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Burden and Risk Factors of All-Cause Dementia in South Asia: An Analysis of Global Health Data and a Framework for Future Dementia Longitudinal Studies in Low-Resource Settings

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Abstract

Background: Dysregulated brain aging leads to dementia in some older adults. South Asia is one of the most populous regions of the world with a rapidly growing older adult population. Yet, very few studies have focused on quantifying the status and risk factors driving aging-related conditions such as dementia in this part of the world. **Objectives***:* We explored multiple sources of global health data to quantify and compare all-cause dementia indices in South Asian countries. **Design**: Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka were considered. Population statistics and dementia as a priority area were examined using US Census Bureau and World Health Organization Global Dementia Observatory data. Crude and age-standardized rates (ASR) of dementia incidence, deaths and disability-adjusted life years (DALYs) were extracted and analyzed from the Global Burden of Disease (GBD) 2019 Study. **Results**: Our analysis reiterated that there are limited resources dedicated to dementia in this region. Sri Lanka and Afghanistan had the highest dementia crude rates and age-standardized rates, respectively [Crude DALYs, Sri Lanka = 321.52 (132.12–736.58); ASR DALYs, Afghanistan = 432.72 (179.01–1001.95)]. The burden of dementia in some South Asian countries was comparable to estimated global averages, and was largely driven by population aging. Analyses of available data on known biological, behavioral, environmental and disease risk factors in the region highlighted the role of metabolic dysregulation in dementia. **Conclusions**: Our preliminary analysis of available global health data highlights an emerging need for resources for dementia prevention and care in South Asia. There is also a critical need for future longitudinal follow-up studies focusing on dementia that are well-designed and can be harmonized with other dementia-related studies. We describe a roadmap for designing them—taking into account cultural, economic, public health and population aging dynamics that may be uniquely applicable to South Asian countries.

Keywords: aging; Alzheimer's disease; dementia; South Asia; risk factors; Metabolism

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1. Introduction

Aging results in multiple morphological and biochemical changes in the central and peripheral nervous systems. In some individuals, these changes may ultimately lead to dementia [1]—characterized by loss of function in brain regions responsible for visuo-spatial memory, orientation, thinking, learning, language skills and reasoning [2]. While aging is the strongest risk factor for dementia, the likelihood of developing the disease is exacerbated by other behavioral, biological, genetic and environmental factors [3]. Modifiable risk factors of dementia include low physical activity, obesity, tobacco smoking, alcohol consumption and unhealthy eating habits. Additionally, factors related to low socioeconomic status (SES), including low levels of education, as well as psychosocial factors related to aging, e.g., loneliness and isolation, are also emerging risk factors of this disease. Dementia is caused by and includes several conditions [4], e.g., Alzheimer's disease, vascular disease, Lewy body disease, frontotemporal dementia, alcohol-related dementia, HIV-related dementia and brain injury-related dementia. Overall, this debilitating disease is characterized by progressive loss of cognitive capacity which leads to increased dependency, reduced quality of life and mortality [5,6]. There are no cures for this disease, and currently, most treatments only focus on symptom management [7]. Dementia also disproportionately affects women, as women live longer and might be subjected to gender-based discrimination throughout their life courses.

The Global Burden of Disease (GBD) 2019 study estimated staggering increases in dementia rates worldwide over the next few decades [8]. Out of these, low-and-middle-income (LMIC) countries may experience a very high financial burden due to dementia [9]. While population growth and aging play a substantial role in this, the poor control of risk factors stemming from lack of awareness, absence of resources and limited research efforts on aging populations may be contributing to this trend [10,11]. Much also remains unknown about regional and country-specific dementia statistics and determinants—which are most relevant to policy-related decision-making.

South Asia is currently the most highly and densely populated region of the world. It is estimated that over 2 billion people live in South Asia, which accounts for more than 25% of the world's population at present. Despite significant economic advancements made in some countries, South Asia has one of the lowest Gross Domestic Product (GDP) per capita in the world ($2000) [12]. A significant proportion of these people are part of a rapidly aging population [13], where one in five adults will be over the age of 65 by 2050 in South Asia. Many South Asian countries are still deeply plagued by communicable diseases. However, with rapidly increasing industrialization, many regions of South Asia are quickly becoming epicenters for aging-related chronic diseases, e.g., heart disease, diabetes mellitus and cancer [14]. Previous studies have already identified risk factors for chronic diseases in South Asian populations, e.g., hypertension, hyperglycemia and hypercholesterolemia [15–17], which may co-occur in individuals as they age. Other studies have also identified genetic factors that appear to strongly contribute to disease phenotypes observed amongst South Asian populations [18,19]. Yet, so much more remains unknown about biological and demographic factors driving health and aging in this part of the world.

According to early reports, the burden of dementia in South Asia is substantial but health policy, awareness, and research areas do not adequately address this pressing need. Even though South Asian countries are typically aggregated in global health classifications, there is high variability and diversity between countries. Therefore, it is important to examine country-specific dementia data. Such an approach can also lead to the identification of potential hotspots for disease and respective risk factors which can help with targeted disease mitigation efforts. Importantly, it can also help quantify the burden of dementia at different levels, e.g., individuals, caregivers, health sectors and the community. In the

present study, we examined dementia-related data from multiple sources to explore and compare the status of the disease as well as risk factors that may be contributing to disease outcomes between different countries.

2. Methods

2.1. Definitions

South Asia was defined according to the World Bank classification of countries which includes Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka [20].

For the present study, the standard definitions of dementia were used as per the GBD 2019 study [21]. It used the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III, DSM-III-R, DSM-IV, or DSM-5, or the International Classification of Diseases (ICD)-8, ICD-9, ICD-10 in representative surveys for dementia cases. This is based on the WHO definition of dementia—an umbrella term used to refer to several diseases affecting memory, other cognitive abilities, and behavior that interfere with a person's ability to maintain their activities of daily living. This definition includes Alzheimer's disease, vascular dementia, dementia with Lewy bodies, frontotemporal dementia and dementia that develops because of HIV, alcohol abuse, brain injury and nutritional deficiencies.

2.2. Datasets

US Census data: Global demographic data were accessed through the international database of the census.gov website [22]. With this publicly available database, demographic measures of 200 countries can be accessed. Data from censuses, administrative records, vital statistics and National statistical offices of countries are compiled here. For the present analysis, we examined total population, population density, life expectancy at birth, dependency ratio for 65+ and percentage of 65+ year-old people in the total population.

WHO Global Dementia Observatory data: Through this data and knowledge exchange platform [23], access to key dementia data from 62 participating countries on policies, service delivery, information and research is provided. For the present analysis, we examined whether each South Asian country has a dementia national plan, contributes to the dementia observatory and the availability and status of dementia reporting in the past two years (2017–2019).

