1. **In patients with early, non-specific signs of cognitive impairment:**
    a. **Suspect dementia as a diagnosis.**

The Canadian Task Force recommends not screening asymptomatic folks 65 and older for cognitive impairment. Of course this doesn't apply to those where there is a concern raised https://canadiantaskforce.ca/guidelines/published-guidelines/cognitive-impairment/

So what is dementia, and when should we suspect it?

The term dementia describes a chronic, insidious syndrome of cognitive impairment that affects one or more areas of cognition and interferes with daily function or independence.This needs to be a significant decline from baseline. This falls in the realm of major neurocognitive disorder under the DSM5.

This is not a normal part of aging. Sure, some changes in memory and cognition speed are expected with aging, but these should be relatively minor and not interfere with function.

- *This is the difference between dementia and mild cognitive impairment. Mild cognitive impairment does not impaire ADLs, while dementia does.*

As a refresher, the 6 areas of cognition can be remembered by a mnemonic I just made up, but I think it is memorable. It's PMS CAMEL: Perceptual Motor, Social, Complex Attention, Memory, Executive Function, Language

The instrumental activities of daily living, IADLs, are unfortunately best remembered with the DEATH mnemonic: dressing, eating, ambulating, toileting, and hygiene. The activities of daily living, ADLs, are captured by SHAFT: shopping, housekeeping, accounting, food preparation, and travel.

Ok so dementia is declining cognition affecting function, what things should make us think about this when seeing a patient?

Functional deficits and more mild cognitive impairment isn't always obvious in short clinic visits, especially if there is a partner or family member present as the support person often unknowingly compensates for the deficits of the patient.
The family might bring up a concern of dementia, but you may have to be the one to ask.

The CDC suggests some signs of dementia, such as:

- Getting lost in a familiar neighborhood
- Using unusual words to refer to familiar objects
- Forgetting the name of a close family member or friend
- Forgetting old memories
- Not being able to complete tasks independently

These are definitely things you can talk to patients and families about, prior to doing any formal assessment.

Perhaps there's caregiver concern, or you've noticed some deficits during the visit or on history, so you're suspecting dementia. Now what?

The objectives would have us jump to formal cognitive assessment, but I think that's a bit premature. Instead, let's talk about a differential and come back to formal cognitive assessment.

2. In patients with obvious cognitive impairment,
a. Select proper laboratory investigations and neuroimaging techniques to complement the history and physical findings and to distinguish between dementia, delirium, and depression
b. Consider possible contributing causes, including mental health, alcohol or substance use problems, or delirium

When a patient presents with cognitive impairment and we're looking to differentiate a delirium from dementia or depression, the first branch in our hypothetical diagnostic algorithm is the time course.

Delirium often progresses over a couple of days, depression may be in the weeks range, and dementia of course is months to years. *The other hallmark of delirium often quoted is the disturbance of attention or an inability to focus, sustain or shift their attention.* We will include a table in the show notes from Tintinalli's that illustrates the differences between these three conditions.

TABLE 142-1 Features of Delirium, Dementia, and Psychiatric Disorder

Characteristic	Delirium	Dementia	Psychiatric Disorder
Onset	Over days	Insidious	Sudden
Course over 24 h	Fluctuating	Stable	Stable
Consciousness	Reduced or hyperalert	Alert	Alert
Attention	Disordered	Normal	May be disordered
Cognition	Disordered	Impaired	May be impaired
Orientation	Impaired	Often impaired	May be impaired
Hallucinations	Visual and/or auditory	Often absent	Usually auditory
Delusions	Transient, poorly organized	Usually absent	Sustained
Movements	Asterixis, tremor may be present	Often absent	Absent

Without going into a tremendous amount of detail, you will want to rule out the numerous causes of delirium. For this we can use the DIMS mnemonic, or your preferred alternative.

- D for drugs, this includes medications, supplements, alcohol and other substances, as well as withdrawal.
- I for infectious or inflammatory, in the older population this is often a urinary or respiratory infection.
- M for metabolic, like electrolyte disturbances, maybe hyponatremia or hypercalcemia, or hepatic encephalopathy, among others.
- S for structural, think about strokes, intracranial hemorrhage, as well as cardiac or respiratory problems that decrease perfusion like ACS, heart failure, or COPD. Don't forget carbon monoxide poisoning either.

For each of these causes of delirium do your history and physical and order appropriate tests if needed to assure yourself the presentation of altered cognition is not delirium. You can also think about neurosyphilis and AIDS dementia, but only test for these if your clinical suspicion is high.

