

Moran, JA et al

Word count: 5529

Number of tables: 3

Number of Supplemental Tables: 3

Number of references: 41

**The National Task Group on Intellectual Disabilities and Dementia Practices
Consensus Recommendations for the Evaluation and Management of Dementia in
Adults with Intellectual Disabilities**

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Financial support and disclosures:

Moran, JA et al

The authors have no disclosures

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Abbreviations:

I/DD: Intellectual and Developmental Disabilities

NTG: National Task Group on Intellectual Disabilities and Dementia Practices

Acknowledgements:

This document represents the collective efforts of many members of the National Task Group on Intellectual Disabilities and Dementia Practices, with the lead for organizing, synthesizing and producing the information attributed to the authors. The NTG is indebted to the NTG members who offered comments, suggestions, and recommendations. Support for these efforts has been provided by the American Academy of Developmental Medicine and Dentistry and by Grant # H133B080009 to the Rehabilitation Research and Training Center on Aging and Developmental Disabilities - Lifespan Health and Function at the University of Illinois at Chicago from the U.S. Department of Education, National Institute on Disability and Rehabilitation Research.

Abstract:

Adults with intellectual and developmental disabilities (I/DD) are now regularly reaching old age, and are increasingly presenting to their health care providers with concerns related to growing older. One particularly challenging clinical question is related to the evaluation of suspected cognitive decline and potential dementia in older adults with I/DD, a question that most physicians feel ill-prepared to answer or address. The National Task Group on Intellectual Disabilities and Dementia Practices (NTG) was convened to help formally address this topic, which remains largely underrepresented in the medical literature. The task group, comprised of specialists who work extensively with adults with I/DD, has promulgated the following Consensus Recommendations for the Evaluation and Management of Dementia in Adults with Intellectual Disabilities as a framework for the practicing physician who seeks to approach this clinical question practically, thoughtfully, and comprehensively.

Introduction: The National Task Group (NTG) on Intellectual Disabilities and Dementia Practices

The National Task Group (NTG) on Intellectual Disabilities and Dementia Practices was formed as a response to the National Alzheimer's Project Act (NAPA), legislation signed into law by President Barack Obama. One objective of the NTG is to highlight the additional needs of individuals with intellectual and developmental disabilities who are affected or will be affected by Alzheimer's disease and related disorders. The American Academy of Developmental Medicine and Dentistry (AADMD), the Rehabilitation Research and Training Center on Aging with Developmental Disabilities-Lifespan Health and Function at the University of Illinois at Chicago, and the American Association on Intellectual and Developmental Disabilities (AAIDD), combined their efforts to form the NTG to ensure that the concerns and needs of people with intellectual disabilities and their families, when affected by dementia, were and continue to be considered as part of the National Plan to Address Alzheimer's Disease¹ issued to address the requirements of NAPA.

Among the NTG's charges were the (a) creation of an early detection screen to help document suspicions of dementia-related decline among adults with intellectual disabilities, (b) development of practice guidelines for health care and supports related to dementia among adults with intellectual disabilities, and (c) identification of models of community-based support and long term care of persons with intellectual disabilities

affected by dementia. In 2012, the NTG issued, “*My Thinker's Not Working': A National Strategy for Enabling Adults with Intellectual Disabilities Affected by Dementia to Remain in Their Community and Receive Quality Supports.*”²

A subgroup of the task group was formed to focus specifically on health practices. The guidelines and recommendations outlined in this document represent the consensus reached amongst said specialists at two plenary meetings and ongoing discussions that followed, informed by review of current literature and drawn from each specialist’s clinical practice, and thus meet level 2 (case-controlled studies) and level 3 (observational studies) for evidence in clinical application. These guidelines are a suggested starting point as we develop more formal methodologies to determine best-practices of evaluation of dementia in this population.

Background

Adults with intellectual and developmental disabilities (I/DD) are now regularly living into old age, with many surviving into their 70s, 80s and beyond. Dementia is among the most clinically challenging co-occurring conditions of aging among a select group within this population (i.e., those adults with Down syndrome and those with brain injury), considering that the approach to evaluation, diagnosis, treatment, and management of dementia in adults with I/DD remains largely undefined in the literature.