Global Burden of Disease (GBD) 2019: Dementia incidence, death and disability-adjusted life years (DALY) rates data as well as risk factor data used in the current study were obtained from the Global Health Data Exchange (GHDx) Query Tool [24]. Detailed methods of the GBD 2019 Study have been published previously [21]. Original sources of GBD data include administrative sources, vital registries, disease registries, census/surveys, surveillance systems, hospital records, environmental and geospatial monitors, and scientific literature. Original data from multiple sources are compiled, corrected for known biases, entered into a database and passed through statistical modeling pipelines (e.g., Space–time and Gaussian Process Regression) that allow for comparison between countries. Modeling and estimation methods are used when reliable statistics cannot be obtained or are missing. Several improvements to the GBD study's data collection and compilation methods have been made since its inception [25]. Since data are publicly available estimates from deidentified sources, informed consent was not applicable. GBD study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [26]. The GBD study utilizes a standardized, data-driven framework to model Alzheimer's and other dementias across 204 countries, employing spatial-temporal regression and comparative risk assessment to estimate burdens from modifiable risk factors. Their protocol

also forecasts dementia trends by isolating the impacts of population growth, aging and changing epidemiological risk profiles.

2.3. Risk Factors

Six behavioral, metabolic and environmental risk factors (low physical activity, tobacco use, alcohol use, obesity, hypertension, and air pollution) and three disease risk factors (diabetes mellitus, depression, hearing loss) were examined through the Global Health Data Exchange (GHDx) Query Tool [24]. Exact queries are available on the GHDx website through dropdown menus. These were selected based on current knowledge and prior literature on dementia risk factors [27–33]. Tobacco included smoking, chewing tobacco and secondhand smoking. Obesity and hypertension were examined through high body mass index and high systolic blood pressure, respectively. Air pollution included particulate matter pollution which consisted of ambient particulate matter pollution, household air pollution from solid fuels and ambient ozone pollution. Diabetes mellitus in this analysis included both type 1 and type 2 diabetes. Depression for the purpose of this analysis included depressive disorders—Major depressive disorder and Dysthymia. No definitive diagnosis criteria or harmonization methods are used in the original data sources, and therefore, GBD-determined definitions of the listed risk factors and conditions were used in the present analysis.

2.4. Data and Statistical Analysis

We examined point estimate numbers (with 95% uncertainty intervals, UI) for crude and age-standardized death rates, incidence rates and DALY rates for dementia in Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka. South Asia and global average estimates were also calculated for comparison purposes. Sex-specific and aggregated data were both examined. We also used GBD 2019 data to examine rates of risk factors related to chronic disease in South Asian countries—low physical activity, tobacco use, alcohol use, obesity, hypertension, diabetes mellitus, depression, hearing loss, and air pollution—that previous studies have identified as relevant risk factors for dementia [34]. Crude and age-standardized DALY rates data pertaining to the all-cause contribution of these risk factors were extracted. Importantly, these data that were available are not dementia-specific population-attributable fractions (PAFs). The contribution and distribution of these risk factors for each South Asian nation was then computed. Linear regression analysis was employed to examine the relationships between the risk factors (independent variables) and dementia (dependent variable). Assumptions for linearity and normality of data were examined. Pearson correlation coefficients (r-values), Spearman rank-order correlation coefficients (ρ-values), Beta (β) coefficients, and statistical significance (p-values) were computed. Multiple testing corrections using Bonferroni and Bonferroni–Hochberg false discovery rate (FDR) adjusted p-values were also computed. Multicollinearity was addressed through calculating variance inflation factors and by conducting dimensionality reduction through a principal component analysis (PCA). $p < 0.05$ was considered statistically significant. All data were analyzed using the Python programming language with Python 3.11, using pandas 1.3.5 and SciPy 1.11.3. Inbuilt functions were used for correlation and other analyses.

3. Results and Discussion

3.1. Population and Aging Statistics, and Dementia as a Health Priority in South Asia

India was the most populated country in South Asia at the time of this analysis, with approximately 1.4 billion people, followed by Pakistan and Bangladesh (Table 1). Maldives was the least populated but most densely populated South Asian country. Dementia

is strongly correlated with advanced age; therefore, life expectancies and proportion of older adults in different countries were examined. Life expectancy at birth was highest in Maldives (77.4 years), followed by Sri Lanka (76.8 years). Life expectancy at birth was lowest in Afghanistan (54.4 years), likely due to high maternal mortality rates, high prevalence of infectious diseases and armed conflicts [35]. The percentage of older adults (individuals who were 65 years or older) was highest in Sri Lanka (12.4%), almost two-times higher than in other South Asian countries. The lowest percentage of older adults was in Afghanistan (2.9%).

Table 1. South Asia statistics on populations and demographics. Data source: US Census Bureau international database (2024). Population density is listed in number of people per km^2. Life expectancy at birth is listed in years.

Country	Total Population	Population Density	Life Expectancy at Birth	Dependency Ratio, 65+ Years	% of 65+ Years
Afghanistan	40,121,552	61.5	54.4	5	2.9
Bangladesh	168,697,184	1296	75.2	11.6	7.8
Bhutan	884,546	23	73.7	9.5	6.7
India	1,409,128,296	473.9	68.2	9.9	6.8
Maldives	388,858	1304.9	77.4	8.6	6.1
Nepal	31,122,387	217.1	73	9.4	6.4
Pakistan	252,363,571	327.4	70.3	8.1	4.9
Sri Lanka	21,982,608	340.1	76.8	19.1	12.4

Setting and following a national-level agenda to assess dementia is an essential component of improving outcomes related to it [34]. Collectively, most LMICs in the world have poor or non-existent policies related to dementia. Compared to other regions of the world, there is limited investment in brain aging and dementia initiatives in South Asia. No countries in South Asia currently have a national plan on dementia, although some discussions are ongoing about establishing these in some countries [36]. Only four South Asian countries (Bangladesh, India, Maldives, and Pakistan) out of the eight currently participate in the WHO Global Dementia Observatory (Table 2). Even in the four countries that participate in the WHO Global Dementia Observatory, no dementia data had been compiled in a report between the period of 2017–2019. The status of other areas related to dementia awareness, dementia risk reduction, diagnosis, treatment and care, dementia carer support, dementia information systems and research is also similar across these countries, highlighting an urgent need for action. Prior reports indicate that there are barriers to dementia assessment and care—stigma about dementia, poor patient engagement, limited trained healthcare professionals who can diagnose and manage dementia, competing healthcare system priorities and insufficient funding [37]. Studies have also identified the importance of establishing research priorities to improve outcomes related to dementia [38]. Research priorities identified are focused on prevention, reduction in dementia risk, delivery and quality of life and care for people with dementia and their caregivers [38]. Other priorities identified in this study were related to diagnosis, biomarkers, treatment development, basic research into disease mechanisms and public awareness of dementia [38]. The South Asian region appears to lack in a majority of these areas owing to poor prioritization of dementia as a public health concern.

Table 2. Dementia as a health priority in South Asia. Data source: WHO Global Dementia Observatory (2019).

