lower for the no dementia group compared to possible ( $t = -4.55; p < 0.001$ ) and probable ( $t = -6.02; p < 0.001$ ) dementia groups.  $DLD\ Cognitive_{trans}$  was significantly lower for the no dementia group compared to possible ( $t = -4.37; p < 0.001$ ) and probable ( $t = -6.08; p < 0.001$ ) dementia groups.  $DLD\ Social_{trans}$  was significantly lower for the no dementia group compared to possible ( $t = -3.96; p < 0.001$ ) and probable ( $t = -4.46; p < 0.001$ ) dementia groups. The  $DLD\ Total$  and subscales appeared to differentiate the no dementia and possible groups, but not possible versus probable dementia groups (Figure 1C–E).

Sensitivity and specificity values of the DLD subscales for levels of dementia diagnosis according to established cutoffs (Evenhuis, 1992; Evenhuis, 1996; Strydom & Hassiotis, 2003) are shown in Table 4. Analyses were undertaken to identify cut scores in the present data that would optimise sensitivity and specificity to dementia status. Overall, measures exhibited similarly fair sensitivity, with the DLD demonstrating more robust specificity compared to the fair BPT and SIB specificity. Exact values and recommended cutoffs based on the present data are provided in Table 5.

ROC curves based on the cutoffs in the present data are presented in Figure 2A for the performance-based measures (BPT and SIB) and Figure 2B for the informant-based measures (DLD and subscales). Performance-based curves are displayed for measures' differentiation of no or possible vs. probable dementia. Informant-based curves are displayed for measures' differentiation of no vs. possible or probable dementia. The different classifications for performance- and informant-based measures were chosen based on the results from the regression models.

The performance-based measures (BPT and SIB Total scores) exhibited fair discrimination ability (AUC = .61 and .66, respectively) when comparing no or possible vs. probable dementia. Regarding the informant-based measures (DLD Total, and Cognitive and Social subscales), the DLD exhibited good discrimination ability (AUC = .75) when comparing no vs. possible or probable dementia, with qualitatively better performance of the Cognitive subscale compared to Social subscale (AUC = .77 and .67, respectively).

## Discussion

This study provides validation evidence for a brief neurocognitive battery, consisting of an informant report (DLD) and two direct cognitive assessments (SIB, BPT) for the detection of dementia in DS. As expected, overall performance on this battery did not differ according to gender (with the exception of a trend for BPT) and did differ according to age, ID severity, and dementia status. Although these factors were significantly associated with test performance, no participants in any group performed at or near floor on the performance measures. This finding suggests that floor effects, a common barrier to accurate cognitive assessment in DS posed by lack of appropriate measures, may be circumvented through the use of this battery. These results imply that the SIB, BPT, and DLD can be used to measure cognition across various demographic factors, lending further support for their use in dementia assessments in this population.

Overall, SIB, BPT, and DLD scores exhibited fair or good discrimination of dementia status, and performance differences on the measures were in the expected directions. Notably, mean scores on the SIB and BPT significantly differed between the possible and probable dementia groups, but not between no dementia and possible. In contrast, performance on the DLD and subscales differed between no and possible dementia groups, but not possible and probable. Further, sensitivity of the measures to dementia presence was modest, as was specificity of the performance-based measures. In contrast, specificity for the DLD was robust, reaching .94 for the Total score and Cognitive subscale. These findings regarding mean scores on the SIB and BPT, low sensitivity across measures, and superior specificity



of the DLD reflect the difficulty in identifying incipient dementia in DS based on cognitive performance.

Frontal deterioration and subsequent personality or behavioural changes may indicate early changes associated with dementia in DS (Ball et al., 2008; Fonseca et al., 2019) and predate clinical diagnoses of dementia (Urv et al., 2008). Thus, informant based measures of behavioural dysfunction may be more capable than performance based measures of identifying incipient dementia symptoms, in keeping with previous findings (Startin et al., 2019). This conclusion is also supported by the ROC curves in the present study, wherein the SIB and BPT exhibited fair discrimination of no/possible dementia vs. probable dementia. The DLD Total and subscales, particularly Cognitive, exhibited good discrimination of no dementia vs. possible/probable dementia. These results not only highlight the known importance of including informant input in the dementia diagnostic process in DS, but also suggest their superior capabilities compared to performance based measures when identifying early dementia symptoms in adult DS persons. Future test development and refinement efforts in this area may benefit from investigation of domain-specific performance on performance-based measures such as the SIB and BPT, as total scores may mask more specific impairments that could be useful in determination of dementia status.

