CARDIOVASCULAR DISEASE AND MOBILITY DISABILITY IN RURAL OLDER INDIANS: THE MOBILITY AND INDEPENDENT LIVING IN ELDERS STUDY (MILES)

by

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ABSTRACT

Increase in older population is most rapid in developing countries and will have major impact on public health. Indian older population is not well described and there is an urgent need to estimate the burden of prevalent disease, disability and risk factors. To accomplish this, we established a longitudinal cohort study – MILES, in a rural population of older Indians. We enrolled a random sample of 562 men and women aged 60+ from rural India. Baseline visit consisted of a comprehensive clinical examination and interview.

We examined the prevalence of CVD and its relationship with traditional CVD risk factors in MILES. CVD was defined as a composite of self-reported history of CVD, major ECG abnormality or peripheral artery disease (PAD). Prevalence of CVD was 24.6% in men and 25.6% in women. In multivariate analyses among men, BMI, hypertension and physical inactivity were associated with higher prevalence of CVD. Among women, chewing tobacco, hypertension and physical inactivity were associated with higher prevalence of CVD.

Additionally, we estimated the prevalence and risk factors for mobility disability in MILES population by using inability to attempt or complete a 400-meter usual paced walk as a measure of mobility disability. Mobility disability prevalence was much higher in women (43.8%) compared to men (27.9%). In men,

knee pain, fair vision, chronic lung disease and greater number of depressive symptoms were associated with mobility disability. Among women, waist circumference, depressive symptoms, knee pain, poor vision, CVD history and PAD were associated with mobility disability. Mean walking times were high in those men (435 seconds) and women (503 seconds) who completed the walk. Higher walking times were associated with higher waist circumference, knee pain and use of walking aid in both men and women.

This dissertation has major public health significance. In this dissertation, we identified the rural older Indian population to be very frail, and with high prevalence of disease and mobility disability. There is a high prevalence of risk factors, low heath awareness and poor health care access. These data indicate urgent need for primary prevention measures and increasing availability of treatment to prevent further complications.

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1.0 INTRODUCTION

1.1 Global aging

Almost all nations in the world are now experiencing a growth in the number of older adults, though there is considerable variability. Most developed countries already have relatively high proportions (15% – 22%) of individuals $\geq$65 years of age. The most rapid increases in the older population are in the developing world. Birth rates are also rapidly declining in many countries, including developing countries like India, further accelerating the shift toward an aging society [1]. This change towards an aging society is unprecedented. The upsurge in proportion of older adults is accompanied by declines in the proportion of the young (under age 15). As per United Nations (UN), by 2050, the number of elderly in the world will exceed the number of young people for the first time in history [2]. Several developed countries have already witnessed this reversal of relative proportions of old and young by the year 1998. This trend is occurring at a faster pace in the youngest age groups. In 1950, about 5% of the world's population was $\geq$65 years of age while 13% was <5 years of age. By 2020, individuals who are $\geq$65 years of age will outnumber children who are <5 years of age [3, 4]. According to a US government report: "An Aging World: 2008", the world population $\geq$65 years of age will double from about 506 million in 2008 to 1.3 billion by 2040, accounting for 14% of the world's total population [3]. Consistent with this, the UN estimates the proportion of older population (60 years and older) to increase to 21% by the year 2050 [2] (Figure 1).

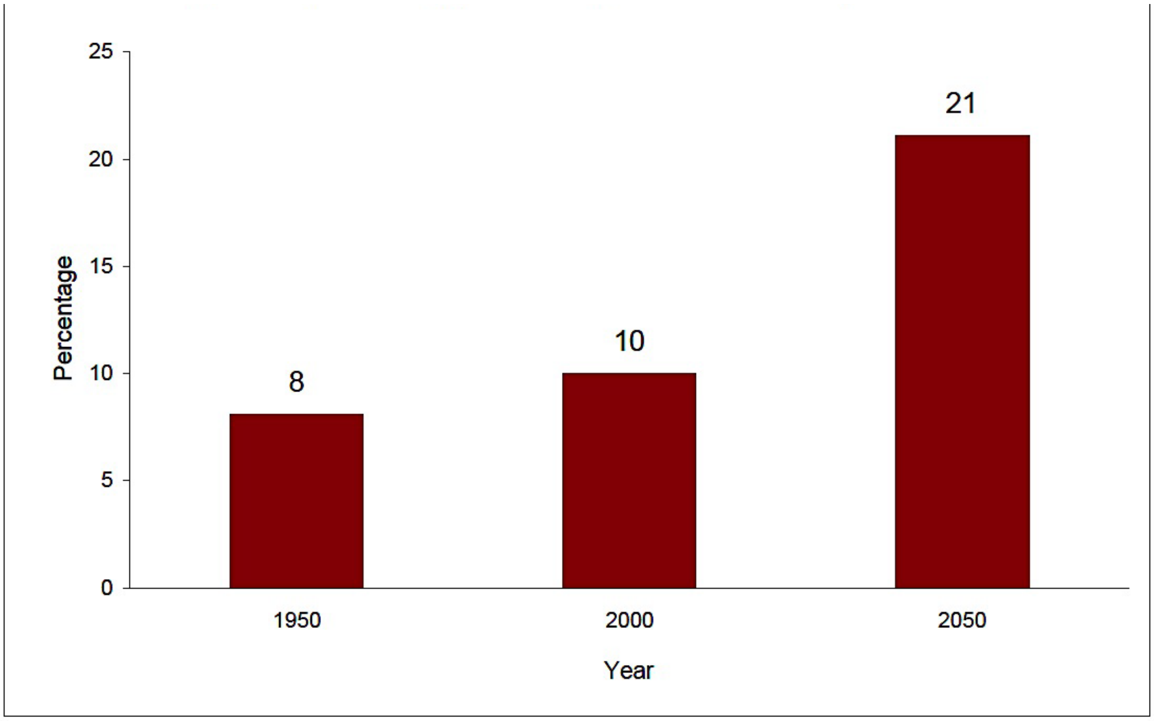


Figure 1: Proportion of population 60 years or older: world, 1950-2050 [2]

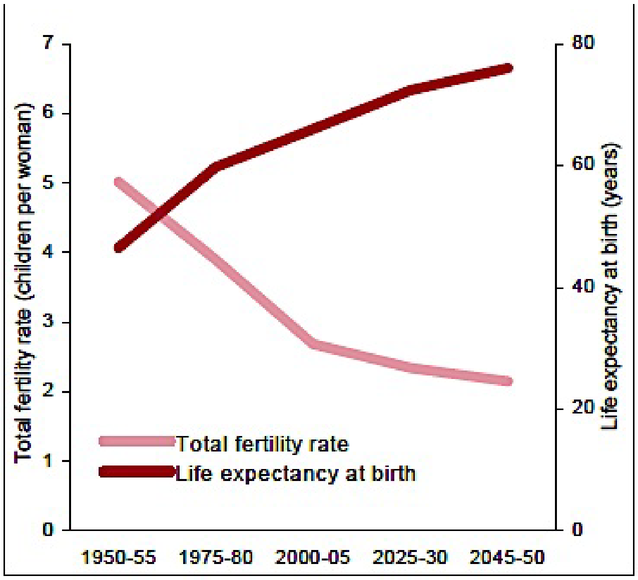


Figure 2: Total fertility rate and life expectancy at birth: world, 1950-2050 [2]

These changes in population structure are a direct consequence of a continuous decline in total fertility rate and increased life expectancy at birth globally (Figure 2).