Country	Included in/Contributes to WHO Global Dementia Observatory?	Availability and Status of Dementia Reporting in the Past 2 Years, 2017–2019
Afghanistan	No	N/A
Bangladesh	Yes	No dementia data have been compiled in a report
Bhutan	No	N/A
India	Yes	No dementia data have been compiled in a report
Maldives	Yes	No dementia data have been compiled in a report
Nepal	No	N/A
Pakistan	Yes	No dementia data have been compiled in a report
Sri Lanka	No	N/A

3.2. Incidence, Deaths and DALYs from All-Cause Dementia in South Asia

Using GBD 2019 data, crude and age-standardized rates of dementia in South Asian nations were considered (Table 3, Figure 1). The crude death rates in South Asian countries (9.48 per 100,000) were lower than the global average (20.98 per 100,000) (Table 3, Figure 1A). Amongst South Asian nations, Sri Lanka showed the highest crude death rate (18.95 per 100,000). Age-standardized death rates in some South Asian countries (Afghanistan and Sri Lanka) were higher than the South Asia and global average (Table 3, Figure 1B). Within South Asian countries, Afghanistan showed the highest age-standardized deaths (30.79 per 100,000), followed by Sri Lanka (23.53 per 100,000). Incidence rates of dementia in South Asia showed similar patterns. Crude incidence rate was highest in Sri Lanka (84.32 per 100,000) which was lower than the estimated global average (93.52 per 100,000) (Table 3, Figure 1C). Age-standardized incidence rate was highest in Afghanistan (109.39 per 100,000) which was much higher than the global average (94.99 per 100,000), followed by Sri Lanka (86.29 per 100,000) (Table 3, Figure 1D). Maldives also showed a relatively high age-adjusted incidence rate of dementia (86.00 per 100,000). For DALYs, the highest crude rates were seen in Sri Lanka (321.52 per 100,000) which was slightly lower than the global average (326.68 per 100,000) (Table 3, Figure 1E). The highest age-standardized DALY rates were observed in Afghanistan (432.72 per 100,000), followed by Sri Lanka (342.98 per 100,000) (Table 3, Figure 1F). Both of these were higher than the global age-standardized DALY rates (338.68 per 1500,000).

Table 3. All ages (crude) and age-standardized death, incidence and DALY rates for all-cause dementia in South Asian countries with uncertainty intervals (UI). Global averages are also shown for comparison. Data source: Global Burden of Disease Study (2019).

Country	Death Rate (per 100,000)		Incidence Rate (per 100,000)		DALYs Rate (per 100,000)	
	All Ages	Age-Standardized	All Ages	Age-Standardized	All Ages	Age-Standardized
Afghanistan	4.64 (1.10–12.54)	30.79 (7.46–82.34)	22.10 (18.56–25.57)	109.39 (92.94–125.60)	80.83 (33.26–192.81)	432.72 (179.01–1001.95)
Bangladesh	9.80 (2.38–27.25)	18.23 (4.45–49.29)	48.14 (41.10–55.88)	71.28 (61.06–82.14)	166.64 (72.32–377.64)	263.10 (114.29–589.70)
Bhutan	10.68 (2.56–28.70)	21.68 (5.25–57.41)	41.53 (35.44–47.99)	69.41 (59.22–79.62)	166.28 68.60–387.64)	294.56 (120.22–672.40)
India	9.28 (2.24–25.90)	19.12 (4.57–52.01)	38.93 (33.37–44.84)	62.29 (53.08–71.43)	152.84 (61.32–367.97)	260.26 (103.52–616.93)
Maldives	9.57 (2.36–24.66)	22.70 (5.59–58.33)	41.34 (35.50–47.11)	86.00 (73.41–98.08)	156.74 (66.96–351.04)	338.10 (145.14–745.14)
Nepal	8.05 (1.87–22.50)	19.51 (4.53–53.31)	37.78 (32.57–43.38)	68.96 (58.69–79.24)	136.76 (57.06–322.81)	270.81 (111.54–636.11)
Pakistan	4.89 (1.18–14.23)	20.98 (5.01–58.43)	21.75 (18.70–24.90)	67.22 (57.19–77.28)	82.02 (32.81–200.65)	280.19 (110.44–683.03)
Sri Lanka	18.95 (4.47–49.76)	23.53 (5.52–60.92)	84.32 (72.77–96.48)	86.29 (73.91–98.61)	321.52 (132.12–736.58)	342.98 (140.10–771.73)
South Asia	9.48 (2.27–25.70)	22.07 (5.30–59.00)	41.98 (36.00–48.30)	77.61 (66.20–89.00)	157.95 (65.56–367.14)	310.34 (128.03–714.62)
Global	20.98 (5.27–54.36)	22.92 (5.83–59.20)	93.52 (80.35–106.40)	94.99 (81.59–107.86)	326.68 (144.81–705.12)	338.64 (151.02–731.27)

