MAYO CLINIC



Population Neuroscience and Dementia Syndemics

Using Systems to Address a Global Health Crisis

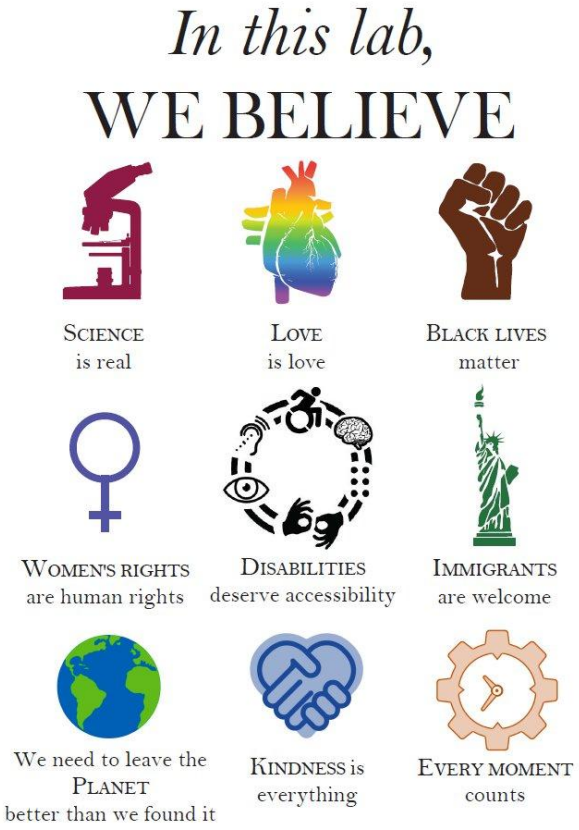
Ganesh M. Babulal
10/07/26

©2026 Mayo Foundation for Medical Education and Research |

Disclosures of Interest

Grant/Research Support

1. R01AG067428 **(PI)**
2. R01AG068183 **(PI)**
3. R01AG074302 **(PI)**
4. R01AG080469 **(MPI)**
5. RF1AG061900 **(Co-I)**
6. U19AG073585 **(Co-I)**
7. U19AG078109 **(Co-I)**



Speakers Bureau

N/A

Clinical Trials

N/A

Consultant

N/A

I own no stocks or equity in any pharmaceutical company

Dementia is a global crisis — and increasingly an LMIC one

152M

people projected to live with dementia by 2050

68%

of dementia cases in low- and middle-income countries (LMICs) by 2050

11.6%

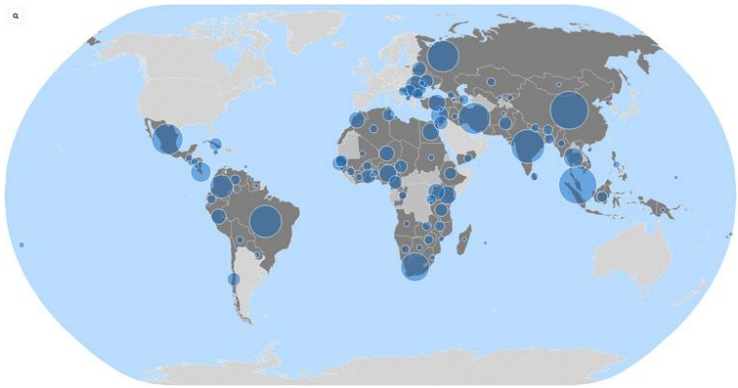
of 1,237 disease-modifying drugs tested in dementia were tested in LMICs

17%

of Sustainable Development Goal targets are on track to be achieved

The burden lands on families. Formal geriatric and long-term care is minimal in most LMICs. Older adults both give and receive care in multigenerational households, so dementia removes income, childcare, and household labor while adding caregiving demand.

The burden is gendered. Women in LMICs carry greater late-life dementia risk and burden, yet most sex/gender evidence comes from high-income countries.



Sources: Shaaban, Trani, Babulal et al., Nature Aging 2026 (PNDS); Nichols et al., Lancet Public Health 2022; Llibre-Guerra et al., Alzheimers Dement 2023; UN SDG Progress Report 2024.

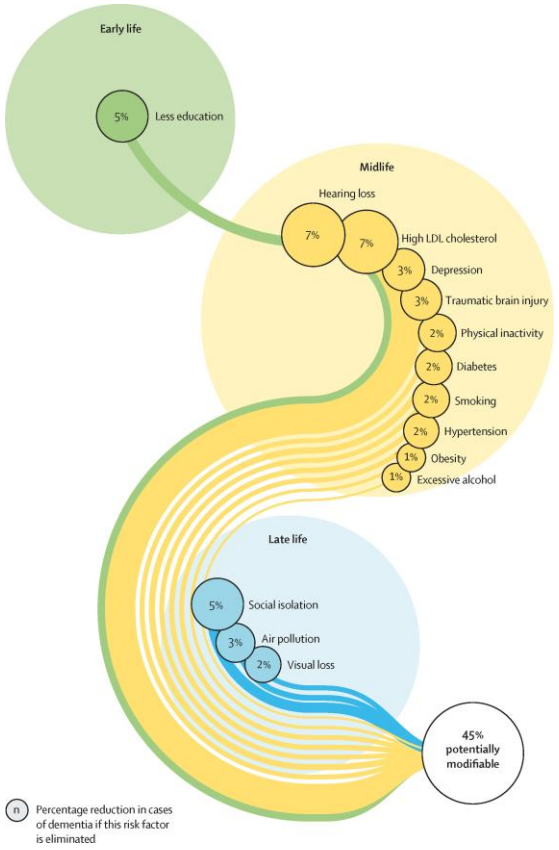
©2026 Mayo Foundation for Medical Education and Research

Why a systems lens?

Risk factors do not arrive alone — they are clustered and produced by structural deprivation

The single-risk-factor model

- The 2024 Lancet Commission lists 14 potentially modifiable risk factors — low education, hypertension, depression, social isolation, air pollution, and more.
- In LMICs these factors co-occur with poverty, conflict, climate shocks, and weak social protection.
- Income-only poverty measures miss overlapping disadvantages that shape exposure and access to care.
- Typical neuroscience samples are small, highly selected, and do not generalize to LMIC target populations.



Three needs to addresses

1. **Integrate** structural and social determinants of health (S/SDOH) with biological determinants of dementia
2. **Identify** context-dependent mechanisms and domains of deprivation that can guide public health intervention
3. **Generalize** with representative, population-based studies conducted in LMICs

Livingston et al., Lancet 2024; Shaaban, Trani, Babulal et al., Nature Aging 2026.

