CHAPTER 25

Neurocognitive Disorders

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DSM-5 replaced the terminology of the dementias with a characterization of these neurodegenerative disorders as neurocognitive disorders. Throughout this chapter, the term "dementia" is avoided and the presentation and diagnosis of the neurocognitive disorders are discussed. In this chapter, we review the diagnosis of the disorders and consider how they are applied. We then go on to examine the etiology and pathology and to suggest changes necessary to the diagnostic criteria for the disorders in people with intellectual disabilities.

Neurocognitive Disorders

Review of Diagnostic Criteria

The disorders in this section concern a clinically significant acquired deficit in cognition that results in a significant decline from a previous level of functioning. They include delirium, major neurocognitive disorder (dementia), and mild neurocognitive disorder. The underlying etiology varies among individuals, but in the case of major neurocognitive disorder (dementia), several subtypes have been recognised.

Delirium is commonly seen in general medical hospitals (American Psychiatric Association, 2006). The essential feature of delirium is an acquired and usually acute disturbance of consciousness accompanied by a change in cognition. The disturbance develops over a short period of time, tends to fluctuate during the course of the day, and is usually a consequence of a medical condition, substance intoxication or withdrawal, or a medication at toxic or even therapeutic doses.

The essential feature of a major neurocognitive disorder is the development of multiple cognitive deficits that are severe enough to cause impairment in daily functioning and represent a decline from a previous level of functioning.

Summary of DSM-5 Criteria

The neurocognitive disorders (known as Dementia, Delirium, Amnestic, and Other Cognitive Disorders in *DSM-IV-TR*) comprise delirium, and major and mild neurocognitive disorder (NCD), divided into etiological subtypes. *DSM-5* introduces the terms "major" and "mild neurocognitive disorder" to indicate severity of the impairment. The term "dementia" is avoided in the *DSM-5* criteria but may still be used where physicians and patients are accustomed to this term. The term "neurocognitive disorder" is often preferred, especially for conditions affecting younger adults. Neurocognitive disorder is also seen as broader and encompasses disorders included under "Amnestic Disorders" in *DSM-IV-TR*.

Delirium

Review of Diagnostic Criteria

A disturbance in attention, awareness, and cognition/perception that develops over a short period of time (less than a few days) and is likely a direct physiological consequence of another medical condition or substance or is due to multiple etiologies and not better explained by a developing or established neurocognitive disorder. The clinician should specify if the delirium is acute or persistent and if the individual is hyper-/hypoactive or has a mixed level of activity. In hospital settings, delirium usually lasts about a week, but it may have a more prolonged course in some individuals. The hyperactive state may be more common (or more frequently recognized) and is typically associated with substance- or medication-related delirium. The hypoactive state is more commonly recognized in older adults. Delirium is frequently accompanied by disturbances in the sleep-wake cycle and emotional/behavioral disturbances. There is additionally often generalized slowing on electroencephalography (EEG) recordings (or, occasionally, abnormally fast activity) although EEG is insufficiently sensitive or specific enough for diagnostic use for delirium.

Delirium should be specified according to its etiological sub-type:

■ *Substance-Intoxication Delirium*

This diagnosis should be made instead of substance intoxication when a disturbance in attention and awareness that has developed over a short period of time predominates in the clinical presentation and the disturbance is sufficiently severe to warrant clinical attention. Coding is done for specific substance intoxication-related delirium.

■ *Substance-Withdrawal Delirium*

Symptoms as above, but etiology of the condition is related to substance withdrawal rather than substance use. Coding is done for specific substance withdrawal-related delirium.

■ *Medication-Induced Delirium*

A disturbance in attention, awareness and cognition that develops as a consequence of a medication taken as prescribed. Specific medication category should be coded for.

■ *Delirium due to Another Medical Condition*

There is evidence that the disturbance may be attributable to another medical condition. The name of the other medical condition should be included in the name of the delirium (e.g. 293.0 [F05]: delirium due to hepatic encephalopathy). The other medical condition should also be coded and listed separately immediately before the delirium.

■ *Delirium due to Multiple Etiologies*

There is evidence that the disturbance may be attributable to multiple etiologies. Multiple separate codes should be used in the same style as delirium due to another medical condition.

There are also categories for other specified delirium and unspecified delirium. Other specified delirium should be used when it is clinically significant but doesn't otherwise meet the full criteria for delirium (e.g., attenuated delirium syndrome). The clinician should specify the reason that the presentation does not meet the criteria for the general diagnosis of delirium. Unspecified delirium can be used when the clinician is unable to specify the reason the presentation does not meet the criteria for the general diagnosis of delirium, such as when there is insufficient information available about the patient or the patient is previously unknown.

Major and Mild Neurocognitive Disorders

Review of Diagnostic Criteria

Major Neurocognitive disorder can be distinguished from mild Neurocognitive disorder by the severity of the cognitive decline and the impact the symptoms have on the individual's ability to carry out his or her daily living activities.

To meet the diagnostic criteria for an Neurocognitive disorder, individuals must present with significant (major Neurocognitive disorder) or modest (mild Neurocognitive disorder) cognitive decline in one or more domains (including complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition). There should be prior

concern that there has been a significant (major) or mild (mild) decline in cognitive function, which is evidenced by substantial (major) or modest (mild) impairment in cognitive performance (preferably evidenced by a standardized cognitive test). The deficits should not occur exclusively in the context of delirium and should not be better explained by another mental disorder. For a diagnosis of mild neurocognitive disorder, the cognitive decline should not interfere with everyday life. For major neurocognitive disorder, the symptoms must interfere with independence in everyday activities. The clinician must specify the severity of the symptoms for major neurocognitive disorder and whether there are any behavioral disturbances with both mild and major neurocognitive disorder. In addition to cognitive decline, psychosis, mood disturbances, agitation, apathy, and other behavioral symptoms are frequently observed.

The neurocognitive disorders are sub-classified according to etiology/pathology as follows, and several include the option to specify whether or not they occur with behavioral disturbance:

■ *Alzheimer's Disease*

Mild or major neurocognitive disorder due to Alzheimer's disease is diagnosed where there is gradual progression of cognitive deficits in one or more domains (for major Neurocognitive disorder, two or more domains must be impaired) and the symptoms are not better explained by cerebrovascular disease, another neurodegenerative disorder, the use of a substance, or another mental, neurological, or systemic disorder. Criteria needs to be met also for either probable or possible Alzheimer's disease as follows: Major Neurocognitive disorder due to probable Alzheimer's disease may be diagnosed where there is evidence of the presence of a known pathogenic mutation, or there is clear evidence of a steadily progressive decline in learning and memory and at least one other cognitive domain and no evidence of mixed etiology; otherwise possible Alzheimer's disease should be diagnosed.

Mild Neurocognitive disorder due to Alzheimer's disease may be diagnosed as *probable* if there is evidence of the presence of a known pathogenic mutation from genetic testing or family history. If no such evidence is available, *possible* Alzheimer's disease may be diagnosed if there is a clear evidence of decline in learning and memory, the cognitive decline is steadily progressive and gradual, and there is no evidence of mixed etiology

Psychological and behavioral manifestations of Alzheimer's disease are very commonly observed in patients upon presentation and, even at the mild stage, depression and/or apathy are often seen, and coding includes the presence of behavioral disturbance. Common behavioral/psychological features in major Neurocognitive disorder due to Alzheimer's disease are psychosis, irritability, agitation, combativeness, and wandering in the moderately severe stage with gait disturbance, dysphagia, incontinence, myoclonus, and seizures frequently being observed in the later stages. Cortical atrophy, amyloid-predominant neuritic plaques, and tau-predominant neurofibrillary tangles are characteristic of Alzheimer's disease and may be observed through neuroimaging or through *post mortem* histopathology. Coding is done for the certainty of the presence of Alzheimer's disease.