The following cut scores maximized sensitivity and specificity for the detection of possible or probable dementia in this sample: BPT cut score of 62; SIB cut score of 69; DLD Total cut score of 17; DLD SCS cut score of 9; DLD SOS cut score of 10. When compared to established cut scores for the DLD SCS and SOS (Evenhuis, 1992; Evenhuis, 1996; Strydom & Hassiotis, 2003), a higher cut score was identified for the SCS in the present study. Thus, lower cut scores are not necessarily unsupported by the data, but a higher cut score may be needed, particularly to minimise false positive dementia diagnoses as much as possible in this population. Given that cut scores have not been established in the extant literature for the SIB and BPT to the authors' knowledge, further validation of these recommendations using independent samples is warranted.

Limitations of the current research include the use of SIB, BPT, and DLD test data in consensus diagnosis decisions, leading to possible circularity in the dementia groupings, a possibility unfortunately not uncommon in clinical dementia research. However, the high percent agreement (96%) between the neurologist's independent diagnostic impression and eventual consensus diagnosis makes the possibility of significant contribution from circularity less likely. It is important to note that care providers often discuss observed changes and symptoms in the participant with DS during the medical examination process. Therefore, the report of symptoms on the DLD and discussion with the neurologist may explain the robust association between DLD and final diagnosis. Future aims of the ADS study include validation of dementia diagnosis against neuropathology found at autopsy. As such data become available, they may serve to further address the issue of possible criterion contamination. Additionally, the sample included relatively small percentages of participants with severe ID as well as possible and probable dementia, as it was designed to examine early cognitive transitions in adults with DS. Lastly, age was predictably associated with performance across measures; thus the possibility exists of a cohort effect on test performances.

The current study provides validation evidence for the SIB, BPT, and DLD serving as a brief (under 30 minutes each; Sano et al., 2005; Strydom & Hassiotis, 2003) and multimethod (informant report, performance assessment) neurocognitive battery in the assessment of dementia in DS. The SIB and BPT demonstrated the ability to differentiate between possible and probable dementia groups, suggesting their utility in discriminating dementia stages once a dementia process is suspected. In contrast, the DLD and subscales discriminated between no dementia and possible dementia groups, suggesting the measure's utility in identifying incipient dementia symptoms. Together with the high specificity demonstrated by the DLD in the current sample, these findings particularly support the use of informant-based measures in early dementia evaluations. Further research is needed to continue to validate these instruments in DS dementia evaluations. Future investigations into individual or sequential application of these measures to identify and eliminate patients without dementia from further evaluation are also warranted.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## References

- Albert M. and Cohen C, 1992. The Test for Severe Impairment: an instrument for the assessment of patients with severe cognitive dysfunction. *Journal of the American Geriatrics Society*, 40(5), 449–453. [PubMed: 1634695]
- American Psychiatric Association (2000). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., Text Revision). Washington, DC.
- Anderson-Mooney AJ, Schmitt FA, Head E, Lott IT, and Heilman KM, 2016. Gait dyspraxia as a clinical marker of cognitive decline in Down syndrome: a review of theory and proposed mechanisms. *Brain and Cognition*, 104, 48–57. [PubMed: 26930369]
- Ball SL, Holland AJ, Hon J, Huppert FA, Treppner P, and Watson PC, 2006a. Personality and behaviour changes mark the early stages of Alzheimer's disease in adults with Down's syndrome: findings from a prospective population-based study. *International Journal of Geriatric Psychiatry*, 21(7), 661–673. [PubMed: 16802281]
- Ball S, Holland T, Huppert FA, Treppner P, and Dodd K, 2006b. *CAMDEX-DS: The Cambridge Examination for Mental Disorders of Older People with Down's Syndrome and Others with Intellectual Disabilities* (Vol. 1). Cambridge University Press.
- Ball SL, Holland AJ, Huppert FA, Treppner P, Watson P, and Hon J, 2004. The modified CAMDEX informant interview is a valid and reliable tool for use in the diagnosis of dementia in adults with Down's syndrome. *Journal of Intellectual Disability Research*, 48(6), 611–620. [PubMed: 15312062]
- Ball SL, Holland AJ, Treppner P, Watson PC and Huppert FA, 2008. Executive dysfunction and its association with personality and behaviour changes in the development of Alzheimer's disease in adults with Down syndrome and mild to moderate learning disabilities. *British Journal of Clinical Psychology*, 47(Pt 1), 1–29.