©2026 Mayo Foundation for Medical Education and Research

PART 1

The Population Neuroscience–Dementia Syndemics (PNDS) Framework

Shaaban, Trani, Babulal et al. Nature Aging 2026;6:38–55 — developed through the ISTAART Diversity & Disparities PIA LMIC Work Group and Sex & Gender SIG

©2026 Mayo Foundation for Medical Education and Research

Two lenses, fused into one framework

Population neuroscience

- Brings epidemiology and demography to cognition, imaging, and blood biomarkers
- Follows community members who start dementia-free — not clinic patients
- Multilevel and lifecourse; uses heterogeneity to learn
- Designs and analyses that protect internal and external validity

+

Dementia syndemics

- "Synergistic epidemics": health conditions that co-occur within S/SDOH contexts
- Conditions and social conditions interact to potentiate harm
- Intersectional: systems of oppression interact
- Biomedical approaches alone are unlikely to produce unbiased health gains

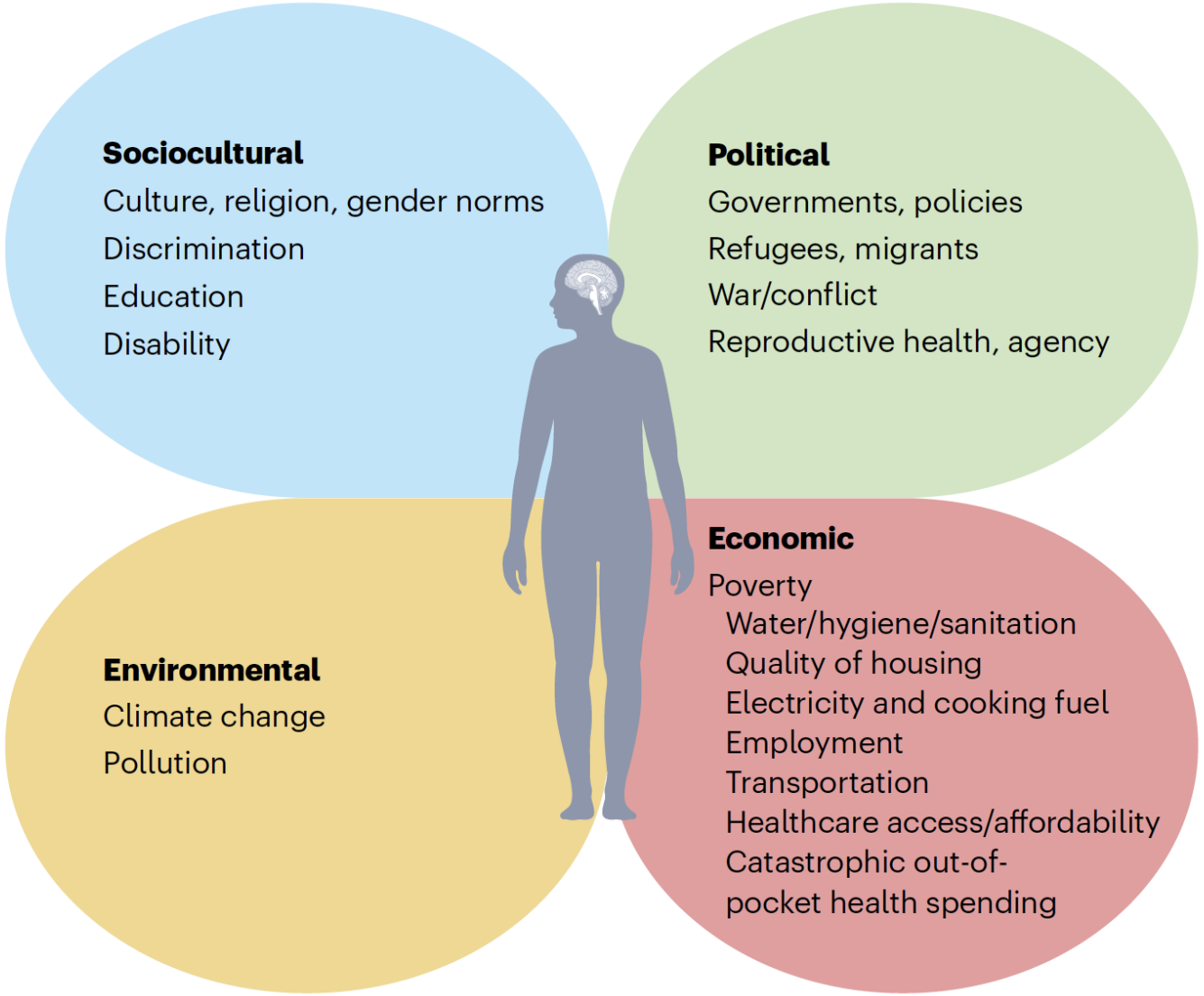
PNDS Multilevel, lifecourse, gender/sex-aware inference about dementia risk — from samples that transport to target populations in LMICs.

Ganguli et al., Alzheimer Dis Assoc Disord 2018; Singer et al., Lancet 2017; Shaaban, Trani, Babulal et al., Nature Aging 2026.

©2026 Mayo Foundation for Medical Education and Research

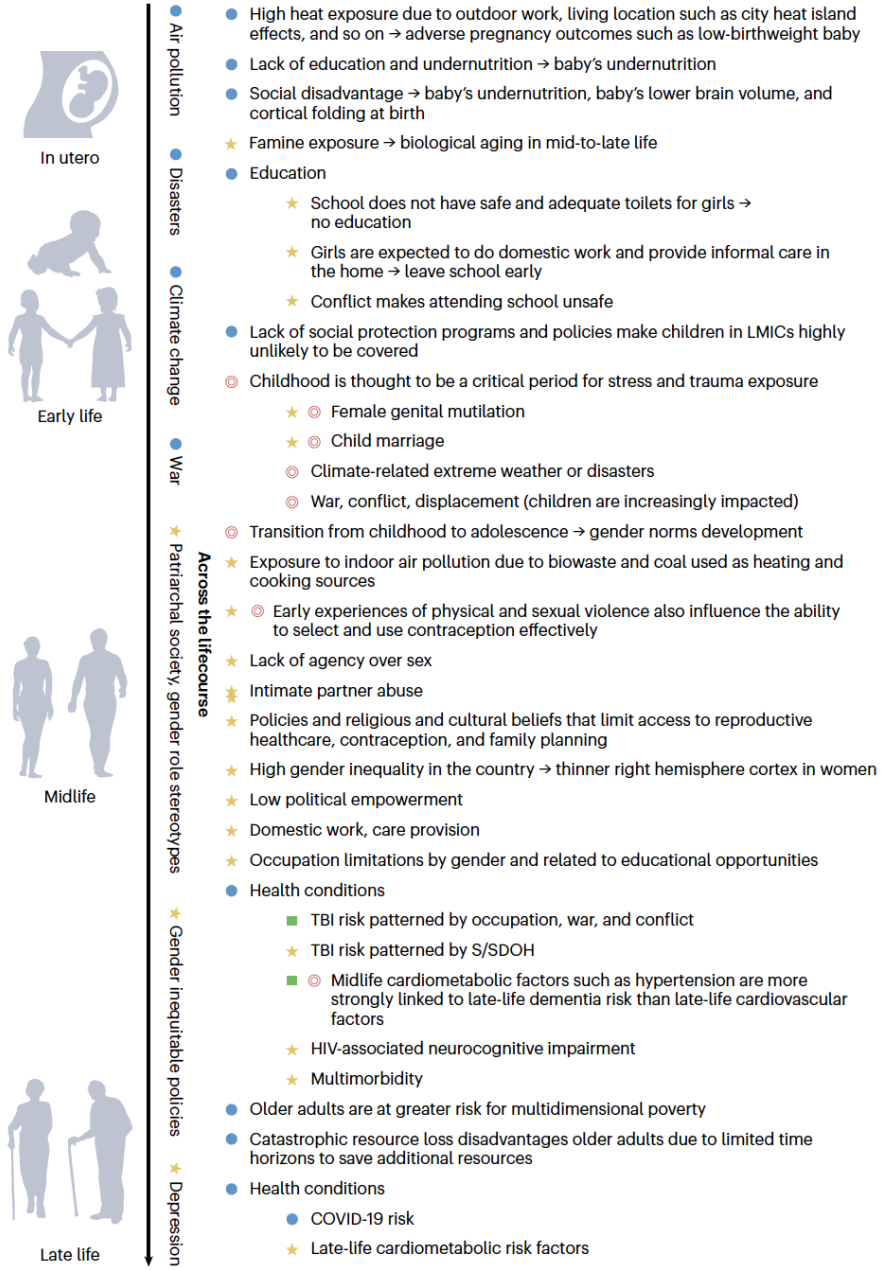
Syndemic risk and protective factors

The body and brain develop and age across the lifecourse within these four contexts



