Cognitive Health Among Middle-aged and Older Adults in India - the Role of Depression

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Technology in Healthcare – India's mantra for Universal Health Coverage

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INTRODUCTION

- Depression affects around 280 million people worldwide (WHO, 2023) and associated with significant functional impairments and reduction in quality of life

- Depression associated with significant cognitive impairment – often termed as “pseudodementia”

- Biological pathways linking depression with cognitive impairment along multiple domains
  - Shared volumetric reductions in particular brain regions such as the insula, associated with socio-emotional processing, sustained attention, executive function, and superior temporal gyrus (STG), a part of the language network (Zackova et al., 2021)

  - These reductions associated with deficits in communication activities, social withdrawal, and reduced participation in mentally stimulating activities – risk factors for both depression and mild cognitive impairment

INTRODUCTION

- Depression → changes in individual's neurochemistry and brain structure → social withdrawal, communication problems, sleep problems, and difficulty in performing regular activities → increases the odds of cognitive decline

- Depression leads to the most pronounced deficits in areas of information processing speed, visual learning and memory, and verbal learning and memory (Krieshche et al., 2022)

- Number of depressive episodes is positively correlated with the extent of cognitive decline across multiple domains - global cognitive status, processing speed, auditory attention capacity, visual attention accuracy, memory (both verbal and visual), verbal fluency, and task-shifting abilities (Semkovska et al., 2019).

OBJECTIVES

- Establishing causal link between depression and cognitive function is challenging
  - ***Unobserved confounders*** correlated with depression status and cognitive function can preclude causal inference (e.g. genetic factors)
  - ***Measurement error*** Self-reports of depressive symptoms can be fraught with errors in measurement if individuals either under-report or over-report their symptoms
  - ***Reverse causality*** Poor cognitive function can lead to depressive symptoms

- Examine the causal effect of depression on cognitive functioning by exploiting a plausibly exogenous variation in the respondent's depression status by using the spouse's depression status as an instrumental variable (IV)

- Examine the role of socio-economic and demographic correlates of cognition and depression

- Assess the role of limitations in Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL, and quality of sleep in mediating the relationship between depression and cognitive function

DATA

- **Longitudinal Ageing Study in India**, Wave 1, 2017-18
  - Nationally representative sample of Indian population aged 45+ (N=73,408)
  - Information on socio-economic and demographic characteristics, health status, mental health, cognition, psychosocial factors, etc.
  - Study sample: 51,658 (24,216 men; 27,442 women)
    - Inclusion criteria: Individuals aged 50+
    - Exclusion criteria: Missing information on depression status

