Optimizing outcomes for patients with Alzheimer's disease: A focus on transdermal therapy

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A conversation between:

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Conversation 1

Optimizing outcomes in AD: Overcoming barriers and addressing symptomatic treatment needs

Prof. George T Grossberg

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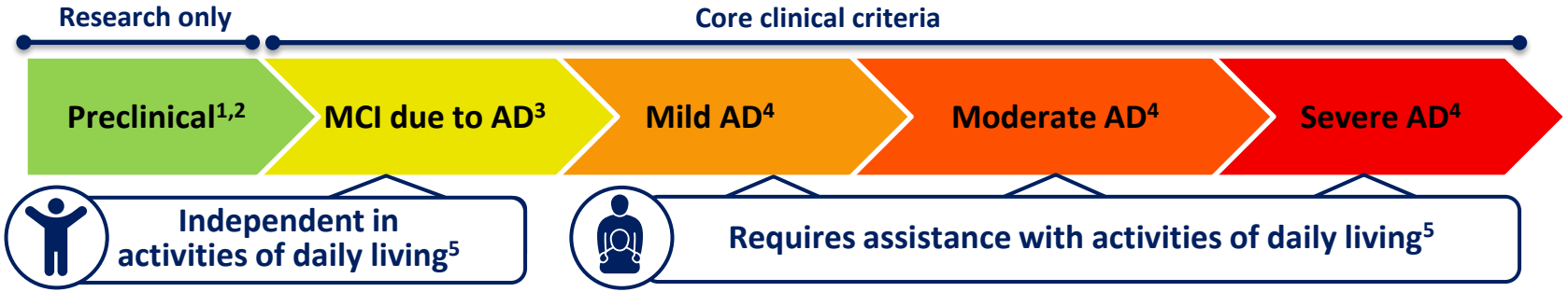
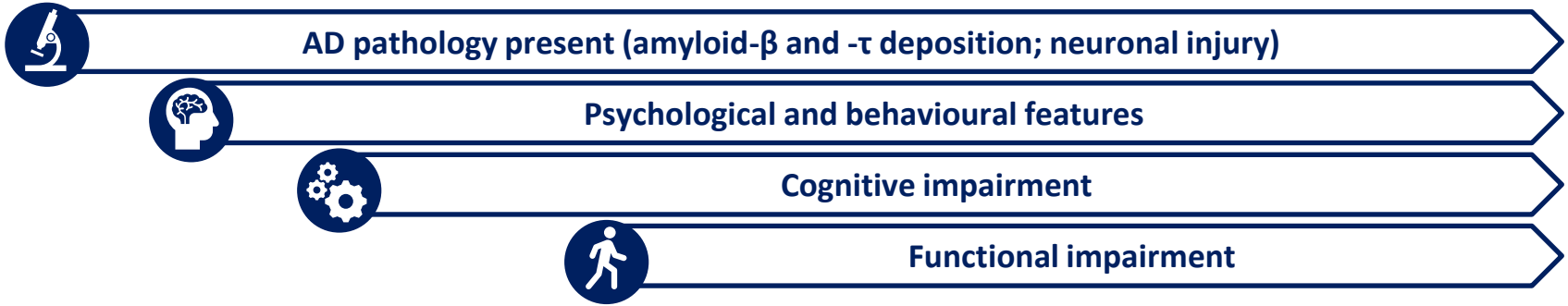
Symptoms and clinical features along the AD continuum

NIA-AA AD classification[1–4]



Underlying pathology and associated symptoms[5]



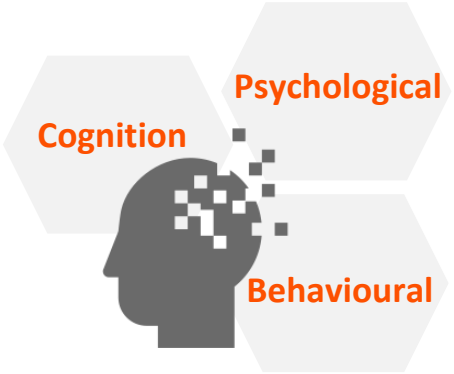
AD, Alzheimer's disease; MCI, mild cognitive impairment; NIA-AA, National Institute of Aging-Alzheimer's Association.

1. Sperling RA, et al. *Alzheimers Dement.* 2011;7:280–92; 2 Jack CR, et al. *Alzheimers Dement.* 2011;7:257–62; 3. Albert MS, et al. *Alzheimers Dement.* 2011;7:270–9; 4. McKhann GM, et al. *Alzheimers Dement.* 2011;7:263–69; 5. Porsteinsonn AP, et al. *J Prev Alzheimers Dis.* 2021;3:371–86.