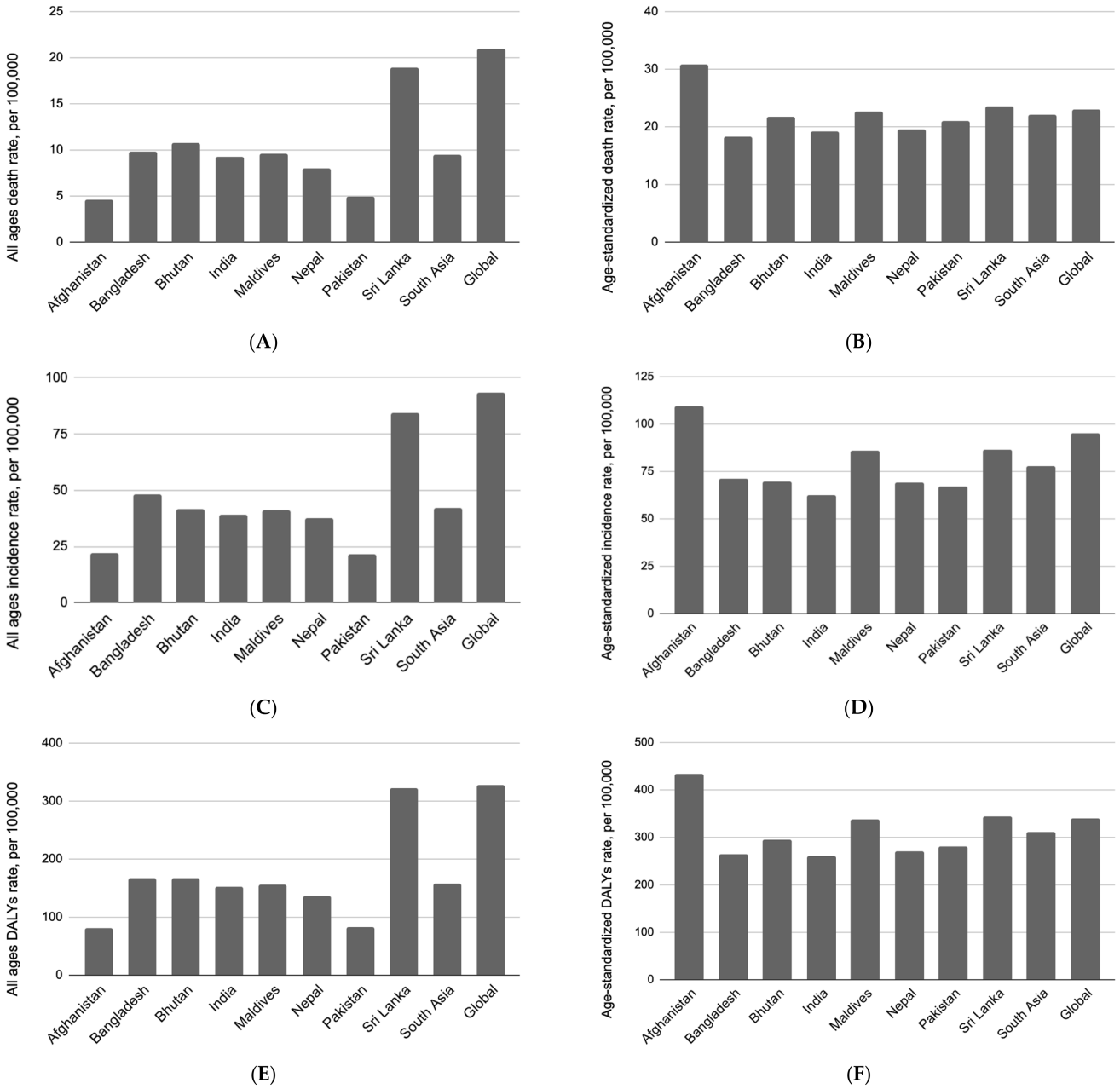


Figure 1. All ages (crude) (**A**) death rates, (**C**) incidence rates, (**E**) DALY rates and age-standardized (**B**) death rates, (**D**) incidence rates, (**F**) DALY rates of dementia in South Asian nations. South Asia and global averages are also shown for comparison. All rates are per 100,000. Disability-adjusted life years, DALYs. Data source: Global Burden of Disease Study (2019).

It is important to highlight the absence of definitive diagnosis criteria leading to underreporting when compiling large amounts of global health data from various sources in the GBD project. For example, dementia is typically diagnosed using cognitive testing (e.g., Montreal Cognitive Assessment, Mini-Mental State Examination), brain imaging (e.g., magnetic resonance imaging), blood or cerebrospinal fluid (CSF) tests (e.g., amyloid β or p-tau levels) and others. It is difficult to ascertain which method was used in aggregated data. Due to the absence of technology and infrastructure, brain MRI or blood/CSF tests might not be available in many low-income settings, so it is likely that cognitive and neurophysiological evaluations are prioritized but they may have limited sensitivity in case detection. Therefore, these broad estimates must be followed up with in-depth studies in order to accurately quantify dementia levels in each population. Previous independent

reports that assessed dementia rates in locally conducted community-based cohort studies show prevalence rates in South Asian nations—8% in Bangladesh [39], 7.4% in India [40], and 4% in Sri Lanka according to a report from 2003 [41].

Sex-specific analysis showed that the burden of dementia in South Asian countries was higher amongst females than males. This is an observation that has been made elsewhere in the world as well, where females are disproportionately affected by the disease [42]. Mechanisms behind this are not fully understood but differential life course exposures and metabolic changes that occur during midlife and menopause appear to play a role [43,44]. Females also have longer lifespans on average compared to males which may further contribute to this. Sex-stratified analyses of risk factors contributing to dementia burden could not be conducted from the present dataset. Future longitudinal studies must be designed so that these sex-specific differences can be captured.

Overall, within South Asian countries, the highest crude rates of deaths, incidence and DALYs related to dementia were seen in Sri Lanka, while the highest age-standardized rates were observed in Afghanistan, followed by Sri Lanka and the Maldives. These findings indicate that population aging likely plays a substantial role in the dementia burden in South Asia, similar to other parts of the world [45]. Previous studies have shown that aging is the strongest predictor of dementia [46], and the findings from this analysis also emphasize this within the context of South Asia. As a result, countries with higher proportions of older adults in this age range may experience a disproportionately higher burden of dementia. Age-specific analyses showed an age-dependent increase in dementia deaths, incidence and burden rates in all eight South Asian countries as well as globally. Dementia rates were higher in younger age groups in Sri Lanka, compared to Afghanistan. Overall, this may also contribute to higher crude dementia rates observed in Sri Lanka. However, the total rates of dementia were much higher in older age groups across all the countries.

There also may be other factors that can contribute to the high dementia burden, in addition to population aging. A recent study showed that multidimensional poverty is associated with dementia in Afghanistan [47]. The main contributors identified during this study were education, employment, health and living conditions. Prior research has shown that trauma is linked to poor mental health outcomes, e.g., post-traumatic stress disorder and dementia amongst US Veterans [48]. Whether these phenomena specifically apply to countries in South Asia that have been in armed conflicts—Afghanistan and Sri Lanka—is currently unknown. Another consideration is how countries are geographically located and are categorized as a result. Afghanistan is geographically close to the Middle East and North African (MENA) region, and is often considered a Middle Eastern nation according to some classifications, including the GBD project. Studies have shown that the prevalence of dementia is very high in the MENA region [49]. How these geographical factors contribute to dementia data of individual countries, particularly where data are sparse or missing, can only be fully ascertained by examining high-quality, country-specific data in rigorous follow-up studies [50].

3.3. Etiological Factors Driving Dementia in South Asia

We interrogated GBD 2019 study data to ascertain whether there were any dementia risk factors that were prevalent in South Asian countries. The GBD 2019 study identified smoking, high body-mass index and high fasting plasma glucose as the major risk factors contributing to global dementia burden [21]. In addition to these, there are many other known risk factors of dementia—air pollution, alcohol use, high systolic blood pressure, low physical activity, hearing loss, depressive disorders and diabetes mellitus, amongst others. We examined crude and age-standardized DALY rates for each risk factor available

through the GBD 2019 study for each South Asian nation (Table 4). There were appreciable similarities as well as differences in crude and age-standardized DALYs for various risk factors within different South Asian nations. High systolic blood pressure and high fasting blood glucose appeared to be notable contributors to the overall burden across South Asian populations (Figure 2). In some nations, other risk factors were more prominent. For example, air pollution made up a large proportion of the contributing risk in Nepal, India and Bangladesh, while diabetes mellitus was disproportionately higher in Sri Lanka. It is important to note that these DALYs were not dementia-specific, but were used to explore the distribution of known risk factors of dementia in different countries. These findings indicate that while there might be common drivers relevant to dementia in different South Asian nations, the burden might be modified by country-specific, unique risk factors as well. The exact contribution of each risk factor to dementia burden specifically was not analyzed here, as the goal was to compare the prominence of well-established dementia risk factors in each South Asian nation.

Table 4. (**A**) All ages (crude) and (**B**) age-standardized DALY rates of known disease risk factors and dementia for 8 South Asian nations. Mean with 95% CI is also shown. BMI, body mass index. Data source: Global Burden of Disease Study (2019).