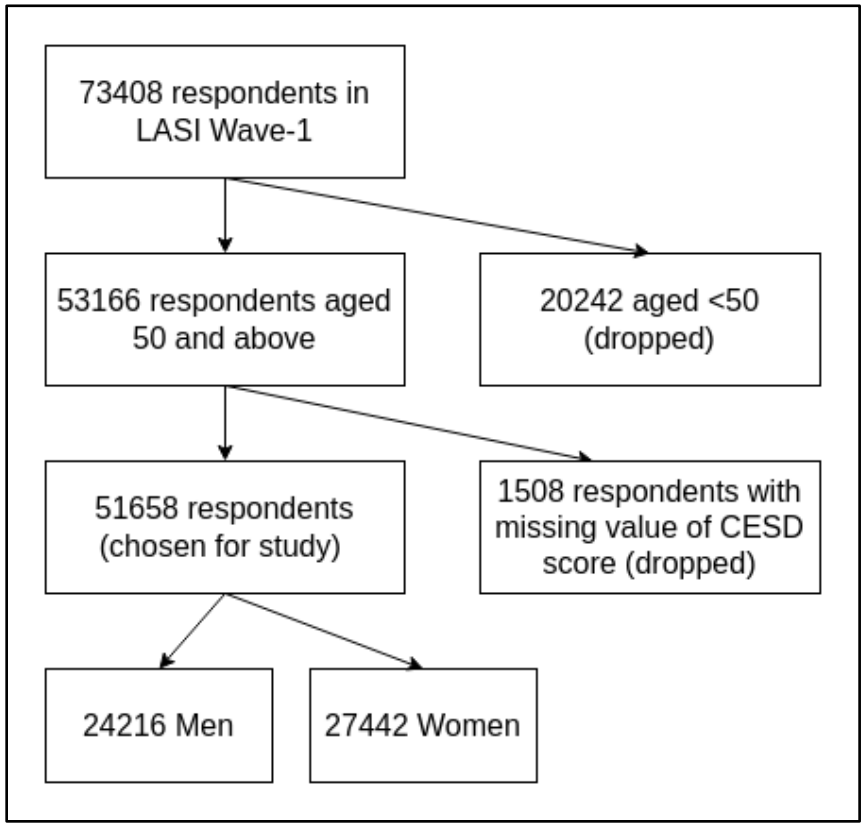


Figure 1: Study sample selection criteria

DATA

Measures of Cognitive Health

- Overall cognitive function: 22 items (Orientation, Memory, Language, Executive Function, Visuospatial)
- Orientation: date, place, city, street, district naming
- Immediate memory: 10-word immediate recall
- Delayed memory: 10-word delayed recall
- Language: verbal fluency, reading a sentence, writing a sentence, 3-stage task, object naming
- Executive function: backward counting from 100, backward counting from 20, serial 7s (number of correct subtractions), computations
- Visuospatial: drawing interlocked pentagons, drawing a clock

- Each measure standardized (mean=0; SD=1)

DATA

Depressive symptom status

- Center for Epidemiologic Studies Depression (CES-D) 10-item Scale
  - Symptoms: trouble concentrating, felt depressed, felt tired or low in energy, everything was an effort, etc.
  - Rating of each item on a scale of 0-3 [rarely/never, sometimes, often, most/all of the time] in the past week
  - Total score 0-30
  - Binary indicator (1 if CES-D score ≥ 10; 0 if CES-D score < 10)

Covariates

- Age, gender, education level, region, coupled status, religion, caste, participation in physical activity, chronic conditions, current working status, and socialization

Instrumental Variable

- Spousal depressive symptoms (1 if CES-D score ≥ 10; 0 if CES-D score < 10)

DATA

Mediators

- Activities of Daily Living (ADL)
  - Bathing, dressing, eating, getting in/out of bed, walking across the room, and using the toilet
- Instrumental Activities of Daily Living (IADL)
  - making telephone calls, managing money, taking medications, shopping for groceries, preparing hot meals, finding an address in an unfamiliar place, and working around the house/garden
- Quality of Sleep
  - difficulty falling asleep, feeling unrested during the day, waking up during the night, and waking up too early.
- Each mediator standardized (mean=0; SD=1)

METHODS

Linear Regression:

$$Cognition = \beta_0 + \beta_1 Depression + \beta_2 X + u$$

2 Stage Least Squares (2SLS):

$$Depression = \alpha_0 + \alpha_1 SpousalDepression + \alpha_2 X + \varepsilon$$

$$Cognition = \delta_0 + \delta_1 \widehat{Depression} + \delta_2 X + \epsilon$$

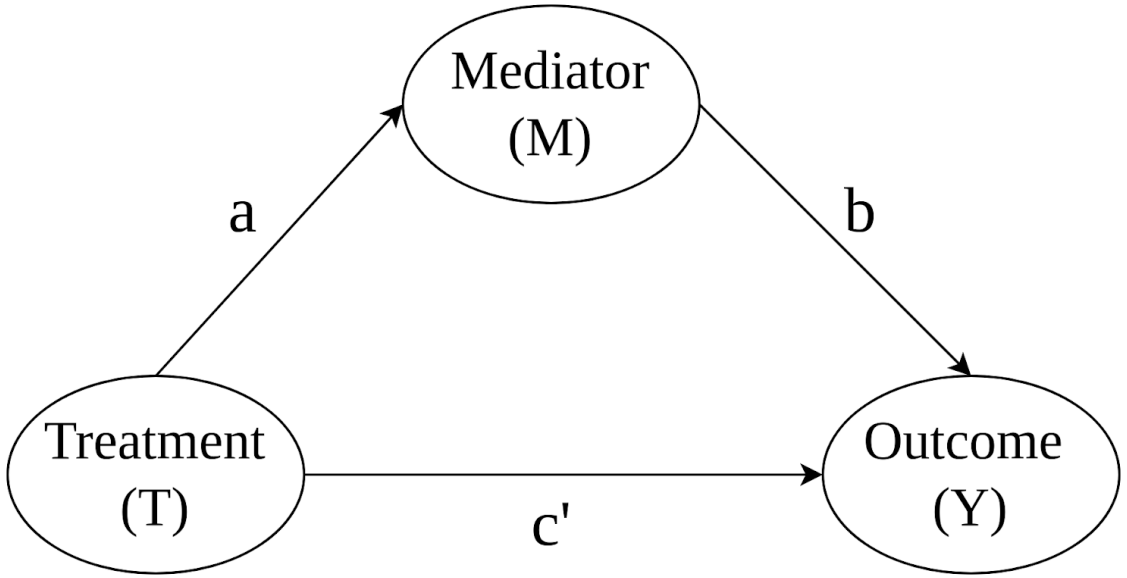
Mediation Analysis:

$$Cognition = \gamma_0 + c' Depression + bMediator + \gamma_1 X + u_1$$

$$Mediator = \pi_0 + aDepression + \pi_2 X + u_2$$

METHODS

Mediation Analysis:



Natural Direct Effect (NDE): c'

Natural Indirect Effect (NIE): ab

Total Effect (TE): $c' + ab$

RESULTS (Overall Cognition Score)

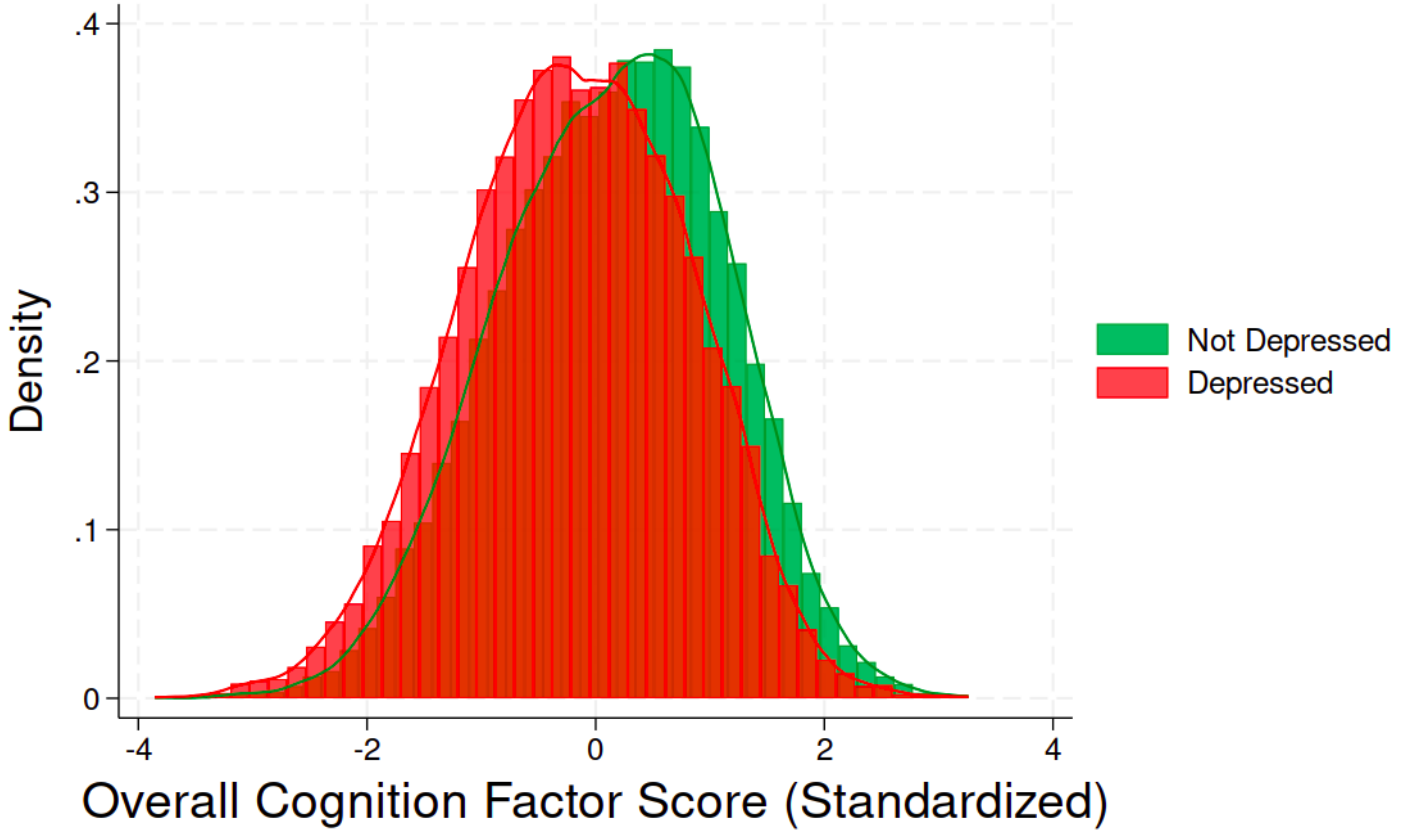


Figure 2a. Distribution of Overall Cognition Score by Depression Status

RESULTS (Cognition Domain Scores)

