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Review

Screening of Cognitive Changes in Adults with Intellectual Disabilities: A Systematic Review

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Abstract: Background and Aims: Screening and assessment of cognitive changes in adults with Intellectual Disabilities (ID), mainly Down Syndrome (DS), is crucial to offer appropriate services to their needs. We present a systematic review of the existing instruments assessing dementia, aiming to support researchers and clinicians' best practice. Methods: Searches were carried out in the databases Web of Science; PubMed; PsycINFO in March 2019 and updated in October 2020. Studies were selected and examined if they: (1) focused on assessing age-related cognitive changes in persons with ID; (2) included adults and/or older adults; (3) included scales and batteries for cognitive assessment. Results: Forty-eight cross-sectional studies and twenty-seven longitudinal studies were selected representing a total sample of 6451 participants (4650 DS and 1801 with other ID). In those studies, we found 39 scales, questionnaires, and inventories, and 13 batteries for assessing cognitive and behavioural changes in adults with DS and other ID. Conclusion: The most used instrument completed by an informant or carer was the Dementia Questionnaire for Learning Disabilities (DLD), and its previous versions. We discuss the strengths and limitations of the instruments and outline recommendations for future use.

Keywords: screening; dementia; intellectual disability; early-onset; neuropsychology

1. Introduction

Individuals with intellectual disabilities (ID) may be at an increased risk of developing dementia when compared to the general population [1]. In people with ID, the prevalence of dementia is as high as 4% in individuals under 40 years, and 40% in those 60 years or older, with an average age of onset between 51 and 56 years [2–4]. Epidemiological studies found that within a population of 222 individuals with ID aged 60 years, a total of 29 had a dementia diagnosis when using the criteria from both the International Classification of Diseases, 10th Revision (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) [5]. Among those diagnosed with dementia, 66% of individuals met criteria for dementia of Alzheimer's type, with a prevalence of 8.6% (95% CI 5.2–13.0). Recently, a cross-sectional study with 493 adults with Down Syndrome (DS) and other ID reported that individuals with other ID may develop dementia and mild neurocognitive disorder at an earlier age and at a higher rate than the general population. The prevalence of dementia in individuals with other ID was 0.8% in the age group of 45 to 54 years, 3.5% in the group of 55 to 64 years and 13.9% for

those aged 65 to 74 years. The study also showed that the prevalence of mild neurocognitive disorder in individuals with other ID was 3.1% in the age group of 45 to 54, 3.5% in the age group of 55 to 64, and 2.8% in the age group of 65 to 74. When analysed by severity of ID in individuals with DS and other ID, 1.5% of the individuals with moderate ID were diagnosed with dementia, 5.0% with severe ID were diagnosed with dementia in relation to 3.0% of individuals with moderate ID and 1.7% with severe ID were diagnosed with mild neurocognitive disorder [6].

Pathological studies also provide evidence for early-onset dementia. One study reported that by the age of 40 years, nearly all individuals with DS presented Alzheimer's Disease (AD) markers [7], while longitudinal studies show that by the age of 65 years over 90% of people with DS and other ID meet diagnostic criteria for dementia [8,9]. Another study carried out with individuals with DS and other ID (n = 526) showed that among individuals with a diagnosis of DS, symptoms of dementia appeared earlier than those in other ID (average age of diagnosis was 52 years of age). In 75% of the cases, the symptoms were consistent with dementia of Alzheimer's type [10].

Early detection of dementia can be challenging in individuals with ID [11]; many of the instruments for assessing dementia-related cognitive changes in the general population are based on the assumption of sound premorbid cognitive functioning, which is difficult to determine in those with ID [12–14]. Furthermore, the clinical presentation of dementia in those with ID may differ compared to the general population, with personality and behavioural changes presenting earlier [15,16].

Single domain cognitive tests are the usual approach to screen for dementia in the general population, as they can identify progressive deterioration in cognitive domains [17]. However, in people with ID, these tests are not appropriate due to pre-existing conditions which makes it difficult to determine baseline cognitive function, meaning the results cannot be interpreted in a substantial and valid way, as there are often no norms for this population [11]. This has been addressed in recent research carried out by Benejam [18], who used the CAMCOG-DS in people with Down syndrome to accurately diagnose Alzheimer's disease. This shows the importance of developing reliable population norms for appropriate instruments when assessing cognitive changes in people with ID.

1.1. Down Syndrome Intellectual Disability

Among adults with ID, there is a well-established link between DS and dementia, particularly AD. Research indicates that 95% of people with DS will develop AD by the age of 65 [4,19,20]. Individuals with DS also have an increased risk of developing early-onset dementia; the clinical presentation of dementia symptoms before the age of 65 [4,19,21]. The increased prevalence of AD in DS is largely due to genetic factors associated with trisomy 21, the most common form of DS. Those with trisomy 21 have a third copy of chromosome 21 [22], which is responsible for the production of β-amyloid precursor protein [23]. The increased presence of β-amyloid precursor protein leads to an accelerated build-up of senile plaque in the brain, which is a primary cause of AD [22]. By age 40, most individuals with DS display neuropathological changes consistent with AD, while most individuals with DS show clinical signs of dementia by age 50 [24]. Similarities of symptoms between AD and DS suggest common risk factors among AD and DS. Prasher and colleagues (2008) [25] examined Apolipoprotein (APOE) genotyping in people with DS, concluding that those with APOE E4 allele had a significantly higher risk of developing AD, had an earlier onset of AD, and a higher rate of progression to death when comparing for participants with APOE 3 allele. Screening for APOE genotype in this population may be of good clinical utility as it helps people obtain early treatment, which can reduce early mortality rates [25,26]. Startin et al. (2019) [27] recently "conducted the largest cognitive study to date" (p. 245) with 312 participants with DS in order to assess typical age-related and AD-related cognitive changes in this population. The authors reported memory and attention measures were most sensitive to decline, although the earliest cognitive markers of AD-related pathology were identified on most outcome measures. They also reported an age-related relationship where older age groups showed poorer performance in neuropsychological tests, except for scores on the Behaviour Rating Inventory of Executive Function—adult version; a measure of executive function. However, other research has

indicated that declines in executive function may precede memory loss in those with DS and AD [28], suggesting further research is needed to determine the typical progression of AD in this population.

1.2. Other Intellectual Disability

There is less conclusive evidence of an increased risk of dementia in those with an intellectual disability not related to DS (herein other ID). While there may be several genetic factors, leading to increased risk of dementia in those with other ID—such as reduced baseline cognitive ability and fewer neurons and synaptic connections [1]—older adults with other ID show protective factors against developing dementia, including lower rates of smoking and greater cardiovascular health compared to the general population [29].

Some research suggests the prevalence of dementia for individuals with other ID may be the same or slightly higher than the general population [30,31], although a longitudinal study by Strydom et al. (2013) [1] reported that dementia might be five times more prevalent in this population. However, epidemiological studies may underestimate true prevalence rates due to several factors. Firstly, dementia is under-diagnosed in the general population—it is likely that this is also present in those with ID [14]. Secondly, those with ID generally have poorer access to health care services [32,33], which could result in lower levels of diagnosis. Finally, dementia presents differently in those with ID compared to those without, leading to difficulty in diagnosis [14].

1.3. The Present Study

Due to the prevalence of dementia in those with ID, particularly DS, it is important that researchers and clinicians have validated, reliable measures for diagnosis. Standardised measures are necessary for determining prevalence within a population, assessing and comparing interventions, and synthesising research findings for meta-analyses; however, a systematic review by Zellinger et al. (2013) [14] noted an "immense" number of instruments assessing cognitive change in those with ID. The present review aims to build on the previous work by Zellinger et al. (2013) [14] by comprehensively reviewing the existing instruments available for screening for cognitive impairments in individuals with ID, considering cross-sectional and longitudinal studies. This systematic review focuses on scales and batteries as they demonstrate a more robust way to screen for dementia in this population [14,17]. The review will look at the strengths and limitations of instruments and aims to provide researchers and clinicians with an up to date, comprehensive list of available tools.