A											
Country	**Air Pollution**	**Alcohol Use**	**High BMI**	**High Fasting Plasma Glucose**	**High Systolic Blood Pressure**	**Low Physical Activity**	**Tobacco**	**Age-Related and Other Hearing Loss**	**Depressive Disorders**	**Diabetes Mellitus**	**Dementia**
Afghanistan	4830.95	92.85	2067.62	2044.50	2664.14	286.18	1635.23	186.18	691.57	660.64	80.83
Bangladesh	3393.18	308.58	1031.10	1676.86	2689.18	129.10	2257.78	443.42	809.61	775.47	166.64
Bhutan	2528.07	629.28	1409.69	1679.06	2143.01	188.25	1368.64	432.64	681.94	787.25	166.28
India	3847.07	1057.15	1511.31	2379.92	2664.82	135.34	2435.27	494.45	608.04	919.02	152.84
Maldives	509.73	208.49	964.37	1296.43	1639.06	128.25	1470.29	464.87	480.46	544.56	156.74
Nepal	3995.84	880.91	1079.82	1523.57	1920.46	105.53	2961.65	385.56	800.43	623.76	136.76
Pakistan	5011.83	432.60	1614.37	2027.54	2806.93	178.71	2296.41	328.08	533.05	890.71	82.02
Sri Lanka	1831.29	1244.65	2443.94	4050.35	3101.04	169.47	1853.01	610.80	473.89	2252.19	321.52
Mean	3243.49	606.82	1515.28	2084.78	2453.58	165.11	2034.78	418.25	634.88	931.70	157.95
95% CI	(1956.87–4530.12)	(256.74–956.89)	(1077.89–1952.67)	(1362.63–2806.92)	2037.65–2869.51)	(117.72–212.49)	(1577.67–2491.90)	(313.95–522.55)	(523.51–746.24)	(472.82–1390.59)	(95.48–220.43)
B											
Country	**Air Pollution**	**Alcohol Use**	**High BMI**	**High Fasting Plasma Glucose**	**High Systolic Blood Pressure**	**Low Physical Activity**	**Tobacco**	**Age-Related and Other Hearing Loss**	**Depressive Disorders**	**Diabetes Mellitus**	**Dementia**
Afghanistan	6992.28	155.57	5098.61	5920.63	7400.80	909.85	3328.98	416.91	890.19	1674.41	432.72
Bangladesh	4106.14	328.94	1149.49	2063.64	3263.86	177.44	2700.96	506.96	822.20	934.34	263.10
Bhutan	3308.22	665.76	1733.59	2264.73	2865.90	283.10	1833.34	517.96	696.86	1026.02	294.56
India	4685.39	1097.78	1697.84	2871.12	3194.22	191.47	2936.77	560.60	616.13	1084.95	260.26
Maldives	744.60	186.13	1229.06	2155.07	2606.23	229.59	2192.92	564.99	459.45	820.94	338.10
Nepal	5271.72	1027.98	1354.34	2089.12	2593.96	167.80	4200.85	482.87	874.04	826.94	270.81
Pakistan	6181.83	597.34	2777.63	3911.09	5207.91	399.80	4134.37	520.99	678.27	1640.62	280.19
Sri Lanka	1641.36	1096.49	2073.38	3543.70	2731.68	160.82	1579.71	554.92	440.87	1948.76	342.98
Mean	4116.44	644.50	2139.24	3102.39	3733.07	314.98	2863.49	515.77	684.75	1244.62	310.34
95% CI	(2319.39–5913.49)	(311.85–977.14)	(1046.77–3231.72)	(1983.00–4221.78	2303.78–5162.36)	(103.26–526.71)	(2038.82–3688.15)	(474.66–556.89)	(539.24–830.26)	(876.01–1613.24)	(261.11–359.57)

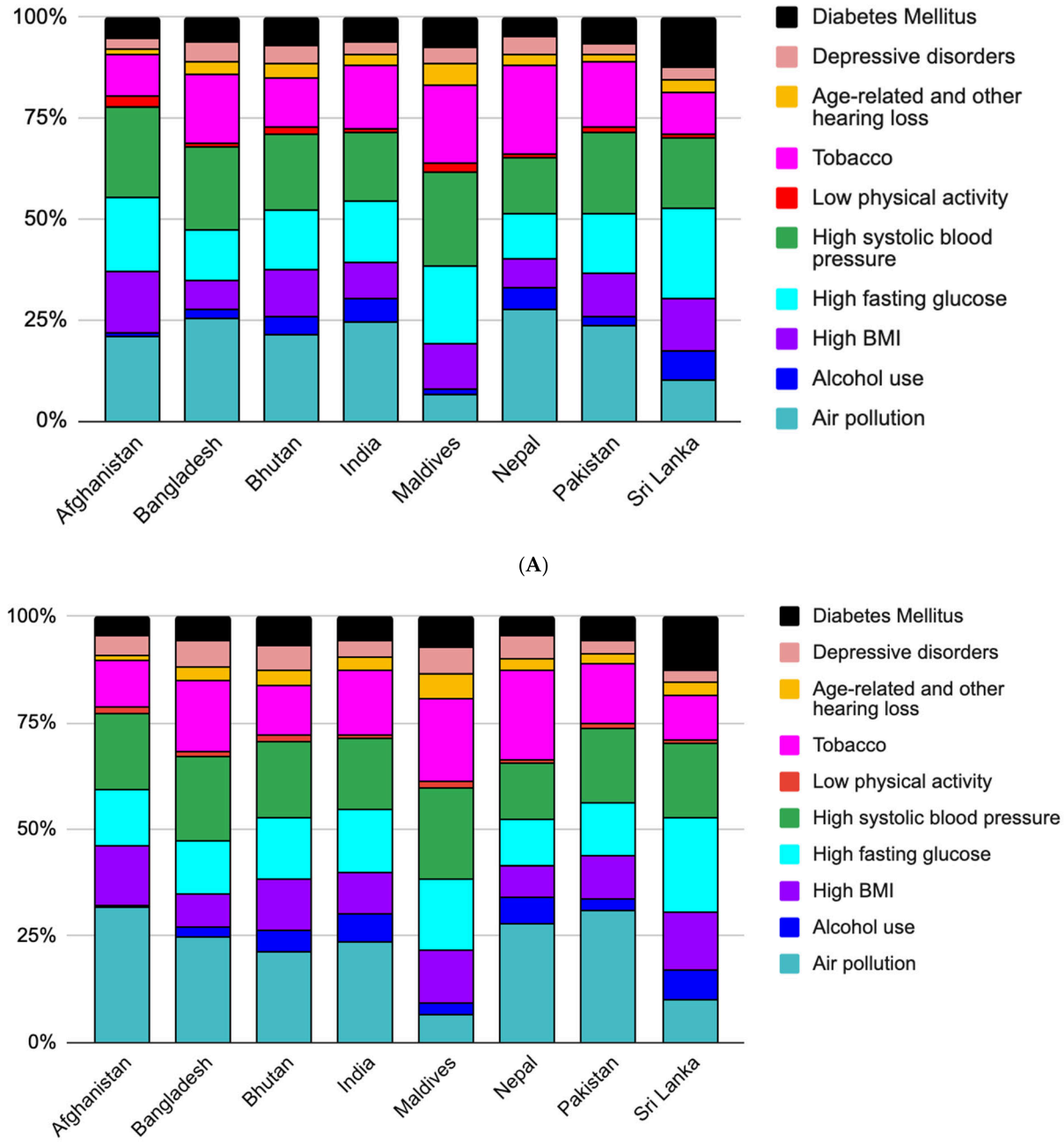


Figure 2. (**A**) All ages (crude) and (**B**) age-standardized DALY rates of known disease risk factors that have implications for dementia, compared between the 8 South Asian nations. BMI, body mass index. Data source: Global Burden of Disease Study (2019).