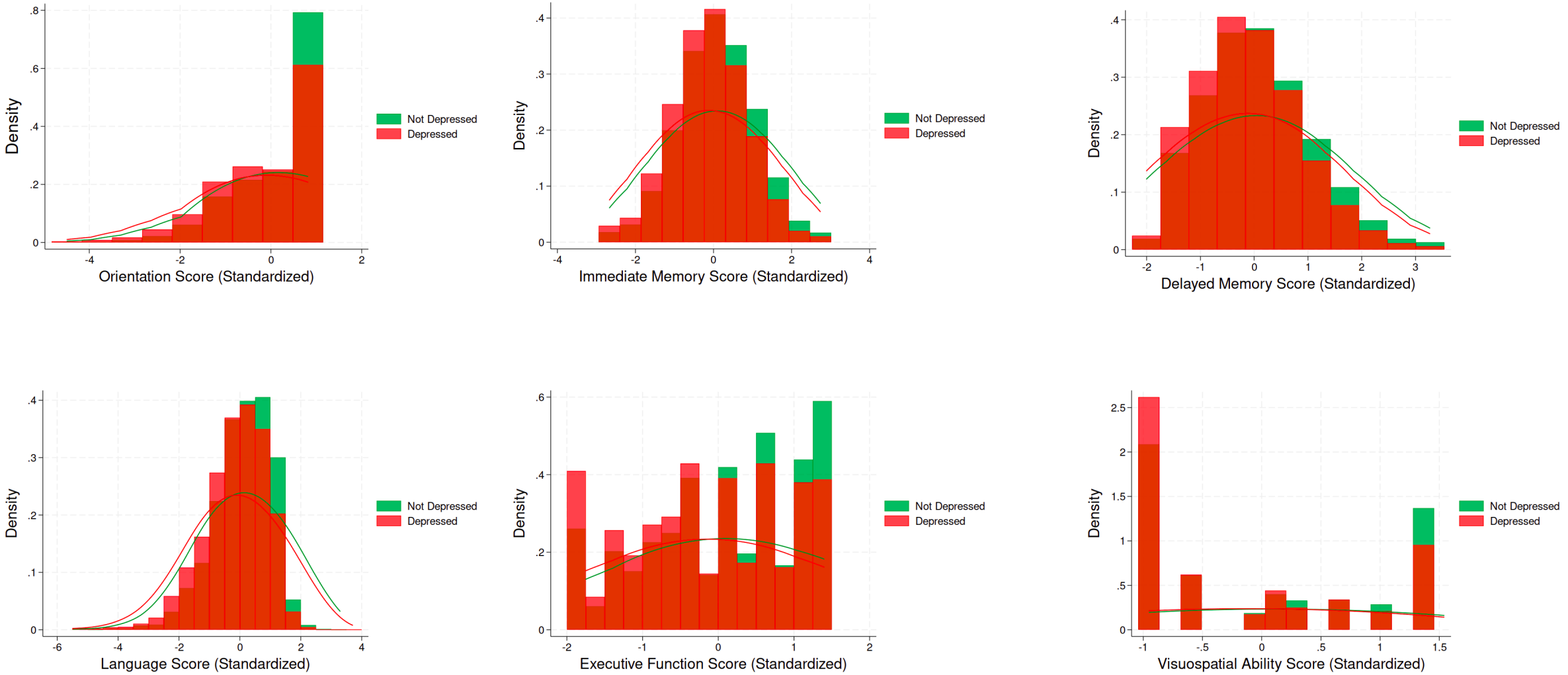


Figure 2b. Distribution of Cognition Domain Scores by Depression Status

RESULTS (Summary Statistics of Overall Cognition Score)

