

Diabetes and Cognitive Impairment: Epidemiology, Mechanisms, Treatment, and Prevention

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knowledge changing life



Presenter Disclosures

- Leonard E. Egede, MD
- Disclosed no conflict of interest

Learning Objectives

- Discuss epidemiology of diabetes
- Discuss epidemiology of cognitive impairment/dementia
- Discuss epidemiology of diabetes and cognitive impairment
- Discuss recognition and diagnosis of cognitive impairment/dementia in adults with diabetes
- Discuss potential pathways, treatment, and prevention of cognitive impairment in adults with diabetes

Case 1

- 72 year old woman with type 2 diabetes, hypertension, and hyperlipidemia
- Presents with poorly controlled diabetes and difficulty with self care
- Daughter states patient is having progressive difficulty remembering to take medications or test her sugars
- Also reports more frequent hypoglycemic episodes in past year
- Family is concerned about her safety living alone
- No recent falls, trauma, or weakness or numbness in upper/lower limbs
- A1c 11; BP 160/97; LDL 160
- Meds: NPH Insulin; Lisinopril; HCTZ; Atorvastatin
- Patient is alert; oriented to time, place, person, but admits to having more difficulty remembering to take medications or track her sugars

Question 1

- What are potential risk factors for cognitive impairment in this patient?