- Burt DB and Aylward EH, 2000. Test battery for the diagnosis of dementia in individuals with intellectual disability. Working Group for the Establishment of Criteria for the Diagnosis of Dementia in Individuals with Intellectual Disability. *Journal of Intellectual Disability Research*, 44(Pt 2).
- Coppus AMW, 2013. People with intellectual disability: what do we know about adulthood and life expectancy? *Developmental Disabilities Research Reviews*, 18(1), 6–16. [PubMed: 23949824]
- Dalton AJ, 1995. Dalton/McMurray Visual Memory Test: Delayed Matching to Sample Cognitive Test. Byte Craft Ltd., Ontario, Canada.
- Dalton AJ, 2008. The Dyspraxia Scale for adults with Down syndrome. In Prasher V. (Ed.), *Neuropsychological Assessments of Dementia in Down Syndrome and Intellectual Disabilities*, 67–89, London: Springer.
- De Graaf G, Buckley F. and Skotko BG, 2017. Estimation of the number of people with Down syndrome in the United States. *Genetics in Medicine*, 19(4), 439–447. [PubMed: 27608174]
- Devenny DA, Zimmerli EJ, Kittler P, & Krinsky-McHale SJ (2002). Cued recall in early-stage dementia in adults with Down's syndrome. *Journal of Intellectual Disability Research*, 46(6), 472–483. [PubMed: 12354318]
- Evenhuis HM, 1992. Evaluation of a screening instrument for dementia in ageing mentally retarded persons. *Journal of Intellectual Disability Research*, 36(4), 337–347. [PubMed: 1525439]
- Evenhuis HM, 1996. Further evaluation of the Dementia Questionnaire for Persons with Mental Retardation (DLD). *Journal of Intellectual Disability Research*, 40(Pt 4), 369–373. [PubMed: 8884592]
- Finch H, 2005. Comparison of the performance of nonparametric and parametric MANOVA test statistics when assumptions are violated. *Methodology*, 1(1), 27–38.
- Folstein MF, Folstein SE and McHugh PR, 1975. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3), 189–198. [PubMed: 1202204]
- Fonseca LM, Mattar GP, Haddad GG, Goncalves AS, Miguel AQC, Guilhoto LM, et al. , 2019. Frontal-subcortical behaviors during Alzheimer's disease in individuals with Down syndrome. *Neurobiology of Aging*, 78, 186–194. [PubMed: 30947114]
- Gedye A, 1995. Dementia scale for Down syndrome: manual. A. Gedye.
- Head E, T Lott I, M Wilcock D. and A Lemere C, 2016. Aging in Down syndrome and the development of Alzheimer's disease neuropathology. *Current Alzheimer Research*, 13(1), 18–29. [PubMed: 26651341]
- Hithersay R, Startin CM, Hamburg S, Mok KY, Hardy J, Fisher EM, ... & Strydom A. (2019). Association of dementia with mortality among adults with Down syndrome older than 35 years. *JAMA Neurology*, 76(2), 152–160. [PubMed: 30452522]
- Johnstone EM, Chaney MO, Norris FH, Pascual R. and Little SP, 1991. Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis. *Molecular Brain Research*, 10(4), 299–305. [PubMed: 1656157]
- Jorm AF, 1994. A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. *Psychological Medicine*, 24(1), 145–153. [PubMed: 8208879]
- Koehl LM, Harp JP, Van Pelt K, Head E. and Schmitt FA, 2020. Longitudinal assessment of dementia measures in Down syndrome. *Alzheimers Dement (Amst)*.
- Landes SD, Stevens JD and Turk MA, 2020. Cause of death in adults with Down syndrome in the US. *Disability and Health Journal*, 100947.
- Lott IT, Doran E, Nguyen VQ, Tournay A, Head E. and Gillen DL, 2011. Down syndrome and dementia: a randomized, controlled trial of antioxidant supplementation. *American Journal of Medical Genetics Part A*, 155(8), 1939–1948.
- Lott IT, Doran E, Nguyen VQ, Tournay A, Movsesyan N. and Gillen DL, 2012. Down syndrome and dementia: seizures and cognitive decline. *Journal of Alzheimer's Disease*, 29(1), 177–185.
- Lott IT and Head E, 2019. Dementia in Down syndrome: unique insights for Alzheimer disease research. *Nature Reviews Neurology*, 15(3), 135–147. [PubMed: 30733618]