Next, rule out depression. This can be challenging with any patient, but even more so if the patient actually has concurrent dementia. Use a questionnaire, and a reasonable dose of collateral for this. The Geriatric Depression Scale would be reasonable here. http://www.stanford.edu/~yesavage/GDS.html

The other psychiatric condition that can overlap with Dementia is schizophrenia. Delusion with or without hallucinations in dementia can occur and misguide you. Look for:

- *A progressive cognitive decline **prior** to the psychotic symptoms*
- *The presence of impairment of multiple cognitive declines*
- Psychosis of AD compared with Schizophrenia in the elderly

Clinical Features:	Psychosis of AD	Schizophrenia
Bizarre or complex delusions	Rare	Frequent
Misidentifications of caregivers	Frequent	Rare
Common form of hallucinations	Visual	Auditory
Schneiderian first-rank symptoms	Rare	Frequent
Active suicidal ideation	Rare	Frequent
Past history of psychosis	Rare	Frequent
Eventual remission of psychosis	Frequent	Uncommon
Need for long-term treatment with antipsychotics	Uncommon	Very common

If you're satisfied that it's not delirium and not depression *or schizophrenia*, then pursue more formal cognitive and functional assessment. Realistically, this is probably going to mean a second or third office visit.

Imaging

Of course dementia is a clinical diagnosis, however, there are some circumstances where some brain imaging is indicated. You should be getting a CT brain if they have cognitive decline, and:

Indications for computed tomography in patients with cognitive decline*

- Age < 60 yr
- Rapid decline in cognition or function (1–2 mo)
- Duration of dementia < 2 yr
- Recent head trauma
- New unexplained neurologic symptoms or localizing signs
- History of cancer
- Use of anticoagulants or history of bleeding disorder
- History of gait disorder or urinary incontinence early in dementia
- Atypical cognitive symptoms or presentation
- Current gait disturbance

https://www.cmaj.ca/content/188/8/603

Objective 1b. Use validated tests of cognitive function and careful functional inquiry, as well as a careful history (including collateral history from family and caregivers if available) and physical examination, to make an early positive diagnosis.

The diagnosis of dementia requires:

- A significant decline from baseline in one of the cognitive domains
- Interference with daily function
- Not due to delirium or another medical or psychiatric cause.

A diagnosis of mild cognitive disorder can be made if the deficits in cognition do not interfere with daily function.

Identifying the cognitive domain deficit can be made easier with the various options for brief cognitive testing. These include the MMSE, MOCA, clock drawing, or Trail Making Test. All of which are reasonable choices.

The Trail Making Test part B is a new one for me, but it seems to have been well studied, and is suggested by the CMA for this purpose. This is a longer version of the first task on the MOCA where the patient connects the numbers and letters in alternating order 1-A-2-B-3-C etc. The cut off is 3 minutes or 3 errors. Link in the notes.
http://apps.usd.edu/coglab/schieber/psyc423/pdf/IowaTrailMaking.pdf

When asking about ADLs and IADLs, keep in mind we're trying to capture cognitive limitations, not necessarily physical or mobility related issues. Ideally, the patient and the family should be asked about these in separate rooms to ensure honesty.

When asking the patient about these you may need to question not just whether they do certain things for themselves, but how. That way the patient isn't just answering your questions on autopilot.
I'm not sure if this is validated but, you can propose a situation and ask what they would do. Like, take me through the steps to make a salad for dinner, or, you need to deposit a cheque, how do you do that? Compare these answers to what you expect, and to what the family tells you.

In the event of a discrepancy between testing and the history, a truly formal assessment can be completed.
https://www.uptodate.com/contents/the-mental-status-examination-in-adults

Remember to address any language barriers when completing cognitive testing or functional inquiry as this can skew results.

3. In patients with dementia, distinguish Alzheimer's disease from other dementias, as treatment and prognosis differ.
Now we get to the different types of dementia, and there are many, although Alzheimer's and vascular dementia account for the vast majority.

Let's talk about **vascular dementia** first, as this is the only non-neurodegenerative type on the list. Vascular dementia refers to cognitive impairment due to cerebrovascular disease or impaired cerebral blood flow. This isn't just strokes and intracranial hemorrhages, but also cerebral small vessel disease, which is often unrecognized initially.

These patients can experience a stepwise deterioration in cognition following strokes both big and small. The presentation here is as varied as the presentation of strokes ranging from executive function impairment to memory impairment with possible associated aphasia and apraxia.