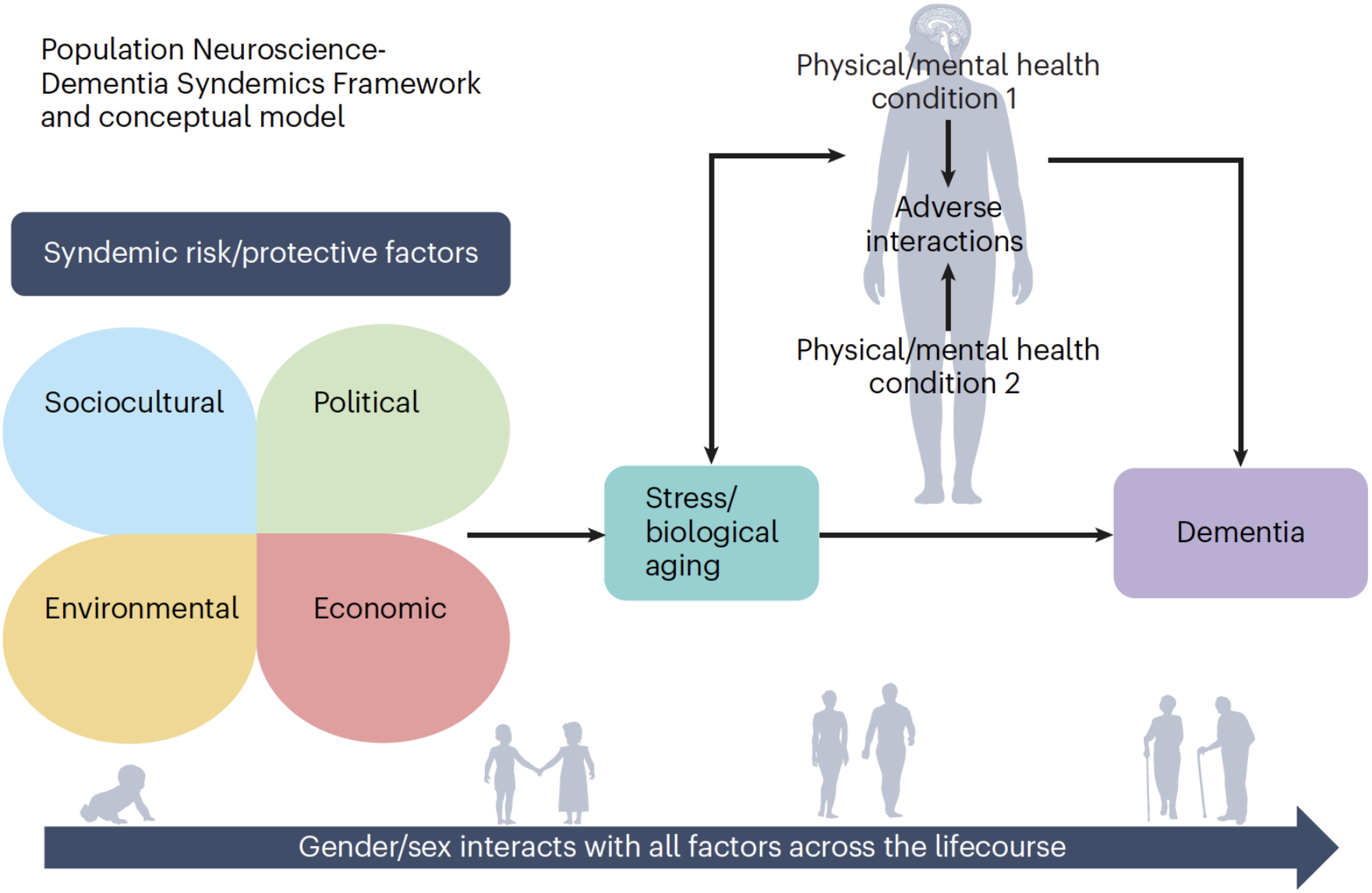
©2026 Mayo Foundation for Medical Education and Research

Lifecourse exposures differ by gender/sex



©2026 Mayo Foundation for Medical Education and Research

The PNDS conceptual model



©2026 Mayo Foundation for Medical Education and Research

What the framework predicts for women and for LMICs

Three gender/sex insights

More exposure
Girls and women face more adverse life events and milieus linked to dementia risk.

Less protection
Reduced or delayed access to education, employment, physical activity, and political participation.

Stronger links
Risk factor–dementia associations may be stronger, and protective associations weaker, in women.

Capacity–load: reserve meets risk

Capacity

set during critical developmental periods

Load

syndemic and health challenges accrued over life

Early developmental challenges lower the capacity set-point. Combined with accruing syndemic load, people in LMICs may develop dementia earlier in the lifecourse and with less mid-to-late-life risk than people in HICs — making early-life prevention even more essential.

PNDS Box 2 and key insights (Shaaban, Trani, Babulal et al., Nature Aging 2026); capacity–load model from Miranda et al., Nat Med 2019.

©2026 Mayo Foundation for Medical Education and Research

Population neuroscience: four design commitments

Characterize richly

Descriptive epidemiology, contexts and environments, disease phenotypes, risk and protective factors, brain health mechanisms

Think in time

Risk and protection across the lifecourse; temporal trends and cohort effects; multigenerational studies

Use heterogeneity

Include participants diverse in characteristics and contexts; examine interactions of factors and contexts

Protect validity

Unbiased selection of the study sample; selection weighting, joint models for attrition and death, transportability estimators

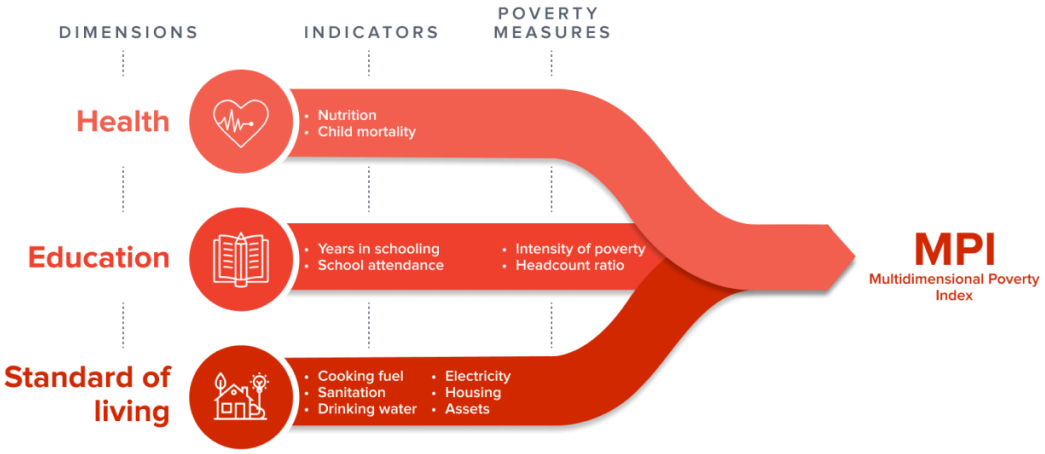
For LMICs, two features are non-negotiable: an unbiased study sample drawn from the community, and analytic methods that transport findings to the target population.