- McCarron M, McCallion P, Reilly E. and Mulryan N, 2014. A prospective 14-year longitudinal follow-up of dementia in persons with Down syndrome. *Journal of Intellectual Disability Research*, 58(1), 61–70.
- McKhann G, Drachman D, Folstein M, Katzman R, Price D, and Stadlan EM, 1984. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group\* under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology*, 34(7), 939–939. [PubMed: 6610841]
- McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, Kawas CH, ... & Phelps CH (2011). The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia*, 7(3), 263–269.
- Nieuwenhuis-Mark RE, 2009. Diagnosing Alzheimer's dementia in Down syndrome: problems and possible solutions. *Research in Developmental Disabilities*, 30(5), 827–838. [PubMed: 19269132]
- O'Caomh R, Clune Y, and Molloy W, 2013. Screening for Alzheimer's disease in Downs syndrome. *Journal of Alzheimer's Disease & Parkinsonism*, 7(001), 2161–0460.
- Panisset M, Roudier M, Saxton J. and Boller F, 1994. Severe impairment battery. A neuropsychological test for severely demented patients. *Archives of Neurology*, 51(1), 41–45. [PubMed: 8274108]
- Prasher VP, 1997. Dementia questionnaire for persons with mental retardation (DLD): modified criteria for adults with Down's syndrome. *Journal of Applied Research in Intellectual Disabilities*, 10(1), 54–60.
- Prasher VP, Huxley A, Haque MS and Down Syndrome Ageing Study Group, 2002. A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Down syndrome and Alzheimer's disease—pilot study. *International Journal of Geriatric Psychiatry*, 17(3), 270–278. [PubMed: 11921156]
- Presson AP, Partyka G, Jensen KM, Devine OJ, Rasmussen SA, McCabe LL, et al. , 2013. Current estimate of Down Syndrome population prevalence in the United States. *Journal of Pediatrics*, 163(4), 1163–1168.
- Rubenstein E, Hartley S. and Bishop L, 2020. Epidemiology of dementia and Alzheimer disease in individuals with Down syndrome. *JAMA Neurology*, 77(2), 262–264. [PubMed: 31657825]
- Salardini A, 2019. An overview of primary dementias as clinicopathological entities. *Seminars in Neurology*, 39(2), 153–166. [PubMed: 30925609]
- Sano M, Aisen PS, Andrews HF, Tsai WY, Lai F. and Dalton AJ, 2016. Vitamin E in aging persons with Down syndrome: a randomized, placebo-controlled clinical trial. *Neurology*, 86(22), 2071–2076. [PubMed: 27164691]
- Sano M, Aisen PS, Dalton AJ, Anderews HF, Tsai W and The International Down Syndrome and Alzheimer's Disease Consortium, 2005. Assessment of aging individuals with Down syndrome in clinical trials: results of baseline measures. *Journal of Policy and Practice in Intellectual Disabilities*, 2(2), 126–138.
- Startin CM, Lowe B, Hamburg S, Hithersay R, Strydom A. and LonDown S. Consortium, 2019. Validating the Cognitive Scale for Down Syndrome (CS-DS) to detect longitudinal cognitive decline in adults with Down syndrome. *Frontiers in Psychiatry*, 10, 158. [PubMed: 31057430]
- Strydom A. and Hassiotis A, 2003. Diagnostic instruments for dementia in older people with intellectual disability in clinical practice. *Ageing & Mental Health*, 7(6), 431–437. [PubMed: 14578004]
- Urv TK, Zigman WB and Silverman W, 2008. Maladaptive behaviors related to dementia status in adults with Down syndrome. *American Journal on Mental Retardation*, 113(2), 73–86. [PubMed: 18240877]
- Visser FE, Aldenkamp AP, Van Huffelen AC, Kuilman M, Overweg J. and van Wijk J, 1997. Early signs of dementia checklist. *American Journal of Mental Retardation*, 101, 400–12. [PubMed: 9017086]
- Walsh DM, Doran E, Silverman W, Tournay A, Movsesyan N. and Lott IT, 2015. Rapid assessment of cognitive function in down syndrome across intellectual level and dementia status. *Journal of Intellectual Disability Research*, 59(11), 1071–1079. [PubMed: 26031550]