■ *Frontotemporal Lobar Degeneration*

Major or mild frontotemporal neurocognitive disorder is diagnosed when there is either a progressive behavioral problem (including three or more symptoms including behavioral disinhibition, apathy or inertia, loss of sympathy or empathy, perseverative, stereotyped or ritualistic behavior, and hyperorality or dietary changes) or a progressive language problem (a prominent decline in language ability, speech production, word-finding, grammar, or word-comprehension).

The language variant of frontotemporal lobar degeneration comprises three types: semantic, agrammatic/nonfluent, and logopenic. The cognitive deficit is relatively sparing of learning and memory and perceptual-motor function and should not be better explained by cerebrovascular disease, another neurodegenerative disorder, the use of a substance, or another mental, neurological, or systemic disorder.

If there is evidence of known pathogenic mutation from either family history or genetic testing or there is evidence of disproportionate involvement of the frontal and/or temporal lobes from neuroimaging, a diagnosis of *probable* frontotemporal lobar degeneration can be made. *Possible* frontotemporal lobar degeneration should be diagnosed otherwise. Patients may present with both the behavioral and the language variant of frontotemporal lobar degeneration concurrently, and coding includes a system for indicating the presence of behavioral disturbance. Extrapyramidal features, features of motor neurone disease, or visual hallucinations may be apparent in some cases.

■ *Lewy Body Disease*

Major or mild neurocognitive disorder with Lewy bodies should be diagnosed in individuals presenting with the following core diagnostic features: Fluctuating cognition with pronounced variations in attention and alertness; recurrent vivid visual hallucinations; spontaneous features of Parkinsonism (with onset after the development of cognitive decline). Suggestive diagnostic features are fulfilling the criteria for REM sleep behavior disorder and severe neuroleptic sensitivity.

For *probable* major or mild neurocognitive disorder with Lewy bodies, the individual must present with two core features, or one suggestive feature and with one or more core features. For *possible* major or mild neurocognitive disorder with Lewy bodies, the individual has only one core feature, or one or more suggestive features. The symptoms should not be better explained by cerebrovascular disease, another neurodegenerative disease, the effects of a substance, or another mental, neurological, or systemic disorder.

A diagnosis of mild neurocognitive disorder with Lewy bodies should be made when the cognitive and functional symptoms presenting are not sufficiently severe to warrant a diagnosis of a major disorder. People with neurocognitive disorder with Lewy bodies frequently report repeated falls and syncope and transient loss of consciousness. Dysfunction of the autonomic nervous system and features of psychosis may also be observed. Coding is done for the certainty of the presence of major or mild neurocognitive disorder with Lewy bodies and the presence/absence of behavioral disturbances.

■ *Vascular Disease*

Major or mild vascular neurocognitive disorder should be diagnosed in individuals whose clinical features are consistent with a vascular etiology (suggested by cognitive deficits with an onset following a cerebrovascular event or decline in complex attention (including processing speed) and frontal-executive functioning, and where there is evidence of cerebrovascular disease from physical examination, history, and/or neuroimaging.

Probable vascular neurocognitive disorder should be diagnosed if one of the following is present (otherwise *possible* vascular neurocognitive disorder should be diagnosed): Cerebrovascular disease is supported by neuroimaging, the symptoms are temporally related to a cerebrovascular event, or both clinical and genetic evidence of cerebrovascular disease is present. Personality and mood changes, lack of initiative, depression, and emotional lability are often present. In older adults with progressive small vessel ischemic disease, depression, psychomotor slowing and executive dysfunction are common. Coding is done for the certainty of the presence of vascular neurocognitive disorder and the presence/absence of behavioral disturbances.

■ *Traumatic Brain Injury*

Major or mild neurocogntive disorder due to traumatic brain injury should be diagnosed in individuals where there is evidence of a traumatic brain injury and loss of consciousness, post-traumatic amnesia, disorientation and confusion, or other neurological signs. The disorder must present immediately after the brain injury or immediately after regaining consciousness and must persist beyond the acute post-injury period. Individuals frequently present with emotional and behavioral disturbances. Coding is done for behavioral disturbances, skull fracture and loss of consciousness, and the severity of the neurocognitive disorder should be rated,

but not the severity of the underlying traumatic brain injury.

■ *Substance/Medication Use*

Substance- or medication-induced major or minor neurocognitive disorder should be diagnosed in individuals presenting with neurocognitive impairments that do not occur exclusively during the course of delirium and persist beyond the ordinary course of intoxication and (acute) withdrawal. The substance and/or medication must be capable of producing the deficits and the temporal course of the symptoms should be consistent with substance and/or medication use. Coding is done for substance, abstinence or intoxication state, and severity and persistence can be specified.

■ *HIV Infection*

Major or mild neurocognitive disorder due to HIV infection should be diagnosed in individuals presenting with cognitive impairments and documented infection with HIV. The symptoms should not be attributable to any other medical condition and should not be explained by another mental disorder. Major or mild Neurocognitive disorder is more common in individuals testing HIV positive who had had prior episodes of severe immunosuppression, high viral loads in the cerebrospinal fluid, and anemia and hypoalbuminemia. Coding is done for behavioral disturbances.

■ *Prion Disease*

Major or mild neurocognitive disorder due to prion disease should be diagnosed in individuals with progressive neurocognitive deficits with motor features of prion disease (such as myoclonus or ataxia) or biomarker evidence and where the symptoms cannot be explained by another medical or mental disorder. Coding is done for the presence/absence of behavioral disturbances.

■ *Parkinson's Disease*

Major or mild neurocognitive disorder due to Parkinson's disease should be diagnosed in individuals presenting with progressive cognitive deficits with established Parkinson's disease and where the symptoms are not better explained by another diagnosis. Other features commonly observed in individuals with neurocognitive disorder due to Parkinson's disease include apathy, mood disturbances, psychotic symptoms, personality changes and sleep problems. Coding is done for the presence/absence of behavioral disturbances.

■ *Huntington's Disease*

Major or mild neurocognitive disorder due to Huntington's disease should be diagnosed in individuals presenting with progressive cognitive deficits with established Huntington's disease (or at risk from family history) and where the symptoms are not better explained by another diagnosis. Other features commonly observed in individuals with Neurocognitive disorder due to Huntington's disease include mood disturbances, obsessive-compulsive symptoms, apathy, and, occasionally, psychotic symptoms. Coding is done for the presence/absence of behavioral disturbances.

■ *Another Medical Condition*

A number of medical conditions can cause neurocognitive impairments. Individuals diagnosed with major or mild neurocognitive disorder due to another medical condition should present with evidence (through history, physical examination, etc.) that the deficits are a pathophysiological consequence of another medical condition (excluding those already covered in the section in the *DSM-5*).