Key stages in the journey to a diagnosis of AD

Community-based healthcare professionals increasingly provide AD management[1–6]

Referral to specialists for more complex cases[1–6]



Detection → Assessments → Diagnosis → Treatment

- In primary care, >50% patients with cognitive impairment are not recognized or correctly diagnosed[7]
- Failure to diagnose results in suboptimal treatment and care, delayed or incorrect therapies, and inaccurate information about disease and prognosis[7]

AD, Alzheimer's disease.

1. Porsteinsonn AP, et al. *J Prev Alzheimers Dis.* 2021;3:371–86; 2. Liss JL, et al. *J Intern Med.* 2021;290:310–34; 3. Park JY, et al. *BMC Geriatrics.* 2022;22:522; 4. Yang M, et al. *JAMDA.* 2016;17:802–6; 5. Reuben DB, Fulmer T. *Am J Geriatr Psychiatry.* 2021;29:527-9; 6. Streeter RA, et al. *Health Serv Res.* 2017;52:481–507; 7. Angioni D, et al. J Prev Alzheimers Dis. 2022;4:569–79.

Diagnostic tests and tools in AD[1–9]

Detection | **Assessments and diagnostic confirmation** | **Treat**

- **Clinical history + input from care partner/reliable informant**
- **Family history**

- **Medication review**
- **Physical + neurological exam**
- **Blood tests**
  CMP, CBC, TSH, B12/folate.
- vitamin D?, CRP?
- **Genotyping**
  APOE4?

- **Cognitive***
  AD8®, MMSE®, MoCA, Mini-Cog, SLUMS
- **Functional/ADL**
  Barthel Index + Katz ADL inventories
- **Behavioural**
  NPI-Q, PHQ-9

- **Neuroimaging**
  CT/MRI
  FDG-PET?

- **Amyloid PET**
- **CSF biomarkers**
  Aβ42, p-tau, t-tau
  Aβ42/Aβ40
- **Blood-based biomarkers?**

- **Lifestyle modifications**
- **Symptomatic therapies**
- **Disease-modifying therapies?**
- **Psychosocial support**
- **Clinical trials**

*Note: Use of cognitive assessment tools may be subject to copyright, with licencing and permissions for use requirements. Check before use.

Aβ, amyloid beta; AD, Alzheimer's disease; AD8®, The Eight-item Informant Interview to Differentiate Aging and Dementia; ADL, activities of daily living; APOE4, apolipoprotein E gene (E4 allele); CMP, comprehensive metabolic panel; CRP, C-reactive protein; CSF, cerebrospinal fluid; CT, computerized tomography; FDG-PET, fluorodeoxyglucose-PET; Mini-Cog, Mini Cognitive Assessment Instrument; MMSE®, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging; NPI-Q, Neuropsychiatric Inventory Questionnaire; PET, positron emission tomography; PHQ-9, Public Health Questionnaire-9; p-tau, phosphorylated tau; SLUMS, The Saint Louis University Mental Status Examination Test; TSH, thyroid-stimulating hormone; t-tau, total tau.

1. Sperling RA, et al. *Alzheimers Dement*. 2011;7:280–92; 2 Jack CR, et al. *Alzheimers Dement*. 2011;7:257–62; 3. Albert MS, et al. *Alzheimers Dement*. 2011;7:270–9;
4. McKhann GM, et al. *Alzheimers Dement*. 2011;7:263–69; 5. Hyman BD, et al. *Alzheimers Dement.* 2012;8:1–13; 6. Porsteinsonn AP, et al. *J Prev Alzheimers Dis.* 2021;3:371–86;
7. Wade DT, Collin C. *Int Disabil Stud.* 1988;10:64–7; 8. Katz S. *J Am Geriatri Soc.* 1983;31:721–7; 9. Hancock P, Larner AJ. *Int J Psychiatry Clin Pract.* 2009;13:188–91.

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Conversation 2

Symptomatic treatment options in AD: What are we learning from the latest data about transdermal and oral therapies?

Prof. George T. Grossberg

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Approved symptomatic treatment options in AD[1–3]

		Indication (AD stage)	Formulation *(frequency)*
ChEI	Donepezil	All	▪ Oral tablet *(once daily)* ▪ Oral solution *(once daily)* ▪ **Transdermal patch *(once weekly)***
ChEI	Galantamine	Mild to moderate	▪ Oral immediate-release tablet *(twice daily)* ▪ Oral solution *(twice daily)* ▪ Oral extended-release capsule *(once daily)*
ChEI	Rivastigmine	Mild to moderate	▪ Oral capsule *(twice daily)* ▪ Oral solution *(twice daily)*
ChEI	Rivastigmine	All	▪ **Transdermal patch *(once daily)***
NMDA RA	Memantine	Moderate to severe	▪ Oral tablet *(twice daily)* ▪ Oral solution *(twice daily)*
	Donepezil + memantine	Moderate to severe	▪ Oral extended-release capsule *(once daily)*

AD, Alzheimer's disease; ChEI, choline esterase inhibitor; NMDA RA, N-methyl-D-aspartate receptor antagonist.