This change in global demography will bring about numerous challenges and opportunities. Population aging is a global phenomenon affecting every human being and is not just limited to a particular region or sections of the world. However, global averages can conceal the presence of considerable heterogeneity both across and within regions. Various countries are at very distinct stages of the process of population aging, and the pace of change differs greatly. There are clear differences between regions in the number and proportion of older adults. In the year 2000, developed countries had almost one-fifth of their population aged 60 or older. This population is expected to reach one-third by the year 2050 [2]. On the other hand, in the year 2010, only 8 per cent of the population was over the age of 60 in the less developed countries. However, by the year 2050 older adults will make up almost 20 percent of the population in these countries (Figures 3 and 4) [2]. The absolute rise in the number of older adults and the change of population dynamics in relation to the working population has a direct bearing on the health and socioeconomic equity and solidarity of society. The pace of population aging is much faster in developing countries compared to developed countries. As a result, developing countries will have less time to adjust to the consequences of this change in population restructuring. Developing countries have not encountered such high numbers of older adults in their population and are not fully equipped to handle the challenges presented by this change. Additionally, population aging in developing countries is taking place at much lower levels of socioeconomic development compared to developed countries, leading to further complications.

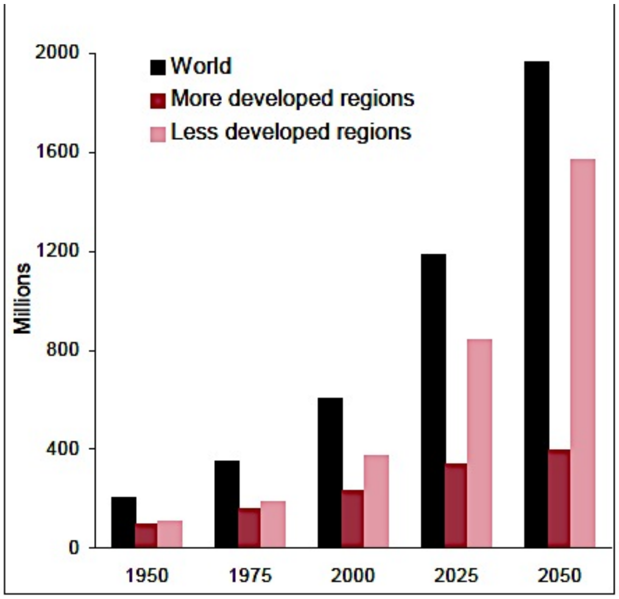


Figure 3: Population aged 60 or over: world and development regions, 1950-2050 [2]

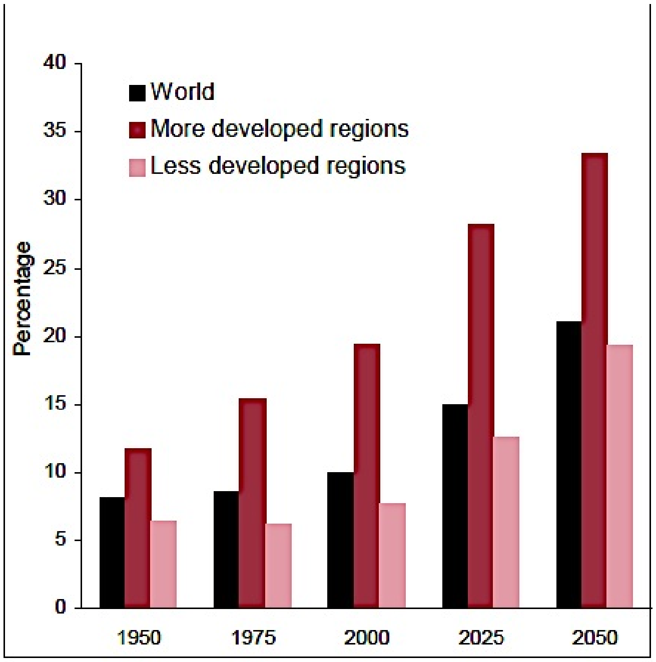


Figure 4: Proportion of population aged 60 or over: world and development regions, 1950-2050

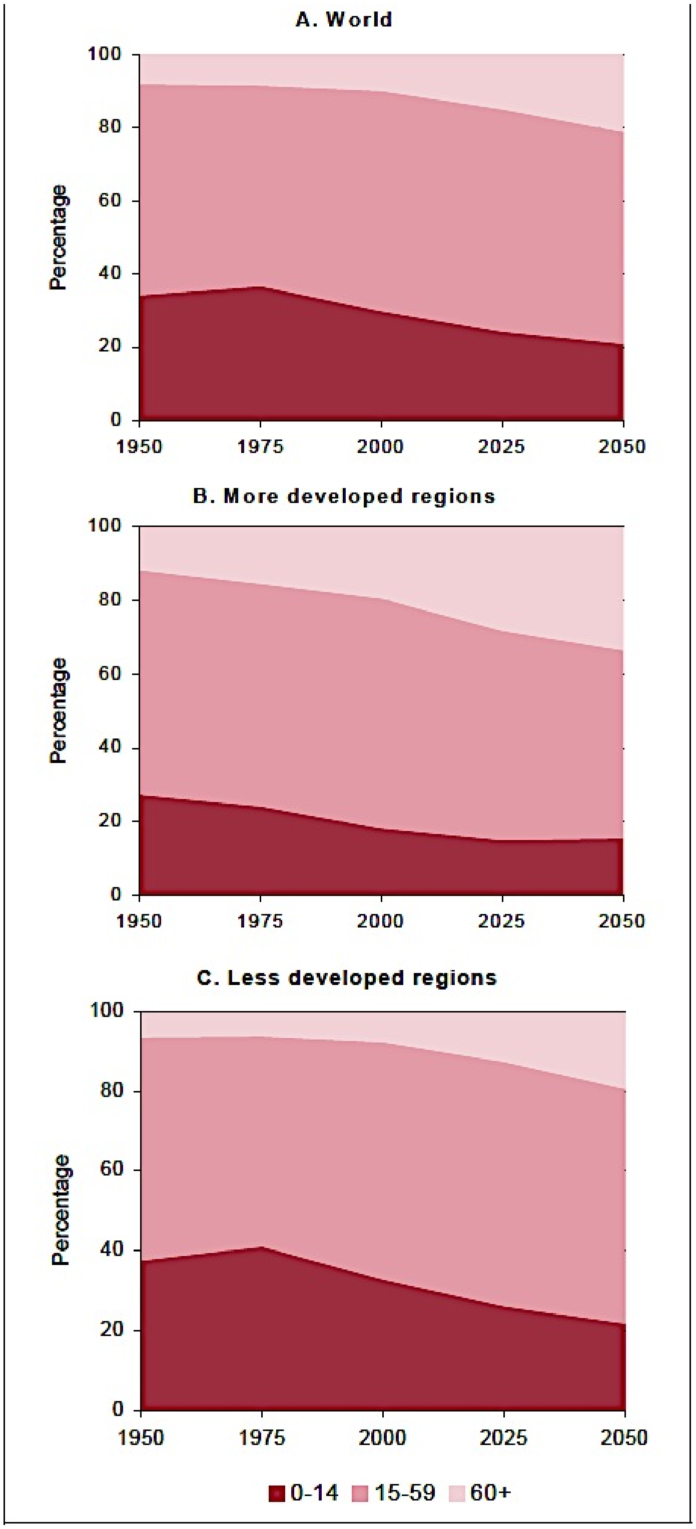


Figure 5: Distribution of population by broad age groups: world and development regions, 1950-2050 [2]

Another challenge that is facing the world and particularly the developing nations is the oldest old population. The older population is itself aging and the fastest growing age group in the world is the oldest old or those aged 80 years or older. The current rate of increase in the population of the oldest old is 3.8 percent per year. According to UN estimates, by the year 2050, one-fifth of older adults will be 80 years or older [2].