It has been well established that adults with I/DD experience poorer health outcomes compared to the general population, a trend seen in mortality, morbidity, and quality of life.^{3,4} The cause of this disparity is complex and multifactorial, but poor training and preparedness among health care providers nationwide ranks among the key contributing factors. Formal didactic training on adults with I/DD throughout the lifespan is not routinely incorporated into U.S. medical school or residency training.⁵

Recognizing these existing disparities in medical training and health care services for adults with I/DD, the National Task Group on Intellectual Disabilities and Dementia Practices organized a targeted effort to help address this gap. The goal of this paper is to clarify key principles of evaluation and management of dementia in adults with I/DD (which, for the purpose of this paper, refers to individuals 20 and older), based on evidence-based research as well as consensus among experts within the NTG.

Prevalence of dementia in intellectual disability

In Down syndrome, one of the most common forms of intellectual disability, the underlying genetic link between trisomy 21 and Alzheimer's disease has been convincingly established.^{6,7} By age 40, all adults with Down's syndrome demonstrate some degree of neuropathologic defects postmortem that meet criteria for Alzheimer's disease.^{8,9} While specific prevalence estimates may vary, generally it is accepted that approximately at minimum 50% of adults age 60 and older will evidence dementia

clinically.^{10, 11, 12} Thus, the development of clinical Alzheimer's disease is not inevitable in aging adults with Down syndrome, although risk increases incrementally with age.

In these practice guidelines we take an encompassing approach and generalize recommendations onto the broad population with intellectual and developmental disabilities, recognizing that distinct genetic and neurological factors associated with specific conditions may compromise these generalizations.

Specific challenges within the aging population in I/DD

One of the hallmark features of all causes of dementia is a decline from baseline level of function and performance of daily skills. While this is usually relatively straightforward to establish in the general population, this can be a much more complicated task in adults with intellectual disability because of variance in cognitive functioning. This is particularly true to the current generation of older adults with I/DD due to a variety of factors, including: poor record-keeping from childhood, lack of ongoing involvement from family, and involvement of multiple staff members (often due to a high degree of turnover), and inconsistencies in the physician-patient relationship that obviates knowing the person over his or her lifespan.¹³

In the absence of a personal historian who is able to accurately and comprehensively attest to an individual's baseline level of functioning, the assessment of a reported or observed change may be exponentially more complicated. The early signs of dementia in

adults with I/DD can be subtle and often require an astute observer to identify these changes proactively. Often individuals with I/DD are served by numerous caregivers throughout their lifetime, and often newly involved care providers will presume that their current level of ability represents their baseline level of functioning, and thus miss signs of early decline.¹⁴

Down syndrome and other forms of intellectual disability

Down syndrome is the only genetically-inherited form of intellectual disability that has been indisputably linked to the early formation of Alzheimer's disease. The leading explanation for this link is tied to the triplication of chromosome 21 (trisomy 21), and the overexpression of the gene coded on this chromosome for amyloid precursor protein (APP). The excessive production of beta amyloid as a result is key to the pathogenesis of Alzheimer's disease. In addition, other genes coded on 21 are also theorized to potentially contribute to both the early emergence of dementia and the phenomenon of accelerated aging seen in adults with Down syndrome.^{15, 16} Down syndrome has the most robust body of literature with regard to the correlation to dementia among persons with I/DD in older age, although there are still many unanswered and under-explored questions that remain. Comparatively, for nearly all other forms of I/DD there is a widespread scarcity of lifespan research.¹⁷

Assessment Guidelines

The NTG recommends the following procedural steps that allow for the accurate assessment of health and function with respect to the identification and validation of symptoms of Alzheimer’s dementia and related disorders (ADRDs). The steps include (a) evaluation, (b) diagnosis, (c) treatment, and (d) follow-up. As noted in the *National Plan to Address Alzheimer’s Disease*, physicians and other health care providers need information on how to implement the “detection of any cognitive impairment” requirement in the Medicare Annual Wellness Visit included in the Affordable Care Act.^{18, 19} The following guidelines also address this process and offer suggestions on how to meet this requirement.

Evaluation

History is the cornerstone of a dementia diagnosis. It is important that a thorough and comprehensive history be conducted to compile evidence consistent with an emerging dementia while probing for other features or patterns that might suggest other contributing factors. Pertinent historical information is particularly useful from personal accounts of caregivers and family members who have known the individual for several years. In addition, other sources of information such as previous neuropsychological testing or school IEP information can greatly assist in accurately characterizing and individual’s baseline. One model for obtaining such a history is elaborated in a separate NTG publication regarding community supports.²⁰ To perform the evaluation process, we recommend the following 9-step approach.

