

Diagnosing dementia and the caregiver role

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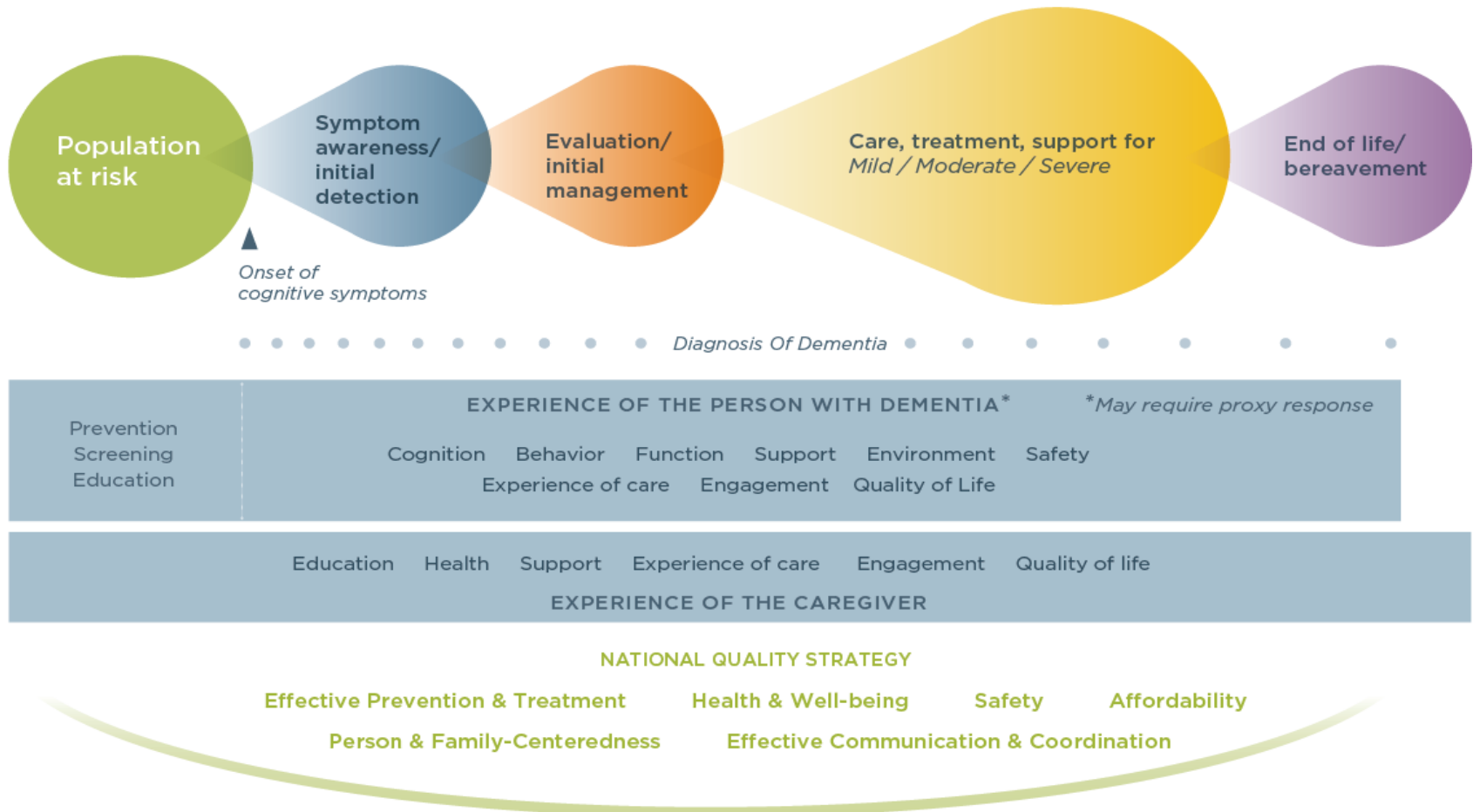
March 21st, 2016

Washington, D.C.

Lilly

When does caregiving begin?

CONCEPTUAL MODEL FOR PERFORMANCE MEASURE DEVELOPMENT FOR DEMENTIA:
Maximizing quality of life, minimizing distress



Passive Approach to Diagnosis of AD

- ◆ There may be a delay of 2 years from first noticing symptoms to the initial doctor visit and 3 years before a firm dementia diagnosis¹
- ◆ Dementia specialists diagnosed AD in only 35%, and patients did not receive adequate work-up even after diagnosis²
- ◆ Less than half of dementia cases are diagnosed by primary care physicians (sensitivity 48.2%, specificity 99.6%) and too few are referred to specialists³

1. Speechly CM et al. *Med J Aust* 2008;189:487-9
2. Phung TK et al. *Dement Geriatr Cogn Disord* 2009;27:534-42
3. Löppönen M et al. *Age Ageing* 2003;32:606-12