2. Materials and Methods

The methods for this review were based on the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [34]. As a complement and extension to the PRISMA protocol, we used the Synthesis Without Meta-Analysis in Systematic Reviews Checklist (SWiM), following the recommendation of the EQUATOR group network ("Enhancing the QUAlity and Transparency Of Health Research") (as seen in https://www.equator-network.org) [35]. Both checklists, quality assessment and eligible studies, are available as Supplementary Material.

2.1. Literature Search

Two systematic literature searches of three databases (Web of Science; PubMed; PsycINFO) were conducted. Searches included the key terms (with the appropriate Boolean operators for each database) "Adult* OR Older adult*"; "Cognit* task OR Cognit* test OR neuropsych* test"; "Instrument* OR Scale OR questionnaire OR screening"; "Dementia"; "Intellectual* Disabilit* OR mental* retar* OR General learn* disabilit*". Filters were applied for the key terms NOT "Child* AND adolesc* AND youth*". Searches were performed with consideration of all articles, without limiting the year of publication or language of publication. Except for two publications, one in Spanish and one in German, both included in the screening phase, all other search results were published in English.

2.2. Eligibility Criteria and Data Extraction

The eligibility criteria for the studies included in this systematic review were:

Population: Studies that included adults aged 18 years and older diagnosed with Intellectual Disability;

Intervention: Screening of cognitive changes in adults with Intellectual Disabilities;

Comparators: Studies using scales and batteries to assess cognitive changes and dementia in individuals with intellectual disabilities including Down Syndrome;

Outcomes: Studies assessing cognitive and behavioural changes in adults with intellectual disabilities;

Studies: Studies with cross-sectional and longitudinal designs.

During the first search in March 2019, 70 articles were found on Web of Science, 76 on PubMed, and 60 on PsycINFO (n = 206). Duplicated records (n = 63) were removed, leaving 143 articles. A second search for new entries to databases using the same key search terms was done in September 2019 and 58 new entries were found. The search was repeated in May of 2020 and no new articles were identified, and one article was added in October 2020.

All 202 titles and abstracts were screened using the following inclusion criteria: (1) studies focusing on assessment of dementia in person with ID; (2) population being adults and/or older adults; (3) studies including scales and batteries for cognitive assessment. Sixty-one articles were excluded based on exclusion criteria (review studies and/or intervention studies, or the age of participants not matching the criteria). In total, 140 articles were included for a thorough review (as shown in Figure 1). A manual search of the reference sections of the retrieved studies and review articles was conducted. However, no new articles meeting the inclusion criteria were found.

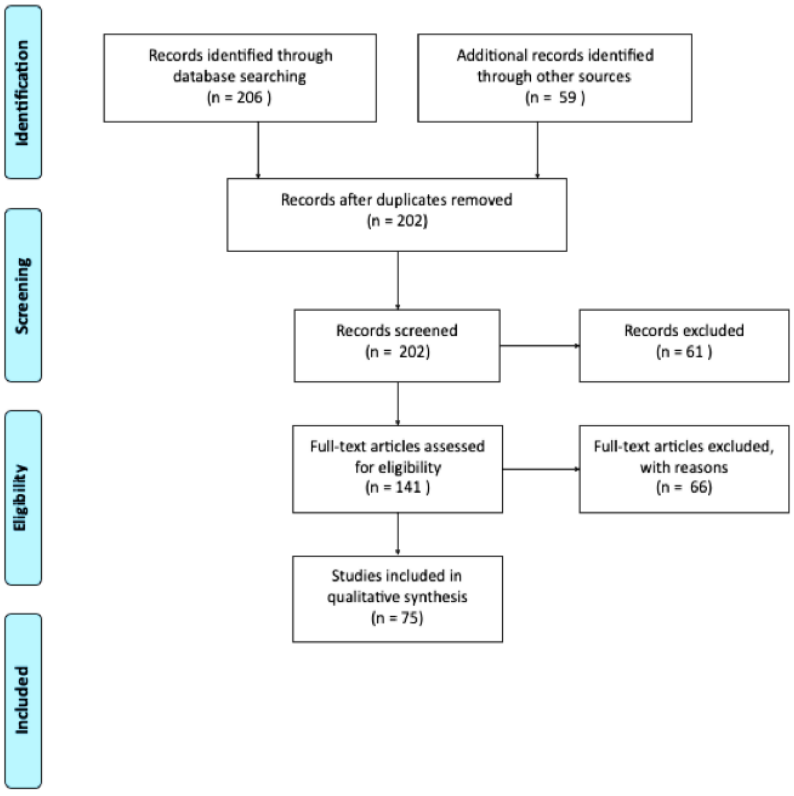

Figure 1. Preferred reporting items for systematic review and meta-analysis (PRISMA) flow chart concerning study retrieval and selection.

We analysed 48 cross-sectional studies and 27 longitudinal studies qualitatively, excluding 66 articles for not meeting inclusion criteria (e.g., review studies, intervention studies, and studies including children or adolescents). In total, 75 articles were included in this review. All articles were

reviewed by two researchers independently. In the few cases of disagreement, discrepancies were solved by consensus.

2.3. Quality Assessment

As for critical appraisal of the studies included in this review, a standardised checklist to identify the risk of bias was used to assess the quality of included studies. The checklist was based on the Newcastle–Ottawa Scale (NOS) [36], embedded on the Tables A2 and A3. A total score with a maximum value of nine points provides a rating for the quality level. Quality levels of evidence were defined as high (9–7 points); medium (6–4 points), and low (3–1 point). No studies presented low-quality range.

3. Results

Descriptive Synthesis

This review identified 48 cross-sectional studies and 27 longitudinal studies with ID population testing. Cross-sectional studies were conducted in the United Kingdom (13), United States (17), Spain (4), Netherlands (4), Italy (4), Ireland (2), Belgium and Switzerland (1), Australia (2) Israel (1), Finland (1) and Canada (1). Longitudinal studies were conducted in the United States (12), the United Kingdom (7), Ireland and the United States (1), Ireland (1), Germany (1), Canada (1), Australia (1), Spain (1), and the Netherlands (1). The most frequent journal in this review was the Journal of Intellectual Disability Research, with a H-index of 93 and an impact factor of 1.94.

Of the 48 cross-sectional studies, 24 included only participants with DS, while the remaining 24 included individuals with DS and other ID. Table 1 represents the demographic information for both cross-sectional and longitudinal studies. In longitudinal studies, the available *n* accounts for the average of individuals in the last wave (follow-up) of each study.

Table 1. Demographics of included individuals in the eligible studies.

Cross-Sectional Studies		Longitudinal Studies	
Down Syndrome	2776	Down Syndrome	1874
Other ID	1231	Other ID	531
Male	1396	Male	110
Female	1143	Female	450
Missing Data	1482	Missing Data	1284
Total	4007	Total	2405

The tables for cross-sectional and longitudinal studies (Appendix A, Tables A2 and A3) present the characteristics of the participants (age, diagnosis), intervention, comparison, outcomes, and study design [37] structured according to the eligibility criteria. The average duration of longitudinal studies was 97.01 months, with no data for one study. This was calculate based on the total amount of months for each study, from baseline to the last follow-up, dividing by the number of studies included (average = average + ((value − average)/nValues).