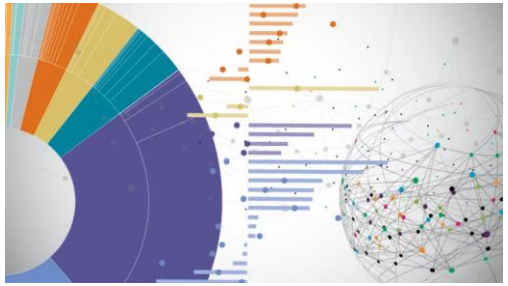
PNDS Box 3 (Shaaban, Trani, Babulal et al., Nature Aging 2026); Keyes et al., Curr Top Behav Neurosci 2024.

©2026 Mayo Foundation for Medical Education and Research

Measuring deprivation: the dual cut-off method

Alkire–Foster multidimensional poverty measurement, applied to dementia





1 **Indicator cut-off** Is the person deprived on each indicator? (e.g., never enrolled in school; CES-D ≥ 15)

2 **Count weighted deprivations** Here: 4 of 6 dimensions

3 **Poverty cut-off d** Multidimensionally poor if deprived in ≥ d dimensions (primary d = 4)

H — **Headcount ratio**
Prevalence: share of people who are multidimensionally poor

A — **Average deprivation share**
Intensity: how many deprivations the poor experience

$M_0 = H \times A$ — **Adjusted headcount ratio**
Depth; decomposable by dimension, sex, age, and country

Why it fits a syndemic frame: it measures co-occurring deprivations in the same person, not one welfare indicator — and low correlations between indicators confirm they capture distinct facets.

Alkire & Foster, J Public Econ 2011. Weighting robustness checked with equal-indicator and equal-nested weights in every study.

©2026 Mayo Foundation for Medical Education and Research

PART 2

Three published studies: the same method in three crisis contexts

South Africa (JAMA Netw Open 2022) · Afghanistan (eClinicalMedicine 2023) · Pakistan (Innovation in Aging 2024)

Soweto, South Africa | **Badakhshan & Ghazni, Afghanistan** | **Punjab & Sindh, Pakistan**

©2026 Mayo Foundation for Medical Education and Research

South Africa

Soweto, Johannesburg

Urban township; legacies of apartheid and Bantu education; more than half the population below the poverty line.

- 227 adults aged ≥ 50
- Random 2-stage cluster sample, 40 census areas
- Nov 2019 – Feb 2020
- AD8 + RUDAS
- 7 dimensions, 11 indicators



Multidimensional poverty doubles among adults with dementia

20.0% vs 9.7%

multidimensionally poor (d = 4): dementia vs no dementia

2.31

adjusted OR for dementia if poor (95% CI 1.08–4.95)

2.03

adjusted OR for women (95% CI 1.00–4.12)

1.27

adjusted OR per additional household member (1.05–1.53)

Main contributors to poverty

Education | **Health** | **Employment**

Deprivation in clean water and sanitation was lower among adults with dementia — a reminder that not every dimension moves together.

Trani, Moodley, Maw, Babulal. JAMA Netw Open 2022;5(3):e224160.

©2026 Mayo Foundation for Medical Education and Research

Afghanistan

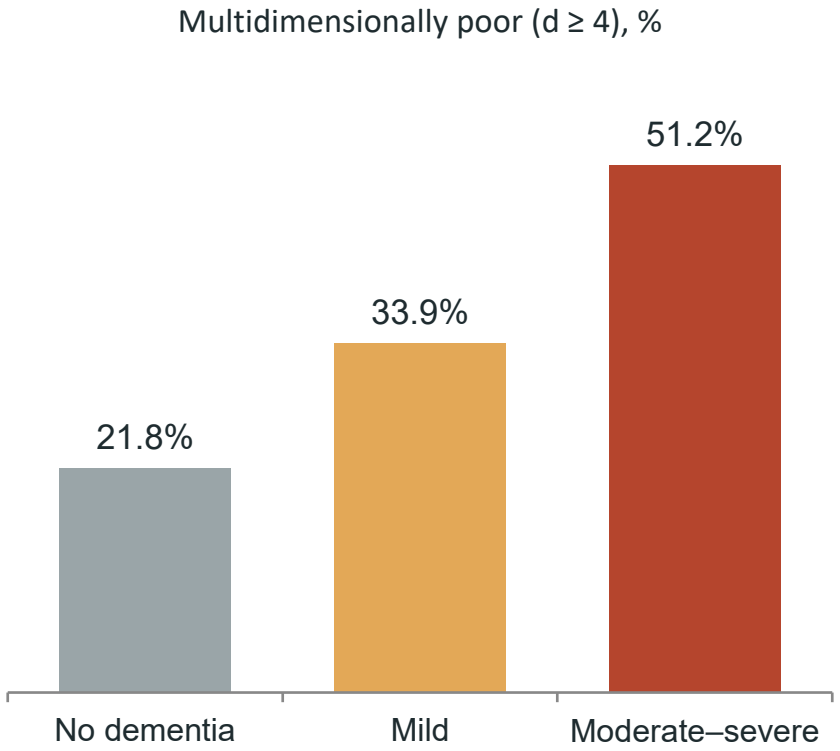
Badakhshan & Ghazni provinces

Four decades of conflict, regime change in 2021, economic collapse, drought and flood. First evidence from a conflict setting.

- 478 adults aged ≥ 50 interviewed
- 43 villages, 3-stage random sample
- Feb – Apr 2022
- RUDAS (Dari, Pashto)
- 6 dimensions, 16 indicators



Poverty rises with dementia severity in a conflict setting



4.42

odds of dementia if multidimensionally poor, unadjusted (95% CI 2.05–9.53)

17.38

adjusted odds among adults aged ≥ 70 (95% CI 2.22–135.6)

Main contributors

Education | **Employment** | **Health** | **Living conditions**

Women were over-represented in moderate–severe dementia; stigma contributed little — respect for elders held.

Trani, Zhu, Park, Khuram, Azami, Fazal, Babulal. eClinicalMedicine 2023;58:101906.

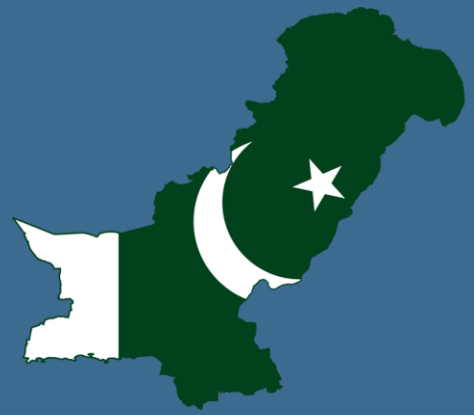
©2026 Mayo Foundation for Medical Education and Research