Differentiating AD From Other Causes of Cognitive Impairment Is Challenging

- ◆ Mild cognitive impairment (MCI) can be confused with normal aging¹
- ◆ Symptoms of AD dementia frequently overlap with those of other conditions¹
- ◆ Patients often present with multiple comorbidities, which can contribute to confusion about their diagnoses¹
- ◆ About 1 in 5 AD dementia diagnoses by experts do not have AD³⁻⁵
- ◆ A definitive diagnosis of AD is only possible at postmortem examination^{6,7}
- ◆ Differentiating degenerative or vascular etiologies from reversible ones is important²

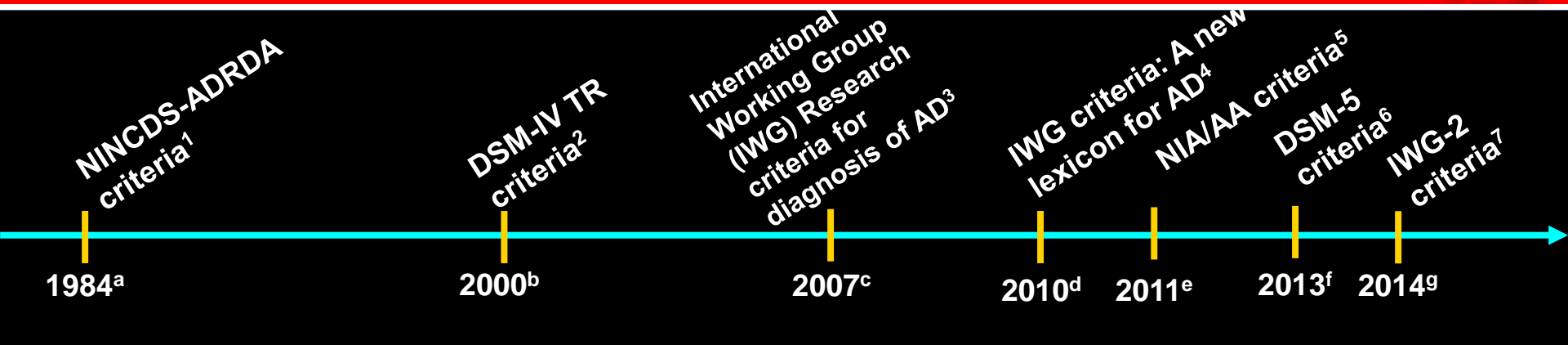
Causes of cognitive impairment include^{1,2}

- Depression
- Delirium
- Thyroid dysfunction
- B₁₂ deficiency
- Vascular dementia
- Parkinson's disease dementia
- Lewy body dementia
- Frontotemporal dementia
- Alzheimer's dementia
- Normal pressure hydrocephalus
- Substance or alcohol abuse
- Tumor
- Stroke
- Infection

1. National Collaborating Centre for Mental Health. Dementia: NICE-SCIE Guideline 2007
2. Piccini C et al. *J Neurol Sci* 1998;153:172-81
3. Lim A et al. *J Am Geriatr Soc* 1999;47:564-9

4. Petrovitch H et al. *Neurology* 2001;57:226-34
5. Witte M et al. *J Neuropsychiatry Clin Neurosci* 2014;26:214-20
6. Beach TG et al. *J Neuropathol Exp Neurol* 2012;71:266-73
7. McKhann GM et al. *Alzheimers Dement* 2011;7:263-9

Alzheimer's Disease: Diagnostic Criteria Timeline



^a Based on correlation between pathology and clinical symptoms; did not incorporate nonamnestic presentations, biomarker information, or concept of MCI; clinical focus and diagnosis of exclusion

^b Criteria for AD dementia and provisional category mild neurocognitive disorder (mild level of cognitive impairment)

^c Included early/prodromal AD stages; incorporated biomarker information, and memory impairment; formalized the idea of a continuum; becomes a diagnosis of inclusion

^d Attempt to provide a common language about disease stages and types of evidence; distinguished MCI from prodromal and incorporated atypical presentations

^e Written to address both research and clinical practices; formalized different stages of continuum: preclinical AD, MCI due to AD, AD dementia; incorporated adjunctive biomarker information; includes atypical presentations

^f Terminology shift from dementia to neurocognitive disorders (NCDs); major or mild NCD subtypes can be due to AD

^g Diagnosis simplified to require clinical phenotype and AD pathology biomarker (amyloid PET; CSF amyloid- β_{1-42} , p-tau, t-tau); MRI, FDG-PET recommended to monitor course of disease

1. McKhann G et al. *Neurology* 1984;34(7):939-44

2. American Psychiatric Association. DSM-IV TR, 2000

3. Dubois B et al. *Lancet Neurol* 2007;6(8):734-46

4. Dubois B et al. *Lancet Neurol* 2010;9(11):1118-27

5. Jack CR Jr et al. *Alzheimers Dement* 2011;7(3):257-62

6. American Psychiatric Association. DSM-5, 2013

7. Dubois B et al. *Lancet Neurol* 2014;13(6):614-29
(Updated 13: p 757)

Differential Diagnosis of Cognitive Impairment¹⁻³

First rule out and/or treat depression and delirium

Assessment of core clinical criteria for different major types of dementia

Medical and neuropsychiatric history, physical examination, informant history, objective cognitive tests