Alternately there may be no history of stroke, but still a concerning history of progressive or stepwise deterioration. This points to the various other cerebrovascular diseases that impair blood flow.

The diagnosis of vascular dementia, requires a diagnosis of dementia, along with neuroimaging findings or history of stroke that would be considered significant enough to cause the impairments seen.

Treatment for vascular dementia involves modifying stroke risk via anticoagulation, antihypertensives, diabetes management, and statins. Cholinesterase inhibitors or memantine can be considered as frequently there is concomitant Alzheimer's. We'll talk more about these at the end of this objective.

Ok onto the rest. These include Lewy Body Dementia, Alzheimer's, Parkinson disease dementia, and frontotemporal dementia. There are some less common dementia types, but diagnosing these is out of the scope of this episode.

The distinguishing features of **Lewy Body Dementia** include visual hallucinations, parkinsonism, cognitive fluctuations, dysautonomia, sleep disorders, and neuroleptic sensitivity. The diagnosis of Lewy Body dementia requires a diagnosis of dementia and two or more features of:

- Fluctuating cognition with pronounced variations in attention and alertness
- Recurrent visual hallucinations that are typically well formed and detailed
- REM sleep behavior disorder, which may precede cognitive decline
- One or more spontaneous cardinal features of parkinsonism (bradykinesia, rest tremor, or rigidity)

SPECT or PET scan can also be used to make a diagnosis.

Treatment of Lewy Body Dementia is primarily focused on environmental and behavioural modification. However, cholinesterase inhibitors may be helpful, and parkinsonism can be treated with the typical medications like carbidopa-levodopa. Antipsychotic drugs and memantine may worsen hallucinations so caution should be used.

Parkinson disease dementia is pretty much how it sounds: dementia that develops in the setting of established parkinson disease. Treat as you would parkinson disease, and consider cholinesterase inhibitors or memantine. Symptoms of psychosis can often be treated with a small dose reduction of the parkinson disease medication, but quetiapine or clozapine can be used if needed.

Frontotemporal dementia actually includes two subtypes depending on the primary location of degeneration and the associated symptoms, either behavioural changes or aphasia. This can start to affect individuals in their 50's and is one of the causes of early onset dementia.

In the behavioural variant there is a progressive and persistent change from baseline. Diagnosis of possible frontotemporal dementia behavioural variant requires 3 of the following:

- Disinhibition
- Apathy
- Loss of empathy
- Hyperorality
- Compulsive behaviours
- Dysexecutive neuropsychologic profile

As well as exclusion of other medical or structural causes. So imaging is typically required in the form of CT or preferably MRI.

Probable frontotemporal dementia behavioural variant is the same as above in addition to a definite associated decline in function.

Hyperorality is the need for oral stimulation by putting edible or non-edible things in the mouth. Often this manifests as taking huge mouthfuls at meals that the patient cannot hope to chew and swallow, or excessive eating in general.

A dysexectutive profile describes a common pattern of dysfunction in planning, abstract thinking, flexibility and behavioural control.

Patients with frontotemporal dementia typically lack insight into their behaviours or the impact on their family so this can be troubling for the family, as well as you, the clinician responsible for them. Also, up to ⅕ may develop motor neuron disease.

The other variation of frontotemporal dementia involves a primary progressive aphasia. This includes deficits in word finding, usage, comprehension, or sentence construction, yet there is relatively intact memory and other cognitive domains.

Diagnosis of frontotemporal dementia aphasia variant requires all of:

- The prominent feature is language difficulty
- The language deficits impair activities of daily living
- Aphasia is the main deficit at symptom onset and early in the course.

They must not have:

- Deficits better explained by other medical, structural or psychiatric disorders.
- Prominent deficits in episodic or visual memory or visuoperceptual impairments
- Behavioural disturbance at onset.

Imaging is once again required to rule out a mass or similar.

There are no good medical treatments for frontotemporal dementia. Conservative interventions should be tried like environmental changes to limit the effects of behavioural issues. If needed an SSRI such as citalopram, paroxetine or trazodone, can be trialed for the behaviour aspects.

On to the main part of this objective... **Alzheimer's Disease**.

Alzheimer's is a neurodegenerative disease caused by accumulation of extracellular amyloid plaques and tau protein within neurofibrillary tangles. Both are neurotoxic.

Development of Alzheimer's is multifactorial and includes both acquired and genetic factors. Risk is increased with hypertension, smoking, diabetes, dyslipidemia, air pollution and pesticides, as well as long term use of certain medications including benzodiazepines and anticholinergics. There is also some concern about PPI use and Alzheimer's. However, risk is reduced in those who are physically active throughout life.