We found 39 scales, questionnaires, and inventories, and 13 batteries for assessing cognitive and behavioural changes in adults with ID (see Appendix B). A total of 23 informant-based measures (scales, questionnaires, and inventories) were used to obtain information on behavioural and cognitive changes from a proxy, while the remaining 29 instruments were self-report measures (13 batteries and 16 scales, questionnaires and inventories). Of the cross-sectional studies included, 15 studies used only self-report instruments, 10 studies used only informant-based instruments, and 15 studies used both type of instruments. Regarding the longitudinal studies, 10 studies used self-report instruments, 5 studies used only informant-based measures, and 7 studies used both types of measures. The remaining studies used single domain tests or tasks (8 cross-sectional studies, 5 longitudinal studies) (see Appendix A, Tables A2 and A3). According to the selected studies, we identified a multitude of different instruments

(single-domain cognitive tests; scales; batteries; tasks), with few replications, and a lack of descriptive data (means, standard deviations, gender ratios, specificity and sensitivity scores) in publishing material, which was not obtained from all authors upon request. Consequently, a meta-analysis could not be performed. Of the 27 longitudinal studies, the majority (n = 19) focused on DS, while the remainder (n = 8) included participants with DS and other ID. There was also a large degree of heterogeneity in measures used in longitudinal studies including those with both DS and other ID. Within the eight studies included, 30 measures and tasks were reported. All datasets generated for this study are included in the article or its supplementary material, including Tables S4–S7 list of instruments used in the studies, PRISMA checklist and SWiM checklist.

4. Discussion and Implications

This study aimed to systematically review scales and batteries for screening for cognitive changes in adults with ID and provide a guide for practitioners and researchers to choose valid, reliable instruments. This review found a multitude of materials used with adults with ID, with much of the research focusing on those with DS. We focused on batteries and scales as the best approach to evaluate cognitive changes and age-related changes in individuals with ID [14,17]. The current evidence encourages the focus on measures such as DLD and CAMCOG-DS, which should be further explored psychometrically, clinically and longitudinally among the essential clinical diagnosis tools to distinguish mild neurocognitive disorder and dementia status in those with ID, particularly DS [38].

Identified instruments can be divided into two categories: informant-based measures (answered by a carer) and self-report measures (answered by the individual). Across the literature, the diagnosis of dementia in this population is a major concern and subject to a disagreement regarding which instrument to use; there is also considerable disagreement surrounding which instruments better discriminate mild neurocognitive disorder and preclinical dementia [8]. Studies are discussed according to the study design and clinical groups.

4.1. Longitudinal Studies

4.1.1. Longitudinal Studies in Participants with Down Syndrome

The present review identified a multitude of measures used to assess cognitive change in those with DS—36 separate measures and tasks were used across the 19 studies. The Dementia Questionnaire for Learning Difficulties (DLD—previously referred to as the Dementia Questionnaire for Persons with Mental Retardation, or DMR) [39–41] was the most frequently used measure, appearing in seven studies [4,8,38,42–45]. The frequent use of the DLD may reflect its recommendation by the National Institute for Health and Clinical Excellence—Social Care Institute for Excellence in the UK [46]. The DLD, an informant-based measure, was developed by Evenhuis (1990) [39] for use with Dutch speakers but has since been translated and used in several countries, allowing cross-cultural comparisons [10,43,45]. The DLD consists of 50 items and eight subscales and provides scores for cognitive and social domains. Previous research has noted that the DLD is widely used due to high levels of agreement between its scores and clinician's diagnosis [47] as well as its good sensitivity and specificity [48].

In the included studies, the DLD was effective in identifying deterioration in cognitive and social skills in adults with DS over time [45], although Nelson et al. (2007) [44] noted that while DLD total scores showed good overall test-retest reliability after one year (r = 0.77), there was low test-retest reliability for the social scale (r = 0.45). In another study, [43], using the cognitive element of the DLD as a secondary measure to examine the impact of seizures on cognitive impairment in adults with DS, Lott et al. (2012) [43] found that the cognitive scale of the DLD identified increased deterioration in adults with DS and AD with seizures compared to those without seizures. Similarly, a 14-year longitudinal study by McCarron et al. (2014) [8] found that epilepsy was identified as a significant predictor of dementia in adults with DS and noted the DLD was the most sensitive instrument for tracking cognitive changes over time. However, another study [45] reported that the DLD showed poor sensitivity in

distinguishing between dementia-related cognitive decline and depression, which is likely due to the inclusion of the social skills element of the questionnaire. Furthermore, Evenhuis et al. (2009) [40] suggested that this measure may not have adequate sensitivity when used with people with severe and/or profound ID due to a floor effect; similarly, it may also be problematic with those with mild ID due to a ceiling effect on cognitive function. A multi-wave study [38] found that the overall summary score of the DLD clearly identified individuals with mild neurocognitive disorder onset.

The Severe Impairment Battery (SIB) [49] is another measure of cognitive functioning which has been used longitudinally. The SIB is a self-report measure assessing cognitive function across nine domains: attention, language, orientation, memory, praxis, visuospatial perception, construction, social skills, and orientating head to name [50]. The SIB was used in four longitudinal studies exclusively examining those with DS [8,38,42,43]. Like the DLD, [43] the SIB was effective at tracking the cognitive decline in adults with DS and seizures; it was used as a secondary measure and provides a limited description of its effectiveness [8,42].

4.1.2. Longitudinal Studies Including Participants with DS and Other ID

There was no overlap between measures used across studies, with no measure included in more than one study. This is illustrative of the lack of standardised measures for assessing cognitive decline in those with other ID and highlights the need for an accepted, recommended measure to allow synthesis across different studies.

It is interesting to note that the DLD was only used in a single study including participants with other ID [10]. The study found that the DLD showed good test-retest reliability within their sample and reported that DLD scores showed agreement with other measures of cognitive change used in their study.

One potentially promising new measure for assessing cognitive decline in those with other ID is the Wolfenbütteler Dementia Test for Individuals with Intellectual Disabilities (WDTIM). The WDTIM was used in a 2-year longitudinal study carried out by Kuske et al. (2017) [51] and was effective at detecting cognitive changes over time. The authors noted that the WDTIM was more effective when used in conjunction with the Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (DSQIID) [52]—an informant-based measure. The combination of a self-report and informant-based measure could provide a useful method to cross-check screening. However, like the DLD, the WDTIM may be problematic when used with individuals with severe and/or profound ID [51].

4.2. Cross-Sectional Studies

4.2.1. Cross-Sectional Studies in Participants with Down Syndrome

As was the case with longitudinal studies, the DLD [39] was the most frequently used instrument, appearing in eight studies [43,47,53–57]. While the DLD was generally reported as a good marker of cognitive decline and dementia in those with DS, [24], one study found no association between scores on the DLD and the presence of beta-amyloid precursor protein, a biological marker of senile plaques and neurofibrillary tangles present in AD. While this may indicate that the DLD lacks sensitivity in identifying early cognitive changes associated with AD in those with DS, the authors suggest that small sample size and lack of statistical power may have influenced their findings.

The SIB [49] was also frequently used, appearing in four cross-sectional studies [22,53,58,59]. Witts and Elder (1994) [59] carried out a preliminary study on the use of the SIB with adults with DS and concluded that the measure was suitable to assess cognitive function in this population. Furthermore, they noted that no floor or ceiling effects were observed in scores on the SIB—this is advantageous as it indicates that the measure can be used to assess cognitive function in a wide range of individuals with ID. A later study [53] reported that the SIB showed good concurrent validity with the DLD. However, unlike Witts and Elder (1994) [59], the authors reported evidence of ceiling effects, which has implications for the clinical usefulness of the measure [53]. They also identified the need for more

longitudinal research to determine the effectiveness of the measure over time. Boada [60], using a between-groups design, observed greater impairment in the group with dementia and DS compared to individuals without dementia when using the DLD, but no difference between groups when using the SIB. According to the authors, the DLD is an appropriate functional instrument to assess for dementia in individuals with DS and other ID, while the SIB was not designed for the diagnosis of dementia of Alzheimer's but rather as a measure to monitor cognitive decline in individuals with DS which offers objective function from a clinical view point. Another potential limitation of the SIB is reported by Head et al. (2011) [24], who noted that, like the DLD, there was no association between scores on the SIB and the presence of beta-amyloid precursor protein, which may indicate that the measure lacks sensitivity.