■ *Multiple Etiologies*

The diagnosis is as above although the etiology is presumed to arise from multiple conditions and/or events, excluding substance use.

There is also an unspecified neurocognitive disorder category, to classify neurocognitive disorders where there is insufficient information and/or the precise etiology of the deficits cannot be determined and the criteria for other neurocognitive disorders in the *DSM-5* cannot be fulfilled.

Issues Related to Diagnosis in Persons with ID

Most of what we know about the course of neurocognitive disorders in individuals with intellectual disability comes from the study of

individuals with Down syndrome and probable Alzheimer's-type dementia. Individuals with Down syndrome often present with an early onset form of Alzheimer's-type disease, with clinical manifestation of dementia in this population often preceding by more than two decades its appearance among individuals with non-Down syndrome intellectual disability or the general population (Strydom, Hassiotis, King, & Livingston, 2009).

Development and Course

Neurocognitive disorders generally have a progressive and unremitting course (although there are exceptions such as vascular dementia and dementia as a result of head injury) as opposed to other conditions that may affect cognition and function such as depression and delirium but which may resolve with timely and targeted treatment. Given that cognitive and functional decline occurs as an overlay upon pre-existing deficits associated with developmental disability, it is important to consider all factors that may complicate both the presentation and the course of the disorder including depression, sensory loss, and other co-morbid psychiatric or medical illness (McCarron, Gill, McCallion, & Begley, 2005, p. 200).

There are few stage-based comparisons of the disorder across developmental subtypes. The disorder is often assumed to be more rapidly progressive among individuals with Down syndrome than the advancement of dementia among those with non-Down syndrome intellectual disability or within the general population, though data on progression is limited (Dodd, Bhaumik, & Benbow, 2009).

Early Stage and Late Stage Symptoms of Neurocognitive Disorder in Down Syndrome

An IASSID dementia and aging work group reviewed the literature published between 1997 and 2008 (Strydom et al., 2009) and described a range of early symptoms of Alzheimer's disease in Down syndrome including memory changes, maladaptive behaviors, decreased social engagement, and neurological signs.

Memory and language skills have been noted to be early cognitive changes (e.g. Devenny, Krinsky-McHale, Sersen, & Silverman, 2000); personality and behavior changes and erosion of social skills are early non-cognitive changes (Adams & Oliver, 2010; Ball et al., 2006; Ball, Holland, Treppner, Watson, & Huppert, 2008; Ball, Holland, Watson, & Huppert, 2010; Holland, Hon, Huppert, & Stevens, 2000; Oliver, Kalsy, McQuillan, & Hall, 2011). Physical changes and functional skills loss can also appear early in the course of the condition. Early compromise of complex activities of daily living may include decline in ability to maintain personal hygiene, housekeeping, and work skills; later progression involves dyspraxia and decline of basic self-help skills such as toileting, dressing, and eating (Dalton & Fedor, 1998; Evenhuis, 1997). An increase in maladaptive behaviors may be evident representing increased impulsivity and personality changes (Kannabiran & Deb, 2010).

Early personality and behavioral changes and cognitive decline associated with frontal lobe degeneration may precede full clinical manifestation of dementia in individuals with Down syndrome (Holland et al., 2000). This initial presentation is considered to be an important difference compared with the general population (Deb, 2003; (Deb, Hare, & Prior, 2007). Individuals are reported to display uncharacteristic apathy, lack of motivation, and stubbornness. Frontal presentation may also include psychiatric symptoms among individuals with no known previous history of mental illness. The preponderance of frontal lobe symptoms reported for the Down syndrome population, which includes neuropsychological findings such as deficits in executive function, has led some researchers to refer to a "frontal-temporal like dementia" (Kannabiran & Deb, 2010). Two types of behavioral problems are manifest in dementia in Down syndrome: Behavioral excesses such as irritability, aggression or self-injury, and then behavioral deficits that would include slowness, apathy, loss of interest, and lessened social engagement (Oliver et al., 2011)

Late stage symptoms of neurocognitive disorders in Down syndrome are characterised by the individual's lack of response to the environment, loss of mobility, loss of communication

skills, incontinence, seizures and may include Parkinsonian features (Strydom et al., 2009; Visser et al., 1997).

Cognitive Changes

Memory and other cognitive deficits do sometimes occur in Down syndrome in advance of formal clinical diagnosis of neurocognitive disorder and may be present before the person meets the clinical criteria for dementia (Devenny et al., 2000; Devenny, Zimmerli, Kittler, & Krinsky-McHale, 2002; Krinsky-McHale, Devenny, & Silverman, 2002). Cognitive decline during early and middle stage dementia involves progressively more areas of cognitive functioning, starting with complex cognitive functions, followed by visual organization as well as verbal memory before affecting semantic and short-term memory (Devenny et al., 2000). Dyspraxia tends to occur at a later stage (Crayton, Oliver, Holland, Bradbury, & Hall, 1998; Patti, 1999). Executive functions, visual organization and verbal memory appear to usually decline before semantic memory and short-term memory (Kittler, Krinsky-McHale, & Devenny, 2006).

Physical Changes

Reduced speech and deterioration in gait may be early symptoms of dementia in Down syndrome (V. P. Prasher, 1995). First time adult onset of seizures among individuals with Down syndrome with no previous history of epilepsy may be a marker for neurocognitive disorder (Kannabiran & Deb, 2010). Neurological changes noted among early presenting symptoms include late onset myoclonic epilepsy in Down syndrome (LOMEDS); this is characterized by myoclonic jerks upon awakening and generalized tonic-clonic seizures and generalized spikes in waves on EKGs (Möller, Hamer, Oertel, & Rosenow, 2001). Incontinence may be among early physiological signs of neurocognitive change.

McCarron et al. (2005) have proposed that there is an increased risk of health comorbidities among individuals with Down syndrome and dementia. Observed medical problems include respiratory problems, gastrointestinal problems, vision, hearing, and weight loss which may further complicate the course of a neurocognitive disorder. Additional physiological signs may include rigidity, postural abnormalities, and pathological grasping and sucking reflexes.

Neurocognitive Disorder Among Individuals with Non-Down Syndrome ID

We do not know the extent to which descriptions of the development and course of neurocognitive disorder based upon Down syndrome are generalizable to adults with intellectual disability who do not have Down syndrome who manifest cognitive and adaptive skills changes.

According to the IASSID workgroup, individuals with non-Down syndrome intellectual disability and dementia display a general deterioration of function and behavioral or emotional changes (Strydom et al., 2009). Further study is required regarding subtypes of developmental disorder and subtypes of neurocognitive disorder.

Generally, the course for those with non-Down syndrome intellectual disability of moderate or more severe disability is similar to those with Down syndrome, but it has been suggested that the course of neurocognitive disorder for individuals with mild intellectual disability is similar to the general population (Dodd et al., 2009). Memory problems and other changes may be observed in early stages, and symptoms of depression, lack of energy, low mood, disturbed sleep, persecutory delusions, and auditory hallucinations or delusions may also be apparent. Observed changes in physical status include urinary and fecal incontinence and gait disturbance (Cooper, 1997; Cooper & Prasher, 1998).

Course of Neurocognitive Disorder

Although it is known that anatomical brain changes precede clinical presentation, it is on the basis of observed behavioral change that neurocognitive disorder is diagnosed. Reported observed changes that bring individuals to the attention of practitioners include changes in daily living skills, work habits, and memory.