A-History of hypertension and hyperlipidemia

B-Poorly controlled diabetes

C-Frequent hypoglycemic episodes

D-All of the above

Question 1 - Answer

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Overview of diabetes

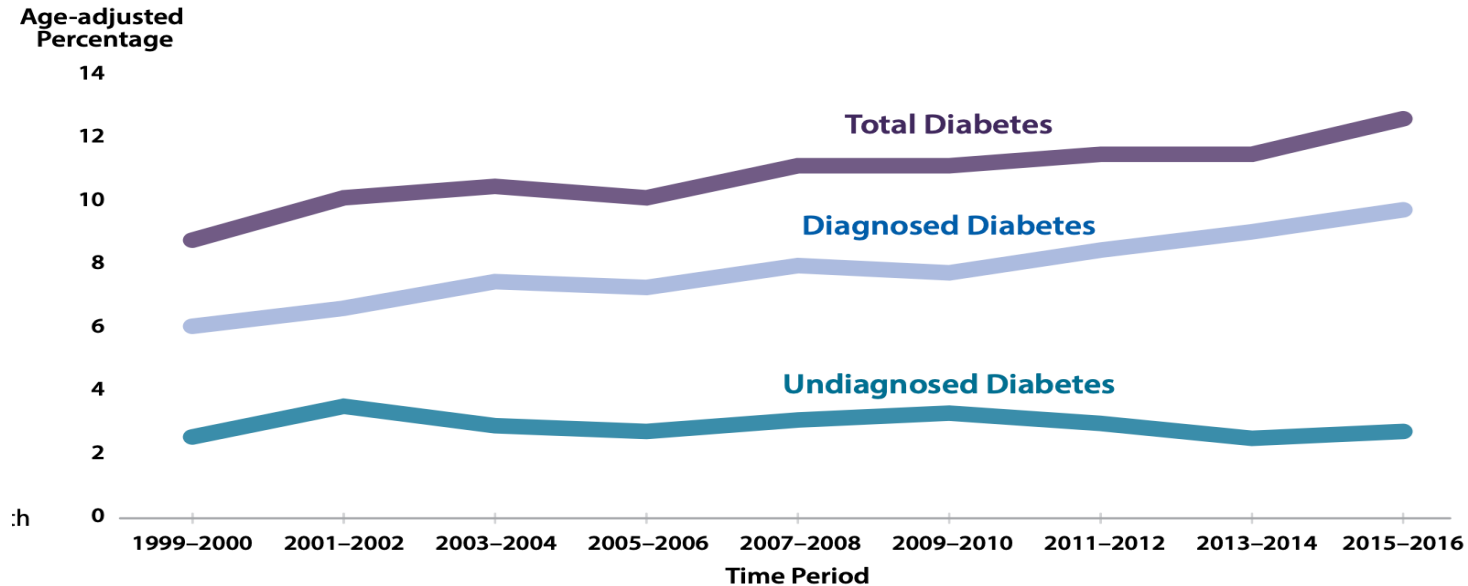
OVERVIEW OF DIABETES: PREVALENCE

Characteristic	Diagnosed diabetes Percentage (95% CI)	Undiagnosed diabetes Percentage (95% CI)	Total diabetes Percentage (95% CI)
Total	10.2 (9.3–11.2)	2.8 (2.4–3.3)	13.0 (12.0–14.1)
Age in years			
18–44	3.0 (2.6–3.6)	1.1 (0.7–1.8)	4.2 (3.4–5.0)
45–64	13.8 (12.2–15.6)	3.6 (2.8–4.8)	17.5 (15.7–19.4)
≥65	21.4 (18.7–24.2)	5.4 (4.1–7.1)	26.8 (23.7–30.1)
Sex			
Men	11.0 (9.7–12.4)	3.1 (2.3–4.2)	14.0 (12.3–15.5)
Women	9.5 (8.5–10.6)	2.5 (2.0–3.2)	12.0 (11.0–13.2)

Estimated crude prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 2013–2016

CDC, 2021

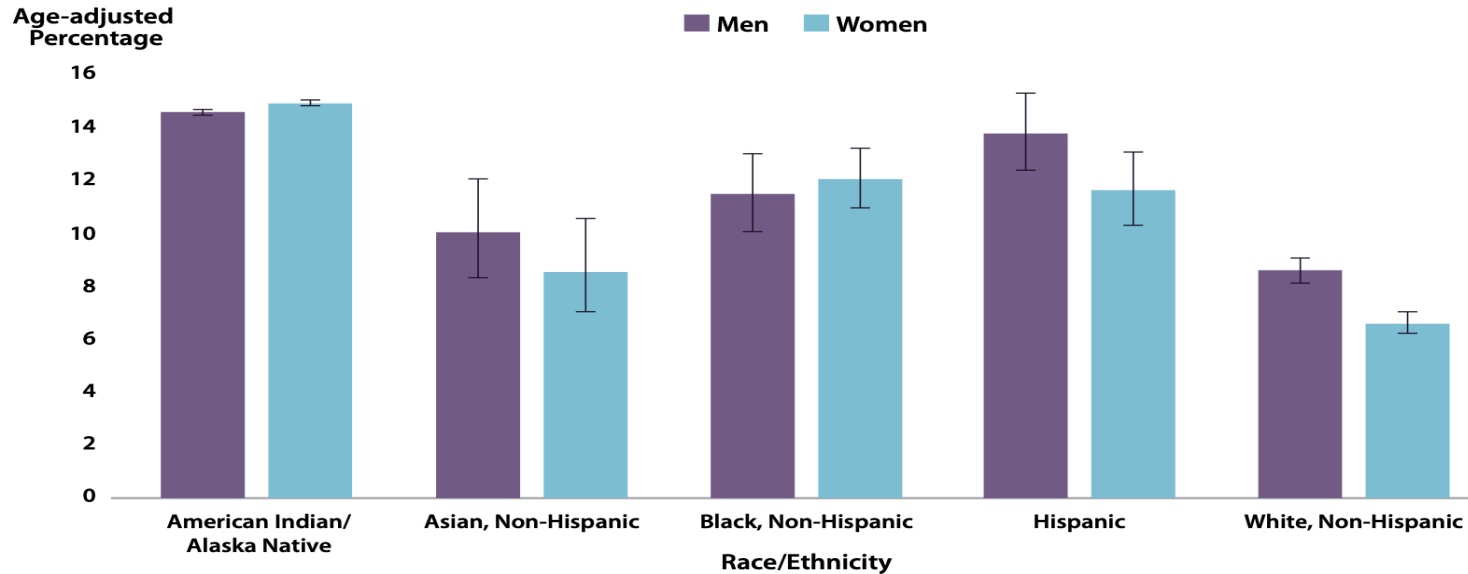
OVERVIEW OF DIABETES: TRENDS



Trends in age-adjusted prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 1999–2016.