4.2.2. Cross-Sectional Studies Including Participants with DS and Other ID

The DLD [39–41] revealed good psychometric properties in studies with participants with both DS as other ID. Eight studies used the DLD [47,61–67]. Shultz et al. (2004) [48] reported the sensitivity of the DLD as 0.65 and specificity 0.93. The instrument was found to be a good marker of the cognitive and affective symptoms observed in the early signs of dementia [65] and displays good inter-test validity with other instruments like the SIB [53] and the Alzheimer's Functional Assessment Tool (AFAST) [63]. The DLD has shown adequate inter-rater reliability for all subscales, except behaviour and disturbance, with correlations of 0.68 or higher [40].

Due to problems with floor and ceiling effects in the assessment of people with ID, researchers have attempted to address this issue. Startin et al. (2016) [56] created a comprehensive neuropsychological assessment to evaluate people with DS and avoid ceiling and floor effects. The LonDownS Consortium identified a set of tests for the evaluation in people with DS with minimum floor and ceiling effects. The authors suggest that the battery is suitable for most adults with DS, although half the participants with both dementia and DS were unable to undertake any of the cognitive tasks in the battery, indicating that it may be useful for screening before the development of dementia [56].

Another measure was the Cambridge Cognitive Examination (CAMCOG). This was originally designed for use with the general population but was later adapted for the assessment of dementia in those with DS (CAMCOG-DS) [68]. Cross-sectional studies have shown that this instrument can reliably differentiate between older and younger participants, is useful when possible dementia is considered, and shows good internal reliability (Cochran's alpha between 0.82–0.89 and test-retest reliability (r = 0.86) [69]. When comparing CAMCOG-DS scores in a sample of DS participants between 30 to 65 years old, a significant difference was found in the cognitive performance between younger participants (30–44 years old) and older participants (>45 years old), except on the Attention/Calculation subscales [68]. This is consistent with the idea that the largest differences between age groups are in memory, praxis, and perception subscales [69,70]. The authors found a good correlation between MMSE and CAMCOG-DS scores (r = 0.97). This inter-test reliability remained after removing MMSE related items in the CAMCOG-DS and excluding participants who achieved zero scores (r = 0.95). Furthermore, recent research has identified recommended cut-off points for the CAMCOG based on a normative sample of adults with DS [18]. However, it has been noted that this measure may not be suitable for those with severe learning disabilities, severe sensory impairments, or advanced dementia due to floor effects [69]. This instrument has also been found to have "limited diagnostic value as a single assessment" because it is not possible to estimate the extent of the decline in cognitive functioning based on scores—the instrument is also limited at determining whether cognitive decline is due to ID, dementia, or other reasons [67].

There is evidence that the Test for Severe Impairment (TSI) is reliable for monitoring the progression of dementia in people with severe ID [71]. The TSI was used in three of the cross-sectional studies including participants with DS and other ID [61,72,73]. This instrument was developed to assess cognition in people with severe cognitive impairment, and most individuals with moderate/severe ID score on this test and only those with advanced dementia fail to score. In addition to its use in

cross-sectional studies, the TSI is reliable and valid in longitudinal studies as it monitors rates of changes and indicates a decline in cognitive function over time that can indicate dementia. In one of the earliest studies using the TSI, [71], the authors assessed the reliability and validity of the instruments in a sample of 60 adults with DS. They found that the convergent validity of the TSI for all samples was good ($r = 0.94$), with satisfactory interrater reliability ($r = 0.97$) and test-retest reliability ($r = 0.98$) over a two-year period. The instrument also showed good internal consistency, with a Cronbach's alpha of 0.89.

Although DLD has been used in most studies showing it to be effective in identifying changes over time in people with DS and other ID [45], one study [51] revealed that it may not be an appropriate measure to assess dementia in people with severe ID. Recently, DLD was used in Benejam [18] and as expected, participants with ID with prodromal AD and AD dementia had worse scores than asymptomatic subjects. These authors also recommend cut-off points for the CAMCOG-DS for a diagnosis of prodromal AD and AD dementia in adults with DS, based on population norms stratified by level of ID impairment: mild ID, a score of 80 and moderate ID, scores of 56.

When screening for cognitive decline in people with ID, we need to highlight and concentrate on the change and decline based on premorbid level of functioning [74]. It is important to keep in mind the ceiling effects of some measures in individuals with DS when compared to severe ID, for example of the SBI, which has implications for the clinical usefulness of the measure [59,64]. When using the same instrument on individuals with DS when compared to other ID, the TSI can be used in both DS and other ID due to the absence of ceiling and floor effects in individuals with moderate and severe ID, it is a valid and reliable measure to both DS and other ID [71,74].

4.2.3. Other Measures

Across most studies, the findings suggest that people with ID performed more poorly in verbal tasks, with significant declines with age [61,75–77]. Phonological tasks are more likely to be sensitive to the detection of cognitive decline among individuals with DS compared to those with other ID, based on significant declines in these tasks [75,78]. This is an important finding when considering which assessment should be used for those with DS and those with other ID.

According to ICD-11 (World Health Organization/2019) and DSM-5 (American Psychiatric Association/2013), the diagnosis of dementia and cognitive changes in the general population and people with ID requires multi domain assessment. Thus, this finding means that phonological tasks are a cognitive marker that should be part of any protocol rather than be taken in isolation [17,18].

Another important aspect of the screening instruments for dementia in ID is their ability to assess the behaviour changes commonly seen during the onset of dementia. An example of this concern is the Assessment for Adults with Developmental Disabilities (AADS) [79]. This instrument assesses prodromal behaviour modifications and deficits associated with dementia in people with ID—such as agitation, stereotypical behaviour, anxiety, or inactivity. The adaptive behaviour dementia questionnaire (ABDQ) is another instrument specifically developed to assess behaviour changes in those with ID and dementia [6]. The ABDQ was used in two cross-sectional studies [80,81].

4.2.4. Limitations

There are some limitations to this review. There is a lack of findings from studies published in other languages. For instance, De Vreese et al. (2011) [62] carried out an Italian adaptation of the AADS (AADS-I) that displays good psychometric properties and satisfactory interrater reliability for the six subscales (coefficients from 0.67 to 0.79). A further limitation is the lack of studies found in grey literature and open science databases; while only including papers from peer-reviewed journals helps to ensure the quality of included studies is high, it also limits a large amount of research which may provide additional insights.

Another limitation is the lack of psychometric data for some of the instruments used. Although we aimed to create a review to help clinicians and researchers to find the most suitable instrument,

many studies did not provide psychometric properties based on their samples, and we considered it inappropriate to use secondary sources, such as tests and batteries handbooks, as they do not reflect characteristics of the current samples.

As with any diagnostic assessment, we recommend following practical medical guidelines with multiple diagnostic approaches assessing cognitive, behavioural, and independent functioning. The use of informant and self-report instruments alongside medical examinations, neuroimaging techniques, and genetic and biological measures of various types of dementia is also recommended [82].

We found no overlap between measures used across studies, with no measure included in more than one study. The use of the same instruments in different languages would favour cross-cultural comparisons. This is illustrative of the lack of standardised measures for assessing cognitive decline in those with other ID and highlights the need for an accepted, recommended measure to allow synthesis across different studies.

This systematic review could not examine neuropsychological assessment in different stages of dementia due to the nature of the articles selected. There is no consensus regarding dementia stages in people with ID and discrepancies with the general population are observed [8,63,83]. This reinforces the need for longitudinal studies to investigate cognitive changes in DS and other ID. Some studies [18,61] show promising examples of the benefit of this approach, as they use baseline and longitudinal data to support and explore factors related to cognitive decline.

5. Conclusions

In conclusion, there is a multitude of instruments being used to screen for cognitive changes associated with dementia in those with ID. This review highlights the variation between measures used across studies and illustrates the need for unified, standardised measures to allow for the synthesis of results in research and greater consistency of diagnosis in clinical practice. Contrasting cross-sectional and longitudinal studies, we recommend the use of specifically designed instruments, such as the DLD [14] and the CAMCOG-DS [67], to assess cognitive functioning and behaviour changes related to ID and dementia. The use of measures designed for the general population should be avoided due to their lack of sensitivity in differentiating between those with and without dementia. Evidence supports the DLD as a promising informant-based screening tool for the diagnosis of dementia, since it covers both cognitive and behavioural symptoms [38,84]. We stress, however, that the DLD is not an instrument for a clear-cut diagnosis, but rather a good screening instrument for follow up assessment which is reliable when used routinely in combination with other objective measures such as, for example, CAMCOG-DS.