Step 1: Gather pertinent medical and psychiatric history. A thorough history should include, of course, a review of past medical and psychiatric history, with particular attention to issues of one's personal health that could potentially influence likelihood for development of a premature dementia. These include:

- history of cardiovascular disease
- history of cerebrovascular disease or stroke
- known underlying neurologic structural abnormalities
- history of head injury, concussion, loss of consciousness
- poorly treated sleep disorders or thyroid disease, vitamin B12 deficiency, metabolic syndrome (obesity, diabetes, hypertension)

Step 2: Obtain a historical description of baseline functioning. As discussed earlier, a dementia diagnosis requires evidence of change from a prior level of functioning, and this 'baseline' is quite individualized in people with I/DD. This is highly dependent on the historian, and thus a family member or caregiver who knows the individual well should be present for this interview.

Supplemental Table 1 outlines the key factors to review when constructing a historical baseline for an individual undergoing assessment for dementia (available online at <http://www.mayoclinicproceedings.org>)

Step 3: Obtain a description of current functioning and compare to baseline.

Information-gathering regarding current functioning is obtained in a similar fashion as

was done in the historical baseline, allowing a side-by-side comparison of scope and degree of change over time. This practice helps systematically assess for the key criteria of dementia, specifically: “dementia is diagnosed when there are cognitive or behavioral symptoms that 1) interfere with the ability to function at work or at usual activities; and 2) represent a decline from previous levels of functioning and performing.”²¹ Key features to look for included reported memory loss or impairment, significant changes in personality, disorientation, and decreasing performance in expected tasks/skills.

Step 4: Perform a focused review of systems. A focused review should take an inventory of common issues that are seen with increasing age and also with possible emerging dementias. Supplemental Table 2 summarizes the system areas that should be highlighted in an assessment of an adult with I/DD (available online at <http://www.mayoclinicproceedings.org>)

Step 5: Review the medication list thoroughly. Medications require specific focus, as the risk of polypharmacy and the involvement of multiple prescribing providers increases with advancing age. Special attention should be paid to all newly-added medications, particularly those that are psychoactive, antiepileptic, or anticholinergic, as well as those with sedating properties. Common side effects and drug-drug interactions should be reviewed, with attention paid to non-specific signs and symptoms that might suggest a drug side effect, such as somnolence, gait instability, urinary retention, to name a few.

Table 1 lists commonly used medications with potential deleterious effects on cognition in this population.

Insert Table 1 about here

Step 6: Obtain pertinent family history. Family history is important primarily for detecting a history of dementia in first-degree relatives, particularly if the disease presented prematurely (generally under age 50, except among adults with Down syndrome), suggesting a stronger possible familial predisposition. Additional factors of note include: history of cerebrovascular disease, stroke, diabetes, heart disease, and rheumatoid arthritis or systemic lupus erythematosus (SLE) in first-degree relatives.

Step 7: Assess for other psychosocial issues or changes. Aging adults with I/DD often confront a wide variety of potentially destabilizing life events merely by virtue of growing older. These events may include: leaving the family home, witnessing the declining health or death of a parent, loved one, or friends/housemates, decline in one's own health, functionality, or employment status, or frequent turnover/departure of caregivers. The cumulative impact of these events in an adult with I/DD who may have limited coping skills or emotional maturity cannot be overstated. A careful assessment for these factors could identify certain triggering events and frequently also help in the identification of other coexisting mood disorders, such as untreated anxiety or depressed mood, which could be strongly influencing an individual's cognitive and functional performance.

Psychiatric illness may present atypically in adults with I/DD and there is a common pitfall of diagnostic overshadowing, where features truly related to an underlying mental illness are instead attributed to the individual's intellectual disability. The method of history taking described above helps account for changes in baseline mood, behavior, or personality, which should raise red flags for a possible emerging psychiatric/mental health disorder. Pay close attention to the review of systems to highlight other potential neurovegetative signs of appetite changes, weight loss, and change in sleep patterns. In Down syndrome, depression and other prefrontal lobe symptoms may be more common in dementia. These include signs and symptoms of: indifference, uncooperativeness, apathy, depression and socially deficient communication or impaired adaptive functioning in general.²² For a review of features of mental disorders that may present atypically in adults with I/DD, the Dementia Manual – Intellectual Disability (DM-ID) is a particularly helpful desk reference.²³

Step 8: Review social history, living environment, and level of supports. Assessment of current living conditions and level of support is increasingly critical when an emerging dementia is suspected, as evaluation of safety concerns and appropriateness of one's current placement is a priority. Even if current supports appear to be adequate it is important to think proactively in the setting of a suspected dementia, knowing that there will be ever-changing and increasing needs.