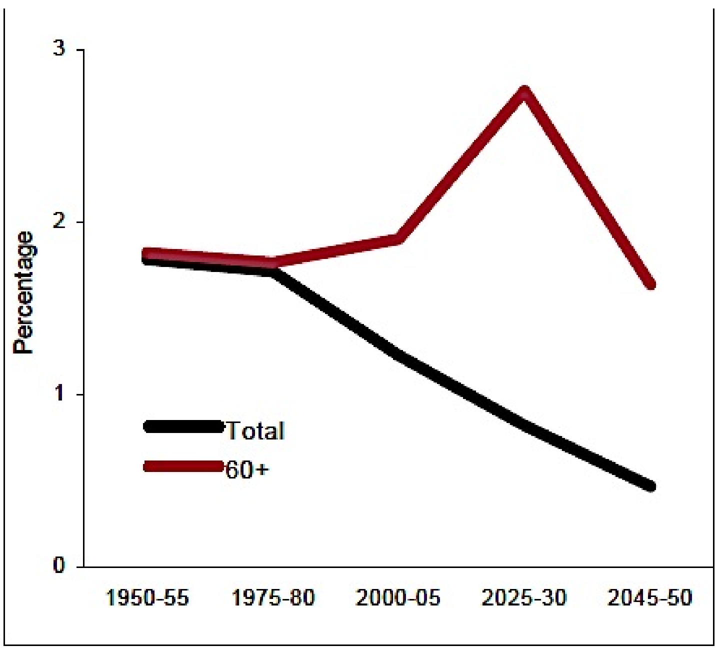


Figure 6: Average annual growth rate of total population and population aged 60 or over: world, 1950-2050 [2]

1.2 Aging in India

India is the second most populous country in the world with 1.21 billion people in its 2011 census [5]. In 2011, the 60+ population accounted for 8% of India population (93 million people). According to estimates, by the year 2050, the 60+ population will climb and account for 19% (323 million people) of the population [3]. The population pyramid of India follows the structure of most of the other developing countries by starting out with a conical shape in the middle of the last century and becoming rectangular by the year 2050 (Figure 7) [2]. Data from the World Population Prospects from the UN show a similar picture of growth in the 65+ years old population, almost till the end of this century [6].

Several forces are driving India's changing age structure, including an upward trend in life expectancy and falling fertility. An Indian born in 1950 could expect to live for 37 years, whereas today India's life expectancy at birth has risen to 65 years; by 2050 it is projected to increase to 74 years. Fertility rates in India have declined sharply, from nearly 6 children per woman in 1950 to 2.6 children per woman in 2010. India has also been experiencing a breakdown of the traditional extended family structure; currently, India's older people are largely cared for privately, but these family networks are coming under stress from a variety of sources [7].

India is in the early stages of establishing government programs to support its aging population. At the current burden of disease levels, rising numbers of older people will likely increase demands on the health system. Less than 10% of the population has health insurance (either public or private), and roughly 72% of healthcare spending is out-of-pocket [8]. The aging population is particularly at risk, as the health insurance scheme for the poor covers only those aged 65 or younger [9].

Older Indians also face economic insecurity; 90% of them have no pension. According to official statistics, labor force participation remains high (39%) among those aged 60 and older and is especially high (45%) in rural areas [10]. These high participation rates reflect an overwhelming reliance on the agriculture and informal sectors, which account for more than 90% of all employment in India. They also reflect the inadequacy of existing social safety nets for older people. In addition, more than two-thirds of India's elderly live in rural areas, limiting their access to modern financial institutions and instruments such as banks and insurance schemes [7, 11].

With India in the early stages of a transition to an older society, little is known about the economic, social, and public health implications. Developing countries like India have mostly focused on infectious diseases as the main health care challenge. However, these trends of a shift to an aging society will lead to increases in the burden of physical and cognitive disability and non-communicable diseases, notably osteoarthritis and cardiovascular disease (CVD) [12]. Indian health system is poorly equipped to address most of these issues associated with this dramatic change in demographics. New institutions and new programs must be implemented and evaluated to determine whether the dual goals of providing income and health security at older ages can be achieved at affordable budgets. Data on the status of older people are needed to analyze population aging and formulate mid- and long-term policies.

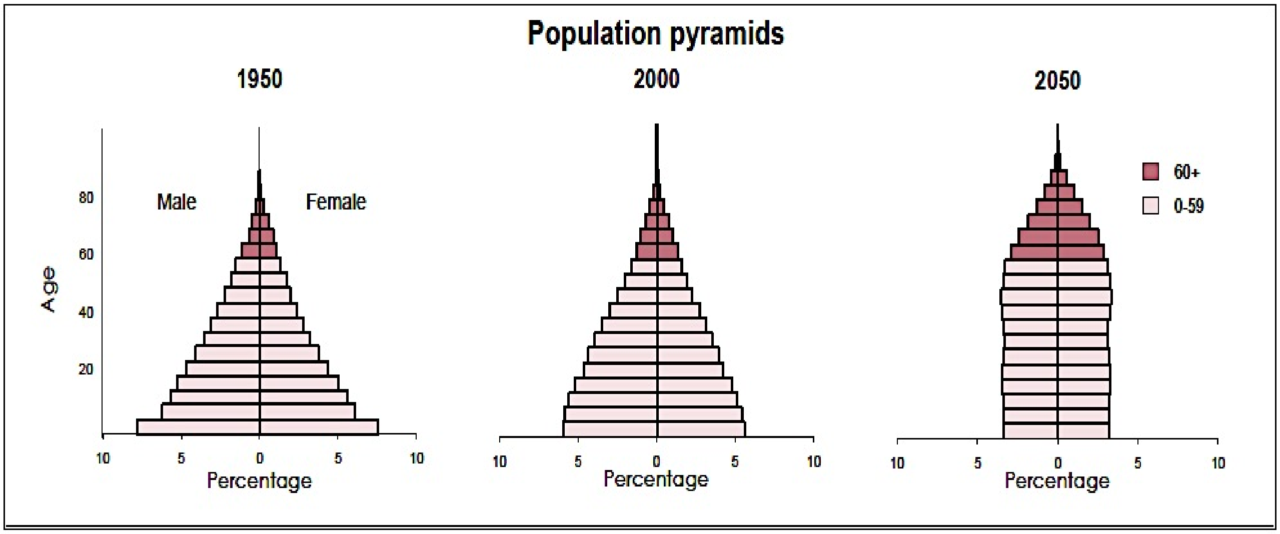


Figure 7: Population pyramids for India showing percentage of population in different age groups from the years 1950, 2000 and 2050 (estimated) [2]