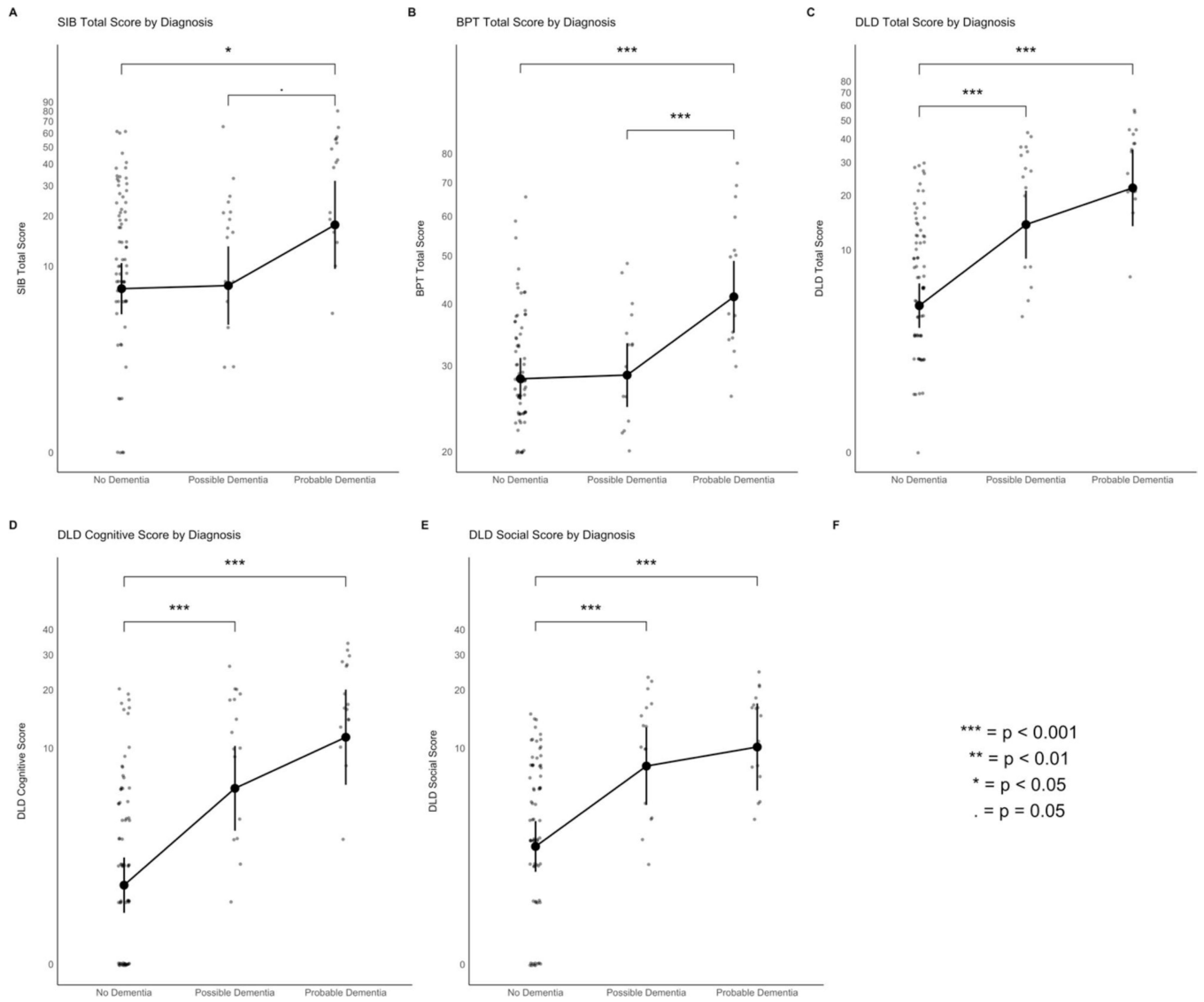
Witts P. and Elders S, 1998. The 'Severe Impairment Battery': assessing cognitive ability in adults with Down syndrome. *British Journal of Clinical Psychology*, 37(Pt 2), 213–216.