Pakistan

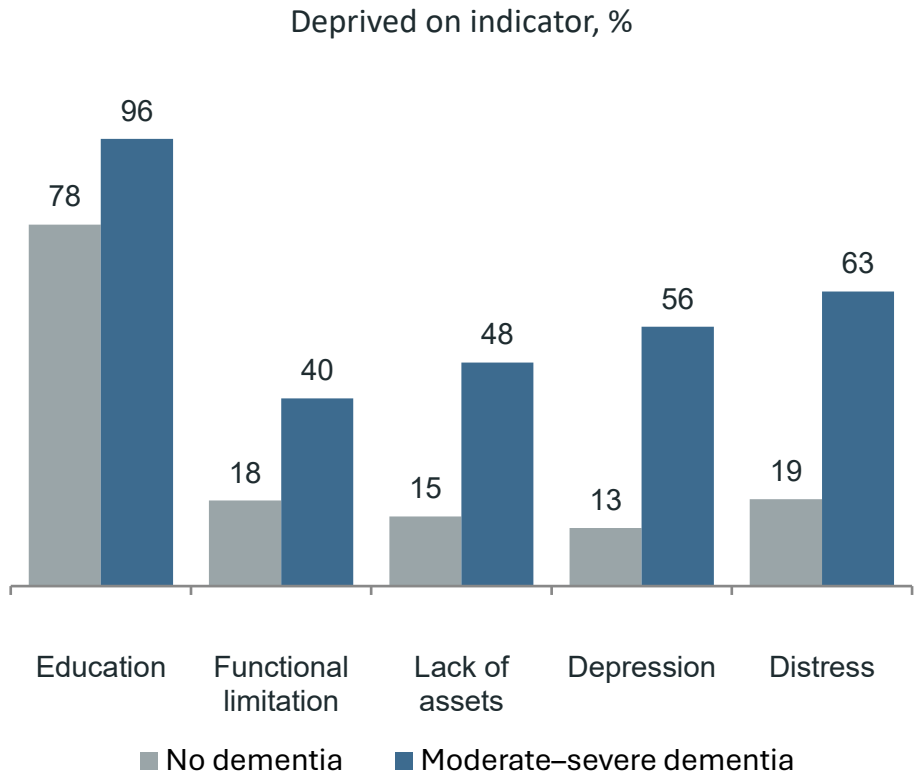
Punjab & Sindh provinces

Chronic political instability, wide inequality, and the 2022 monsoon floods that submerged a third of the country during fieldwork.

- 817 adults aged ≥ 50 analyzed
- 136 villages, 3-stage random sample
- Mar – Aug 2022
- RUDAS (Urdu, Sindhi)
- 6 dimensions, 15 indicators



Psychological deprivation stands out alongside education



32.7%

of adults with moderate–severe dementia poor at d = 4, vs 13.2% without

3.88

adjusted OR if poor (95% CI 1.61–9.31); 65.5 among adults ≥ 70

2.07

adjusted OR for women (95% CI 1.44–2.95)

Main contributors

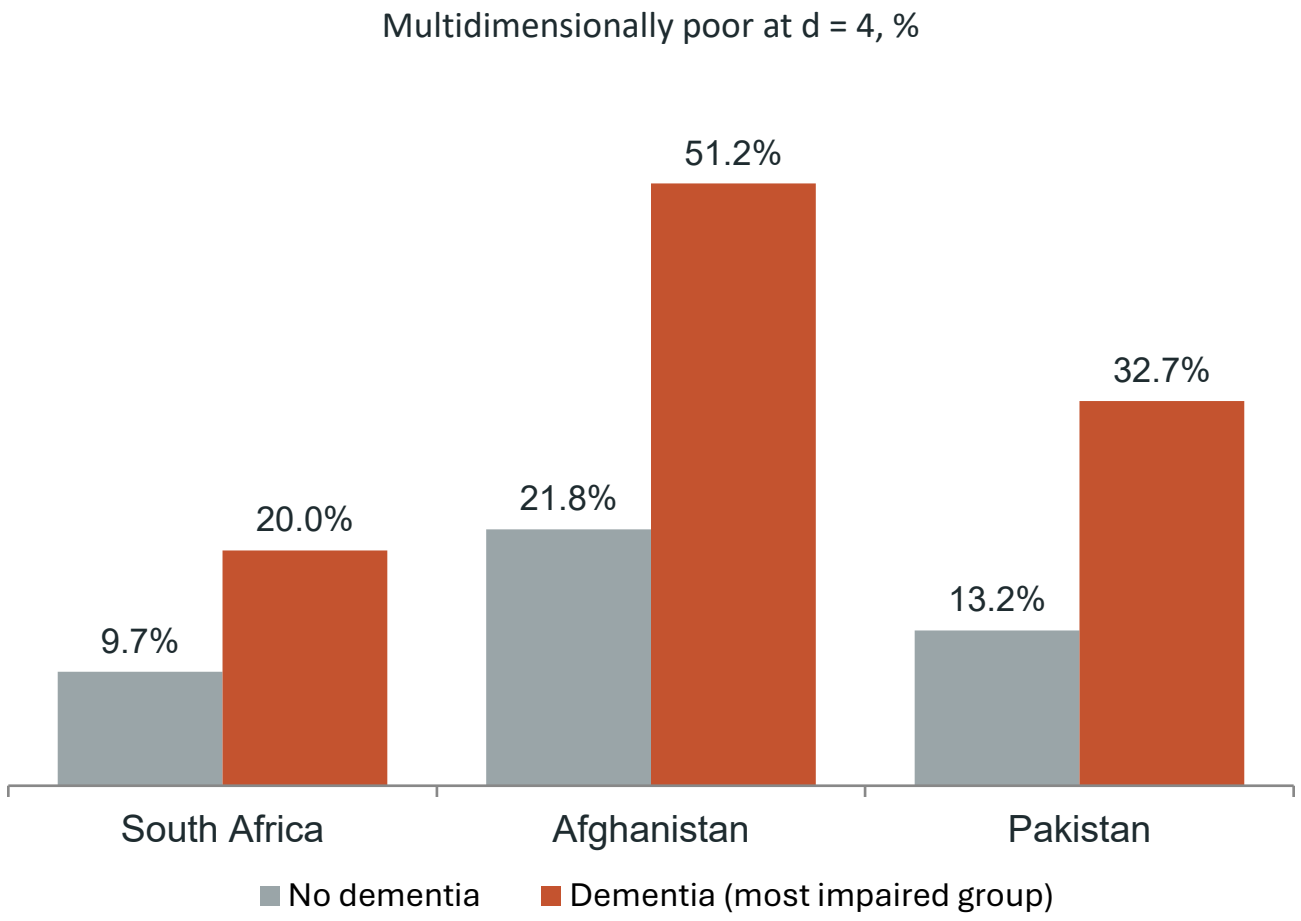
Education | **Health** | **Psych. well-being** | **Living conditions**

Trani, Zhu, Park, Babulal. Innovation in Aging 2024;8(2):igae007. ORs from Table 5 (adjusted for sex, marital status, age, household size).

©2026 Mayo Foundation for Medical Education and Research

Same signal, three contexts

The poverty–dementia association replicates; the dimensions driving it differ



South Africa — **2.31**

adjusted OR (1.08–4.95)

Education · health · employment

Afghanistan — **4.42**

unadjusted OR; 17.38 adjusted at ≥ 70

Education · employment · health

Pakistan — **3.88**

adjusted OR; 65.5 at ≥ 70

Education · health · psych. well-being

Most impaired group: AD8 or RUDAS dementia (South Africa); RUDAS moderate–severe (Afghanistan, Pakistan). Indicators and cut-offs were country-specific, so levels are not directly comparable — which motivated harmonization.