Step 9: Synthesize the information. As the history and all supporting data are obtained in a stepwise fashion, the interviewer is advised to continually mentally cross-reference the information with the criteria for a dementia diagnosis, building a case of evidence for or against the diagnosis. By the end of the history taking a fairly strong level of suspicion should already be built.

Physical Examination

A physical examination in the setting of a suspected dementia should keep a keen eye out for physical findings that may suggest underlying medical issues that may be contributing to the patient's current presentation. Supplemental Table 3 summarizes the key components of focus during an office examination for suspected dementia (available online at <http://www.mayoclinicproceedings.org>).

Cognitive Assessment

Currently, there is no generally accepted gold standard for memory screening or assessment in adults with I/DD. Assessment tools used in the general population (e.g, Folstein Mini Mental Status Examination, Montreal Cognitive Assessment; see also Cordell et al., 2013 for a recent compendium of assessment tools appropriate for the Annual Wellness Visit under the Affordable Care Act)²⁴ have not been normed for adults with intellectual disabilities, and thus results cannot be interpreted meaningfully in adults with I/DD. The NTG has made the following recommendations for a general framework of cognitive assessment:

Inclusion of at least one standardized tool for cognitive assessment is recommended, as it generates a score that can be tracked over time and provides an additional rigid data point that can be repeated on subsequent encounters. Many instruments of been developed and validated for diagnosis of dementia in this population including the Dementia Scale for Down's Syndrome (DSDS),²⁵ the Dementia Questionnaire for People with Learning Disabilities (DLD)^{26, 27} and the Cambridge Examination for Mental Disorders of Older People with Down's Syndrome,²⁸ the DSMSE - Down's syndrome Mental Status Examination,²⁹ and the Test for Severe Impairment.³⁰ Regardless of the clinician's choice of instrument, the focus should be centered on recognizing change and decline in relation to a premorbid baseline.

In addition, the initial interview and exam can be adapted to assess performance in a variety of cognitive domains. This could be performed in the office or at the bedside if questions are flexible enough to be appropriate for the individual's baseline intellectual ability. To further enhance the information provided by the test batteries suggested above, providers are encouraged to include additional questioning to assess the individual's general orientation, writing/writing/math skills (if applicable), naming abilities (body parts, common objects), basic motor skills, general knowledge (counting, days of the week), language comprehension, and recall of newly learned information. All of these components could be fairly easily added to a provider's questioning repertoire and can help point to changes if abilities decay over subsequent visits.

Diagnosis

There exists great heterogeneity in adults with I/DD and thus there is no basis for comparison against any other set of peer-based percentiles, standards, or generalized sets of expectations when assessing an individual for dementia. Assessment of decline should always be individualized and patient-specific, with judgments made based on a deterioration from the patient's own individual baseline level of intellectual disability, function, and achievement (i.e., their 'personal best').

A dementia diagnosis should never be arrived upon at the expense of a proper investigation into other contributing factors that are potentially correctable. There are several co-occurring issues that frequently masquerade as dementia or negatively compound the effects of an early dementia. Table 2 summarizes these common conditions that should be assessed during a general evaluation in an effort to identify contributors, and more importantly, to look for elements that can be treated or improved.

Insert Table 2 about here

The workup following an office cognitive assessment should be customized to the specific signs and concerns of each individual patient. Further assessment of one or more of the above components may comprise the "homework" that a patient's caregiver or referral agency may be instructed to complete following their first assessment.

Laboratory testing is justifiable in nearly every patient seeking cognitive assessment, as blood work is potentially high-yield for uncovering or ruling out multiple common conditions that might influence cognition. Complete metabolic panel, thyroid function

tests, B₁₂, folate, liver function tests and complete blood count should routinely be performed. Use of neuroimaging is recommended on a case-by-case basis, and features that should prompt consideration of brain imaging would include: focal findings on neurologic examination, underlying known structural abnormalities without recent imaging, suspicion of/high risk factors for cerebrovascular disease, rapid and sudden neurologic/cognitive deterioration, history of recent fall with head injury, or past history of repeated head trauma. Particularly in patients where the history is quite fragmented, treatable causes of functional decline such demyelinating disease, infection, intracranial mass and infections may be missed if imaging is not considered. Thus, proceeding with MRI or noncontrast CT scan is recommended, particularly if select brain features may lead to a differential diagnosis of the type of dementia.