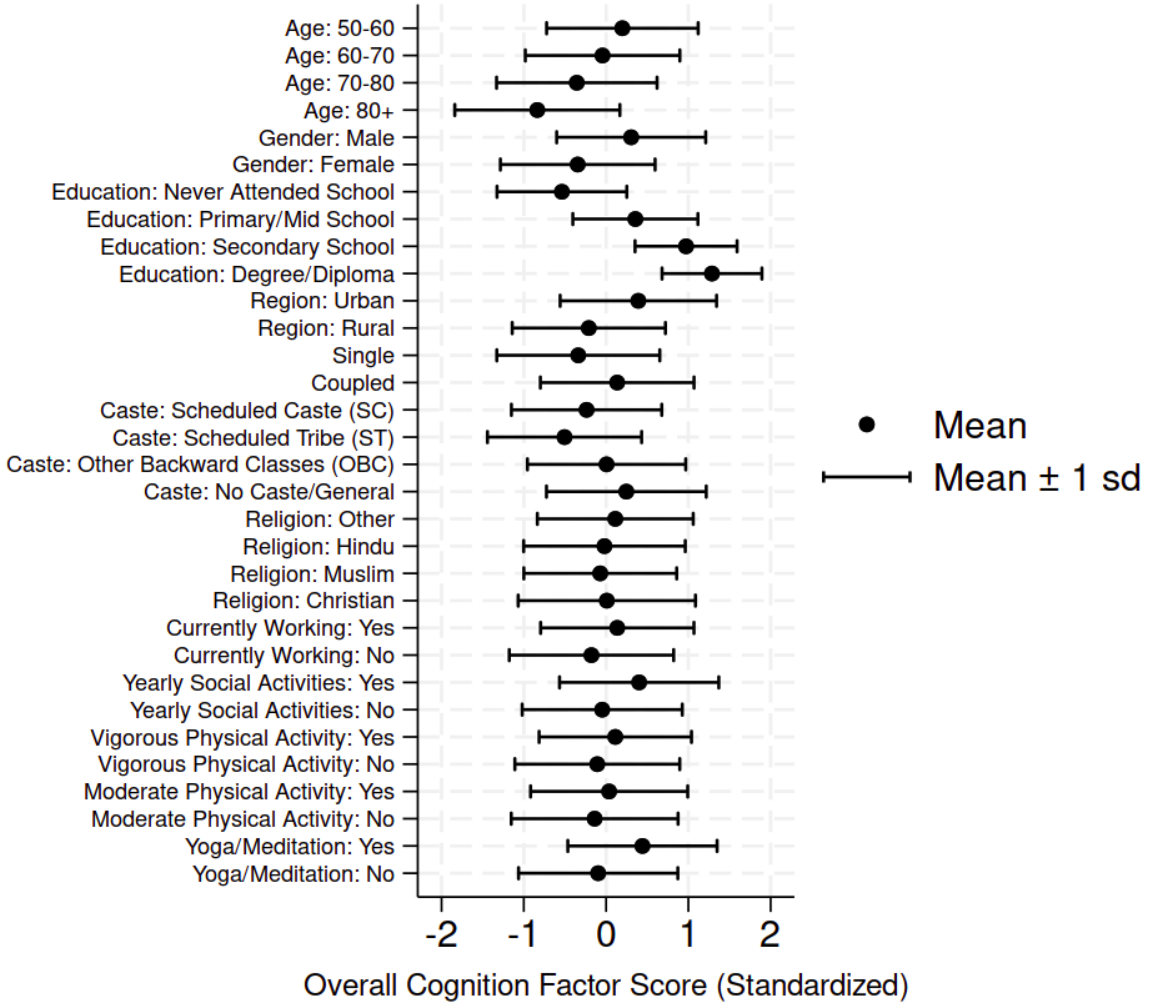


Figure 3. Summary Statistics of Overall Cognition Score

RESULTS (Summary Statistics by Depression Status)

Table 1. Weighted Summary Statistics by Depression Status

	Total (N=51,658)	**Depressed** (N=22,691)	**Not depressed** (N=28,967)	**p-value***
Overall Cognition, Mean (SD)‡	-0.020 (0.978)	-0.183 (0.957)	0.119 (0.975)	<0.001
Orientation, Mean (SD)‡	-0.035 (0.981)	-0.165 (1.028)	0.076 (0.924)	<0.001
Immediate Memory, Mean (SD)‡	-0.001 (0.978)	-0.112 (0.954)	0.095 (0.987)	<0.001
Delayed Memory, Mean (SD)‡	0.001 (0.981)	-0.092 (0.938)	0.080 (1.010)	<0.001
Language, Mean (SD)‡	0.049 (0.960)	-0.087 (0.983)	0.140 (0.933)	<0.001
Executive Function, Mean (SD)‡	0.019 (0.990)	-0.102 (0.989)	0.123 (0.978)	<0.001
Visuospatial Ability, Mean (SD)‡	-0.074 (0.978)	-0.180 (0.936)	0.017 (1.003)	<0.001
Activities of Daily Living (ADL), Mean (SD)‡	-0.030 (0.922)	0.096 (1.091)	-0.138 (0.732)	<0.001
Instrumental Activities of Daily Living (IADL), Mean (SD)‡	-0.001 (0.981)	0.179 (1.091)	-0.155 (0.846)	<0.001
Sleep Quality, Mean (SD)‡	-0.026 (1.027)	-0.247 (1.150)	0.162 (0.865)	<0.001
Spousal Depression, N (%)	13,533 (43.6%)	9,230 (69.2%)	4,303 (24.2%)	<0.001

RESULTS

Table 2. Association of Depression with Overall Cognition Score

Coefficient (SE)	**Overall Cognition Score**	
	OLS	**2SLS**
Depressed	-0.112***	-0.137***
	(0.008)	(0.022)
Mean (Overall Cognition Score)	0.001	0.166
Sample size (N)	51,094	32,693
Adjusted R-squared	0.501	0.47
First stage F-stat		7849.14