Description of the progression of neurocognitive disorder is complicated by several factors including when during the course of the disorder individuals receive a formal diagnosis. Given the difficulties with early recognition, an individual may progress to advanced stages

of dementia before receiving formal diagnosis. Changes in behavior may not be considered as possible signs of dementia in a population with pre-existing neurobehavioral problems.

Determination of the trajectory of decline depends upon the point at which significant change is identified and whether or not change is effectively tracked over time. Perception of decline and how decline is manifest depends upon such factors as premorbid level of intellectual disability and patterns of cognitive abilities, sensory and mood problems as well as environmental demands placed upon the person (Aylward, Burt, Thorpe, Lai, & Dalton, 1997; Strydom et al., 2009).

A variety of factors impede establishing a reliable pre-morbid baseline which is needed in order to track the progression of symptoms. Careful assessment of baseline functioning would help in differentiating among delirium, dementia, and depression and therefore aid in the description of the course of change in cognitive and adaptive skills. We currently lack the tools to reliably and directly assess individuals on the lower end of the range of intellectual functioning.

There are insufficient data on the extent to which patient characteristics such as pre-morbid severity of intellectual ability, pre-morbid cognitive and adaptive skills, or co-morbid psychiatric illness may influence trajectory of neurocognitive decline (Dodd et al., 2009). However, the presence of neurocognitive disorder and the severity of intellectual disability are significant predictors of decline in adaptive skills (Deb, Prior, & Bhaumik, 2007). It has also been suggested that the residential setting in which care is delivered and other environmental factors may also influence outcomes (Courtenay, Jokinen, & Strydom, 2010).

More research is needed with regards to the natural history of cognition and adaptive skills in aging adults with intellectual disability across levels of intellectual impairment and types of developmental disorder to allow for clearer distinction between normative and non-normative changes in function as individuals age. Further research is required to determine the extent to which subtype of dementia, level of intellectual disability, type of developmental disorder, or caregiving factors may influence the course of dementia.

Prevalence and Incidence

Major Neurocognitive Disorder in People With Down Syndrome

Several of studies have confirmed that dementia is frequent in older adults with Down syndrome. Prevalence appears to increase sharply in this group between ages 40 and 60. Prevalence estimates have ranged from 1.4% in those with Down syndrome under 40 (Tyrrell et al., 2001) to 40% in the 50-59 age group (Holland, Hon, Huppert, Stevens, & Watson, 1998). Coppus and colleagues (2006) found that up to the age of 60 the prevalence of dementia doubled with each 5-year interval (from >49 to 60 years). Studies have varied in their findings beyond the age of 60. Some studies have found that prevalence continues to increase, with most individuals eventually diagnosed with dementia (major neurocognitive disorder) (Tyrrell et al., 2001; Visser et al., 1997); whilst others (Coppus et al., 2006) described a decrease in prevalence to 25.6% at ages 60 and over due to the increased mortality associated with neurocognitive disorder.

Incidence increased steadily with increasing age, from 2.5 per 100 person years in those aged <50 to 13.31 per 100 person years in those aged 60 and older (Coppus et al., 2006).

Major Neurocognitive Disorder in People With ID Without Down Syndrome

Estimates of the prevalence and incidence of dementia in people with intellectual disabilities (without Down syndrome) are lower than in the Down syndrome population but may be higher than the general population average.

Cooper (1997) found a prevalence rate of 20% in people aged 65 years and over. Later Strydom and colleagues (2007) found a similar prevalence rate of 18.3% among those aged 65 and older. Alzheimer's disease was found to be the most common type of dementia and had a prevalence of 12%, three times greater than comparable general older adult population rates. One study has, however, found demen-

tia rates comparable to the general population in the over 65 age group (Zigman et al., 2004) though this group later reanalyzed their data due to diagnostic issues and adjusted their estimate to a slightly higher rate (Zigman, 2013). This group also found an incidence rate for Alzheimer's disease to be 8 cases over 3 years in a cohort of approximately 100 participants over the age of 65. Strydom, Chan, King, Hassiotis, & Livingston (2013) found an overall incidence rate for those aged 60 of 54.6/1000 person years with the highest incidence rate in the age group 70–74 years.

Differential Diagnosis and Comorbidity

Any condition that affects cognitive functioning should be considered in the differential diagnosis of a neurocognitive disorder – the possibilities to consider has been reviewed elsewhere (Knopman et al., 2001). It is particularly important to exclude common comorbidities in intellectual disability such as hearing or vision loss, thyroid function disorders (particular in individuals with Down syndrome; (Määttä, Kaski, Taanila, Keinänen-Kiukaanniemi, & Iivanainen, 2006; Määttä et al., 2011), and mental health concerns such as depression – see the section below on general considerations for more detail.

Functional Consequences

Overall, the natural history of the disorder involves a progressive loss of skills, increased loss of independence and increased dependence upon others for personal assistance and maintenance of daily routine. Later stages of dementia among individuals with Down syndrome are associated with dyspraxia and extensive loss of self-help skills (Prasher, 1995), as well as the development of neurological symptoms such as problems with swallowing, myoclonic jerks and seizures.

Neurocognitive decline and its functional implications impact upon caregiving and health care practices including the level of supervision at which an individual needs to stay safe, staffing to provide personal assistance, and planning including allocation of resources and environmental modifications.

Application of Diagnostic Criteria to People with ID

General Considerations

Due to generally better access to medical and social care and healthier lifestyles, people with intellectual disability are living longer and therefore increasingly at risk of age-related disorders such as neurocognitive disorders. Although neurocognitive disorders are more common in this population, a number of factors make diagnosis of neurocognitive disorders in adults with intellectual disability difficult (for reviews see (Evans et al., 2013; Moran, Rafii, Keller, Singh, & Janicki, 2013; Strydom et al., 2010).

The main difficulties include that 1) baseline functioning varies widely between individuals, making it difficult to interpret change and to apply screening approaches across the population; 2) individuals with intellectual disability may be unable to answer questions about their memory or higher cognitive functioning; 3) there are many other treatable conditions that could explain an apparent decline in cognitive and functional abilities, including medical co-morbidities, mental health problems, and behavioral responses to stress or change in environment, and 4) in many geographic areas, there is a relative paucity of qualified healthcare providers for this population relative to the general population (Moran et al., 2013). The diagnosis of dementia in people with intellectual disability is further hampered by the lack of reliable and standardized diagnostic tools and procedures, especially in the early stages of decline. Furthermore, the use of investigations such as neuroimaging and lumbar puncture is limited by its acceptability in this population, as well as the complexities of interpreting results.

As previously discussed, the presentation of major neurocognitive disorders may differ in people with intellectual disability compared to the general population. Memory loss may not be prominent in the early stages. Cognitive changes are frequently present, but they may be difficult to evaluate because of limitations in the individual's language, communication, and functional abilities. In contrast to the general population, people with intellectual disability

may experience a predominance of changes in functioning (i.e. activities of daily living and work habits) early in the course (Aylward et al., 1997; Strydom et al., 2010). Functional abilities can be influenced by many different factors and are more dependent on disability level and comorbidity than dementia (Lin et al., 2014). Behavioral problems, such as behavioral excesses (e.g. restlessness, aggression) or deficits (e.g. withdrawal, inactivity), may also be an early sign associated with neurocognitive disorders (Adams et al., 2008, p. 200; Oliver et al., 2011).