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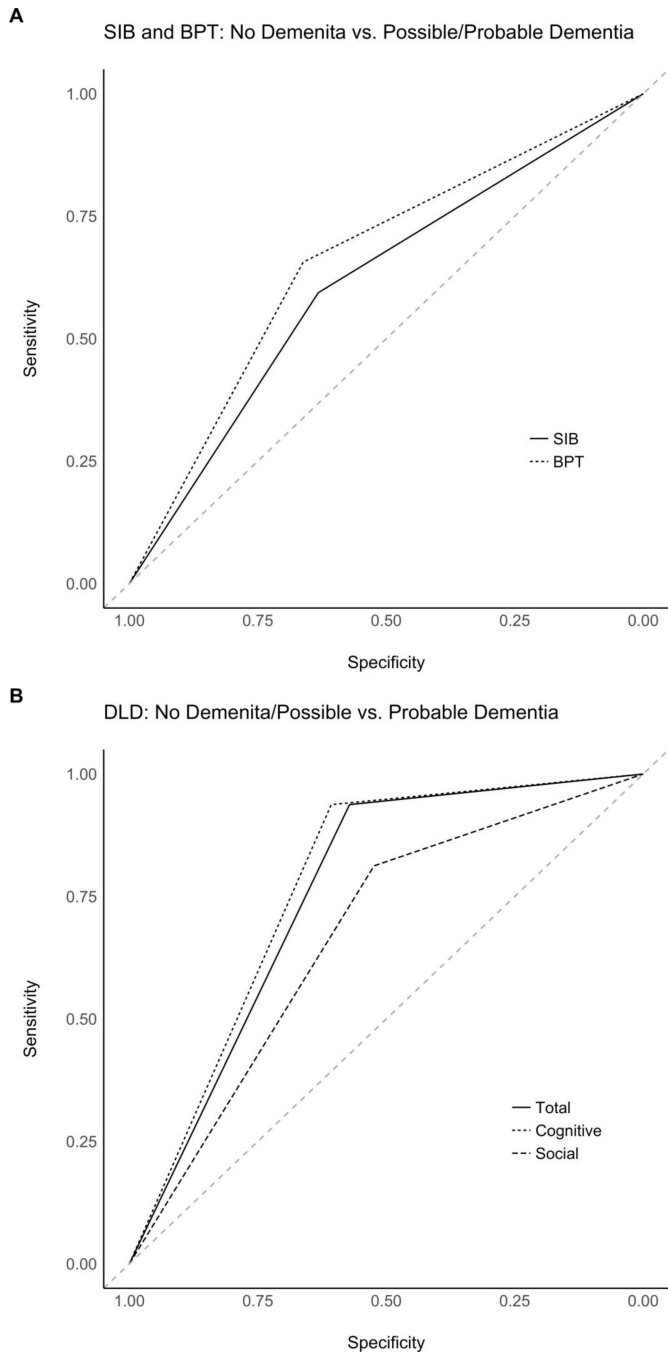
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**Figure 1.** Predicted test scores and 95% confidence intervals by dementia status.  
*Note:* A) SIB Total score; B) BPT Total score; C) DLD Total score; D) DLD Cognitive subscale; E) DLD Social subscale