Supplementary Materials: The following are available online at http://www.mdpi.com/2076-3425/10/11/848/s1, Tables S4–S7: List of instruments; PRISMA checklist; Synthesis-without-Meta-analysis-SWiM-Checklist.

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Appendix A

Table A1. Cross-Sectional Studies assessing cognitive changes in ID and ID-DS participants.

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[3] ^	USA	DS: N = 30 DAT: N = 18 Elderly controls N = 25	MMSE; NBAP	Between groups	DS individuals showed more signs of indifference; inappropriateness; pragnosia and scores were consistent also in individuals with DAT	7
[11] ^	UK	DS N = 14	The Prudhoe Cognitive Function Test (PCFT)	inter-rater reliability and test retest reliability	0.99 ($p < 0.01$) represents excellent inter-rater reliability to detect cognitive deterioration aspects of dementia. High reliability and temporal stability.	4
[16] #	UK	DS N = 78; Mild ID N = 33	CAMCOG; CaD; SR; ToL; SB; CaODB	Changes in behaviour	Disinhibited behaviour and apathy were both associated with impaired performance in executive function.	5
[20] #	USA	oID N = 10 DS no dementia N = 10 DS/dementia N = 10	BPT; SIB	Between groups	The BPT test was sensitive to functional declines because of dementia in DS.	5
[24] * #	USA	DS/NO AD N = 17 Normal controls N = 11 DS/AD N = 17 Normal AD controls N = 12 Group 2 DS/AD N = 52 DS/NO AD N = 78	BPT; SIB; DMR	Between groups A beta levels in plasma	No association between plasma Aβ and scores on the SIB and DMR; Lack of sensitivity of SIB and DMR to detect dementia or cognitive decline in DS adults.	7
[47] *	UK	Ntotal = 62 DS N = 26 DS/dementia N = 36 DS no dementia	MMSE; DMR; DSDS	Between instruments	Positive correlation in the diagnosis of dementia between DMR and the DSDS with specificity and sensitivity at 0.92 in both cases.	4
[48] *	USA	ID N = 38 ID/DS N = 26 ID with dementia N = 19 ID no dementia N = 19	DSDS; DMR; Reiss Screen; Shultz MMSE	Between groups	Both DSDS and DQMR assess similar elements of dementia; Both subscales of DSDS differentiated between groups	5
[85] * #	Netherlands	DS N = 39	WPPSI-R; FANT; NPEMID; DMR; SRZ/SRZ-P; FP/FS	Between instruments	56% of participants preferred facial pictograms scales over drawn face stimuli	4
[53] * #	UK	DS N = 90 (mean age 38.97, SD ± 9.18) N = 37 males; N = 16 females	SIB; DMR	SIB vs. DMR criterion validity	The SIB has good concurrent criterion validity when compared to DMR; The SIB has a good validity specifically as a measure of cognitive ability in people with DS: It correlates only with the cognitive functioning component of the DMR.	4

Table A1. *Cont.*

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[54] * #	The Netherlands	DS N = 106 (mean age = 37; *n* = 56 men) DS/possible dementia N = 49 (age range = 40 years and over)	SRZ/SRZ-P; DMR; FAS; CAS; NRS	Between instruments	Adults with DS have generally a better comprehension of faces rather than numbers and more comprehension of pain affect rather than pain intensity.	4
[55] * #	USA	DS N = 20	WAIS-III; DMR; WGTA; Tasks: ODL, RL; DNMP; DNMS	Between instruments	DMR is the strongest predictor of reversal learning error scores, suggesting symptoms of dementia effect on reversal learning	4
[56] * #	UK	36 > age DS/no dementia N = 130; 36 > age DS/dementia N = 51;16–35 DS N = 124	KBIT-2; Short ABS; DLD; CANTAB; CAMCOG; NAID; ACTB; OMQ; ToL; BRIEF-A; NEPSY	Between groups and instruments	Poor performance for adults with cognitive decline and dementia; Majority of tasks have high completion rate for adults who do not have a diagnosis of dementia	4
[57] * #	Netherlands	DS N = 26 N = 14 More able group N = 12 Less able group	DLD; DRS-2; VABD-II; ABAS-II; PAS-ADD	Inter-informant agreement	Differences in scores are merely attributable to differing informants' perspectives.	4
[58] #	USA	DS N = 63, *n* = 31 male; *n* = 32 female age range (30–53)	Several neuropsychological batteries	Between groups	Many adults with Down syndrome can tolerate amyloid-β deposition without deleterious effects on cognitive functioning.	4
[59] #	UK	N = 33 DS	SIB; VABS	The utility of SIB in people with DS	For DS and DAT, SIB could be of used in the longitudinal study by comparing age-matched DS and other ID groups	4
[61] * #	USA	DS N = 55; oID N = 75;	BVSR; PPVT; SICD-AASH; LIPS; BSID; TSI-M; PP; DTVMI; DSADS; DSDS; DMR; SoIB; RSMB; PIMRA; DASH-II; DSI; MAS	Between groups and age groups	Performance of older adults did not change over time, but that of younger adults with DS and adults without DS improved; Adults with DS showed significant and unique declines only in test of verbal fluency	5
[62] *	Italy	ID N = 63 ID/DAT N = 15 DAT/DS N = 13	Italian translation of the AADS scale (AADS-I) DMR		Subjects with DAT scored significantly higher on both DMR subscales compared to the subgroup without DAT	4
[63] *	Italy	ID N = 61 ID/DS N = 22 ID/oID N = 39	AFAST; ADL; IADL; DMR	AFAST-I clinical significance	Good internal consistency of the AFAST-I (0.92); AFAST-I assesses several difficulty levels of autonomy.	4
[64] * #	Spain	ID N = 146; Mild ID N = 62; Moderate ID N = 84; ID/DS N = 103, ID/oID N = 43;	DMR; K-BIT I; CAMDEX-DS; CAMCOG-DS	Between instruments	High degree of diagnostic validity between the CAMDEX-DS and the CAMCOG-DS; Reliability scored 0.93.	4
[65] *	Italy	N = 58 DS; *n* = 40 no dementia; *n* = 3 dementia N = 142 oID, *n* = 126 no dementia; *n* = 2 dementia	DSQIID; DMR	Between instruments	Reliability of the DSQIID-I was 0.94;	5

Table A1. *Cont.*

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[66] *	UK	ID/oID N = 76 DS N = 12	DMR; ABS	Between instruments	DMR gives a general indicator of cognitive and affective symptoms that could indicate dementia.	5

[67] * #	USA	N = 63 men;
		mild ID N = 40; moderate ID N = 44;
		severe and profound ID N = 30;
		ID/DAT N = 71; ID/no DAT N = 43
			RADD; DMR; BADLS; SIB; BPT	Between groups	RADD has efficacy for assessing cognitive functions relevant to AD in DS; RADD differentiated participants based on their dementia status	5