©2026 Mayo Foundation for Medical Education and Research

PART 3

A harmonized three-country analysis

Multidimensional poverty and dementia in Afghanistan, Pakistan, and South Africa: a cross-sectional analysis of three harmonized population-based surveys — manuscript under review

©2026 Mayo Foundation for Medical Education and Research

One framework, three settings, 2,008 older adults

Under review

2,008

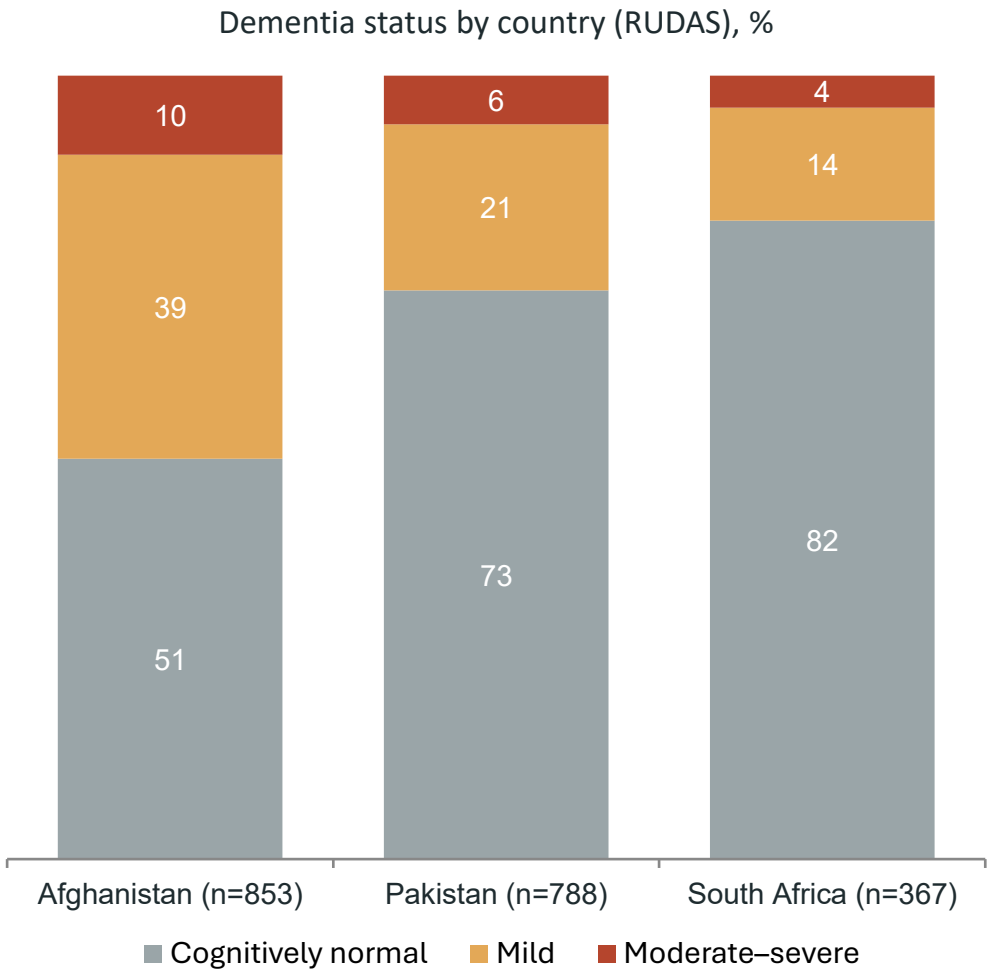
adults aged ≥ 50 · 1,307 cognitively normal, 551 mild, 150 moderate–severe dementia

Settings Afghanistan: rural Badakhshan & Ghazni + Kabul · Pakistan: Punjab & Sindh · South Africa: Soweto

Exposure 6 dimensions, 12 harmonized indicators; country-specific cut-offs defined a priori (e.g., education = never enrolled in AFG/PAK, primary only in SA)

Outcome RUDAS: no, mild, or moderate–severe dementia

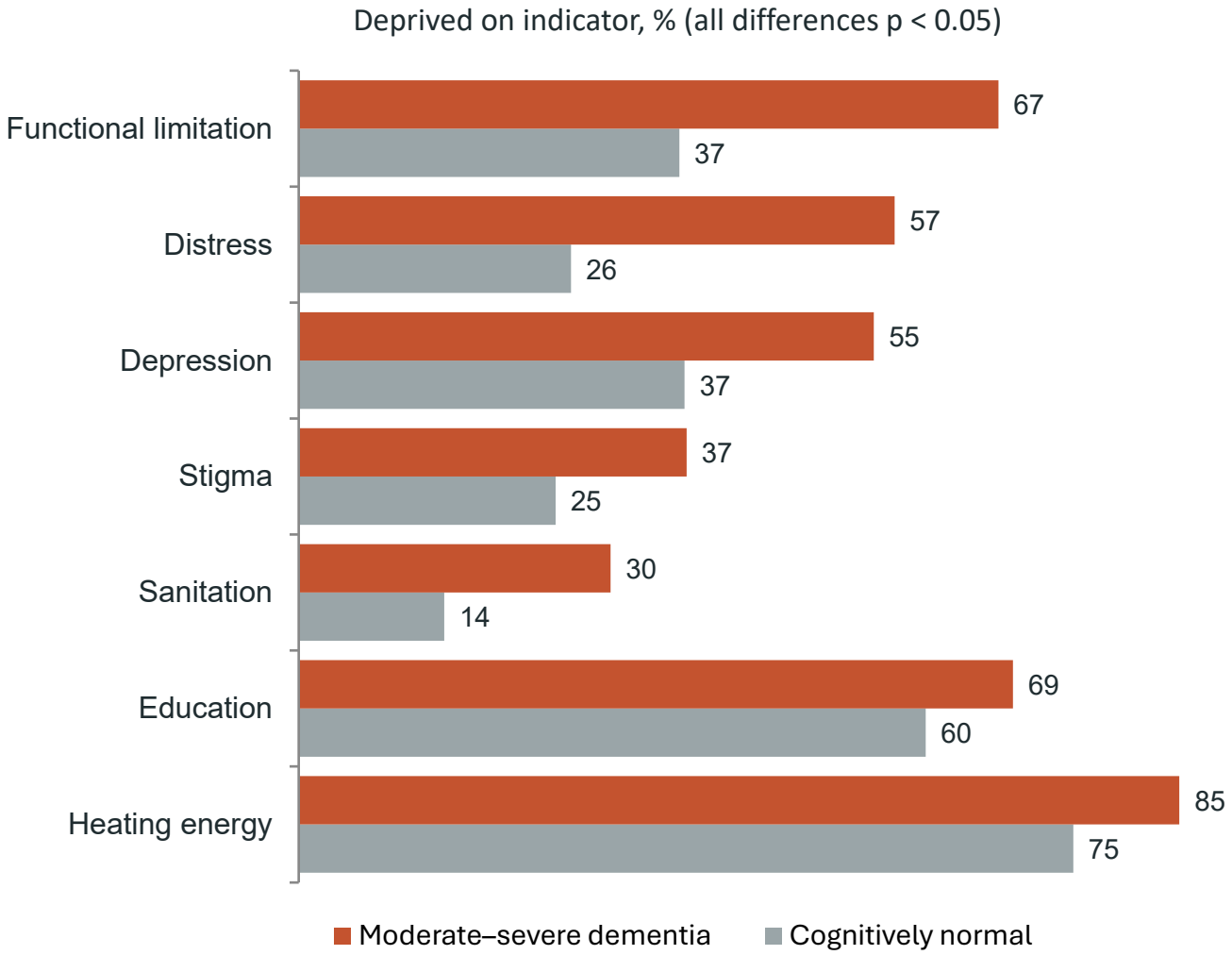
Analysis H, A, M_0 at d = 1–12 (primary d = 4); ordered logistic regression adjusted for age, sex, marital status, household size, country



Trani, Babulal et al., under review. Percentages computed from manuscript Table 2 counts.