RESULTS

Table 3. Association of Depression with Cognition Scores

Panel A	**Orientation**		**Immediate Memory**		**Delayed Memory**	
Coefficient (SE)	**OLS**	**2SLS**	**OLS**	**2SLS**	**OLS**	**2SLS**
Depression	-0.090***	-0.102***	-0.100***	-0.134***	-0.078***	-0.082**
	(0.009)	(0.025)	(0.010)	(0.029)	(0.010)	(0.030)
Sample Size (N)	51,094	32,693	51,094	32,693	51,094	32,693
Adjusted R-squared	0.325	0.296	0.167	0.138	0.134	0.112
First stage F-stat		7849.14		7849.14		7849.14
Mean (Cognition Score)	0.002	0.153	0.002	0.105	0.000	0.085
Panel B	**Language**		**Executive Function**		**Visuospatial Ability**	
Coefficient (SE)	**OLS**	**2SLS**	**OLS**	**2SLS**	**OLS**	**2SLS**
Depression	-0.145***	-0.280***	-0.060***	-0.049*	-0.026**	-0.029
	(0.015)	(0.041)	(0.009)	(0.025)	(0.008)	(0.025)
Sample Size (N)	24,812	17,718	51,094	32,693	51,094	32,693
Adjusted R-squared	0.17	0.142	0.396	0.367	0.406	0.394
First stage F-stat		3882.77		7849.14		7849.14
Mean (Cognition Score)	0.008	0.052	0.000	0.149	-0.001	0.118

RESULTS

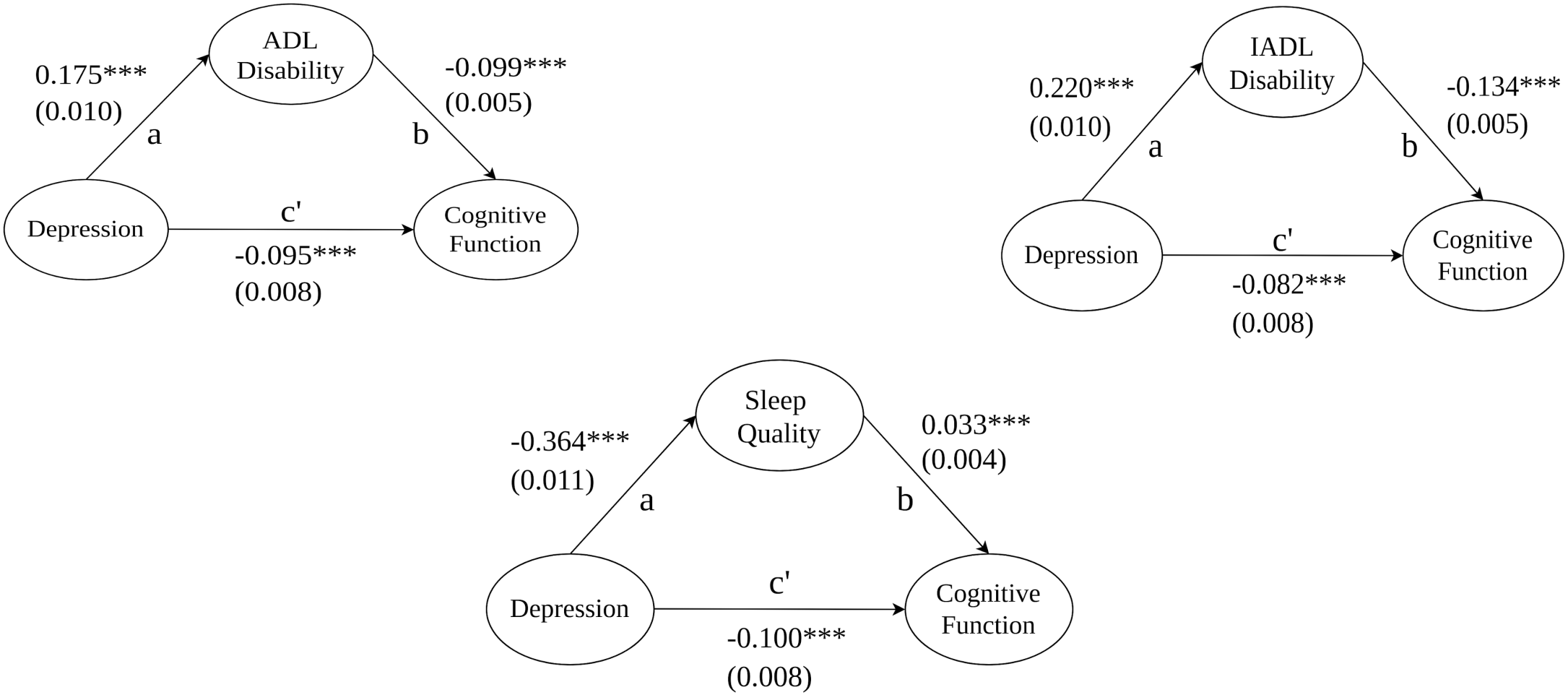


Figure 4. Mediation of the Association of Depression with Overall Cognitive Function