[69] #	UK	N = 77 DS Group 1 age 30–44 (N = 45) Group 2 age 45 years and over (N = 29)	CAMCOG; MMSE	Between instruments	Younger group scored higher in the total CAMCOG and MMSE scores on all subtests except Attention/Calculation; CAMCOG can be used when possible dementia is being considered.	4
[71] #	Ireland	Moderate ID group: ID/dementia *n* = 19 ID/no dementia *n* = 29 Severe ID group: ID/dementia *n* = 11 ID/no dementia *n* = 11	DSMSE; TSI	Between groups	The TSI is useful to monitor the progression of dementia longitudinally in severe MR. TSI-Reliability 0.89.	5
[72] * #	Ireland	No DAT/DS N = 14 DS/DAT N = 16	CAS-ID; DSMSE; TSI; DLSQ	CAS-ID to other validated tests	Good measure cognitive and functional decline in individuals with DS and AD.	5
[73] ^	USA	DAT N = 13 DAT/DS N = 6 Normal controls N = 31	OMT; TSI; ABMT; O; PRT; NEPSY; PPV-III	Between groups	The functional level of the DAT group was significantly lower than that of the normal control group; DAT groups scores significantly lower than the normal group;	7
[75] ^	Canada	N = 31 DS N = 41 oID	Tasks: VS; MN; RA; NF; SAE; CO; WR; FM; Matrices	Between groups	People with DS performed poorly in two verbal tasks; Phonological tasks are more likely to be sensitive in the detection of cognitive decline among people with DS	5
[76] #	USA	DS young: N = 16 DS old: N = 16 oID young: N = 16 oID old: N = 15	WAIS or WAIS-R; Stanford-Binet ratio IQ; DRS; PPVT-R-Form M; MAT; CAS	Between groups	DS old group performed poorly in most test. In the tasks that involved verbal output both DS groups performed poorly	5
[77] *	USA	Dementia N = 10 DS = 6; ID/oID = 4 No dementia N = 12 DS = 4; ID/oID = 8	CTT; BNT; TCOWAT; FOME; ESDCL	Between groups	Deficits in the Dementia group in areas consistent with diagnosis of dementia for persons with ID	7
[78] ^	Finland	DS: N = 15 group ID/oID: N = 15	Tasks: DSB; CS; NWR; NWS; DSF; CB; VST	working memory performance	The DS group performed significantly more poorly in working memory tasks that measured phonological loop	5
[80] *	Australia	DS = 33	PPVT-4; DBC-A; ABDQ; ABAS-II		Age is associated with decrease in adaptive behaviour independent of dementia and health status; Age-related changes are domain specific rather than pervasive	4
[81] *	Australia	N = 55 total; DS N = 47; AD or suspected: N = 10	ABDQ; RCPM; PPV; ASM; VSM; TACL-III	Between groups	Adults with DS may show failure in continuing developing in productive syntax.	5

Table A1. *Cont.*

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[86] #	Switzerland & Belgium	DS N = 47	EVIP; PN; ISADYLE; STMT; CBTT; NEPSY; RPCM	Vocabulary knowledge verbal abilities	Dissociation between productive and receptive vocabulary measures in verbal short-term memory abilities in DS participants.	4
[87] #	USA	DS *n* = 28 N = 19 young adults N = 9 older adults	PPVT-R, Block Pattern subtest of HNTLA; WISC-R; BDDE; DSF; OPS; BTS; DS	The relation of EEG alpha background to cognitive function	Older patients with DS with decreased alpha waves backgrounds had fewer visuospatial skills, decreased attention span, and dementia	4
[88] #	UK	N = 70 DS; *n* = 39 female, *n* = 31 male.	BPVS; VABS; CAMDEX; ECT	Between age groups	Participants with highest risk of developing dementia scored significantly higher in identification test	4
[89] * #	UK	N = 63 DS; N = 74 oID; Mild ID *n* = 27; Moderate ID *n* = 69; Severe ID *n* = 38; profound ID *n* = 4	DQ; IBR-MSE	Between instruments	Good agreement between DQ and the IBR Mental Status Exam; Disagreement is greater for individuals who are lower functioning and for those with DS	5
[90] #	USA	ID/oID N = 40 ID/DS:Healthy N = 44 Questionable DAT N = 10 Early-Stage DAT N = 5 Middle-Stage DAT N = 7	WISC-R; CRT; SRT;	Levels of decline across stages of dementia	Group differences: (i.e., healthy with DS, 'questionable', early-stage dementia and middle-stage dementia) for each subtest	4
[91] * #	UK	DS N = 48 Control group oID N = 42	CAMCOG; BPVS	Between groups	Significant negative correlation between mean myo-inositol concentration and overall cognitive ability in DS group	5
[92] ^	USA	DS *n* = 53 Williams syndrome *n* = 10 Mixed aetiology *n* = 39	Short term memory and dual task processing tasks	Between groups	Dual task performance declined significantly in DS; No aetiology group differences on single tasks.	6
[93] ^	USA	DS N = 9 oID N = 24 DAT/DS N = 15 DAT/oID N = 11	r-PRMT; OMT; TSI; NEPSY	Between groups	The r-PRMT discriminates between those with DAT from those without DAT; Controls with DS showed higher scores.	5
[94] *	USA	DS N = 14 Typically, Development N = 82 WS *n* = 41	DLD; KBIT	Between groups	Individuals with DS demonstrated age-related effects on gray matter associated with dementia	5
[95] ^	Spain	DS/no DAT N = 75; DS/DAT N = 15	Modified Cued Recall Test (mCRT)	Between groups	Healthy DS achieved higher total scores and committed fewer intrusion errors; In DS-DAT with advanced DAT the mCRT is not useful.	5
[96] #	UK	DS Total N = 49 DS/dementia N = 19 DS/no dementia N = 30	ACTB; CANTAB; NAID; ToL; VF; F-NT; GA; OM	ACTB validity	Only 3 tests of the ACTB differentiated between demented and non-demented DS groups.	5
[97] * #	UK	Total DS N = 128 DS/Dementia N = 23/128	CSDS; CAMDEX; KBIT-2	Development of CS-DS	Good reliability (0.84) and validity using two raters and over two time points.	5

Table A1. *Cont.*

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[98] #	Israel	NSD N = 18; DS N = 14;	LLPI; PPVS; RSPM; PFT; S; CVMT; IC; TFB; HMGT; MTT; NVMT; TMT	Between groups	Participation in cognitively stimulating activities influence cognitive performance in adults with ID with and without DS.	5
[99] #	Spain	ID N = 69 ID/DS N = 65/69 COMTVal158Met N = 93; VNTR-DAT1 N = 57	K-BIT; CANTAB; WAIS-III; SFWGT; WCFST; TOLDx	Between groups	Met allele carriers showed worse adaptive social skills and self-direction.	6
[100] * #	Netherlands	DS N = 224	PS; DFPA; WPPSI-R; FANT; NPEMID; FSID	Pain experience	Structural differences and atypical patterns of brain activation in DS individuals.	4
[101] * #	Spain	DS N = 63 adults ID_{mild} N = 39 ID_{mod} N = 24	KBIT-2; ABS-RC:2; CAMDEX-DS; BT-ID; WCFST; BRIEF; TOL^{DXTM}	Between groups	Psychometric properties of the TOL^{DXTM} version for people with ID were satisfactory on all variables; Sensitivity (0.76), Specificity (0.81).	4

Legend: DAT (Dementia of Alzheimer's type); HD (Huntington Disease); MR (Mental Retardation); DS (Down Syndrome); ID (Intellectual Disability); AD (Alzheimer Disease); WS (Williams Syndrome); ID (Intellectual Disability); NSID (Non Specific ID); Cd (Cognitive decline); oID (other Intellectual disability) CD (Cognitive Deterioration). For acronyms of instruments (scales, questionnaires investors and batteries) see Appendix B and Supplementary Material; * means the study used an informant based measure; # means the study used a self-report measures; ^ single domain tests and tasks.

Table A2. Longitudinal Studies assessing cognitive changes in mixed groups of ID participants.