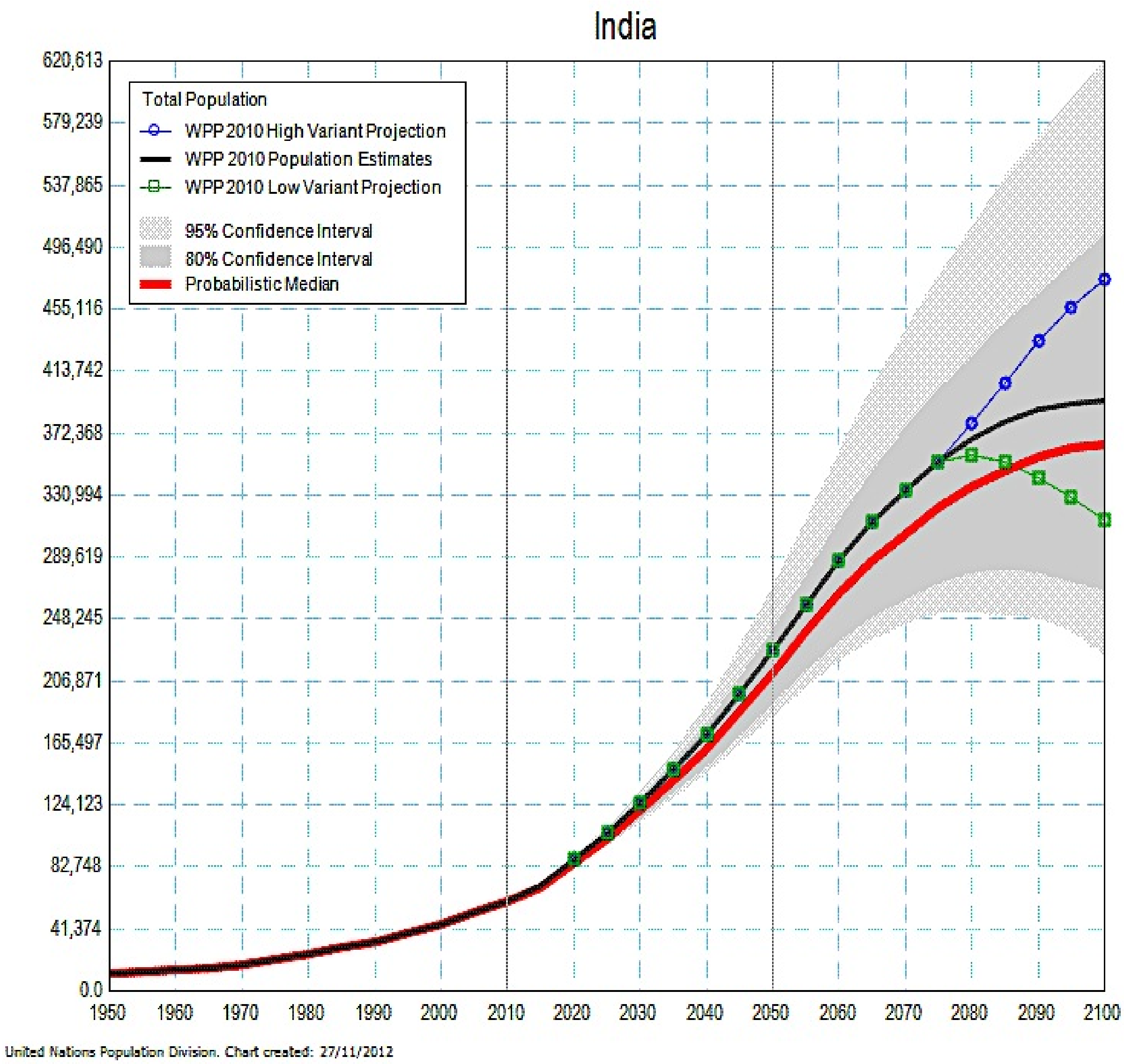


Figure 8: Probabilistic Population Projections: Population age 65 and over (thousands) Based on the 2010 Revision of the World Population Prospects [6]

1.3 Aging and mobility disability

1.3.1 Introduction

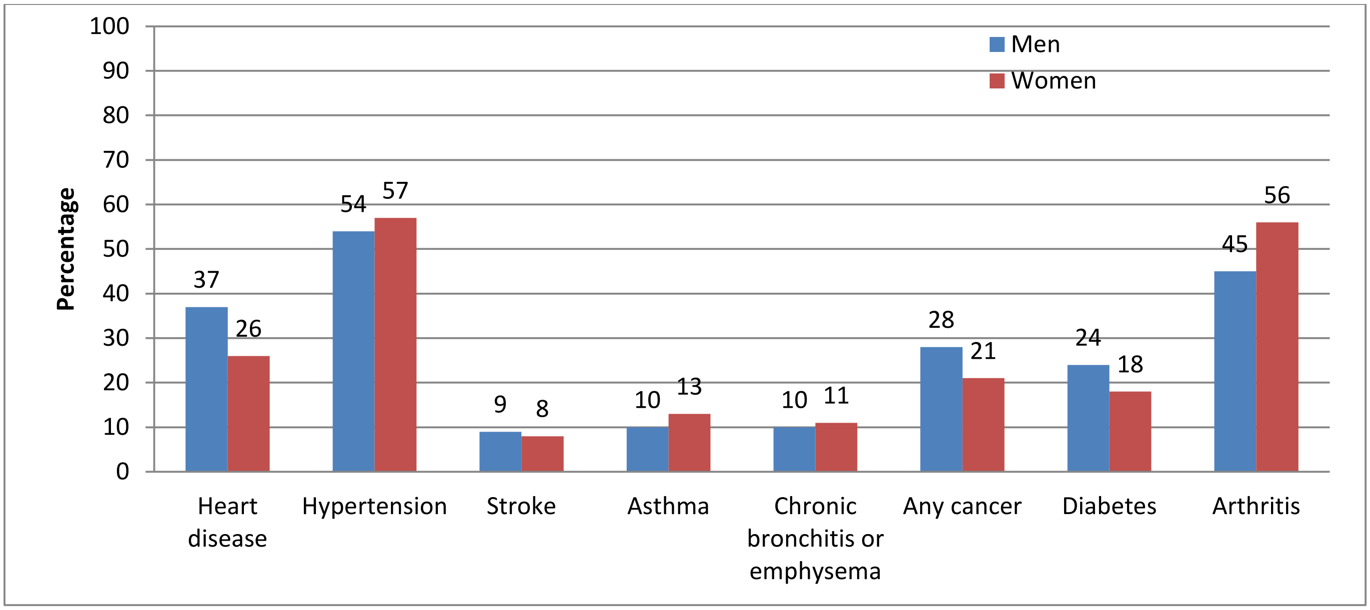
Mobility can be defined as the ability to move independently in the environment. It is considered one of the most important and basic functions of daily life, and is crucial for retaining the capability to fulfill the activities of daily living, social functioning, and overall to maintain a good quality of life.

The most common way to identify mobility impairment is by evaluating the capacity of an individual to move around on their own feet, with or without the aid of assistive devices. Presence of limitations or difficulties in walking is considered to be mobility disability. The severity of mobility disability can be segregated into different levels. Most commonly, limitation in getting around outside the house, neighborhood or the community is considered as community mobility disability. Serious mobility disability is described as difficulty in the capacity to move around inside the house. The most severe form of mobility disability is considered to be the inability to walk completely (Table 1) [13].

Table 1: Mobility disability according to severity of condition

Community mobility disability	Limitation in getting around outside the house, neighborhood or the community
Serious mobility disability	Difficulty in the capacity to move around inside the house
Severe mobility disability	Inability to walk completely

Older population has high prevalence and incidence of chronic disease and disability. Data from Centers for Disease Control and Prevention from 2009-10 shows that almost 50% of older Americans suffer from Arthritis and more than a quarter of them have heart disease (Figure 9)[14].



(Data are based on a 2-year average from 2009–2010 for civilian non-institutionalized population.
SOURCE: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey)

Figure 9: Percentage of US population age 65 and over who reported having selected health conditions, by sex, 2009-2010

Mobility disability is one of the leading health issues in older adults globally and is the cause for poor quality of life in this age group [15, 16]. According to data from the Federal Interagency Forum on Aging Related Statistics, age-adjusted percentage of chronically disabled Medicare enrollees aged ≥65 years has been decreasing over the years. However, in 2009, 41% of the older population still had at least one ADL or IADL disability or were institutionalized (Figure 10)[14]. The aging process itself is often accompanied by impairments in mobility and gait disturbances. The prevalence and incidence of mobility disability can be variable, as several factors can influence the extent and duration for the condition. Epidemiologic studies have identified several diseases and disease processes to be related with mobility disability, including cardiovascular, musculoskeletal and neurological diseases [13]. Mobility disability can be sudden, following an acute and severe disease process, e.g. myocardial infarction, stroke, fractures, etc. More commonly, the process of mobility disability is more gradual and progressive, usually as a result of chronic disease or age-related changes in biology and physiology. Depending on the main cause, the onset of mobility disability can be acute and catastrophic or gradual and progressive, and follow a dynamic pathway characterized by periods of deterioration and recuperation [13, 17, 18]. The duration of mobility disability might also vary from a few days (e.g. after a fracture) to lifetime (e.g. after a stroke or other chronic conditions). Another variation in estimates of mobility disability is due to differences in definitions and methods used to identify the condition (Table 2). However, regardless of the method or definition used, the estimated prevalence of mobility disability is high in community dwelling older adults.