CDC, 2021

OVERVIEW OF DIABETES: DISPARITIES



Age-adjusted estimated prevalence of diagnosed diabetes by race/ethnicity group and sex for adults aged 18 years or older, United States, 2017-2018

CDC, 2021

OVERVIEW OF DIABETES: ABCs

Risk Factor	ABCs Goals for Many Adults	Less Stringent ABCs Goals
A1C	<7.0%	<8.0%
Blood Pressure	<140/90 mmHg	<140/90 mmHg
Cholesterol, non-HDL	<130 mg/dL	<160 mg/dL
Smoking, current	Nonsmoker	Nonsmoker
Percentage meeting all ABCs goals	19.2 (15.3–23.9)	36.4 (15.3–23.9)

- 19.2% met all of these criteria: A1C value <7.0%, blood pressure <140/90 mmHg, non-HDL cholesterol <130 mg/dL, and being a nonsmoker
- 36.4% met all of these criteria: A1C value <8.0%, blood pressure <140/90 mmHg, non-HDL cholesterol <160 mg/dL, and being a nonsmoker

CDC, 2021

EPIDEMIOLOGY OF DEMENTIA

PREVALENCE OF DEMENTIA

- 6.5 million individuals age 65+ living with Alzheimer's Dementia in 2022
- Translates to 1 in 9 or 10.7% of adults 65 years or older
- 2/3 are women
- Older African Americans are 2X more likely to have AD compared to Whites
- Older Hispanics are 1.5X more likely to have AD compared to Whites

Alzheimer's Association - <https://www.alz.org/alzheimers-dementia/facts-figures>

ECONOMIC BURDEN OF DEMENTIA

- Cost \$321 billion in 2022
- Of that, \$206 billion was cost to Medicare and Medicaid
- Projected to cost \$1 trillion in 2050
- 2X higher hospital stays compared to other older adults

Alzheimer's Association - <https://www.alz.org/alzheimers-dementia/facts-figures>

RISK FACTORS FOR COGNITIVE IMPAIRMENT/DEMENTIA

- Non modifiable: age; sex; genetics; family history
- 40% of dementia related to 12 modifiable risk factors
 - High blood pressure
 - Smoking
 - Diabetes
 - Obesity
 - Lack of physical activity
 - Poor diet
 - High alcohol consumption
 - Low levels of cognitive engagement
 - Depression
 - Traumatic brain injury
 - Hearing loss
 - Social isolation

Alzheimer's Society, Canada - <https://alzheimer.ca/en/about-dementia/how-can-i-prevent-dementia/risk-factors-dementia>

EPIDEMIOLOGY OF COGNITIVE
IMPAIRMENT/DEMENTIA IN
INDIVIDUALS WITH DIABETES

ASSOCIATION BETWEEN DM AND CI/DEMENTIA

- Historical Cohort -Rochester, MN (1970-1984; N=1,455)
 - RR 1.66 for dementia; RR 2.27 for AD
- Canadian Study of Aging (1991-1992; N=5,574)
 - RR 2.03 for vascular dementia
- New York City Cohort (1999-2007; N=1,488)
 - HR 1.6 for AD; HR 5.4 for vascular dementia

Luchsinger, Ryan, Launer, 2016 – Diabetes in America; Chapter 24; Diabetes and Cognitive Impairment

ASSOCIATION BETWEEN DM AND CI/DEMENTIA

- Honolulu Asia Aging Study (1991-1994; N=2,574)
 - RR 1.5 for dementia; RR 1.8 for AD; RR 2.3 for vascular dementia
- Group Health Cooperative (1994-2004; N=2,067)
 - HR 1.40 for dementia

Luchsinger, Ryan, Launer, 2016 – Diabetes in America; Chapter 24; Diabetes and Cognitive Impairment

POTENTIAL MECHANISMS AND
PATHWAYS LINKING DIABETES TO
COGNITIVE IMPAIRMENT/DEMENTIA

POTENTIAL BIOLOGICAL MECHANISMS

- Cerebrovascular
 - Mini-strokes/White matter disease
 - Cerebral amyloid angiopathy
 - Inflammation
 - Demyelinating processes
- Non-Cerebrovascular
 - Hyperinsulinemia (insulin resistance)
 - Advanced glycation endproducts
 - Hypoglycemia