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[2] #	UK	DS N = 30	Several multidomain	Follow up	Those with cognitive deterioration show a significant decline on measures of executive function between baseline and 16 months follow up	7
[4] * #	Ireland	N = 77	DLSQ-NIA; DLD; DSMSE; TSI	Follow-up	Over 20 years follow-up, 97.4% developed dementia	6
[8] #	Ireland, USA	DS N = 77	SIB; DSMSE; DLSQ; DMR	Follow-up	After 20 years, 75 individuals developed dementia at a 20-year follow-up.	6
[10] *	USA	MR/oID N = 117 MR/DS N = 126	DMR; RS; Part I of AMDAB	Between groups	Equivalent or maybe lower risk for dementia between MR participants and general population	7
[15] #	UK	DS N = 61	CAMDEX; CAMCOG;	Longitudinal comparison	People with a diagnosis of AD at baseline were at least 6 more times likely to diagnosed with AD at time 2	7

Table A2. *Cont.*

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[42] * #	USA	N = 1	BPT; DMR; SIB; RADD; WAIS III; VABS-II	Follow-up	The prevalence of APP disomy in patients with DS resulting from PT21 appears to be very rare since only 2 cases.	7
[43] * #	USA	DS/DAT No seizure N = 29; Seizure group N = 24	SIB; BPT; DMR; VABS	Between groups;	Cognitive decline is more marked in demented individuals with DS who have seizures compared to those who do not.	6
[44] * #	USA	DS N = 34 N = 19/34 retested one year later	WAIS-III; NBAP; DMR; and other tests	Validity and reliability of instruments.	NBAP was the strongest predictor of dementia-status. Strong correlation between the pragnosia scale scores and the DMR	6
[45] # *	UK	DS N = 8	HSSA; DMR; RCPM; WAIS-R; MEAMS;	Neuropsychological assessment	All patients score below normal population in RCPM Difficult sensitivity in the DMR to distinguished between dementia and depression	6
[38] # *	USA	DS N = 561	MSRT; MMMSE-DS; TSI; CF-T; WISC-R-blocks tests; DSMSE (BLOCK-T); DLD; ABSI; Reiss Screen	Follow-up Assessment	The overall summary score of the DLD showed clear changes with MNI onset	5
[51] *	Germany	baseline sample *n* = 102 ID; *n* = 22 DS;	WDTIM; DSQIDD	Follow up	WDTIM very suitable for mild to moderate ID but limited for severe ID.	5
[83] *	UK	DS N = 92	The PCFT; The ABS	Longitudinal comparison	Participants with low scores and deterioration on PCFT and ABS later showed dementia	6
[84] * #	UK	DS N = 14; ID/oID N = 4 males	RCPM; BPVS-II; CAMCOG; DMR; Mini PASADD; ABS-CR2	Longitudinal comparison	After 2 years, 38.8% of participants were diagnosed with dementia.	7
[102] ^	USA	DS N = 14	NeuroTrax	Follow-up	No significant changes in scores from point to the next in memory, executive function, verbal, visual spatial and global scores	6
[103] # ^	Canada	N = 18 DS; N = 18 oID	PPVT; WISC	Between groups	Younger DS participants, showed less decline in full-scale scores; Cognitive ability, is more stable over time in DS sample	7
[104] #	USA	N = 90	WAIS-R; ICAT	Between individuals	The declining group with initial lower scores had lower levels of adaptive behaviour, were rated as more depressed and had a higher frequency of problem behaviours.	6
[105] ^	USA	DS N = 28; ID/oID N = 5; MR/oID N = 13	Tasks: O; ON; VMC; C MS Test: BMT	Between groups	All groups showed comparable improvements in performance tasks from initial testing to second testing on memory; Functional deterioration did not occur among adults with DS.	7
[106] #	USA	DS/MR N = 91, MR/oID N = 64	IBR-MSE; SRT; VMT; WISC	Between groups	All individuals with possible DAT declined in tasks regarding orientation to time, and object naming.	7

Table A2. *Cont.*

Article	Study City/Country	Population	Instruments	Comparison	Outcomes	Quality Assessment Scale (0/8)
[107] ^	Netherlands	DS N = 307	ESDC; SSIMR	Scores between instruments	ESDC it is easy to use, and the symptoms can be assessed quantitatively.	6
[108] *	USA	DS/DAT N = 14; DS/NO-DAT N = 71	DSDS; SRT	Follow up	Participants with early-stage DAT exhibited significantly greater decline over the 3-year period preceding their diagnosis; Decline in SRT distinguished between groups.	6
[9] ^	USA	ID/oID N = 66; DS/no DAT N = 75 DS/DAT N = 19	mCRT	Between groups	Participants with DAT had lower total scores that participants without DAT; Poor performance on the adaptation of CRT was associated with early-stage DAT.	7
[109] #	USA	ID/oID N = 28; ID/DS N = 42	WISC-R	Sex-related changes	Male participants with ID no DS performed better than female participants with ID oID; Females with DS performed better than males with ID in object assembly and block design	6
[110] ^	UK	DS N = 57	Single domain tasks	Between groups	Poor performance and decline in performance on delayed response and conditioned associative learning is associated with dementia in DS adults.	6
[111] #	USA	DS/DA N = 5, DS no-dementia N = 25	Multi-domain	Longitudinal comparison	DS adults who developed DA at early stages showed progressive impairment in selective attention and in ability to selectively attend to stimuli.	7
[112] *	Australia	Time 2 *n* = 28; Mild/moderate ID *n* = 20 Severe/profound ID *n* = 8	PPVT-4; ABDQ; DBC-A	Follow-up	Adults with DS may experience different ageing patterns for behavioural and emotional problems	6
[113] #	UK	DS N = 27 of 50	LIPS; BPVS; WPPSI; RBMT-C; NAID	Cognitive changes over a 50-year period	Tests of dementia showed falling off in performance even for those without confirmed dementia	6
[114] #	Spain	DS sample N = 41; DS-AD *n* = 13; DS-MNI *n* = 14; DS-Control *n* = 14	CAMCOG-DS; ADVM; WM; DVM; TO	Between groups	DS-AD groups showed significant poorer performance in all tests, especially in verbal and working memory; MNI-DS showed poorer performance than control DS in the CAMCOG and DVM.	7

Legend: MNI (mild neurocognitive impairment) DAT (Dementia of Alzheimer's type); HD (Huntington Disease); MR (Mental Retardation); DS (Down Syndrome); ID (Intellectual Disability); AD (Alzheimer Disease); WS (Williams Syndrome); ID (Intellectual Disability); NSID (Non Specific ID); Cd (Cognitive decline); oID (other Intellectual Disability) CD (Cognitive Deterioration). For acronyms of instruments (scales, questionnaires investors and batteries) see Appendix B and Supplementary Material; * means the study used an informant based measure; # means the study used a self-report measures; ^ single domain tests and tasks.

Appendix B. List of Instruments and Acronyms

Table A3. List of Scales, Questionnaires, and Inventories.

	Scales, Questionnaires and Inventories
1.	Adaptive Behaviour Scale–Residential and Community (ABS)
2.	Adaptive Behaviour Assessment System-II Adult (ABAS-II)
3.	Adaptive Behaviour Dementia Questionnaire (ABDQ)
4.	Alzheimer's Functional Assessment Tool scale for informants (AFAST)
5.	Association on Mental Disability Adaptive Behaviour (AMDAB)
6.	Bayley Scales of Infant Development (BSID)
7.	Behaviour Rating Inventory of Executive Function (BRIEF)
8.	Bristol Activities of Daily Living Scale (BADLS)
9.	British Picture Vocabulary Scale (BPVS)
10.	Caregiver Activity Survey modified (CAS-ID)
11.	Cognitive Scale for down Syndrome (CSDS)
12.	Daily Living Skills Questionnaire (DLSQ)
13.	Dementia Questionnaire (DQ)
14.	Dementia Questionnaire for People with Learning Disabilities (DLD/DMR)
15.	Dementia Rating Scale (DRS)
16.	Dementia scale for Down Syndrome (DSDS)
17.	Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (DSQIDD)
18.	Developmental Behaviour Checklist–Adult (DBC-A)
19.	Diagnostic Assessment for the Severely Handicapped II—DASH II
20.	Down Syndrome Mental State Examination (DSMSE)
21.	Dyspraxia Scale for Adults with Down Syndrome (DSADS)
22.	Early Signs of Dementia Checklist (ESDCL)
23.	Facial Pictograms and Facial Scales (FP/FS)
24.	Functioning Scale for Intellectual Disability (FSID)
25.	Hampshire Social Services Assessment (HSSA)
26.	Instrumental Activities of Daily Living (IADL)
27.	Italian translation of the AADS scale (AADS-I)
28.	Later Life Planning Inventory (LLPI)
29.	Leiter International Performance Scale (LIPS)
30.	Middlesex Elderly Assessment of Mental State (MEAMS)
31.	PAS-ADD Checklist
32.	Rapid Assessment for Developmental Disabilities (RAAD)
33.	Reiss Screen for Maladaptive Behaviour (RSMB)
34.	Scales of Independent Behaviour (SoIB)
35.	Sequences Inventory of Communication Development for Adolescents and Adults with Severe Handicaps (SICD-AASH)
36.	Shultz Mini Mental State Exam (S-MMSE)
37.	Social Functioning Scale for Intellectual Disability (SRZ/SRZ-P);
38.	Vineland Adaptive Behaviour Scales (VABS)
39.	Columbia University Scale to Assess Psychopathology scale informant based

Table A4. List of Batteries.