Recommendations for additional testing or procedures are patient-specific, based on the components listed above re: suspicion for other contributing factors. These may commonly include, and are not limited to: ophthalmology testing, cerumen disimpaction, audiology testing, referral for sleep studies, consideration of anti-depressant trial (if symptoms are present), referral to psychiatry, or a therapist or behaviorist, EEG, EKG (if arrhythmias or dysautonomia suspected), or additional recommendations to minimize polypharmacy.

Treatment

Treatment of dementia involves both a pharmacologic and non-pharmacologic approach. The pharmacologic treatment of dementia may include medications that are meant to

slow the progression of cognitive decline, as methods of neuroprotection or curative treatment are not yet available. Medications may also be used to help with challenging behaviors in adults with I/DD and dementia. Treating affective behavior and psychotic behavior is a challenge which may improve the individual's function but the benefits must be carefully weighed against potential side effects, and one may consider partnering with a psychiatrist for further expert guidance in this situation.

Data specifically focused on pharmacologic treatment interventions for adults with I/DD (and Down syndrome specifically) are quite limited, with many studies flawed by small sample sizes, non-blindedness of study design, and variable inclusion criteria for dementia. The current FDA approved medications for Alzheimer's disease either raise the levels of acetylcholine (Donepezil, Rivastigmine, Galantamine) or block the activity of the neurotransmitter glutamate within the brain (Memantine). In the 2009 Cochrane Collaboration conducted reviews of Donepezil, Rivastigmine, Galantamine, and Memantine^{31, 32, 33, 34} and their use in treating adults with Down syndrome indicated that there is a dearth of rigorous data in this field, as only one study was identified to meet criteria for review. Further, a 2011 study focused on Memantine in adults with Down syndrome provided discouraging results, with no significant improvement noted in the treatment group vs. placebo at one year follow up.³⁵ Table 3 summarizes the some of the limited studies in of cholinesterase inhibitors on DS.

Insert table 3 here

There remains little evidence from the current literature about the efficacy, safety, and tolerability of pharmacologic interventions for dementia in adults with I/DD. Current practice now is largely variable and typically extrapolated from standard treatment principles applied to the general population with dementia. The question of efficacy and response to cholinesterase inhibitors and Memantine in the general population is challenging in and of itself, with outcomes often reflected as a very modest improvement in cognitive subscales and measurements of functionality.

Other treatment options are dictated by what is uncovered in the workup of other contributing factors. Treatment of these issues may be quite gratifying, as some underlying issues may be highly improvable, such as: correction for vision impairment, cerumen disimpaction, amplification for hearing deficits, initiation of antidepressant therapy, initiation or adjustment of thyroid supplementation, adjustment, elimination, or dose-reduction of problematic medications, initiation of CPAP or other non-invasive measures for improvement of sleep disorders, behavioral or environmental modifications, and treatment for suspected underlying pain, discomfort, and mobility difficulties.

Occupational and physical therapy consults should be considered in helping to enable the individual and care staff in helping with current difficulties in ADLs and trying to sustain current levels of function.

Pharmacologic treatment of dementia comprises only a portion of the treatment plan.

The large majority of the treatment approach should be non-pharmacologic, via

communication and environmental and behavioral strategies. This topic is addressed and outlined in rigorous detail in Jokinen et al, 2013, another publication by the NTG.

Follow up

At the conclusion of the initial assessment, it is recommended that a follow-up visit be planned with the goal of reviewing results of requested studies and to assess response to any recommended interventions. If there is any question, it is often prudent to suspend any formal diagnosis of dementia until at least the second meeting, to allow for proper investigation into other contributing factors in the intervening months.

There is no consensus or formal framework by which a provider treating an individual with I/DD can judge an individual's response to dementia treatment. Outcome measures used in drug studies for adults with Down syndrome and dementia typically include: measures of cognition, neuropsychiatric features, adaptive behavior, or scores on subsequent standardized testing. Certainly, assessment of compliance and tolerance of these medications should be a priority in all first follow-up visits. Thereafter, response to medication and decision-making for continuing treatment is judged primarily based on subjective and objective findings during the interview and follow up memory testing. As the impact of these drugs is often subtle and the theoretical mechanism is to slow the progression of disease, if the patient is tolerating the medication, it is often generally justifiable to continue treatment until at least moderate-stage disease or beyond.