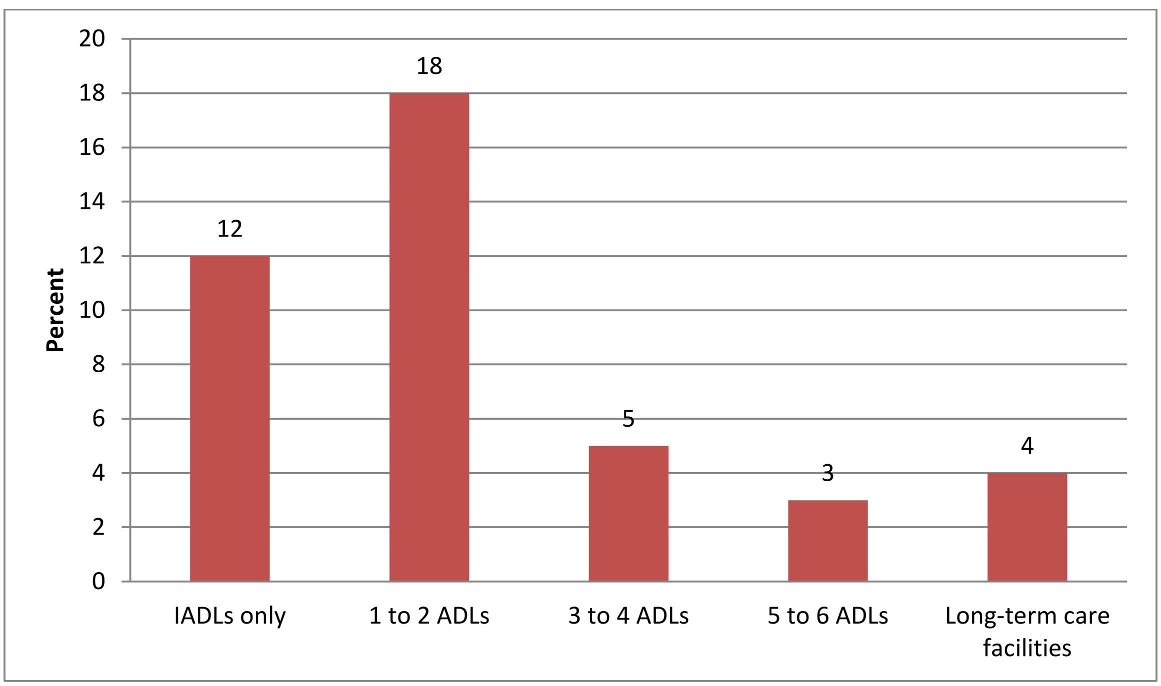


Figure 10: Percentage of Medicare enrollees age 65 and over with limitations in activities of daily living (ADLs) or instrumental activities of daily living (IADLs), or who are in a long-term care facility, in 2009

Table 2: Definition of disability or poor mobility used in epidemiologic studies according to different examinations

Examination	Definition of disability or poor mobility
Self-reported measures of disability	
Activities of Daily Living	Categorized as Disabled or not disabled: Disabled in the specific domain if difficulty in 1 or more tasks
	Categorized in 3 categories: 1 ADL, 2-3 ADLs, >3 ADLs
	More complicated subscales also used in studies
Instrumental Activities of Daily Living	Categorized as Disabled or not disabled: Disabled in the specific domain if difficulty in 1 or more tasks
	Categorized in 3 categories: 1 IADL, 2-3 IADLs, >3 IADLs
	More complicated subscales also used in studies
SF-36 Physical Functioning Subscale (PF-10)	Scores are standardized to range from 0 – 100, with a mean of 50, standard deviation of 10, and higher scores reflecting better function. Disability is categorized using specific domains or as a continuous scale.
Other self-report	Inability/ lot of difficulty to walk a quarter/half a mile
	Inability/ lot of difficulty to climb a flight of stairs
	Require personal assistance in 2 or more ADLs
Objective measures of disability	
Short Physical Performance Battery (SPPB)	Similarly, an SPPB score of <=9 is considered as evidence of limited mobility and a score of <=6 relates to more serious mobility disability.
Usual gait speed (4, 6 or 10 meters)	A gait speed of <1 m/s is considered an important cutoff predicting future events. A gait sped <0.8 m/s predicts more severe disability. In prospective studies, a decline in gait speed of 0.1 m/s in one year is considered an important cutoff in predicting future mortality.
Physical Performance Test (PPT)	The total score ranges from 0 (worst performance) to 36 (best performance) for the 9-item test.
Timed up and go test	A cutoff of 12 seconds is used in some studies. Sometimes used as a continuous measure.
400 meter walk	Mobility disability defined as the inability to complete 400-meter walk test within 15 minutes.

Mobility disability usually has a very subtle and gradual progress and can remain clinically unrecognized for several years before it starts to affect daily living activities, including basic self-care. Mobility disability research is essential in understanding its effects on quality of life, particularly for older adults. The mobility disability process is multifactorial and has discernable and definable causes. The concept of disability can be explained as the difficulty or inability to perform functions due to the gap in a person's ability and social/physical environmental demands [19]. One of the most prominent models used to conceptualize disability is based on the Nagi framework [20]. According to this model, the disablement process starts with pathology at the cellular or tissue level, which leads to impairments. Impairments are defined as abnormalities, defects or losses in specific organs or organ systems, e.g. cardiovascular, neurological or musculoskeletal systems. This leads to functional limitations, defined as impairments at the level of the organism, or restrictions in basic functioning of the individual, e.g. mobility, climbing stairs, grasping, etc. Finally, disability is defined as limitations of the individual in performing socially defined roles, tasks and activities, e.g. self-care, household management, etc. Most epidemiologic studies test functional limitations by using objective measures of physical performance to link impairments (e.g. musculoskeletal disease) with disability (e.g. problems with self-care). Figure 9 shows the Nagi framework for disability.