In order to understand the relationship between these risk factors and dementia within South Asia, a linear regression analysis was conducted where correlation coefficients and *p*-values were computed. Given the small sample size, in addition to the Pearson correlation test, we also conducted a non-parametric Spearman's rank-order test which is more stable against limited observations, outliers and non-normality. For crude DALYs, the strongest positive significant correlations for dementia were observed with age-related and other hearing loss (r = 0.87, $p = 0.005$), diabetes mellitus (r = 0.85, $p = 0.001$) and high fasting blood glucose (r = 0.74, $p = 0.04$) (Table 5). For age-standardized DALYs, the strongest correlations for dementia were seen with low physical activity (r = 0.78, $p = 0.02$) and high BMI (r = 0.78, $p = 0.02$) and high fasting blood glucose (r = 0.77, $p = 0.03$). In addition, high systolic

blood pressure (r = 0.64, p = 0.09) and diabetes mellitus (r = 0.52, p = 0.19) also showed noteworthy correlations which were not statistically significant. When the non-parametric testing was conducted, the correlations dropped substantially, whereas for crude DALYs, hearing loss (r = 0.79, p = 0.02) maintained a significant positive correlation with dementia. Interestingly, air pollution gained a significant negative correlation with dementia under the non-parametric testing. For the age-standardized DALYs, none of the correlations remained statistically significant with the non-parametric testing. Beta (β) coefficients were also considered in this analysis and across both crude and age-standardized DALYs—most of them were very close to zero, indicating that most risk factors have a weak unique predictive power. We also conducted a correction for multiple testing (Supplemental Table S1). According to this, in the crude DALYs, hearing loss and diabetes mellitus remained significant after applying a Bonferroni–Hochberg FDR correction. All the others (Spearman matrices and age-standardized matrices) either reduced substantially or flattened out.

Table 5. Correlation between biological, behavioral and environmental risk factors and dementia in South Asia. Pearson correlation coefficients (r), Spearman rank-order correlation coefficients (ρ) and statistical significance (p-values; p_1 denotes p-value for Pearson correlation test and p_2 denotes p-value for Spearman's rank-order correlation test), and β-coefficients are shown for crude and age-standardized DALYs. β-coefficients denote the slope output generated via univariate linear regression models. * Statistically significant ($p < 0.05$). Original data source: Global Burden of Disease Study (2019).

	Crude DALYs					**Age-Standardized DALYs**				
Risk Factor	**Pearson *r***	**p_1**	**Spearman ρ**	**p_2**	**Beta (β)**	**Pearson *r***	**p_1**	**Spearman ρ**	**p_2**	**Beta (β)**
Air pollution	−0.63	0.09	**−0.81**	**0.01** *	−0.03	0.06	0.89	−0.10	0.82	0.002
Alcohol use	0.67	0.07	0.43	0.29	0.12	−0.49	0.22	−0.48	0.23	−0.07
High BMI	0.39	0.34	−0.17	0.69	0.06	**0.78**	**0.02** *	0.57	0.14	0.04
High fasting glucose	0.74	0.04	0.05	0.91	0.06	**0.77**	**0.03** *	0.55	0.16	0.03
High systolic BP	0.28	0.50	0.26	0.53	0.04	0.64	0.09	0.07	0.87	0.02
Low physical activity	−0.28	0.05	−0.24	0.57	−0.37	**0.78**	**0.02** *	0.31	0.46	0.18
Tobacco	−0.15	0.72	−0.29	0.49	−0.02	−0.18	0.66	−0.33	0.42	−0.01
Hearing loss (Age-related)	**0.87**	**0.005** *	**0.79**	**0.02** *	0.52	−0.50	0.21	−0.12	0.78	−0.60
Depressive disorders	−0.35	0.40	−0.21	0.61	−0.20	0.01	0.99	−0.05	0.91	0.002
Diabetes Mellitus	**0.85**	**0.001** *	0.33	0.42	0.12	0.52	0.19	0.40	0.32	0.07

An important point to note is that many of these risk factors also exhibit strong correlations with each other, which can have a direct bearing on the results. Multicollinearity is indeed a concern for this type of analysis as many of the risk factors considered are related to overlapping biological processes. It is important to note that including many such variables in the same model can lead to unstable correlation coefficients and inflated standard errors. Indeed, Variance Inflation Factors (VIF) were >4 for all of the risk factors considered– which indicated that these predictors were largely capturing common underlying health constructs. Dimensionality reduction through Principal Component Analysis (PCA) can be used to cluster related variables together, reducing effects of multiple testing and multicollinearity. We examined this by constructing three principal components—Metabolic health (PC1), socio-environmental (PC2) and behavioral habits (PC3). With this, we compressed the 9 highly correlated risk factors into these three independent components that captured the majority of the total dataset variance (Supplemental Table S2). The findings from the PCA indicated that the metabolic health group (combination of high blood glucose, high blood pressure, and high BMI) posed the highest risk for dementia in

the South Asian region. Interestingly, this analysis also indicated that environmental factors (air pollution) and physical inactivity were important risk factors for dementia when older populations were concerned. Tobacco and alcohol use do play a moderate role but it is not as pronounced as metabolic risk factors.

Ascertaining the exact causal role of a given risk factor on dementia is not possible through an analysis of this nature. Future analyses should consider this, where larger datasets and more advanced statistical models will be more useful. Collectively, the findings from this study align closely with other studies showing that metabolic risk factors, particularly hyperglycemia, obesity and high blood pressure, play an important role in dementia incidence and progression [51,52]. Preventing and controlling metabolic dysfunction should therefore be an urgent priority for South Asians in order to prevent and control a host of chronic diseases, including dementia [53].

Other studies have also shown that some of these metabolic risk factors are abundantly prevalent in some South Asian countries. A recent publication by an independent group showed that the prevalence of type 2 diabetes amongst Sri Lankans is 23% [54]. The same group showed that the prevalence of prediabetes is 30.5%. These levels are significantly higher than the global average and other countries in the Asia-Pacific region [55]. The exact reasons for the high prevalence of metabolic risk factors in South Asian countries are not fully understood but poor diets, lack of physical activity, genetic predispositions and life course factors, e.g., biological programming, may all be contributing [56].

The role of high glucose in dementia has been previously seen in other populations. A 2013 analysis using data from the Adult Changes in Thought Study, published in the *New England Journal of Medicine*, showed that high blood glucose levels were linked to dementia, even in people without type 2 diabetes [57]. Chronically elevated plasma glucose can result in vascular damage and inflammation and contribute to insulin resistance in the brain [51]. Collectively, these existing studies bolster the observation made during this present analysis and provide a strong rationale to consider high glucose as a strong risk factor for dementia.

However, it is important to note that there are several other dementia risk factors that were not considered here. For example, low educational attainment has been associated with poorer dementia outcomes in previous studies [58]. Vision loss and muscle strength are also emerging as predictors of dementia [59,60]. Even though some of these data are not challenging to collect, many of them are not considered in population-level studies, leading to missed opportunities to better understand dementia determinants. There are other risk factors that are costlier to measure and therefore might not be feasible to measure in low-income and population-level settings. For example, genetic factors such as apolipoprotein E ε4 (APOE ε4) are also strongly linked with dementia incidence and progression [61] but require laboratory-based genotyping. Due to the absence of appropriate current data, these factors could not be considered in the present analysis. It is also important to note that the data used for the present analysis was country-level data, not individual-level data, and therefore, ecological fallacy must be noted as a potential point of caution.