RESULTS

Table 4. Mediation Analysis: Pathways from Depression to Cognitive Function

Coefficient (SE)	**ADL**	**IADL**	**Sleep Quality**
Natural Indirect Effect (NIE)	-0.017***	-0.029***	-0.012***
	(0.001)	(0.002)	(0.002)
Natural Direct Effect (NDE)	-0.095***	-0.082***	-0.100***
	(0.008)	(0.008)	(0.008)
Total Effect (TE)	-0.112***	-0.112***	-0.112***
	(0.008)	(0.008)	(0.008)
Proportion Mediated (NIE/TE)	15.45%	26.29%	10.78%

RESULTS

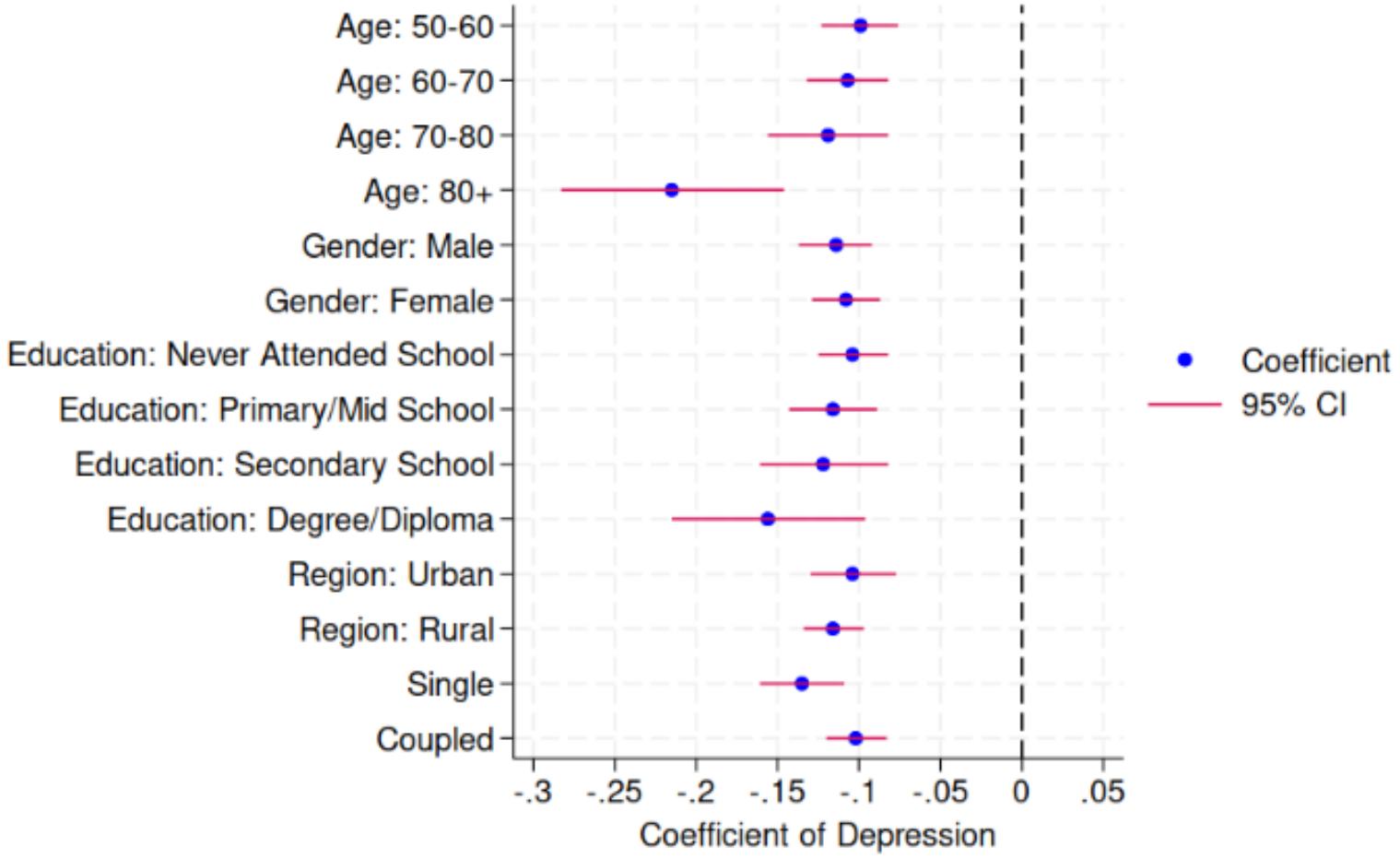


Figure 5. Heterogeneity Analysis: Association of Depression with Overall Cognitive Function