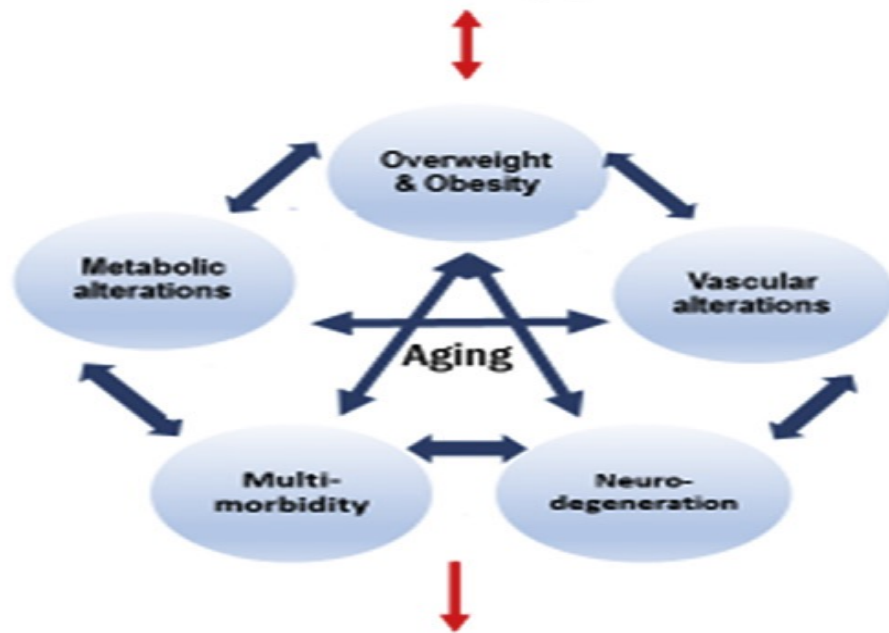
Luchsinger, Ryan, Launer, 2016 – Diabetes in America; Chapter 24; Diabetes and Cognitive Impairment

POTENTIAL SOCIO-BIOLOGICAL PATHWAYS

Pre-diabetes and Type 2 Diabetes

Health disparities

- Socioeconomic status
- Social network
- Built environment
- Food insecurity
- Ethnoracial background
- Access to healthcare
- Control of multi-morbidity
- Medication adherence



Cognitive Impairments and Dementias

Gustafson, McFarlane 2018: Chapter 2; Type 2 Diabetes and Dementia

CLASSIFICATION OF COGNITIVE
IMPAIRMENT/DEMENTIA IN
INDIVIDUALS WITH DIABETES

THREE STAGE CLASSIFICATION – STAGE 1

- Mild changes in cognition
- May represent normal cognitive aging
- Unlikely to significantly interfere with ADLs
- May interfere with diabetes self management if regimen is complex
- Only detectable in neuropsychological testing

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016

THREE STAGE CLASSIFICATION – STAGE 2

- Mild to moderate cognitive impairment
- Testing shows cognitive impairment in one or more domains
- Does not meet criteria for dementia
- Subtle impairment in ADLs
- Can interfere with diabetes self management

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016

THREE STAGE CLASSIFICATION – STAGE 3

- Dementia
- Tends to occur in those 60 years or older
- Progresses over time
- Cognitive impairment in two or more domains
- Decline in executive function and impairment of ADLs
- Inability to understand or remember instructions
- Leads to poor diabetes self management

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016

SCREENING FOR COGNITIVE
IMPAIRMENT/DEMENTIA IN
INDIVIDUALS WITH DIABETES

AMERICAN DIABETES ASSOC. GUIDELINES

- Screen adults 65 years and older at initial visit, annually and as appropriate
 - MMSE
 - MiniCog
 - Montreal Cognitive Assessment (MOCA)
- Referral to behavioral health for formal cognitive/neuropsychological testing

ADA Guidelines; Diabetes Care Jan 2022

ESTABLISHING A DIAGNOSIS

- Detailed social history (assess effect of CI on function)
- Exclude other conditions (e.g., depression, hearing loss)
- Exclude organic causes
 - Hypothyroidism; Vit B12/Folate Def; Anemia; Hepatic dysfunction; Renal dysfunction; Hypercalcemia
- Consider age of the patient
 - <65 yrs, thorough eval for other underlying causes
- Brief cognitive assessment – MOCA, MMSE, MiniCog
- Refer and Follow up

Moulton, Diabetes & Primary care 2016

Question 2

- Which of the following are recommended tools for brief cognitive assessment in individuals with diabetes and cognitive impairment?