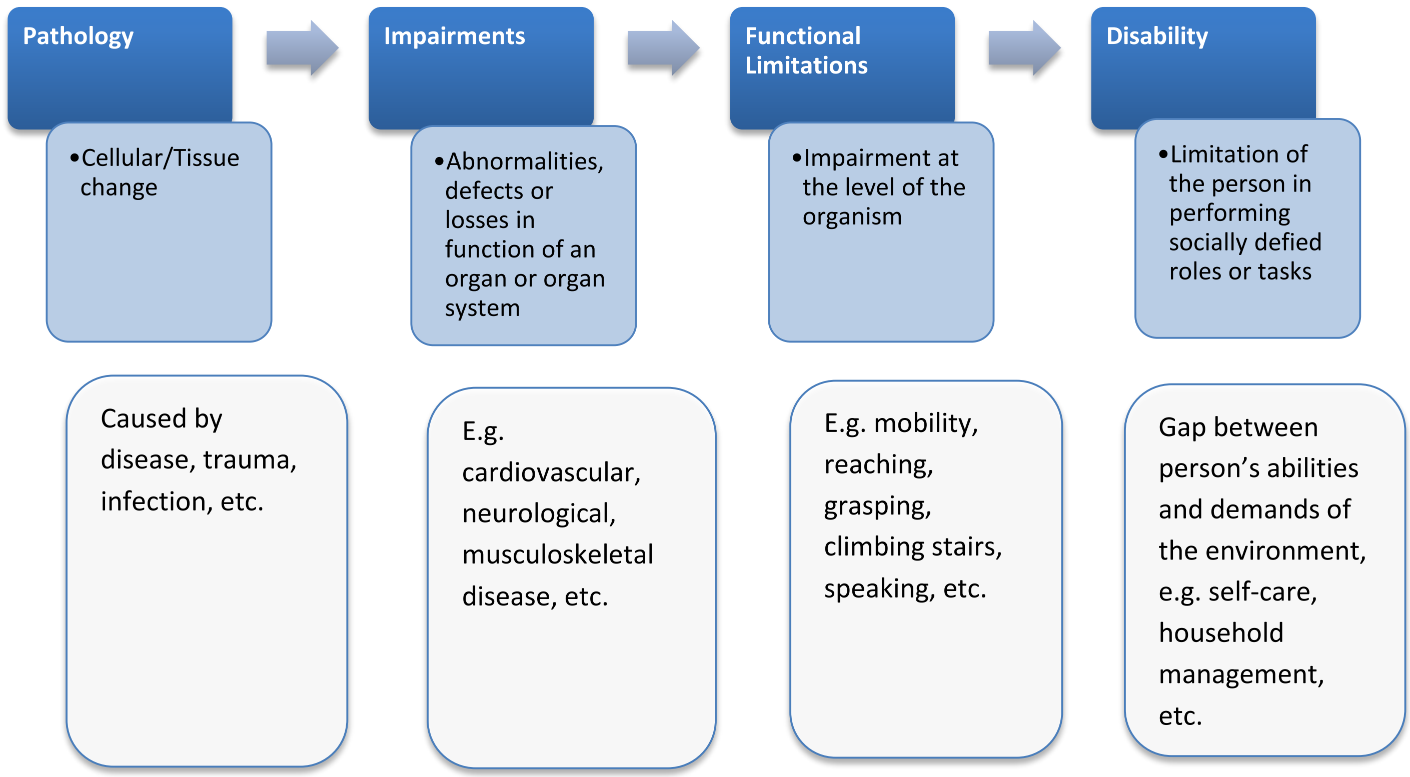


Figure 11: Nagi framework for disability

1.3.2 Major determinants of mobility disability

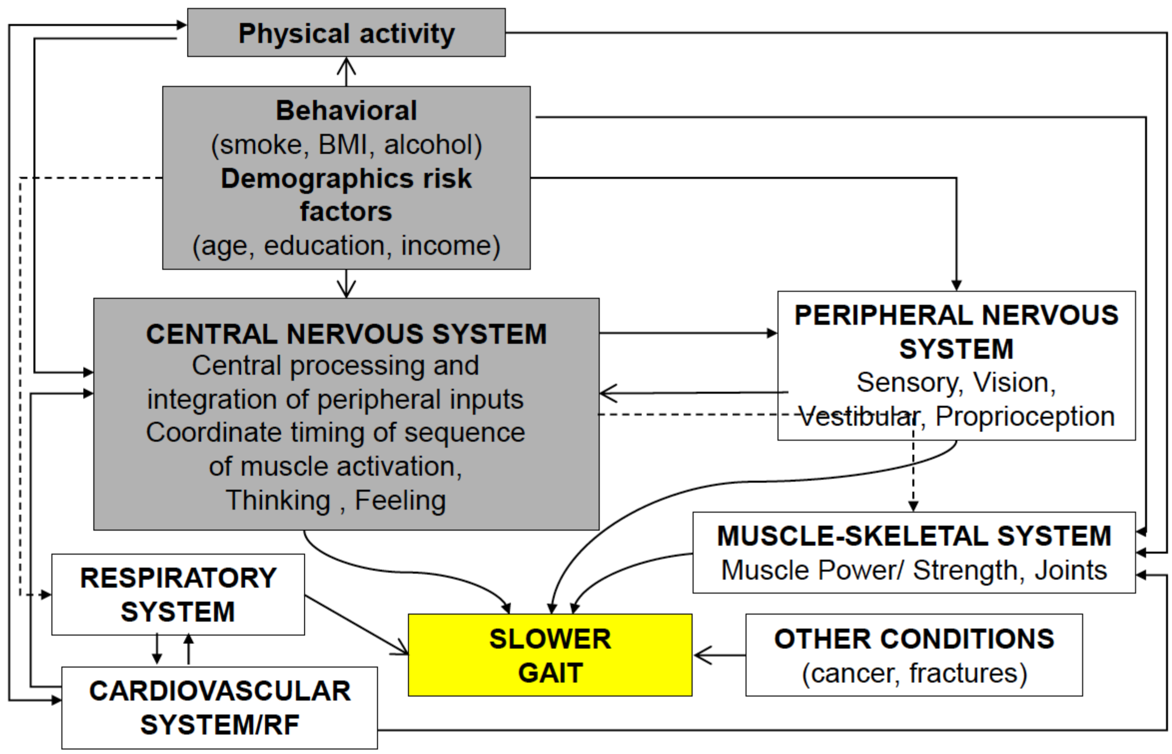
Epidemiologic studies have shown mobility disability to be associated with several factors, including single or multiple chronic diseases, health behaviors, lifestyle and other risk factors. However, major proportion of mobility impairment is not clearly related to a specific medical condition, and is recognized very late in the process to receive adequate medical care. This issue becomes more complicated because of the high prevalence of comorbidity in older adults (Table 9).

Mobility impairment is associated with disorders and diseases or several organs and organ systems in the human body. Majorly, impairments in joints, bones and muscles, brain and cardiovascular system are the main factors associated with mobility disability [21]. There are many other modifiable or non-modifiable risk factors that might contribute to mobility disability. Demographic and socioeconomic factors, including female sex, older age, lower education and lower income are associated with mobility disability [19, 22]. In-home mobility disability increases from 5% at age 65 to 30% at age 85%[13, 22]. Smoking, alcohol use, low physical activity and high BMI are considered lifestyle risk factors for disability [23]. Some musculoskeletal conditions, including sarcopenia are also highly correlated with declines in mobility [13, 24]. Sarcopenia is defined as involuntary loss of muscle mass and strength and is shown to be highly associated with mobility disability in several cross-sectional and longitudinal studies. However, there are controversies and inconsistencies in defining and measuring sarcopenia, because of the lack of an operative definition and standardized methodologies to measure muscle decline. Sarcopenia, in turn, is related to many other causal factors, including age-related loss of motor neurons, hormonal deficiencies, changes in inflammatory markers, and impaired protein synthesis [25]. Another geriatric syndrome, sarcopenic obesity – low muscle mass and obesity, is associated with mobility impairments [26]. Several other chronic clinical and subclinical diseases that have an effect on different organs and organ systems also contribute to progression of mobility disability, particularly in older adults [13, 19, 27].

Impairment in central nervous system, sensory system and effector outputs can influence balance negatively, which is a significant component of mobility [28, 29]. Some studies have shown association of cognitive impairment and subclinical brain disorders with mobility in older adults [30]. New studies have shown deficiency in vitamin D to play a role in mobility impairment [31, 32].

A model in Figure 10 shows the effect of multisystem disorders on gait speed.

Most research indicates that mobility disability is a multifactorial condition, as there is no clear primary cause for the condition in majority of the cases [33]. Even though there is no established path for treatment yet, the approach for management and prevention of mobility disability will have to be multifaceted to be successful.



(Modified from: Brach J, Rosano C, Studenski S. **Mobility**, In: Hazzard WR et al, Principles of Geriatric Medicine and Gerontology, 2007 [22].)