Neurological symptoms associated with dementia such as epileptic seizures and depth perception difficulties may occur more often than in the general population, particularly in those with Down syndrome (Lott & Dierssen, 2010; McCarron, McCallion, Reilly, & Mulryan, 2014). Sensory deficits (particularly hearing loss) are also associated with cognitive decline or dementia in Down syndrome (Lott & Dierssen, 2010; McCarron et al., 2014). Therefore, the assessment and identification of dementia should take into account a nuanced consideration of functional abilities, cognitive status, behavioral indicators, and clinical factors.

There is no universal test for dementia that can be used for older people with intellectual disability who are showing deterioration in function, though an assessment of cognitive function is recommended (Moran et al., 2013). Furthermore, the standard tests used on the general population are inappropriate for people with intellectual disability and different types of assessment tools are required for those with mild intellectual disability compared to those with more severe intellectual disability. The options for formal assessment in this population have been reviewed elsewhere (Zeilinger, Stiehl, & Weber, 2013) and include proxy-rated (i.e. caregiver-rated) dementia screening questionnaires (e.g. Dementia Questionnaire for people with Mental Retardation or Learning disabilities - also referred to as DMR or DLD; (Evenhuis, 1997); Dementia Screening Questionnaire for Individuals with Intellectual disabilities, DSQIID (Deb, Hare, Prior, & Bhaumik, 2007, p. 200); The Adaptive Behavior Questionnare, ABDQ ; (Prasher, Farooq, & Holder, 2004)), several cognitive functioning test batteries completed with the person (e.g. Burt-Aylward battery [Burt & Aylward, 2000]; NAID [Crayton et al., 1998]), and proxy ratings of adaptive ability or everyday functioning (e.g. Vineland Adaptive behavior scale, (Sparrow, 2011) or dementia symptoms (e.g. CAMDEX-DS informant interview, (Ball et al., 2004). Although proxy report has limitations, this remains the most feasible option to track change over time from all individuals with intellectual disabilities regardless of their ability.

Ultimately diagnosis of a neurocognitive disorder requires the exclusion of other conditions that may be implicated in either apparent or actual cognitive or functional decline. A comprehensive medical history (Moran et al., 2013) and a physical work-up should therefore be conducted as part of any assessment (Dodd et al., 2009). The impact of sensory losses such as impaired sight and hearing should be considered (Haveman et al., 2010; Haveman et al., 2011). People with Down syndrome often experience the effects of premature aging including cataracts (Evenhuis, 1997; Evenhuis, Theunissen, Denkers, Verschuure, & Kemme, 2001) and presbyacusis (Haveman et al., 2010), which can impact on function.

A recent Finnish population-based study of case records of older people with Down syndrome also found that thyroid disease was common (Määttä et al., 2006; Määttä et al., 2011), which should be excluded as the cause of cognitive decline. Seizures may also be common in this population, but it needs to be established whether this preceded the onset of decline, as seizures often develop with Alzheimer's-type dementia in individuals with Down syndrome and affect the progression of the disorder (Lott et al., 2012).

Other physical causes of cognitive decline including vitamin deficiencies, electrolyte imbalances, chronic diseases including central nervous system manifestations of untreated coeliac disease, occult malignancies, and central nervous system conditions such as tumors, inflammatory conditions, hydrocephalus, and

infections such as neuro-syphilis should be excluded. Mental health conditions such as depression are common in older individuals with intellectual disability regardless of etiology of the intellectual disability (Cooper, Smiley, Morrison, Williamson, & Allan, 2007) and affect functional and cognitive abilities in people with intellectual disability (Hermans & Evenhuis, 2013). A psychiatric and life events examination is therefore also recommended as part of a comprehensive work-up for neurocognitive disorders.

Methodology

We undertook a comprehensive literature search across several databases (EMBASE, Medline, Cinahl) using all equivalent terms for intellectual disability (e.g. mental retardation and learning disabilities) and combining these with terms for neurocognitive disorders (dementia, Alzheimer's disease). Additionally, we completed searches using terms for other types of neurocognitive disorders, including fronto-temporal dementia, Lewy body dementia, and vascular dementia. We also completed searches for delirium and mild neurocognitive disorder and equivalent terms (e.g. mild cognitive impairment).

Searches were limited to English and the time frame 2008-February 2014 because a comprehensive series of reviews included the literature prior to that date (Haveman et al., 2010; Strydom et al., 2010; Torr, Strydom, Patti, & Jokinen, 2010), and we also consulted the reference lists of these reviews.

Review of Research Applying to People with ID

No research studies were identified concerning the application or modification of criteria for delirium in individuals with intellectual disability.

A small number of studies have considered the diagnostic issues related to mild neurocognitive disorder (similar to but not exactly the same as mild cognitive impairment) and associated symptoms in individuals with intellectual disability. While there is generally an emphasis on earlier detection of underlying disease, this presents challenges in individuals with intellectual disability. One approach has been to identify adults with intellectual disability who show declines in excess of "normal aging," which may be viewed as a prodromal stage of dementia, particularly in older adults with Down syndrome. Using this type of approach, several groups found that the prodromal signs of Alzheimer's disease in older adults with Down syndrome often included signs of frontal lobe dysfunction such as emotional changes, behavioral problems and frontal release signs (Ball et al., 2006; NelsonOrme, Osann, & Lott, 2001; Urv, Zigman, & Silverman, 2010; Urv, Zigman, Silverman, & MacLean, 2008).

In adults with intellectual disability without Down syndrome, informants tended to report general deterioration of functioning more than memory or other cognitive changes (Strydom et al., 2007). However, in individuals who can complete cognitive testing, change in cognitive functioning (particularly episodic memory) has been observed in adults with Down syndrome several years before clinical diagnosis of dementia (Crayton et al., 1998; Devenny et al., 2002; Krinsky-McHale et al., 2002). Nevertheless, changes in behavior and personality now form the basis of several caregiver-reported screening tools for dementia, particularly for individuals with Down syndrome (Oliver et al., 2011; Deb et al., 2007; Whitwham, McBrien, & Broom, 2011).

Strydom, Chan, Fenton, et al. (2013) defined mild cognitive impairment as individuals who had previously screened positive for possible dementia on the Dementia Questionnaire for People with Intellectual Disability screening tool (DMR; Evenhuis, 1992), or because of concerns about decline in functioning or memory, and explored its predictive value for dementia diagnoses two years later using ICD-10 and *DSM-IV* criteria. Only 13% of those with mild cognitive impairment were diagnosed with dementia after follow-up of approximately 2.9 years, which was not much different than that of a "normal" state. This compares to an annual dementia conversion rate of 5-10% for mild cognitive impairment reported in the general population (Petersen, 2011).

Silverman, Zigman, Krinsky-McHale, Ryan, and Schupf (2013) defined mild cognitive impairment as those showing cognitive decline

larger than expected with aging but having insufficient "breadth or severity" to be considered dementia and applied this to their study of dementia in older adults with intellectual disability without Down syndrome. Although they identified dementia or mild cognitive impairment in more than 20% of their sample, they had difficulty designating the majority of these with certainty to a specific category. In their review of the literature on mild cognitive impairment in intellectual disability, Krinsky-McHale & Silverman (2013) emphasized the need for empirically based assessment methods and classification criteria for mild cognitive impairment.