Over the course of the disease, regular support and education are critical. It is helpful to provide a general estimate of the stage of the disease (early, mid-stage, or late stage) to the caregiver, to help provide stage-specific education and expectations. Early stage disease warrants counseling regarding communication strategies, modification of expectations at home/day/work program, safety concerns, behavior or personality changes, and adapting level of supervision and support to account for short-term memory loss.

Anticipatory guidance is necessary to prepare caregivers for changes and for setting realistic expectations going forward. In the early stages of disease, it is recommended to educate caregivers on certain features that commonly accompany progression to mid-stage, including: dysphagia, mobility impairments, new or worsening urinary incontinence, and seizures. When the individual begins to exhibit changes consistent with mid-stage disease, anticipatory guidance should shift to more goal-directed discussions about future planning, advance directives, and goals of care. Having this discussion proactively allows for the caregiver to consider scenarios that may be encountered in late-stage disease, while avoiding having to make decisions in a crisis situation.

One important complicating factor that adds a significant layer of complexity to this discussion when caring for individuals with I/DD is the issue of guardianship and/or proper identification of a decision-maker. The discussion described above would ideally be held in-person during an office encounter with the health care proxy or guardian present. It is common for some older adults with I/DD to have a court-appointed guardian

or health care proxy who may be a family member or someone else. Thus engaging the decision-maker in this important discussion may often be easier said than done, but nonetheless extremely important.

Need for future research and study

As more individuals with I/DD regularly reach old age, the need for further lifespan research within this field cannot be overstated. There is a dearth of syndrome-specific information that can provide insight into common co-incident conditions encountered as individuals progress into adulthood and old age. There remains conflicting information and uncertainty about the relative risk of dementia for adults with all forms of intellectual disability, and this is a major barrier to proper assessment, risk stratification, and guidance. The emerging field of adult developmental medicine has extensively fertile grounds for research, both in basic science and clinical areas, especially clinical trials. This field remains small in number, but large in passion and commitment. Consensus guidelines are necessary to help standardize assessment practices among providers performing memory assessments in this growing population, and this is one of the primary aims of the NTG. In addition, continued training on lifespan issues for adults with I/DD needs to be incorporated into the general medical training of providers of adult medicine, and there are other national efforts underway in this regard. Lastly, the efforts of specialists currently working within this field need to be harnessed in a formal fashion and supported through funding opportunities, so that efforts such as those undertaken by this National Task Group can be continued.

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Table 1. Medications associated with possible worsening cognitive function in patients with dementia.

| Common Offensive Medication Classes | Examples | Comments |
|--|--|---|
| Antihistamines, especially first generation | Diphenhydramine Hydroxyzine Promethazine | Anticholinergic adverse effects, urine retention, confusion, sedation |
| Bladder agents | Oxybutynin Tolterodine | Anticholinergic adverse effects, urine retention, confusion, sedation. |
| Certain pain medications | Meperidine Propoxyphene | Meperidine –increased risk of seizures with renal impairment. |
| Tricyclic Antidepressants (TCAs) | Amitriptyline Clomipramine Doxepin | The risks and benefits of this medication should be guided by a psychiatrist with familiarity with patients with I/DD. |
| Certain antipsychotics | Chlorpromazine Clozapine Pimozide | Atypicals have been associated with increased mortality when used to treat behavioral problems in elderly with dementia but no such studies have been conducted in Down syndrome or I/DD in general |
| Long acting benzodiazepines | Clonazepam Temazepam | Very sedating. Caution for gait impairment, dizziness If benzodiazepine required |

| | | |
|--|----------|---|
| | Diazepam | for anxiety, consider short acting agent (appropriately dosed): alprazolam, lorazepam |
|--|----------|---|