Alzheimer's can be classified by age of onset and family history:

- Typical Alzheimer's occurs over the age of 65.
- Early-onset Alzheimer's occurs before 65 without family history.
- Inherited Alzheimer's often occurs in the patient's 40's or 50's with a family history of similar.

Also, those with down syndrome invariably develop Alzheimer's 10 to 20 years earlier than the general population.

There are several cardinal symptoms of Alzheimer's which we'll list then talk about in depth. These are:

- Memory impairment
- Executive function and judgement
- Impairment in other cognitive domains
- Behavioural disturbance and neuropsychiatric symptoms

In Alzheimer's, episodic memory is severely affected. Episodic memory is defined as the ability to recall and mentally reexperience specific episodes from one's personal past. So events from a specific date and place. Early in Alzheimer's this is especially apparent with memory of recent events, several minutes to recent months, whereas immediate recall and distant memory are retained.

The distinction here is that one's attention has shifted away from the event or information then must shift back. This is what's tested with the delayed word recall during the MOCA or MMSE tests.

Other types of memory including procedural memory, motor learning and specific vocabulary or concepts also remain intact until much later in the disease course.

With respect to the executive function impairments, these can include reduced organization, motivation, judgement and foresight, combined with a distinct lack of insight into the impairment. As we'll talk about, this poses a problem for driving as patients will think they are capable when they are not.

Visuospatial deficits can be present early in Alzheimer's, posing further risk with driving. Language deficits are often delayed however.

The neuropsychiatric and behavioural symptoms often appear later in the disease course. These include apathy, social disengagement and irritability - which unfortunately makes this challenging to distinguish from depression. The behavioural disturbances can include agitation, aggression, wandering, and symptoms of psychosis, mainly hallucinations, delusions and misidentifcation syndromes.

Misidentification syndromes are a new one for me. This describes the delusional phenomena in which patients misidentify familiar persons, objects, or even themself, and believe that they have been replaced or transformed. It's delusional because the misidentifications are false and are not correctable by experience or reason.

There are a few other signs or symptoms of Alzheimer's which are worth mentioning. These are

- Apraxia, or difficulty performing learned motor tasks, which can be tested early on by asking the patient to pantomime the use of a comb for example.
- Olfactory dysfunction
- Sleep disturbance, including insomnia and fragmentation of sleep
- Seizures, more in the later stages of Alzheimer's or those with strong genetic components.
- Some motor changes can be seen but these are definitely late signs and presence early in the disease should prompt further work up. These include pyramidal or extrapyramidal motor signs, myoclonus, as well as return of primitive reflexes.

Two diagnostic criteria for Alzheimer's are available, the DSM-5 and the National Institute on Aging and Alzheimer's Association. These are both similar. The criteria for major cognitive disorder due to Alzheimer's, paraphrased by us, requires:

- The diagnostic criteria for dementia are met - A significant decline from baseline in one of the cognitive domains, interference with daily function, and not due to delirium or another medical or psychiatric cause.
- As well as, insidious onset and gradual progression of impairment in at least two cognitive domains, and
- Either
    - evidence of a causative Alzheimer disease genetic mutation from family history or genetic testing, or
    - all three of:
        - Clear evidence of decline in memory and learning and at least one other cognitive domain.

- Steadily progressive, gradual decline in cognition, without extended plateaus.
- No evidence of mixed etiology (ie, absence of other neurodegenerative disorders or cerebrovascular disease, or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline).

When it comes to treatment for Alzheimer's, there are a couple options to help treat the symptoms of cognitive decline. For the most part, these are not disease modifying.

The first class of medications are the cholinesterase inhibitors, including donepezil, galantamine and rivastigmine. Any one of these medications can be trialled for those with mild to moderate Alzheimer's, corresponding to a MMSE score of 10 to 26.

The next medication is memantine, an NDMA receptor antagonist. This can be added to the cholinesterase inhibitor for those with moderate to advanced dementia, which is an MMSE of 18 or less.

Up To Date suggests continuing memantine in those with advanced dementia with an MMSE less than 10 as it may have some disease modifying effect. However, given that the goal of care may be shifting toward deprescribing and a focus on quality of life at that time, it could certainly be stopped as the effect is small.

Another new medication is aducanumab, which is approved in the USA for patients with mild cognitive impairment and presence of amyloid plaques on imaging. This is supposed to be a disease modifying drug so it will be interesting to see what comes of it going forward.