RESULTS

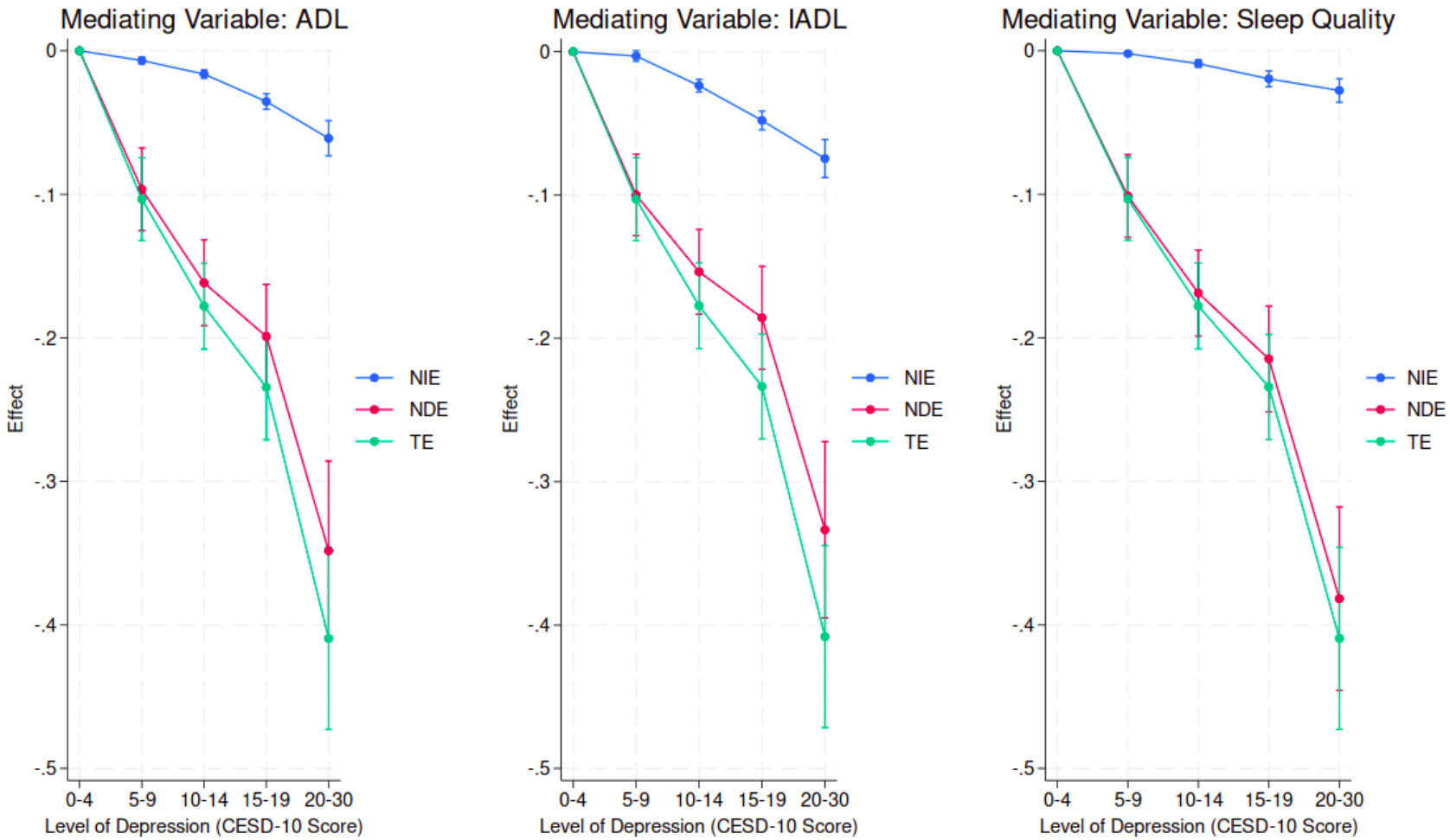


Figure 6. Heterogeneity Analysis: Mediation Analysis for Different Levels of Depressive Symptoms

CONCLUSIONS

- Study highlights the causal effect of depression on cognitive function

- Key findings:
  - Depressive symptoms associated with poor overall cognitive function as well as on orientation, memory, executive function, and language
  - Association of depressive symptoms with over cognitive function mediated by limitations in ADL, IADL, and quality of sleep
  - Age 80+ significant risk factor for poor cognitive health due to depression, compared to younger adults

- Interventions targeting mental health issues, particularly depression, can lead to improved cognitive function and may reduce risk of dementia and related disorders and/or delay onset of ADRD (Alzheimer's disease and Related Dementias)

- Role of Universal Health Coverage, including for elderly people, should be examined to mitigate the adverse impacts on aging related disorders