3.4. The Need for More Data

The GBD Study is a useful resource to identify global health trends and patterns that can help drive policy focus [50]. These data are largely based on estimates arrived at through various statistical models. These data are also compiled from thousands of different sources which may lead to underreporting and missing data for some countries. Furthermore, some conditions are aggregated together in the GBD which may affect the findings presented here. For example, in the GBD, hearing loss that is aging-related and other causes-related are combined. Aging-associated hearing loss is a strong predictor of

dementia but by merging these data with other types of hearing loss, some trends may be lost. In the absence of data collected through local studies, which is often the case with LMIC countries, sources such as the GBD provide valuable starting points for health trend analyses. However, the need for further research on unique factors that may drive dementia and also trajectories of dementia trends in individual countries is pressing. For example, there is also very limited data on mild cognitive impairment (MCI) and how cognitive decline progresses as individuals age in South Asia. Furthermore, there is also poor understanding of the different types of dementia in the region. The paucity of reliable data from this region has been previously noted for many years [62]. The Harmonized Cognitive Assessment Protocol (HCAP) is a network of studies associated with the Health and Retirement Study (HRS) that attempts to provide a flexible yet comparable instrument to measure cognitive function among older adults around the world. Currently, India and Nepal are part of the HCAP network but this must be expanded to include other South Asian nations. Additionally, other standardized measurement, evaluation and reporting approaches specific to healthy aging and dementia must be incorporated [63]. These include the WHO Healthy Aging Framework, WHO Integrated Care for Older People (ICOPE) and other methodologies used by longitudinal studies for studying aging populations. This will ensure that new data for cognitive testing, biomarker assessment, and longitudinal tracking will be collected, stored, analyzed, shared and reported as per standardized, globally accepted protocols.

A major limitation of this analysis is the reliance on modeled estimates of dementia burden and risk-factor exposure in settings where primary epidemiological data remain sparse. In many South Asian countries, dementia is substantially underdiagnosed due to limited specialist services, low public awareness, cultural perceptions of cognitive decline as a normal consequence of aging, and the absence of routine cognitive screening in primary care. Consequently, GBD estimates often rely on statistical modeling and covariate borrowing from neighboring countries or regions with more complete data, which may obscure true within-country heterogeneity. These challenges are likely exacerbated in conflict-affected settings such as Afghanistan and parts of Pakistan, where healthcare disruption, population displacement, trauma exposure, and weakened surveillance systems may further reduce case ascertainment [64]. As a result, the observed dementia burden may reflect both true disease occurrence and variation in diagnostic capacity. Furthermore, the risk-factor DALYs used in this study are themselves modelled estimates and may compound uncertainty when analyzed against modelled dementia outcomes. Although several independent local studies and community-based surveys have reported dementia prevalence estimates broadly consistent with GBD trends, substantial quantitative discrepancies remain. For example, community surveys conducted in India and Sri Lanka have reported prevalence estimates ranging from approximately 1–8% among older adults depending on age structure, diagnostic criteria, and study location, highlighting the sensitivity of estimates to methodological approach. Future studies should formally compare GBD-derived estimates with nationally representative aging surveys, cognitive screening programs, and cohort studies. Expanding the use of community-based surveillance, point-of-care cognitive assessment tools, and portable biomarker technologies may also help address current data gaps, particularly in underserved, rural, and conflict-affected regions where centralized data collection is challenging. Such approaches could improve both the accuracy of dementia burden estimates and the reliability of risk-factor attribution across South Asia.

3.5. Considerations for Future Studies

Findings from broad, large global health projects must be followed up using more specific analyses that focus on interrogating observations made. Several unique challenges must be overcome when planning and executing longitudinal follow-up studies aiming to characterize cognitive decline and dementia in South Asian countries. These include financial, cultural and structural barriers. Table 6 highlights major considerations applicable to countries in South Asia, as well as others that are LMIC. One of the foremost challenges facing South Asian countries in this regard is that dementia is often perceived as a normal part of the aging process. This can lead to delays in diagnosis, care-seeking and treatment. For research studies, this means that "healthy populations" may include a substantial number of undiagnosed cases of dementia.

Table 6. Considerations for setting up future longitudinal studies examining cognitive decline and dementia in low-income settings such as countries in South Asia.

Study Planning-Related	Study Design-Related	Study Data-Related	Study Expansion-Related
How feasible is the study?	How long will the study last? What is the timeline?	What data on biomarkers of cognitive decline and dementia will be collected?	Will there be training and education opportunities arising from this study?
How much will the study cost? And what are the funding sources? What instruments and personnel are needed?	Who are the participants and what is the inclusion/exclusion criteria? What are the considerations for working with older adults?	What biological samples will be collected? How will they be biobanked?	Will there be public awareness opportunities arising from this study?
Who are the major stakeholders?	How will participants be recruited? What are the cultural, language and other barriers to recruitment?	What other supporting data will be collected?	How will findings from this study impact policy changes in the country?
What are the country-specific cultural, language and other considerations?	What are safety, ethical and consent requirements?	What data infrastructures are needed?	Will there be follow-up studies arising from this larger study?
How can local languages be incorporated into communication?	What is the sample size?	What is the data sharing policy?	Are there additional funding sources that could support different parts of the study?
How can instruments be translated and validated for the local setting?	What is the frequency of measurement?	How will study findings be communicated? What are the deliverables?	If the study is to continue beyond the anticipated timeline, how will it be sustained?

Most countries in South Asia have limited medical research funding (Figure 3), which poses a major problem for establishing state-funded programs that are sustainable and continuous. Health record systems are also typically manually handled which can lead to problems in diagnosis and higher loss to follow-up. However, overcoming these initial barriers through strategic partnerships and local investments [65] can help set up powerful data and biological sample repositories that can also serve as strong platforms for research, training, education and public awareness. Our preliminary analysis of the status of dementia in South Asia strongly suggests that the absence of funding is no longer a

viable excuse for not investing more into dementia prevention, care and research. Overreliance on international funding mechanisms has proved detrimental to many global health programs—and therefore, more sustainable and viable local or regional partnership options must be considered for dementia research programs in South Asia. Establishing standard definitions and diagnostic criteria for dementia and utilizing biomarkers, both behavioral and imaging, are important. These long-term studies can also add immense value to overall understanding of dementia and risk factors, ultimately paving the way for prevention and therapeutic strategies that encompass global populations.