	Batteries
1.	ACTB—Arizona Cognitive Test Battery
2.	Cambridge Cognition Examination (CAMCOG)
3.	CAMDEX (Cambridge Mental Disorders of the Elderly Examination)
4.	CANTAB—Cambridge Neuropsychological Test Automated Battery
5.	Crayton and Oliver Dementia Battery (CaODB)
6.	Das–Naglieri Cognitive Assessment System (CAS)
7.	ISADYLE language assessment battery (ISADYLE)
8.	NAID object memory and memory for sequences
9.	Neuropsychological Test series for Elderly with Mild Intellectual Disability (NPEMID)
10.	Severe Impairment Battery (SIB)
11.	Wechsler Adult Intelligence Scale (WAIS/WAIS-R)
12.	WISC-R (Wechsler Intelligence Scale for Children-Revised)
13.	WPPSI-R (Wechsler Preschool and Primary Scale of Intelligence-Revised)

Table A5. List of Tests.

	Tests
1.	Autobiographical Memory Test (ABMT)
2.	Block design (BD)
3.	Block design downward extension (BDDE)
4.	BT-ID Barcelona Test-Intellectual Disability
5.	Buschke Memory test (BMT)
6.	Buschke Verbal Selective Reminding 4–6 years version (BVSR)
7.	Conventional Verbal Metaphor Test (CVMT)
8.	Corsi block tapping task (CBTT)
9.	Corsi Blocks (CB)
10.	Developmental Test of Visual Motor Integration (DTVMI)
11.	Experimental Computerized Test (ECT)
12.	Finger-Nose Test (F-NT)
13.	Foundation Aphasia Netherlands Test (FANT)
14.	Hiskey-Nebraska Test of Learning Aptitude (HNTLA)
15.	Homophone Meaning Generation Test (HMGT)
16.	IBR Mental Status Exam (IBR-MSE)
17.	Iowa Cognitive Abilities Test (ICAT)
18.	KBIT-2—Kaufman Brief Intelligence Test, Second Edition
19.	Matrix Analogies Test-Expanded Form (MAT)
20.	Metaphoric Triad Test (MTT)
21.	Mini Mental State Examination (MMSE)
22.	Modified Cued Recall Test (mCRT)
23.	NEPSY comprehension test (NEPSY)
24.	Neuropsychological Test series for Elderly with Mild Intellectual Disability (NPEMID)
25.	Novel Verbal Metaphor Test (NVMT)
26.	Objective Memory Test (OMT)
27.	Peabody Picture Vocabulary Test (PPVT)
28.	Peabody Picture Vocabulary Test-Revised, Form M—(PPVT-R)
29.	Picture Recognition Memory Test (r-PRMT)
30.	Purdue Pegboard (PP)
31.	Raven Coloured Progressive Matrices (RCPM)
32.	Reiss Screen (RS);
33.	Rivermead Behavioural Memory Test for Children (RBMT-C)
34.	Stanford-Binet ration IQ (S-B IQ)
35.	Test for Severe Impairment (TSI)
36.	Test of Auditory Comprehension of Language-3 (TACL-III)
37.	Test of severe impairment-modified (TSI-M)
38.	The Boston naming Test (BNT)
39.	The Brief Praxis Test (BPT)
40.	The Colour Trails Test (CTT)
41.	The controlled Oral Word Association Test (COWAT)
42.	The Cued Recall Test (CRT)
43.	The Fluid Battery (TFB)
44.	The Fuld Object-Memory Evaluation (FOME)
45.	The modified Objective Memory Test (OMT)
46.	The Neuropsychological Behaviour and Affect Profile (NBAD)
47.	The Prudhoe Cognitive Function Test (PCFT)
48.	The Selective Reminding Test (SRT)
49.	The Standard Progressive Matrices (RSPM)
50.	TOL^{dxtm}—Tower of London-Drexel University: 2nd Edition
51.	Tower of London (ToL)
52.	Trail Making Test (TMT)
53.	Visuo-Spatial Test (VST)
54.	Weigl Colour-Form Sort Test (WCFST);
55.	Wisconsin General Testing Apparatus (WGTA)
56.	Wolfenbütteler Dementia Test for Individuals with Intellectual Disabilities (WDTIM)
57.	Modified Mini Mental Status Evaluation—Down Syndrome MMMSE-DS
58.	Down Syndrome Mental Status Examination
59.	McCarthy Category Fluency Test (CF-T)
60.	Beery Buktenica Developmental test Visual-Motor Integration

Table A6. List of Tasks.

	Tasks
1.	Acting on request (AoR)
2.	Auditory delayed verbal memory (ADVM)
3.	Auditory sequential memory (ASM)
4.	Block tapping span (BTS)
5.	Card sorting task (CST)
6.	Cats and Dogs (CaD)
7.	Colour Ordering (CO)
8.	Complex Span (CS)
9.	Concentration (C)
10.	Delayed match-to-sample (DMTS)
11.	Delayed Visual Memory (DVM)
12.	Design Span (DS)
13.	Digit Span backwards (DSB)
14.	Digit Span forwards (DSF)
15.	Digital Recall (DR)
16.	Experimental Computerized Test (ECT)
17.	Expressive Attention (EA)
18.	Expressive One-word Picture Vocabulary (EOWPV)
19.	Figure Memory (FM)
20.	Fragmented Pictures (FP)
21.	Gait Assessment (GA)
22.	Idiom Comprehension (IC)
23.	Matching Numbers (MN)
24.	Matching shapes (MS)
25.	Matching-to-Sample (MtS)
26.	Matrices
27.	Memory for objects (MfO)
28.	Non-Word Repetition (NWR)
29.	Non-Word Span (NWS)
30.	Number Finding (NF)
31.	Object delayed non-match-to-sample (DNMS)
32.	Object discrimination learning (ODL)
33.	Object Memory (OM)
34.	Object Naming (ON)
35.	Objetct pointing span (OPS)
36.	Orientation (O)
37.	Pattern Recognition (PR)
38.	Picture Description (PD)
39.	Picture Identification (PI)
40.	Picture Naming (PN)
41.	Planned Search (PS)
42.	Receptive Attention (RA)
43.	Reversal learning (RL)
44.	Scramble boxes (SB)
45.	scrambled boxes (SB)
46.	Selective Attention-Expressive (SAE)
47.	Semantic Fluency Word Generation Task (SFWGT)
48.	Sentence Recall (SR)
49.	Shoebox memory task (SbMT)
50.	Short Term Memory Task (STMT)
51.	Simultaneous Coding Tasks (SCT)
52.	Simultaneous Verbal (SV)
53.	Spatial delayed non-match-to-position (DNMP)
54.	Spatial Recognition (SR)
55.	Spatial Reversal (SReversal)
56.	Speech Rate (SRate)
57.	Successive Coding Tasks (SucCT)
58.	Synonyms (S)
59.	Temporal Orientation (TO)
60.	Verbal Fluency (VF)
61.	Visual memory test (VMT)
62.	Visual Search (VS)
63.	Visual sequential memory (VSM)
64.	Visuomotor coordination (VMC)
65.	Word Recall (WR)
66.	Word Series (WS)
67.	Working memory (WM)
68.	DSMSE (BLOCK-T)

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