Several studies were identified which applied ICD-10 and *DSM-IV* dementia criteria for major neurocognitive disorder (dementia) in individuals with intellectual disability. Clinical judgment, based on ICD-10 criteria, resulted in more adults with Down syndrome diagnosed with dementia than methods based on test batteries (Diana B. Burt et al., 2005). DSM IV criteria showed substantial inter-rater reliability (Kappa = 0.68) (Strydom, Chan, Fenton, et al., 2013) and were found to diagnose more people with dementia than ICD-10 criteria (A. Strydom et al., 2007). However, diagnostic instability may be more common in individuals with intellectual disability compared to the general population, affecting the predictive validity of diagnoses. *DSM-IV* criteria diagnosed a few false positive cases with dementia because of the extent of pre-existing cognitive deficits, but cases were occasionally missed when caregivers did not report memory loss in those who did not have sequential cognitive test data. Sensitivity and specificity for either dying or being re-diagnosed with dementia after approximately 2.9 years after a *DSM-IV* diagnosis of dementia was 0.28 and 0.95, respectively (Andre Strydom, Chan, Fenton, et al., 2013).

The challenges in diagnosing dementia in this population included variable quality of informant reports with poor judging of indicators of early and intermediary dementia (Herron & Priest, 2013), difficulties in the assessment of those with moderate and severe intellectual disability (Bell, Turnbull, & Bruce Kidd, 2009), or sensory impairments (Moran et al., 2013), and difficulties in interpreting periods of plateau in vascular dementia and the floor effect in advanced dementia when longitudinal information is not available.

DSM-5 criteria for major neurocognitive disorder could improve the ability to diagnose dementia in individuals with intellectual disabilities. The hierarchical approach to subtyping (i.e. requiring that criteria for major or mild neurocognitive disorder are met before applying criteria for neurocognitive disorder subtypes such as Alzheimer's disease, frontotemporal lobar degeneration, vascular disease, and Lewy body disease) could be helpful. The de-emphasis of a central focus on memory deficits (*DSM-IV*) in favor of the broader inclusion of six possible cognitive domains, as well emphasis on "decline" from a previous level of performance (criterion A) rather than "impairment," are important changes. Coupled with the option for cognitive decline to be reported by the individual, a knowledgeable informant, or a clinician (A1), these changes should improve predictive validity of the criteria.

However, some aspects of the criteria may prove difficult in their application to people with an intellectual disability, particularly those with more severe disabilities or those with communication difficulties. Firstly, it is important to distinguish neurocognitive disorder from premorbid cognitive impairment or impairments due to non-degenerative or stable conditions such as brain injury. Secondly, the requirement that evidence of cognitive decline be documented by standardized neuropsychiatric testing or another quantified clinical assessment (A2) is particularly difficult in the context of intellectual disability. For people in whom standardized neuropsychological assessment or other quantified assessment is not feasible, it is suggested that caregiver ratings of cognitive functioning should be sufficient to meet this criterion (level of evidence: IV). A limitation of this approach is that some people with intellectual disability may already be

performing at the floor of such instruments. Furthermore, criterion B suggests that the cognitive deficits should be severe enough to interfere with independence in daily activities – however, individuals with intellectual disability will by definition already have limitations in functioning, and it should therefore be clarified that a significant change from pre-existing ability in everyday functioning is required (Moran et al., 2013).

The diagnostic criteria for mild neurocognitive disorder requires modest cognitive decline from previous level of function in at least one of six possible cognitive domains. The presence of cognitive decline is determined by a combination of the concern of an individual, informant or clinician, together with modest impairment in performance in comparison to prior or expected results or clinical assessment. There is a specific requirement that cognitive deficits do not result in additional supports being required by the individual.

The existing literature in people with intellectual disability highlights the difficulty in identifying cognitive deficits of such fine granularity from pre-existing cognitive deficits, and highlights the poor predictive validity of mild cognitive impairment definitions in people with intellectual disability. There may be several reasons for changes in cognitive function in individuals with intellectual disability who may be particularly sensitive to the cognitive effects of physical illness, environmental disturbance, changes in support, or mental illness and stress. These factors need to be considered in addition to the possibility of mild neurocognitive disorder. However, most clinicians working with older individuals with Down syndrome will recognize the value in being able to apply a diagnosis of mild neurocognitive disorder when symptoms of Alzheimer's disease are recognized early, i.e. before it has a significant impact on the person's level of functioning. On the flipside, there is a risk of overdiagnosis, and there is not sufficient evidence that people with this diagnosis will progress to major neurocognitive disorder.

In the absence of evidence for the *DSM-5* diagnostic criteria of mild neurocognitive disorders, we suggest that this diagnostic category should be used with caution in individuals with intellectual disabilities, and further research to help identify biomarkers and neurocognitive tests that improve the predictive validity of mild neurocognitive diagnosis will be useful.

Evaluating the Level of Evidence

There is limited evidence on the use of diagnostic criteria for dementia (major neurocognitive disorder) in this population and extremely limited evidence for the use of criteria for mild cognitive impairment and mild neurocognitive disorder.

Adults with ID

Most of the existing studies on dementia criteria in individuals with intellectual disability have been with adults with mild to moderate intellectual disability. Jamieson-Craig, Scior, Chan, Fenton, & Strydom (2010) examined retrospective caregiver reports of early symptoms of dementia in adults with intellectual disability and found that reports of change in memory were a better indicator for possible dementia in those with mild intellectual disability, while in those with more severe intellectual disability decline in everyday functioning was a more reliable indicator of possible dementia. In general, caution is advised when applying dementia criteria in people with more severe intellectual disability.

Children and Adolescents with ID

We have not found any studies that have applied diagnostic criteria for delirium or dementia in children and adolescents with intellectual disability.

Summary of Limitations in Applying DSM-5 *Criteria to People with ID*

Several limitations in applying the criteria for neurocognitive disorders in individuals with intellectual disability are apparent:

1. Difficulty in objectively defining cognitive impairment and decline in a population with pre-morbid deficits (very difficult when cognitive deficits are more subtle). This is the main concern with applying the criteria for mild neurocognitive disorder, which does not

require functional decline to be present and could thus result in over-diagnosis in this population. However, this label may be useful to identify individuals at high risk for future decline, particularly in research settings, as long as it is not prematurely concluded that all persons with more subtle cognitive decline will progress to full-blown dementia.

2. Formal neuropsychological testing:
    a. People with intellectual disability contrast with the general population where clinicians may have greater control over factors which "optimize" cognitive test performance, whereas clinicians working with this population have to deal with considerable unpredictability (factors include contextual issues, emotional states, sensory problems, medical status, medications etc.).
    b. Limited range of tests suitable for this population, especially for those with more severe intellectual disability.
    c. Individuals may have a wide range of baseline abilities across different domains, and there is considerable between-individual variation.
3. Questionnaire-based assessment of cognitive functioning completed with or by caregivers.
    a. Questions often do not map well onto specific cognitive domains.
    b. The "context" is not considered, e.g. whether a task is regularly ignored because the person is unwilling to do it rather than unable to do it, or the familiarity of the person with his/her caregivers.
4. Questionnaires do not discriminate between "physical" and "cognitive" reasons for functional impairments.
5. Reliability of informant reports of impairment or decline is also occasionally an issue, particularly when information is obtained from different caregivers at different times.