Tests to help distinguish Alzheimer's disease from other conditions and identify comorbidities

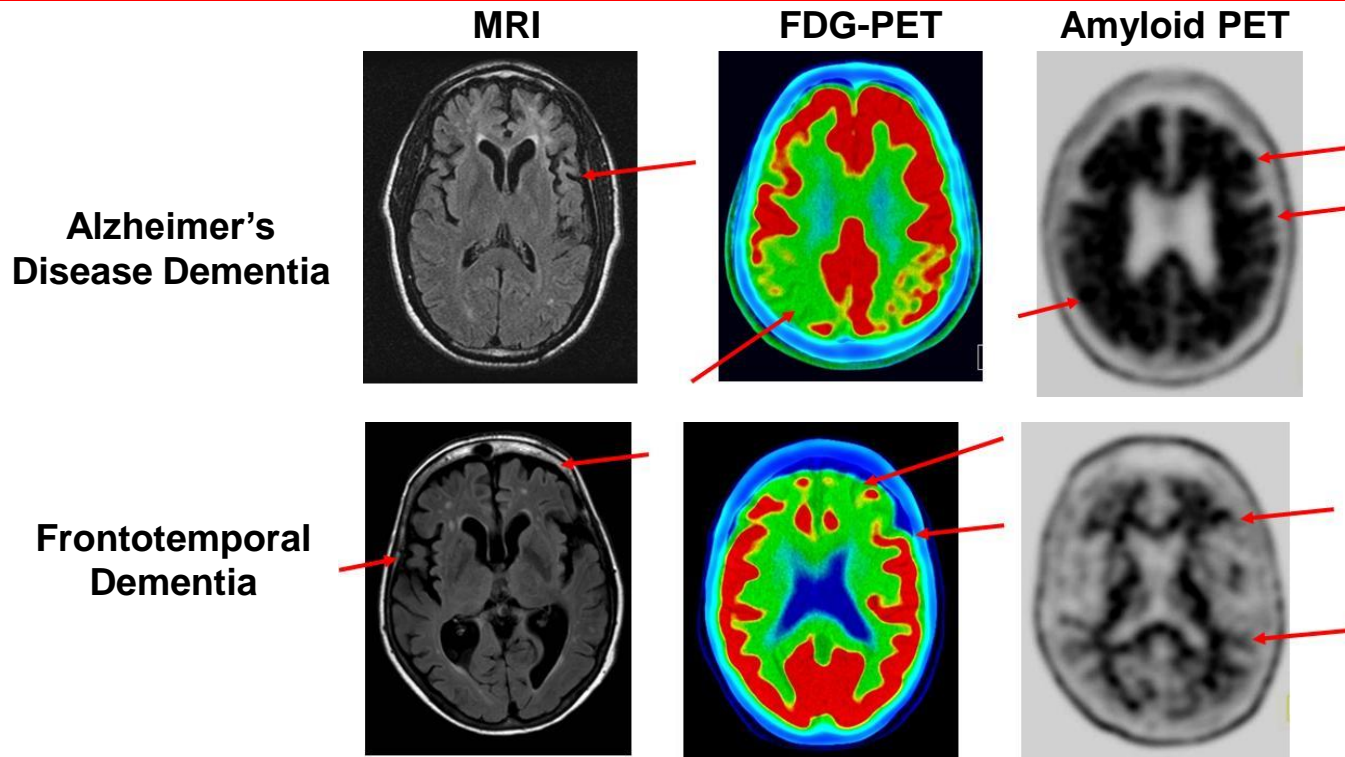
Laboratory tests (CBC, folate, vitamin B₁₂; renal, liver, and thyroid function; syphilis, HIV),
Structural neuroimaging (eg, CT or MRI scan)

Advanced diagnostics may be undertaken if uncertainty remains after the initial work-up

Advanced MRI (volumetric, DTI), molecular neuroimaging (amyloid PET, dopamine transporter SPECT), functional neuroimaging (FDG-PET, SPECT), cerebrospinal fluid analysis (A β , tau), genomic (Huntington's), neuropsychological testing

1. Hort J et al. *Eur J Neurol* 2010;17:1236-48
2. McKhann GM et al. *Alzheimers Dement* 2011;7:263-69
3. Scharre DW, Trzepacz PT. *FOCUS* 2013;11:482-500

Transverse Images From Different Neuroimaging Methods in AD and FTD Cases



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- ◆ AD example shows diffuse cortical atrophy on MRI FLAIR, temporoparietal hypometabolism on FDG-PET fused with CT, and loss of the gray-white matter border indicating abnormal amyloid burden on florbetapir PET
- ◆ In FDG-PET images, red areas represent the highest metabolism
- ◆ FTD example shows bilateral-frontal and temporal cortex atrophy on MRI FLAIR, bilateral-frontal and anterior-temporal cortex hypometabolism on FDG-PET fused with CT, and clear gray-white matter borders negative for amyloid plaque on florbetapir PET

The caregiver matters