A-Montreal Cognitive Assessment (MOCA)

B-MiniCog

C-Mini Mental Status Exam (MMSE)

D-All of the above

Question 2 - Answer

- Which of the following are recommended tools for brief cognitive assessment in individuals with diabetes and cognitive impairment?

A-Montreal Cognitive Assessment (MOCA)

B-MiniCog

C-Mini Mental Status Exam (MMSE)

D-All of the above

PHARMACOLOGIC/NON-PHARMACOLOGIC INTERVENTIONS

- Few medications available for managing dementia in general
- None modify the underlying disease
- No treatments target CI in diabetes
- Blood pressure lowering and certain glucose lowering agents may be beneficial
 - Metformin; TZDs; DPP IV Inhibitors; GLP-1 agonists
- Diet/exercise may be beneficial
- Treatment of CVD risk factors may be beneficial

Calisaya & Moran, Type 2 Diabetes and Dementia; Chapter 12, 2018

PHARMACOLOGIC INTERVENTIONS FOR ALZHEIMERS

- Cholinesterase inhibitors
 - Mild to moderate AD
 - Donepezil; Galantamine; Rivastigmine
- Memantine
 - Moderate to advanced AD
 - Alone or in combination with cholinesterase inhibitors
- Aducanumab
 - FDA approved for mild AD
- Vitamin E (1000 IU BID may be beneficial)

Question 3

- Which of the following are true about treatment options for cognitive impairment in individuals with diabetes?

A-Few medications are available for managing CI

B-None modify the underlying disease process

C-Treatment of CVD risk factors may be beneficial

D-Diet and exercise may be beneficial

E-All of the above

Question 3 - Answer

- Which of the following are true about treatment options for cognitive impairment in individuals with diabetes?

A-Few medications are available for managing CI

B-None modify the underlying disease process

C-Treatment of CVD risk factors may be beneficial

D-Diet and exercise may be beneficial

E-All of the above

ASSISTIVE DEVICES FOR CI IN DM

- 1. Recording and alarming devices
 - Records reminder message
 - Photo albums with audio/video reminders
 - Automated pill dispensers
 - Vibrating or audio watch
 - Diabetes Sentry wrist alarm for tracking hypoglycemia
- 2. Insulin/Injectable devices
 - Insulin pens with memory of time/dose
 - Insulin pump

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016

ASSISTIVE DEVICES FOR CI IN DM

- 3. GPS tracking with emergency alarm
- 4. Talking glucose meters
- 5. CGM devices
- 6. Electrical use monitors

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016

Case 1 - Revisted

- 72 year old woman with **type 2 diabetes, hypertension, and hyperlipidemia**
- Presents with **poorly controlled diabetes** and difficulty with self care
- Daughter states patient is having **progressive difficulty remembering** to take medications or test her sugars
- Also reports more frequent hypoglycemic episodes in past year
- Family is concerned about her safety living alone
- **No recent falls, trauma, or weakness or numbness in upper/lower limbs**
- A1c 11; BP 160/97; LDL 160
- Meds: NPH Insulin; Lisinopril; HCTZ; Atorvastatin
- **Patient is alert; oriented to time, place, person**, but admits to having more difficulty remembering to take medications or track her sugars

Conclusions

- Strong assoc. between diabetes and CI/dementia
- Potential pathways include cerebrovascular and non-cerebrovascular mechanisms
- Annual screening recommended for adults 65 years and older
- Brief screening tools include MOCA, MiniCog and MMSE
- No targeted treatment options are currently available
- CVD risk factor control and diet/exercise may be beneficial
- FDA approved medications for AD including cholinesterase inhibitors, memantine, and adacantumab may be options

Questions?