Etiology and Pathogenesis

Biological Factors for Delirium

Delirium is always caused by an underlying medical condition or combination of conditions but may be exacerbated in the context of functional impairment, immobility, a history of falls, low levels of activity, and use of illicit drugs and medications with psychoactive properties (particularly alcohol and anticholinergic drugs) (American Psychiatric Association, 2013).

Genetic Factors for Major and Mild Neurocognitive Disorders

The amyloid cascade hypothesis remains the most prominent etiological theory for Alzheimer's disease and is of much interest in Down syndrome, as the APP gene on chromosome 21 is strongly implicated in the development of Alzheimer's neuropathology in these patients. Recent advances in Positron Emission Tomography (PET) imaging using new ligands have enabled researchers to show deposition of cerebral amyloid and tau in people with Down syndrome (Nelson et al., 2005) supporting the role of these proteins in the development of Alzheimer's disease in Down syndrome. ApoE4 is a strong risk factor for Alzheimer's disease in the general population, and also relevant in Down syndrome (Prasher, Chowdhury, Rowe, & Bain, 1997). Oxidative stress is also thought to play a role in the pathophysiology of Alzheimer's disease and is particularly of interest in Down syndrome, as the dosage sensitive superoxide dismutase gene (SOD1) is located on chromosome 21. However, a randomized controlled trial of antioxidant supplementation in people with Down syndrome and dementia had disappointing results (Lott et al., 2011). Nevertheless, understanding the link between Down syndrome and Alzheimer's disease would contribute substantially to our understanding of the disease in general.

Little attention has been paid to the risk of dementia in other specific intellectual disability syndromes. Several intellectual disability syndromes have neurocognitive decline as a common characteristic — these include Cockayne syndrome, Rett syndrome, and Sanfilippo syndrome. Cockayne syndrome (progeria-like syndrome), a rare autosomal recessive dis-

order, is characterized by premature aging, including neurodegeneration and dementia (Rapin et al., 2006). Sanfilippo syndrome, or mucopolysaccharidosis III, is a lysosomal storage disease caused by the impaired degradation of heparan sulfate and characterized by severe central nervous system degeneration. There are several types, depending on the genetic origin of the disease. Although most people with the disease die during childhood, those with type B disease (i.e. affecting alpha-N-acetylglucosaminidase) may survive into adulthood. A very high proportion of adults with Sanfilippo syndrome type B developed dementia (Moog et al., 2007; Skandar, Schoonbrood-Lenssen, Van den Akker, & Maaskant, 2005).

There are controversial findings in the literature regarding whether or not severity of intellectual disability acts as a risk factor for dementia (see review by Evans et al., 2013).

Traumatic brain injury may increase the risk of major or mild neurocognitive disorder due to Alzheimer's disease in the general population (Fleminger, Oliver, Lovestone, Rabe-Hesketh, & Giora, 2003). Age is the strongest risk factor for Alzheimer's disease, and in the case of people with Down syndrome the effect of age is independent of severity of intellectual disabilities and gender (Strydom et al., 2009). Multiple vascular risk factors influence risk for Alzheimer's disease and may act by increasing cerebrovascular pathology or also through direct effect on Alzheimer's disease pathology (see review by Deb & McHugh, 2010). A positive family history of Alzheimer's disease and inactive lifestyle may also act as risk factors (Deb, 2003).

Coppus et al. (2012) showed that in individuals with Down syndrome, higher levels of plasma Aβ40 and Aβ42 were associated with increased risk of dementia. Others have failed to show this association with dementia but showed Aβ40 level to be associated with cognitive decline in people with Down syndrome (Head et al., 2011). On the other hand (Matsuoka et al., 2009) showed that the ratio of Aβ42 to Aβ40 rather than absolute levels of the peptides is important to the pathophysiology of Alzheimer's disease in genetically vulnerable population such as people with Down syndrome. Other factors such as the raised mean corpuscular volume (MCV) of red blood cells (RBC) (Prasher, Uppal, Parveen, Adams, & Haque, 2013), impaired balance between excitatory and inhibitory neurotransmitter system, particularly involving GABAA system (Rissman & Mobley, 2011), and higher levels of macrophage inflammatory protein-1 (MIP-1) (Carta et al. cited in Kannabiran & Deb, 2010) have been implicated as risk factors but further proof is required to confirm these findings.

Use of certain medications particularly those with anticholinergic properties may enhance the expression of neurocognitive disorder. A number of medication classes have been reported to be associated with possible worsening of cognitive function in people with dementia. These include antihistamines, especially first generation (diphenhydramine, hydroxyzine, promethazine), bladder agents (oxybutynin, tolterodine), certain pain medications (meperidine, propoxiphene), tricyclic antidepressants, certain antipsychotics (chlorpromazine, clozapine, pimozide) ,and benzodiazepines (see review by Moran et al., 2013).

Psychosocial Factors

Esbensen, Mailick, & Silverman (2013) found that higher initial maternal and paternal levels of depressive symptoms and lower initial levels of paternal relationship quality were significant predictors of a higher likelihood of a dementia diagnosis in the adults with Down syndrome ten years later. Furthermore, lower initial levels of maternal positive psychological well-being predicted a higher likelihood of developing dementia in adults with Down syndrome ten years later, but the effect was only marginally significant.

Poorer overall physical health and depression were shown to be associated with an increased rate of dementia in people with intellectual disability (Evenhuis, 1997). However, it is not clear to what extent other known risk factors for dementia in the non- intellectual disability general population such as lack of engagement in mentally stimulating leisure and social activities, poor educational achievement, emotional trauma and associated post-traumatic stress disorder, poor diet, and lack of exercise also have a role in individuals with intellectual disability.

Neurocognitive Disorders
Delirium

DSM-5 Diagnostic Criteria	Applying Criteria for Mild-Profound ID
A. A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).	A. Needs to be interpreted as a change from baseline levels of attention and awareness
B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate during the course of the day.	B. No change
C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).	C. Needs to be interpreted as a change from baseline cognitive ability
D. These cognitive disturbances are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.	D. No change
E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.	E. No change
Substance intoxication delirium: This diagnosis should be made instead of substance intoxication when the symptoms in criteria A and C predominate in the clinical picture and they are sufficiently severe to warrant clinical attention.	No change
Substance withdrawal delirium: This diagnosis should be made instead of substance withdrawal when the symptoms in criteria A and C predominate in the clinical picture and they are sufficiently severe to warrant clinical attention.	No change
Other specified delirium: as for delirium but symptoms do not meet the full criteria but cause clinically significant distress or impairment. **NOTE:** The clinician must specify the reason the delirium does not meet the full criteria.	No change
Unspecified delirium: as for delirium but symptoms do not meet the full criteria but cause clinically significant distress or impairment. **NOTE:** The clinician does not specify the reason the delirium does not meet the full criteria.	No change

Major Neurocognitive Disorder

DSM-5 Diagnostic Criteria	Applying Criteria for Mild-Profound ID
A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on: 1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and 2. A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.	A. Take care to determine previous level of performance and change in performance need to be clearly established Neuropsychological tools should have been designed for individuals with an intellectual disability and/or validated in this population; including proxy-rated tools of cognitive performance
B. The cognitive deficits interfere with independence in everyday activities (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).	B. Needs to be a change from previous level of functioning (i.e. measured against the person's own premorbid baseline)
C. The cognitive deficits do not occur exclusively in the context of a delirium.	C. No change
D. The cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia).	D. No change

Mild Neurocognitive Disorder

DSM-5 mild neurocognitive disorder has the same criteria as for major neurocognitive disorder, except that the cognitive decline is modest/mild and does not interfere with capacity for independence in everyday activities.