©2026 Mayo Foundation for Medical Education and Research

4 in 5 adults with dementia are multidimensionally poor



Multidimensionally poor at d = 4

50.7% Cognitively normal

79.5% Mild dementia

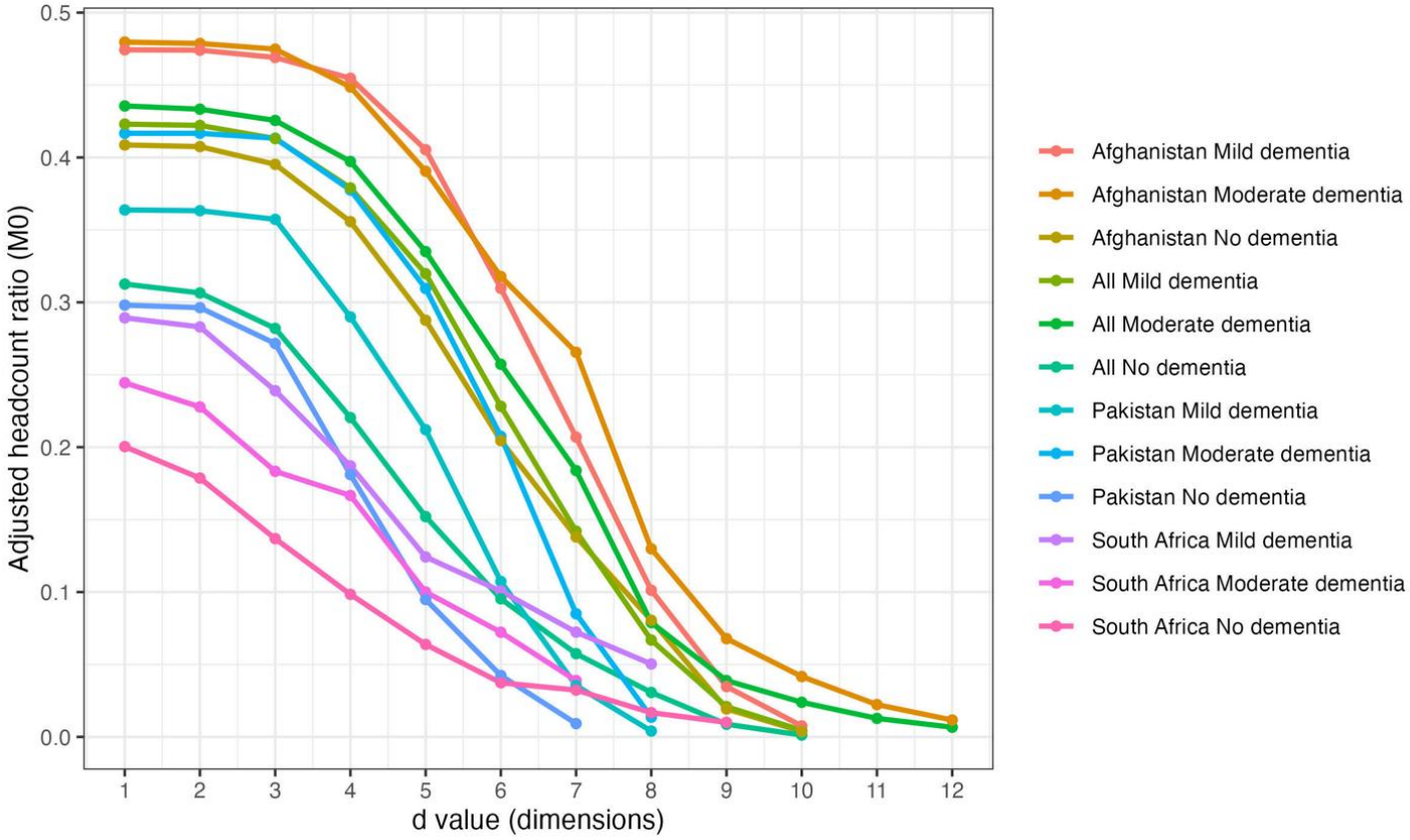
80.1% Moderate–severe dementia

Among women: education deprivation 84.0% vs 64.5% and heating-energy deprivation 80.2% vs 60.2% (moderate–severe vs cognitively normal); no significant gap among men.

Trani, Babulal et al., under review (Supplement Table 1). Pooled Afghanistan, Pakistan, South Africa; n = 2,008.

©2026 Mayo Foundation for Medical Education and Research

The poverty gap deepens as deprivations stack up



+46% to +413%

Gap in M_0 vs no dementia, from d = 1 to d = 9

+104% vs +75%

Gap at d = 4 for women vs men

+62% to +117%

Gap at d = 4 from age 50–59 to age ≥ 70

+112% · +94% · +31%

Gap at d = 4 in Pakistan, South Africa, Afghanistan

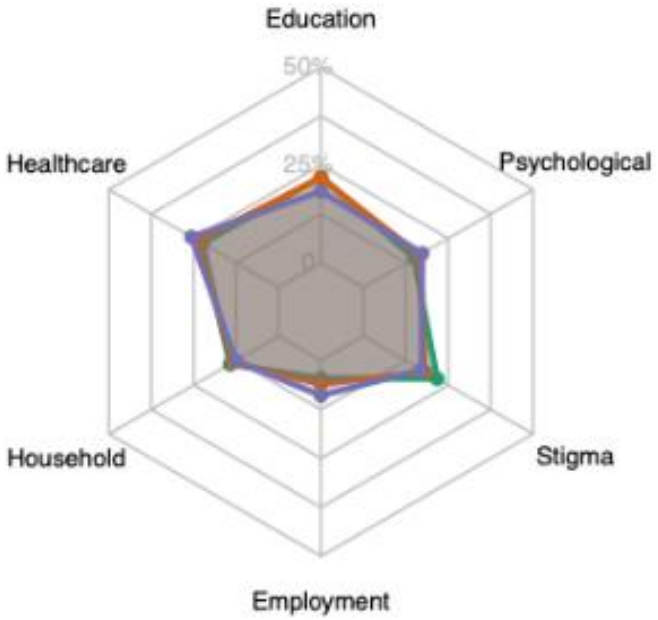
Afghanistan has the deepest poverty overall, but the largest dementia-related gap is in Pakistan.

Adjusted headcount ratio (M_0) by country and dementia status; manuscript Figure 1A. Trani, Babulal et al., under review.

©2026 Mayo Foundation for Medical Education and Research

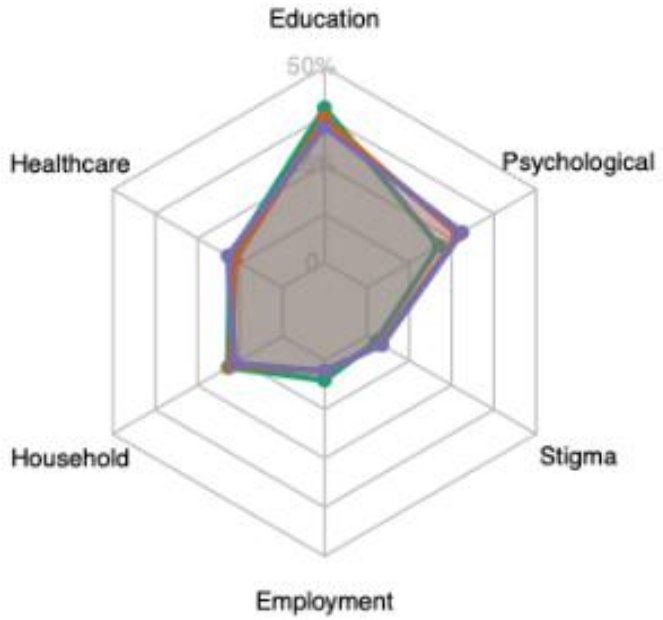
Education leads everywhere; next drivers vary by setting