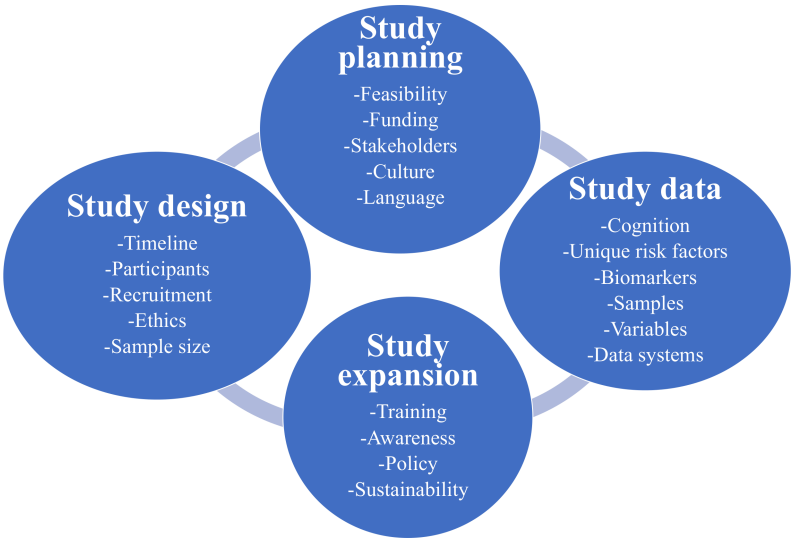


Figure 3. Conceptual framework outlining key considerations for the design and implementation of longitudinal studies examining cognitive decline and dementia in low- and middle-income settings, including South Asia. The framework is organized into four sequential and interrelated domains: (1) Study Planning, which includes feasibility assessment, funding, stakeholder engagement, and cultural adaptation; (2) Study Design, which encompasses participant selection, recruitment, ethical considerations, and study timelines; (3) Study Data, which focuses on cognitive assessments, biomarker collection, biological sampling, and data infrastructure; and (4) Study Expansion, which highlights capacity building, public engagement, policy translation, and long-term sustainability. The framework emphasizes a systems-level approach to generating harmonized, high-quality longitudinal data to inform dementia prevention and care strategies in resource-limited settings.

Such follow-up, focused studies have shown that dementia rates in some South Asian countries have historically been underestimated due to underdiagnosis and underreporting. For example, a recent report from the Longitudinal Aging Study in India (LASI) showed that there are a few million more cases of dementia in India than previously estimated [40]. This is likely the case for many other LMICs that do not have dedicated resources to track and monitor the status of aging-associated conditions like dementia. This can be exacerbated by classifying dementia as a normal part of the aging process. It is also noteworthy that the COVID-19 pandemic has negatively affected diagnosis, management and research related to dementia in many South Asian countries. Additionally, country-specific concerns have also significantly worsened the dementia burden. For example, Sri Lanka was hit by an economic crisis in 2022, leading to serious financial and societal issues that have invariably affected the health sector. The exact magnitude of this crisis and its effects on human health outcomes particularly is unknown.

Conducting longitudinal studies in low-resource environments can be challenging due to logistical issues. For example, biological sample collection, transportation and storage must happen under optimal conditions to ensure accuracy of test results—which can be hindered if necessary equipment is not available or not affordable. Low-cost, high-quality

alternatives must be considered to mitigate this. Point-of-Care Testing devices can be utilized to eliminate the need for expensive and time-consuming laboratory testing in low-resource environments and in settings that are affected by conflicts [66,67]. For the case of dementia and related risk factors, these include rapid, digitized neurocognitive assessments and blood biomarkers that are currently under development. Absence of personnel with *hands-on* training and experience in dementia research can also pose a substantial problem to setting up these specialized longitudinal studies. Setting up collaborative studies with education and exchange components can help offset this to some degree.

There are also specific cultural, religious, education and language factors that must be considered when examining dementia burden in South Asia. Many South Asian countries tend to have high diversity which can introduce specific barriers. These factors are often not captured in cognitive assessment tools that are used for case diagnosis (e.g., MMSE, MoCA) [68]. Most South Asian countries promote strong family structures, and therefore, have multi-generational households where older adults live with younger individuals. When older adults are diagnosed with dementia, caretaking responsibilities may be taken up by younger members of the family due to value systems. Not being adequately equipped and trained to care for a dementia patient can lead to a significant caregiver burden [69,70]. South Asian countries also do not have formal caregiver structures in place, e.g., nursing homes, social workers, community-based healthcare teams, which are essential to effectively reducing overall burden of dementia. Even the existing workforce that provides services has little formal training on dementia-related care. Reliable data on caregiver systems are also sparse in South Asian countries and are not addressed in large studies such as the GDB. Given the socioeconomic status of many South Asian countries, migration (especially younger family members) is a reality for many. This can directly affect follow-up logistics of dementia studies.

The present study did not examine dementia burden amongst South Asians who live in other parts of the world [71]. In spite of dementia outcomes being better in high-income countries, South Asians living in these parts of the world may experience bias and discrimination when seeking dementia-related care [72]. There is also dementia-related stigma within South Asian communities which must be addressed [73] and negligence of diseases that mostly affect older adults such as dementia.

With rapidly growing older adult populations, these concerns are expected to magnify, and countries that are not prepared will likely experience the heaviest financial, societal and public health burden. Efforts dedicated to accurately diagnosing and measuring dementia and dementia biomarkers using standard as well as streamlined tools [74], and also collecting accurate dementia statistics and determinants are vital first steps that must be undertaken in order to understand the true situation of dementia in these countries. Emerging risk factors of dementia are increasingly affecting several South Asian countries, including air pollution [75], as shown in these data. Specific and unique risk factors, including environmental exposures like pesticides [76] that may disproportionately affect South Asian dementia cases due to the use of certain agrochemicals, must be examined in future studies. Many of the risk factors of dementia (e.g., cardiometabolic risk factors) are shared with other diseases that affect many South Asians, including heart disease and type 2 diabetes. By identifying and characterizing these risk factors, they can be controlled, where possible, ultimately leading to improved outcomes in multiple diseases, including dementia. Studies have shown that dementia prevention potential in low- and middle-income countries is high through controlling risk factors [10], but several barriers, as highlighted through the present analysis, must be successfully tackled. Follow-up studies can also help facilitate a better understanding of dementia subtypes, timelines, and molecular targets that may be critical for identifying therapeutic interventions in the future.

4. Conclusions

In this analysis using publicly available dementia data, we highlight the status and risk factors of dementia burden in 8 South Asian nations. Our findings highlight that South Asian countries are lagging behind other regions with regard to prioritization of brain aging and dementia as healthcare and research items that require urgent attention. Sri Lanka (highest proportion of older adults in South Asia) and Afghanistan (lowest proportion of older adults in South Asia) are experiencing the most significant burden of dementia, driven by population aging and other factors, respectively. We also identify that metabolic dysfunction strongly contributes to the dementia burden in South Asian countries. Overall, this analysis emphasizes the need for country-specific, longitudinally collected high-quality data on risk factors and biomarkers of dementia in South Asia. Therefore, prioritizing research, awareness and services related to dementia can help South Asian countries prepare for the impending public health and social challenges related to population aging.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/jdad3030038/s1: Table S1: Multiple testing corrections. Bonf = Bonferroni adjusted *p*-value (capped at 1.000). BH = Bonferroni-Hochberg FDR adjusted *p*-value; Table S2: Multivariable principle component mapping. Beta represents the standardized beta coefficient. Bolded values highlight the strongest directional drivers within each respective model layout.

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Conflicts of Interest: D.L.P. is affiliated with HealthSurveil LC. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

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