The reliability and validity of this diagnosis in individuals with ID has not been established and we advise caution in using this diagnosis.

Major or Mild Neurocognitive Disorder Due to Alzheimer's Disease

DSM-5 Diagnostic Criteria	Applying Criteria for Mild-Profound ID
A. The criteria are met for major or mild neurocognitive disorder	A. No change, but see concerns about mild neurocognitive change
B. There is insidious onset and gradual progression of impairment in one or more cognitive domains (for major neurocognitive disorder, at least two domains must be impaired).	B. No change, but see comments above about change from previous level of performance
C. Criteria are met for either probable or possible Alzheimer's disease as follows: **For major neurocognitive disorder:** Probable Alzheimer's disease is diagnosed if either of the following is present; otherwise, possible Alzheimer's disease should be diagnosed: 1. Evidence of a causative Alzheimer's disease genetic mutation from family history or genetic testing. 2. All three of the following are present: a. Clear evidence of decline in memory and learning and at least one other cognitive domain (based on detailed history or serial neuropsychological testing). b. Steadily progressive, gradual decline in cognition, without extended plateaus. c. No evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease, or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline). **For mild neurocognitive disorder:** Probable Alzheimer's disease is diagnosed if there is evidence of a causative Alzheimer's disease genetic mutation from either genetic testing or family history. Possible Alzheimer's disease is diagnosed if there is no evidence of a causative Alzheimer's disease genetic mutation from either genetic testing or family history, and all three of the following are present: 1. Clear evidence of decline in memory and learning. 2. Steady progressive, gradual decline in cognition, without extended plateaus. 3. No evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease, or another neurological or systemic disease or condition likely contributing to cognitive decline).	C. No change
D. The disturbance is not better explained by cerebrovascular disease, another neurodegenerative disease, the effects of a substance, or another mental, neurological, or systemic disorder.	D. No change

Major or Mild Frontotemporal Neurocognitive Disorder

No change from DSM-5 criteria, but see concerns about mild neurocognitive change.

Major or Mild Neurocognitive Disorder with Lewy Bodies

DSM-5 Diagnostic Criteria	Applying Criteria for Mild-Profound ID
A. The criteria are met for major or mild neurocognitive disorder.	A. No change, but see concerns about mild neurocognitive change
B. The disorder has an insidious and gradual progression	B. No Change
C. The disorder meets a combination of core diagnostic features and suggestive diagnostic features for either probable or possible neurocognitive disorder with Lewy bodies. For probable major or mild neurocognitive disorder with Lewy bodies, the individual has two core features, or one suggestive feature with one or more core features. For possible major or mild neurocognitive disorder with Lewy bodies, the individual has only one core feature, or one or more suggestive features. 1. Core diagnostic features: a. Fluctuating cognition with pronounced variations in attention and alertness. b. Recurrent visual hallucinations that are well-formed and detailed. c. Spontaneous features of Parkinsonism, with onset subsequent to the development of cognitive decline 2. Suggestive diagnostic features: a. Meets criteria for rapid eye movement sleep behavior disorder b. Severe neuroleptic sensitivity	C. No Change
D. The disturbance is not better explained by cerebrovascular disease, another neurodegenerative disease, the effects of a substance, or another mental, neurological, or systemic disorder.	D. No Change

Major or Mild Vascular Neurocognitive Disorder

DSM-5 Diagnostic Criteria	Applying Criteria for Mild-Profound ID
A. The criteria are met for major or mild neurocognitive disorder	A. No change, but see concerns about mild neurocognitive change
B. The clinical features are consistent with a vascular etiology, as suggested by either of the following: 1. Onset of the cognitive deficits is temporally related to one or more cerebrovascular events. 2. Evidence for decline is prominent in complex attention (including processing speed) and fronto-executive function.	B. No Change
C. There is evidence of the presence of cerebrovascular disease from history, physical examination, and/or neuroimaging considered sufficient to account for the neurocognitive deficits.	C. No Change
D. The symptoms are not better explained by another brain disease or systemic disorder.	D. No Change

Major or Mild Vascular Neurocognitive Disorder (continue)

DSM-5 Diagnostic Criteria	Applying Criteria for Mild-Profound ID
Probable vascular neurocognitive disorder is diagnosed if one of the following is present; otherwise possible vascular neurocognitive disorder should be diagnosed: 1. Clinical criteria are supported by neuroimaging evidence of significant parenchymal injury attributed to cerebrovascular disease (neuroimaging-supported). 2. The neurocognitive syndrome is temporally related to one or more documented cerebrovascular events. 3. Both clinical and genetic (e.g., cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) evidence of cerebrovascular disease is present. Possible vascular neurocognitive disorder is diagnosed if the clinical criteria are met but neuroimaging is not available and the temporal relationship of the neurocognitive syndrome with one or more cerebrovascular events is not established.	

Major or Mild Neurocognitive Disorder Due to Traumatic Brain Injury

DSM-5 Diagnostic Criteria	Applying Criteria for Mild-Profound ID
A. The criteria are met for major or mild neurocognitive disorder	A. No change, but see concerns about mild neurocognitive change
B. There is evidence of a traumatic brain injury – that is, an impact to the head or other mechanisms of rapid movement or displacement of the brain within the skull, with one or more of the following: 1. Loss of consciousness 2. Posttraumatic amnesia 3. Disorientation and confusion 4. Neurological signs (e.g. neuroimaging demonstrating injury; a new onset of seizures; a marked worsening of a pre-existing seizure disorder; visual field cuts; anosmia; hemiparesis	B. No Change
C. The neurocognitive disorder presents immediately after the occurrence of the traumatic brain injury or immediately after recovery of consciousness and persists past the acute post-injury period.	C. No Change

Substance-/Medication-induced Major or Mild Neurocognitive Disorder

DSM-5 criteria for substance-medication-induced neurocognitive disorder are the same as for other mental disorders, without adaptation, with the additional need for presence of the criteria for major or mild neurocognitive disorder.

Major or Mild Neurocognitive Disorder Due to HIV Infection

Major or Mild Neurocognitive Disorder Due to Prion Disease

Major or Mild Neurocognitive Disorder Due to Parkinson's Disease

Major or Mild Neurocognitive Disorder Due to Huntington's Disease

Major or Mild Neurocognitive Disorder Due to Another Medical Condition

Major or Mild Neurocognitive Disorder Due to Multiple Etiologies

Unspecified Neurocognitive Disorder

DSM-5 also provides criteria for major and mild neurocognitive disorders due to HIV, prion disease, Parkinson's disease, Huntington's disease, or multiple etiologies. No modifications are suggested to these criteria. There is also a category for unspecified neurocognitive disorder.

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