Afghanistan



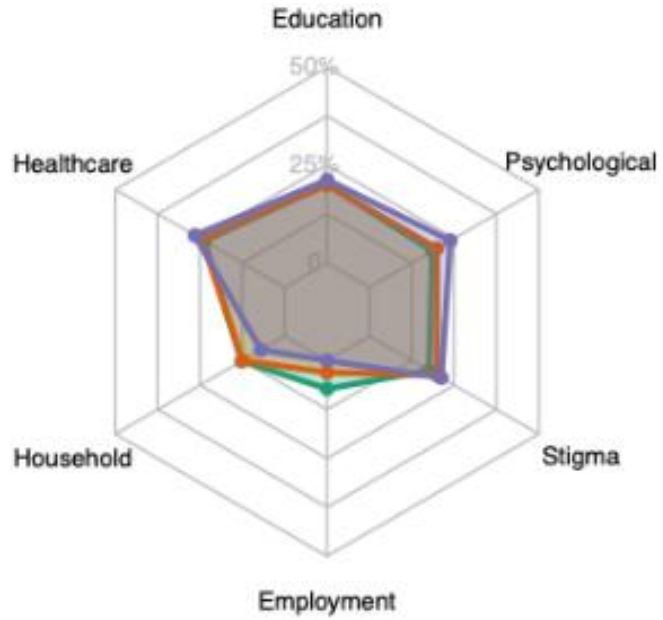
Functioning limits and stigma prominent; living standards salient amid conflict and economic collapse

Pakistan



Education contributes over one-third of deprivation; psychological well-being most salient

South Africa



Functioning limits and stigma prominent; smaller living-standards contribution in this urban sample

Cognitively normal Mild dementia Moderate–severe dementia

Percentage contribution of each dimension to M_0 (d = 4); manuscript Figure 2, country panels. Trani, Babulal et al., under review.

©2026 Mayo Foundation for Medical Education and Research

Three things the harmonized study adds



Magnitude

A 2.5-fold increase in odds is larger than reported for most single modifiable risk factors — consistent with risk factors being clustered and produced by structural deprivation.



Actionability

The leading contributors — education, functional limitation, living standards, psychological well-being — sit largely outside dementia services and within existing global health and development programs.



Bidirectionality

Deprivation plausibly raises risk across the life course, and dementia erodes earnings, function, and standing. South Africa's older-person and disability grants may buffer this; households in rural Pakistan and Afghanistan are largely unsupported.

Policy responses should be context-specific and prioritize education, health (including mental health), and livelihoods.

Trani, Babulal et al., under review; Livingston et al., Lancet 2024.

©2026 Mayo Foundation for Medical Education and Research

St. Louis, USA

The ARCHES cohort

Does the framework travel to a high-income setting? Black adults bear about twice the dementia risk of non-Hispanic White Americans.

- 312 Black adults aged ≥ 45, cognitively normal at phone screen
- S/SDOH composite index: 37 indicators, 10 factors of the NIA Health Disparities Research Framework
- PCI: MoCA ≤ 23 (n = 105)
- PCP: PACC < −1 SD (n = 47)



Individual-level S/SDOH deprivation outperforms area indices

11.48	**S/SDOH composite index** adjusted OR for PCI (2.08–65.00); 13.84 for PCP (1.27–152.07)
1.13	**Social Vulnerability Index** adjusted OR for PCI (1.01–1.25); not significant for PCP
n.s.	**Area Deprivation Index** not associated with PCI or PCP

What drives deprivation (share of index, PCI)

Healthcare barriers ~20% | **Psychological factors >20%** | **Health behaviors ~16%**

Education and reading contributed ~9%, nearly double the share among cognitively normal adults. S/SDOH-CI was 62.4% higher with PCI (p = 0.009).

Trani, Zhu, Walker, Hudson, Babulal. J Racial Ethn Health Disparities 2025. PCI/PCP: potential impairment / poor performance.

©2026 Mayo Foundation for Medical Education and Research

Across five analyses, one consistent pattern

Setting	Sample	Deprivation measure	Headline association	Leading contributors
South Africa — urban Soweto	227, age ≥ 50	7 dimensions / 11 indicators	**aOR 2.31 (1.08–4.95)**	Education, health, employment
Afghanistan — rural, conflict	478, age ≥ 50	6 dimensions / 16 indicators	**OR 4.42 unadj.; aOR 17.38 at ≥ 70**	Education, employment, health, living standards
Pakistan — rural, climate shock	817, age ≥ 50	6 dimensions / 15 indicators	**aOR 3.88 (1.61–9.31)**	Education, health, psychological well-being
Harmonized 3-country (under review)	2,008, age ≥ 50	6 dimensions / 12 indicators	**aOR 2.49 (1.96–3.17)**	Education, functioning, psych. well-being, stigma
St. Louis, USA — ARCHES	312 Black adults, age ≥ 45	10 NIA HDRF factors / 37 indicators	**aOR 11.48 (PCI); 13.84 (PCP)**	Healthcare barriers, psychological factors, health behaviors

Consistent: deprivation clusters and is associated with worse cognition; women and older adults are more exposed. **Context-specific:** which dimensions drive it.

Models differ in outcome definition and covariates; ORs are not directly comparable across rows.

©2026 Mayo Foundation for Medical Education and Research

Operationalizing PNDS: recommendations

Policy

- Universal, high-quality, affordable primary healthcare
- Brain-health diplomacy: education access, reproductive health, climate, pollution

Planning & funding

- Plan at least a generation ahead
- Follow the Dementia Charter of Conduct against research imperialism
- Fund LMIC-led research, early-career leaders, resilient infrastructure

Study design

- Sample the target population, including diverse participants
- Measure gender/sex and syndemic factors together
- Add dementia outcomes to existing LMIC cohorts
- Strengths-based framing (e.g., multilingualism)

Analysis

- Multilevel models; test additive and multiplicative interactions
- Selection weighting and joint models for validity
- Transportability estimators
- Ethical AI per WHO guidance

PNDS Table 2 (Shaaban, Trani, Babulal et al., Nature Aging 2026). Example cohorts: ELSA-Brasil, ELSI-Brasil, Pelotas Birth Cohort, CARRS, and our South Africa and Afghanistan cohorts.

©2026 Mayo Foundation for Medical Education and Research

What we cannot yet say — and where we go next

Current limits

- Cross-sectional: poverty may be a cause and a consequence of dementia
- Screening instruments (RUDAS, AD8, MoCA), not clinical diagnosis or biomarkers
- Attrition and missing interviews (roughly 22–54%) may not be random
- Small samples at the oldest ages; South Africa urban-only
- Wide CIs for age-stratified and US estimates

Next steps

- Longitudinal follow-up to establish temporal ordering
- Low-cost biomarkers: blood-based assays, portable low-field MRI
- Transportability to national target populations
- Test PNDS-informed interventions: education, social protection, rehabilitation, mental health
- Reciprocal innovation between LMICs and HICs

Limitations as reported in each study; next steps from PNDS recommendations and study discussions.

©2026 Mayo Foundation for Medical Education and Research

Dementia is not simply a biomedical condition of aging. It is bound up with cumulative, life-course deprivation; many sources of deprivation are modifiable.

©2026 Mayo Foundation for Medical Education and Research

Thank you




I JOINED THE FIGHT AGAINST
ALZHEIMER'S
AND ALL OTHER DEMENTIA.
WALK TO END ALZHEIMER'S


EXIT


MERRY CHRISTMAS