1. Porsteinsonn AP, et al. *J Prev Alzheimers Dis.* 2021;3:371–86; 2. Grossberg GT, et al. *J Alzheimers Dis.* 2019;67:1157–71;
3. FDA Prescribing information. Searchable for respective agents at www.accessdata.fda.gov/scripts/cder/daf/ (accessed 21 November 2022).

Route to transdermal symptomatic therapies in AD

Rivastigmine[1]

2007

24 h transdermal patch vs oral: Mild-to-moderate AD[3,4]

- **Transdermal patch 9.5 mg/24 h (10 cm²) vs 17.4 mg/24 h (20 cm²) vs rivastigmine oral capsule 6 mg (twice daily)**
- **10 cm² patch demonstrated comparable efficacy to capsules** (ADAS-Cog; ADCS-CGIC) and **lower rates of nausea** (7.2% vs 23.1%) and **vomiting** (6.2% vs 17.0%)

2013

24 h transdermal patch dose comparison: Severe AD[5]

- **Transdermal patch 13.3 mg/24 h vs 4.6 mg/24 h**
- **13.3 mg/24 h patch demonstrated superior efficacy** to 4.6 mg/24 h patch (SIB, ADCS-ADL-SIV)
- **Comparable AE and SAE rates**: 13.3 mg (74.6%; 14.9%) vs 4.6 mg (73.3%; 13.6%)

Donepezil[2]

2022

Once-weekly transdermal patch vs oral: Mild-to-moderate AD[6]

- **Once-weekly 87.5 mg/25 cm² transdermal patch or 5 mg donepezil tablets for 6 weeks, 175 mg/50 cm² transdermal patch or 10-mg donepezil tablets**
- **Bioequivalence** in healthy volunteer study[7]
- **Comparable efficacy** (ADAS-Cog)
- **Comparable SAE rates:** patch (8.21%); oral (7.58%); more topical side effects in transdermal patch cohort (erythema, pruritus)

AD, Alzheimer's disease; ADAS-Cog, AD Assessment Scale–Cognitive; ADCS-ADL-SIV, AD Cooperative Study–Activities of Daily Living scale–Severe Impairment Version; ADCS-CGIC, AD Cooperative Study–Clinical Global Impression of Change; AE, adverse event; h, hours; SAE, serious AE; SIB, Severe Impairment Battery.

1. FDA. Rivastigmine PI. Available at: www.accessdata.fda.gov/scripts/cder/daf/ (accessed 25 November 2022); 2. FDA. Donepezil PI. Available at: www.accessdata.fda.gov/scripts/cder/daf/ (accessed 25 November 2022); 3. Winblad B, et al. *Neurology.* 2007;69(Suppl. 1):S14–22; 4. Winblad B, et al. *Int J Geriatr Psych.* 2007;22:456–67; 5. Farlow MR, et al. *CNS Neurosci Ther.* 2013;19:745–52; 6. Han HJ, et al. *J Clin Neurol.* 2022;18:428–36; 7. Tariot PN, et al. *J Alzheimers Dis.* 2022:90;161–72.

Conversation 3

Addressing shared management needs in AD: Understanding the role of transdermal therapies

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Supporting shared-management needs in AD

Social and emotional[1–5]

- Sense of grief + isolation
- Need for peer support + social contact

Health and well-being[2–4,6]

- Stress + burden of complex care
- Physical + mental care partner strain

Informational[6–8]

- Primary intermediary with HCPs
- Need for written information, care plans + designated point of contact

Care partner needs are often only partially met, or not at all[7]

Treatment and care[1–8]

- Person-centred approach
- Inclusive focus on care partner well-being
- Improved symptomatic therapies
- Support with daily activities

Care partner needs should be regularly assessed, as they evolve over time with AD progression[2]

AD, Alzheimer's disease; HCP, healthcare professional.

1. Fieldhouse JLP, et al. *Psychogeriatrics* 2022; doi:10.1111/psyg.12898; 2. Novais T, et al. *BMC Geriatrics.* 2017;17:86; 3. Vu M, et al. *Health Psychol Res*. 2022;10:37454; 4. Janssen N, et al. *J Am Med Dir Assoc.* 2020;21:1609; 5. Alzheimer's Society. 2022. Available at: www.alzheimers.org.uk/sites/default/files/2022-07/left-to-cope-alone-after-diagnosis-report.pdf (accessed 24 November 2022); 6. Gately ME, et al. *Aging Health Res.* 2022;2:100061; 7. Khanassov V, et al. *BMC Fam Pract.* 2021;22:186; 8. Aworinde J, et al. *Alzheimers Dement.* 2022;8:e12304.