**Figure 2.**  
ROC curves.

*Note:* Curves display the differentiating ability of the: A) SIB and BPT when comparing no vs. possible or probable dementia; B) DLN when comparing no or possible vs. probable dementia

**Table 1.**

## NINCDS-ADRDA Criteria

Diagnosis	Criteria
Probable Dementia	1. Dementia established by clinical examination and documented by cognitive testing 2. Deficits in 2 or more areas of cognition 3. Progression worsening of memory and other cognitive functions 4. No disturbance of consciousness 5. Onset at age >40* 6. Absence of systemic disorders or other brain diseases that could account for cognitive deficits
Possible Dementia	1. Dementia syndrome (core clinical criteria for AD dementia cognitive deficits), in the absence of other neurologic, psychiatric, or systemic disorders sufficient to cause dementia 2. Presence of a second systemic or brain disorder sufficient to produce dementia but is not considered the cause of the dementia 3. Single, gradually progressive severe cognitive deficit identified in the absence of other identifiable cause
No Dementia	Criteria for possible/probable dementia are not met

\* Age criterion not strictly applied for DS.



**Table 2.**

## Demographic and Clinical Characteristics

Characteristic	No Dementia (N=68)	Possible Dementia (N=16)	Probable Dementia (N=16)	F
Gender (female) <i>n</i> (%)	37 (54.41)	11 (68.75)	10 (62.5)	.615
Age (Mean, SD)	37.98 (9.33) <sup>a</sup>	46.66 (9.74) <sup>b</sup>	51.50 (8.79) <sup>b</sup>	16.52 *
ID Level ( <i>n</i> )				2.783
Borderline/Mild	39	8	5	
Moderate/Severe	29	8	10	
Not Documented	-	-	1	

\*  $p < .05$ .

<sup>abc</sup> Within each row, means with different letters are statistically significantly ( $p < .05$ , two-tailed, Bonferroni corrected for multiple comparisons) different from each other.

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**Table 3.**

## Descriptive Test Statistics

Measure	No Dementia (N = 68)		Possible Dementia (N = 16)		Probable Dementia (N = 16)	
	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)
BPT Total	34–80	69.43 (9.31)	52–80	68.50 (8.45)	23–74	54.31 (15.40)
SIB Total	39–100	83.13 (14.98)	35–98	82.06 (15.53)	20–95	61.19 (22.23)
DLD Total	0–30	9.15 (7.71)	4–43	23.50 (13.56)	7–57	32.50 (14.43)
DLD SCS	0–20	4.10 (5.20)	1–26	11.81 (7.80)	3–34	19.19 (9.22)
DLD SOS	0–15	5.04 (4.13)	2–23	11.69 (6.86)	4–25	13.31 (6.54)

Note. BPT = Brief Praxis Test; SIB = Severe Impairment Battery; DLD = Dementia Scale for People with Learning Disabilities; SCS = sum of cognitive scores; SOS = sum of social scores

**Table 4.**

Sensitivity and Specificity of the DLD According to Established Cut Scores

Measure	Cut Score	Consensus Diagnosis	Sensitivity	Specificity
DLD SCS	7	Possible AD	.65	.80
	7	Probable AD	.95	.80
DLD SOS	10	Possible AD	.71	.83
	10	Probable AD	.68	.83

Note. DLD = Dementia Scale for People with Learning Disabilities; SCS = sum of cognitive scores; SOS = sum of social scores. Cut scores taken from Evenhuis, 1992; Evenhuis, 1996; Strydom & Hassiotis, 2003.

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**Table 5.**

Cut Scores Optimising Sensitivity and Specificity of the SIB, BPT, and DLD According to Present Data

Measure	Cut Score	Consensus Diagnosis	Sensitivity	Specificity
BPT Total	62	Possible/Probable AD	.66	.66
SIB Total	69	Possible/Probable AD	.63	.59
DLD Total	17	Probable AD	.57	.94
DLD SCS	9	Probable AD	.61	.94
DLD SOS	10	Probable AD	.52	.81

Note. BPT = Brief Praxis Test; SIB = Severe Impairment Battery; DLD = Dementia Scale for People with Learning Disabilities; SCS = sum of cognitive scores; SOS = sum of social scores.

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