Figure 12: A model showing the effect of multisystem disorders on gait speed

Table 3: Major determinants contributing to mobility disability

Category	**Determinant**
Demographic factors	Older age
	Female sex
Socioeconomic factors	Lower income
	Lower education
Behavioral factors	Smoking, alcohol
	High BMI
Cardiovascular disorders	Stroke
	Peripheral artery disease
Musculoskeletal disorders	Sarcopenia/ low muscle strength and power/ sarcopenic obesity
	Osteoarthritis
	Other bone and joint disorders
	Fractures
Neurological disorders	Central Nervous System
	Peripheral Nervous System
Respiratory disorders	
Vision and hearing disorders	
Other factors	Inflammation
	Hormonal disturbances
	Low physical activity
	Cancer
	Nutritional deficiency (Vitamin D)

1.3.3 Assessment of mobility disability in epidemiologic studies

Mobility disability has been defined in several different ways in epidemiologic studies. Studies have used many different qualitative as well as quantitative methods to describe mobility and gait impairments in older adults. However, most of the assessments offer relevant and complementary information to detect mobility disability, each with its own strengths and limitations.

Table 4: Usual approaches used for assessment of disability in epidemiologic studies

Self-reported measures
Participant self-report
Proxy report
Self-report questionnaires (ADLs, IADLs, SF-36: PF-10, etc.)
Professional report
Objective measures
Short Physical Performance Battery (SPPB)
Balance tests
Chair stands
Usual gait speed
Physical Performance Test (PPT)
Writing a sentence
Simulated eating
Lifting a book and putting it on a shelf
Putting on and removing a jacket
Picking up a penny from the floor
Turning 360 degrees
50-foor walk test
Climbing one flight of stairs
Climbing up to four flights of stairs
Wearable electronic monitoring (accelerometers, GIS devices, etc.)
Timed up and go test
400 meter walk

The most commonly used method for detecting mobility problems is self-report. Self-report questions on mobility (e.g. difficulty in performing activities of daily living, walking, climbing stairs, etc.) can provide clear and evident data on disability [17, 34-36]. These questions are widely used in epidemiologic studies, as they are simple, inexpensive and easy to administer. However, there is a lot of variability within self-report questions. There are single item questions based on difficulty or dependence in mobility. There are many validated questionnaires that assess mobility impairments focusing on different levels and severity of disability (e.g. difficulty in walking short or long distances), different parts of the body (e.g. lower extremity – walking, or upper extremity – grasping, lifting), and several other criteria [13]. The most commonly used questionnaires are Activities of Daily Living (ADLs) that has questions about difficulties in bathing, dressing, eating, ambulating, toilet use and continence

[21, 34-37]; and the Instrumental Activities of Daily Living (IADLs) that has questions about difficulties in managing personal finances, taking medication, using a telephone, preparing meals, housekeeping and shopping [35, 36, 38]. The Barthel Index of Activities of Daily Living is a variant of the original ADLs and uses expanded response options to determine the degree of independence of the individual in performing the basic tasks of daily living [39, 40]. Another questionnaire, PF-10 is a 10-question, generic outcome measure designed to examine a person's perceived limitation with physical functioning and is a subscale within the 36-item Short Form Health Survey (SF-36) [41]. It has questions on difficulties in bathing or dressing, lifting or carrying groceries, bending, kneeling or stooping, walking 100 yards, walking several hundred yards, walking more than a mile, climbing one flight of stairs, climbing several flights of stairs, moderate activities (moving a table, pushing a vacuum cleaner, etc.) and vigorous activities (running, lifting heavy objects, participating in strenuous sports). There are several other variants of these questionnaires used in epidemiologic studies.

However, most self-report questionnaires identify an advanced stage of disability, and do not discriminate at the level of high physical function. They provide very little information about the physical function of higher functioning individuals (ceiling effect) and identify persons whose ability to perform basic functions has already been impaired. Therefore, these measures are appropriate as final outcomes to understand the effect of impairment on function leading to disability.

Table 5: Components of three self-reported questionnaires on physical function (ADLs, IADLs and PF-10)

Activities of Daily Living	**Instrumental Activities of Daily Living**	**SF-36 Physical Functioning Subscale: PF-10**
Bathing	Managing personal finances	Bathing or dressing
Dressing	Taking medication	Lifting or carrying groceries
Eating	Using a telephone	Bending, kneeling or stooping
Ambulating	Preparing meals	Walking 100 yards
Toilet use	Housekeeping	Walking several hundred yards
Continence	Shopping	Walking more than a mile
		Climbing one flight of stairs
		Climbing several flights of stairs
		Moderate activities (moving a table, pushing a vacuum cleaner, etc.)
		Vigorous activities (running, lifting heavy objects, participating in strenuous sports)

As the research in mobility disability has become more advanced, several objective methods of physical performance have been developed. These methods range from simple measures of usual short-distance gait speed to comprehensive measures of assessment of upper and lower limb function [19]. A commonly used test is the Short Physical Performance Battery (SPPB – figure 11) [28, 42]. This test consists of a balance, gait speed and chair stand test. The balance test consists of three components – side-by-side stands, semi-tandem stands and tandem stands. The gait speed test is a timed 4-meter walk at usual pace. The chair-stand test is a timed 5-time repeated chair stands from a sitting position with arms folded. Each test is given a minimum score of 0 and a maximum score of 4. While the individual performance measure can be used to evaluate specific functional abilities, the scores from each of the tests are usually added together to obtain an aggregate or summary score for each participant and used to determine mobility disability. This test has been shown to independently predict mobility disability, activities of daily living disability, future hospitalization, nursing home requirement and mortality in many large epidemiologic studies [28, 42-45].

The short distance usual gait speed (4, 6 or 10 meters) alone has also been used in studies and has proven to be predictive of many negative health outcomes [16, 30, 46, 47]. Longer distance walking tests, including the 400 meters walk, have been included in several studies, as they have also shown to predict disability in older adults [13, 23, 45, 48-50]. These tests are not considered substitutive but are complementary to short walking tests and other lower extremity examinations, as they can better explain the aerobic fitness component and distinguish mobility disability among higher functioning older adults [51-53]. Moreover, this measure is associated with measures of subclinical cardiovascular, neurological and musculoskeletal conditions [51, 54].

Another assessment, the physical performance test (PPT) has been used frequently in many studies. This test assesses multiple domains of physical function by observing the performance of timed tasks that simulate activities of daily living with varying levels of difficulty [38]. It consists of tasks such as writing a sentence, simulated eating, lifting a book and putting it on a shelf, putting on and removing a jacket, picking up a penny from the floor, turning 360 degrees, 50-foor walk test, climbing one flight of stairs and climbing up to four flights of stairs. There are several variants and shortened versions of this test. Each task has a minimum score of 0 and a maximum score of 4. The total score ranges from 0 (worst performance) to 36 (best performance) for the 9-item test.

The timed up and go test is another effective method of assessing mobility and quantifying performance in older adults. [44, 55] This test is objective, quick and easy to perform and includes basic mobility skills. In this test, the individual is required to get up from a chair, walk 3 meters, turn and sit back down on the same chair. Faster completion time indicates better mobility.

Recent studies have used more sophisticated methods to describe mobility, function and activity using wearable electronic monitoring devices, including accelerometers, gait tracking equipment and Geographic Information System (GIS) tracking [13]. However, these techniques are still developing and expensive, but do show a lot of promise for future studies and open up more avenues for research in this field.