Table 2: Common contributors to memory changes in adults with I/DD

| Condition | Presentation |
|--|--|
| Sensory deficits | <ul style="list-style-type: none"> • <i>Hearing loss</i> • <i>Vision loss, low vision, depth perception changes</i> |
| Metabolic disturbances | <ul style="list-style-type: none"> • <i>Electrolyte abnormalities</i> • <i>Hypo/hyperglycemia</i> • <i>B₁₂ or folate deficiencies</i> • <i>Undetected thyroid dysfunction</i> • <i>Anemia</i> • <i>Toxic levels of anti-epileptic or psychoactive medications</i> • <i>Toxic side-effects of certain medications (e.g., hyperammonemia in chronic Depakote use).</i> |
| Coexisting mood disorder | <ul style="list-style-type: none"> • <i>Either newly detected or subacute worsening of baseline mood disorder</i> • <i>Note: Depression can cause symptoms that appear similar to dementia and can also co-occur with an early dementia.</i> |
| Pharmacologic concerns | <ul style="list-style-type: none"> • <i>Polypharmacy, drug-drug interactions and altered pharmacokinetics</i> |
| Sleep problems | <ul style="list-style-type: none"> • <i>Sleep apnea and other undetected sleep disorders</i> |
| Seizures | <ul style="list-style-type: none"> • <i>Undetected or worsening seizure disorders</i> |
| Pain | <ul style="list-style-type: none"> • <i>Undiagnosed pain or undertreated pain</i> |
| Mobility problems | <ul style="list-style-type: none"> • <i>Mobility disorders and loss of functionality</i> |
| Psychosocial or environmental stressors | <ul style="list-style-type: none"> • <i>Changes in routines, death or impairment of family members or close acquaintance, new regime at home or in work place, reactions to threatening situations</i> |
| Others | <ul style="list-style-type: none"> • <i>Conditions that may be associated with cognitive deficit (chronic subdural hematoma,, brain tumors, multiple sclerosis, human immunodeficiency virus and cryptococcal infection)</i> |
| Additional considerations: Prevalent conditions in adults with Down | <ul style="list-style-type: none"> • <i>Vision impairment, due to early development of cataracts and increased risk of keratoconus</i> • <i>Hearing loss, due to conductive hearing deficits</i> • <i>Thyroid dysfunction, particularly hypothyroidism</i> |

| | |
|-----------------|---|
| syndrome | <ul style="list-style-type: none"> • <i>Ostructive sleep apnea</i> • <i>Celiac disease</i> • <i>Atlantoaxial instability and other cervical spine disorders, including osteoarthritis and spinal stenosis</i> • <i>Osteoarthritis and associated pain and/or mobility limitations</i> |
|-----------------|---|

Table 3: Cholinesterase inhibitors in Adults with Down Syndrome with and without Dementia

| Author | # of subjects | Study Type | Results |
|--|----------------------|-----------------------------|-----------------------------|
| Kishnani, PS et al., Lancet 1999 ³⁶ | 4 | Case Reports | Improvement |
| Prasher VP et al. Int J of Geriatric Psych, 2013 ³⁷ | 23 | Case Control | Non-significant Improvement |
| Heller JH et al AJ Medical Genetics 2003 ³⁸ | 6 | Case Reports | Improvement in language |
| Johnson N et al, AJMR, 2003 ³⁹ | 19 | Randomized controlled trial | Improvement in language |
| Prasher, VP et al., Intl J Ger Psych. 2002 ⁴⁰ | 27 | Randomized controlled trial | Non significant improvement |
| Lott, IT et al., Arch Neuro 2002 ⁴¹ | 15 | Case Control | Significant Improvement |

Supplemental Table 1: Key factors of a historical baseline description:

| Baseline domains | Examples of specific questions to ask |
|-------------------------|--|
| Function | <i>What was the highest level of independence achieved with self-care tasks? Review all basic activities of daily living (ADLs): dressing, bathing, grooming, toileting, eating, walking.</i> |
| Skills | <i>What level of academic achievement was reached? Did he/she obtain reading, writing, math or money skills? Inquire about employment history. Did he/she hold a job in the community? Earned a paycheck? Worked in a workshop? If no employment history, did he/she attend a day program? What activities would he/she do at program? Describe chores or responsibilities the individual was capable of in the home. Any other talents or skills throughout lifetime?</i> |
| Memory | <i>Describe the individual's ability to remember short term information. Was he/she able to keep track of the day of the week, upcoming events? Was he/she able to learn and remember names of people? Any particular memory strengths? E.g, Memorizing family birthdays, phone numbers, words to songs, sports statistics, etc.</i> |
| Behavior | <i>Any history of problematic behavior that is longstanding? Obtain description of verbal or physical aggression, self-injurious behavior (skin picking, head banging, etc.), wandering, , pica, hoarding, and history of self-talk?*</i> |
| Language | <i>Describe baseline expressive abilities: Did he/she speak in full sentences? Phrases or single words? Used words to communicate basic needs and wants? Describe baseline receptive abilities: was he/she able to understand spoken language? Could follow a basic verbal instruction, carry on a conversation?</i> |
| Personality | <i>Was he/she social? Loved people? Loved attention? Preferred to be alone? Was he/she outgoing? Fun loving? Dramatic? Liked to joke around?</i> |
| Mood | <i>Generally calm and easy-going? Happy? Labile? Grouchy?</i> |

**Self-talk is common and frequently developmentally appropriate, given the baseline intellectual levels of intellect. It is very helpful to ascertain whether tendency toward*

self-talk is a baseline characteristic, as it may be wrongly interpreted as a feature of psychosis if not thoroughly probed.

Supplemental Table 2. Review of systems

| System/Domain | Specific questions and symptoms |
|---------------------------------------|---|
| Constitutional: | <ul style="list-style-type: none"> • <i>Does the patient typically reliably report pain?</i> • <i>Any reports of pain or any nonverbal signs/suspicion of underlying unreported pain?</i> |
| Head, Eyes, Ears, Nose, Throat | <ul style="list-style-type: none"> • <i>Any low vision or other known underlying vision deficits</i> • <i>Evidence of poor depth perception</i> • <i>Details of recent eye exams</i> • <i>Low hearing or any known underlying hearing deficits</i> • <i>History of frequent cerumen impactions</i> • <i>Date of last audiology examination</i> • <i>Frequency of dental visits</i> • <i>Any current or past dental disease, specifically any issues that are potential sources of pain/discomfort</i> |
| Gastrointestinal: | <ul style="list-style-type: none"> • <i>Any nausea, vomiting, diarrhea, constipation, abdominal pain or heartburn</i> • <i>Any recent weight changes (loss or gain)</i> • <i>Loss of appetite, disinterest in food.</i> • <i>Any previous investigations for weight loss (GI evaluation, endoscopy, etc)</i> • <i>History or current signs/concerns of dysphagia or choking</i> • <i>details of prior swallowing assessments</i> |
| Pulmonary | <ul style="list-style-type: none"> • <i>history of sleep disorders, past sleep assessments</i> • <i>Review sleep patterns: fragmented sleep, difficulty arousing, daytime somnolence and napping</i> |

| | |
|---|--|
| Neurologic: | <ul style="list-style-type: none"> • <i>Any headaches, weakness, change in voice, change in sensation</i> • <i>Trouble walking, balance problem, coordination problem, tremors</i> • <i>Any recent falls, date of last fall, timing, frequency, and descriptive details as known</i> • <i>Speech problem, difficulty following commands</i> • <i>Past seizure history, including date of last seizure.</i> • <i>Any staring spells, or confusional episodes</i> • <i>Recent neurology visits and medication adjustments.</i> • <i>For patients without a seizure disorder, inquire generally about any recent activity that was suspicious for seizure (behavior change or episodes of confusion, staring, drooling and incontinence).</i> |
| <i>Remainder of standard review of systems questions would be determined by patient's clinical history and individual complaints.</i> | |

Supplemental Table 3: Key components of physical examination

| Body area | Assessment |
|------------------------|---|
| Eyes | <ul style="list-style-type: none"> • <i>fundoscopic assessment for cataracts</i> • <i>gross evaluation for changes of keratoconus</i> • <i>assessment for other signs of eye disease</i> |
| Ears | <ul style="list-style-type: none"> • <i>detection of cerumen impactions (and cleaning if possible)</i> • <i>look for underlying middle ear concerns</i> • <i>perform gross hearing testing</i> |
| Oral/Dental | <ul style="list-style-type: none"> • <i>assess for gross signs of dental disease and sources of unreported pain or discomfort</i> |
| Thyroid | <ul style="list-style-type: none"> • <i>assess for enlargement or nodules</i> |
| Abdominal | <ul style="list-style-type: none"> • <i>assess for signs of constipation, reproducible pain, distended bladder</i> |
| Musculoskeletal | <ul style="list-style-type: none"> • <i>look for signs of contractures, crepitus, range-of-motion deficits, valgus deformities, or any other underlying sources of pain or discomfort</i> |
| Back | <ul style="list-style-type: none"> • <i>look for signs of kyphosis, suspected osteoporosis, range of motion deficits, bony tenderness</i> |

| | |
|-------------------|--|
| Neurologic | <ul style="list-style-type: none">• <i>assess for focal deficits, including signs of peripheral neuropathy</i>• <i>Look for frontal release signs</i>• <i>Any rigidity or cogwheeling</i>• <i>Any apraxia, aphasia, agnosia or anomia</i> |
| Gait | <ul style="list-style-type: none">• <i>assess for instability, poor safety awareness, and other gross mobility deficits</i> |