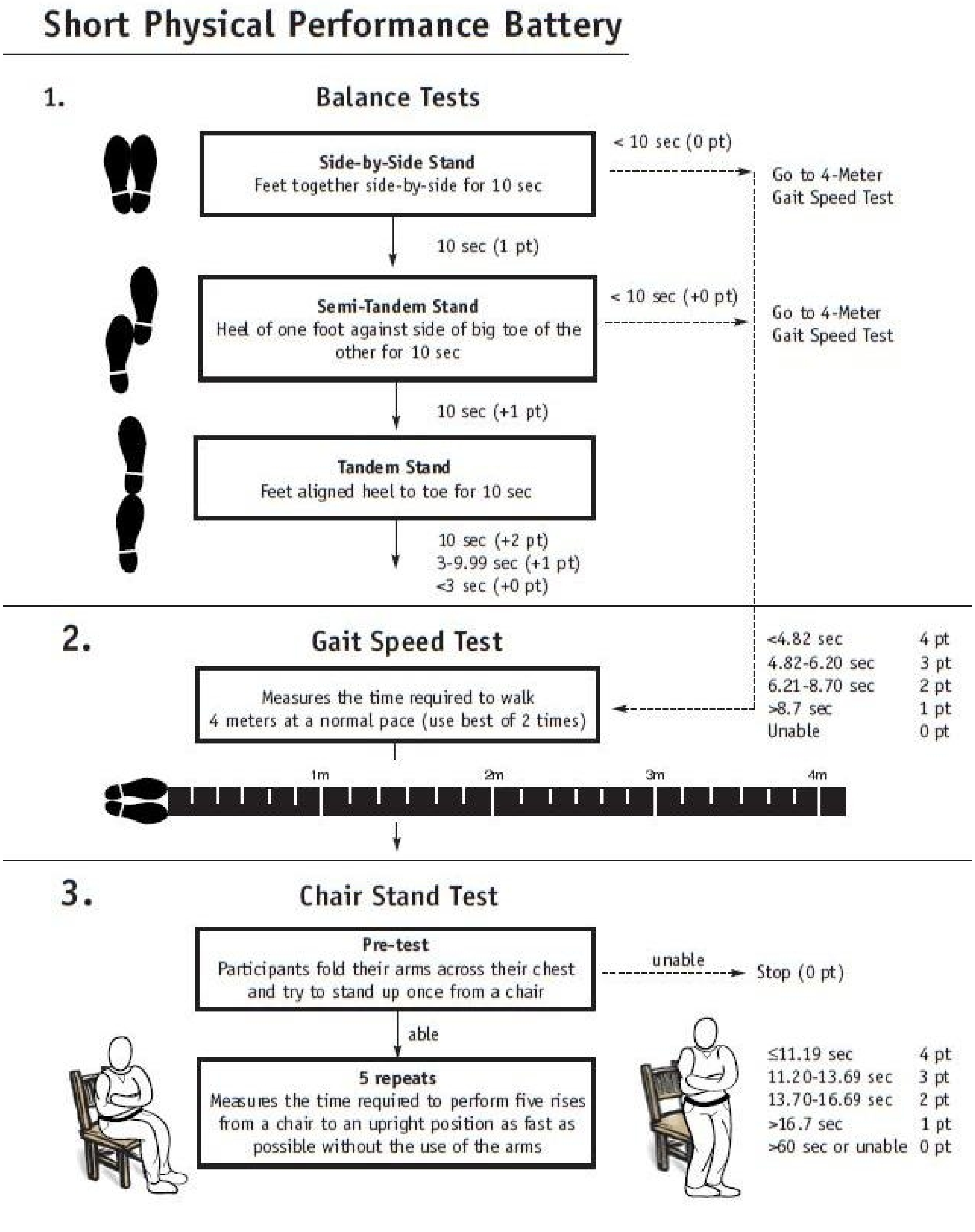


Figure 13: Components of the Short Physical Performance Battery

Table 6: Advantages and disadvantages of self-reported measures of disability

Advantages	Disadvantages
Easy to administer	High ceiling effect
Inexpensive	Depend heavily on environment
Easier in severely disabled	Capture advanced stage of disability
Better assessment according to the individual's own environment	Difficult to use cross-culturally, across different SES levels, ethnic and racial groups
	Difficult to observe deterioration longitudinally if the levels or performance are still high

Table 7: Advantages and disadvantages of objective measures of disability

Advantages	Disadvantages
Identify a whole spectrum of individuals based on performance, including higher functioning ones.	Need more intensive staff training
Identify non-disabled persons at risk of disability	More expensive than self-report
Better indicators of change in functioning over time	Need specialized personnel and space
Better for cross-national, cross-cultural studies,	Difficult to measure in severely disabled persons, particularly with incident disability in longitudinal studies
Used as endpoints in intervention studies	
Predict future disability, need for long-term care and mortality	

1.3.4 Consequences of mobility disability

Loss of mobility is one of the major factors in increasing dependence and decreasing quality of life in older adults. Mobility impairments lead to functional disorders, which further result in increased social isolation and healthcare expenditure [13, 22].

Self-reported mobility impairment has been shown to predict disability and mortality in older populations from several countries and cultures globally [56]. More importantly, objective measures for mobility disability have allowed researchers to explore the early stages of functional decline with more precision without adding too much difficulty in implementation. They have allowed the identification of older adults who are independent and do not have any overt symptoms of mobility disability, but are at risk for developing impairment in the near future. In general, poor performance on these examinations predicts future mobility disability and difficulties in self-care. Of all these measures, short usual pace gait speed is the most predictive of incident mobility disability [16, 30, 46, 47, 57, 58]. Several cutoff points have been proposed to make the values of all the exams meaningful clinically. A gait speed of <1 m/s predicts lower extremity limitations, hospitalizations, falls and death. A gait speed of <0.8 m/s predicts more severe disability. In prospective studies, a decline in gait speed of 0.1 m/s in one year led to an increase in 5-year mortality rate [16, 59]. Similarly, an SPPB score of <=9 is considered as evidence of limited mobility and a score of <=6 relates to more serious mobility disability [60]. In older adults >70 years of age and without any self-care disability at baseline, the SPPB was shown to be a powerful predictor of incident disability in higher-level mobility disability and activities of daily living. Poor performance scores also predict future hospitalizations and nursing home placements in several studies [28, 43, 45]. Mobility impairment is shown to be risk factor for several geriatric conditions, including falls, fractures, cognitive decline, dementia and functional decline. Decreased mobility due to impaired mobility leads to further increase in health problems in older adults, including loss of muscle mass and strength, and deterioration of other chronic conditions, increasing the risk of institutionalization and death. The rates of mobility impairment are higher in women and in long-term care settings. The rates almost invariable increase with age among all ethnicities and geographical regions [16, 43, 47, 58, 61, 62].

1.4 Aging, mobility disability and chronic disease in India

There is very little and inconsistent data about mobility disability from India. According to the Census from 2001, there were a total of 21.9 million (2.13%) disabled people living in India [63]. According to estimates from the National Sample Survey (NSS), which uses a nationally representative stratified sample to get estimates, the total number of disabled people in India in 2002 was 20.8 million. These disabilities included locomotor, hearing, speech, vision and mental disabilities. However, the numbers vary too much within specific categories. The estimate of locomotor or mobility disability according to NSS was 10.6 million and according to the Census was 6.1 million (0.6%) [63]. These large differences were mostly because of difference in definitions and no standardized approach used to arrive at these numbers [64]. All estimates are from self-report, but the NSS uses a much broader classification for locomotor disability by including persons with paralysis, amputation, deformity, dysfunction of joints and dwarfism. In the census, locomotor disability covers the absence of all toes, all fingers, deformity, inability to move without aid, and inability to lift and carry any small article [64]. The Census 2011 is supposed to include more detailed information on disability for each age group.

There are very few epidemiologic studies on prevalence and determinants of mobility disability in India, especially in the elderly. One of the major factors leading to disability in older adults in India is cardiovascular disease (CVD) [65]. CVD is a global problem, but its presence in developing countries has been escalating in the last few years. There are numerous factors contributing to this rise, including demographic shifts with altered age profiles, lifestyle and diet changes related to rapid urbanization, among several others. According to estimates, by 2020, CVD will become the leading cause of morbidity and mortality in most developing nations around the world. With advances in healthcare in developing countries, the population suffering from CVD is living to be older than ever before, which may contribute to an increase in disability in this population.

Several techniques have been developed for the early detection of arterial damage that have provided important insights into patterns and pathogenesis of cardiovascular disease and possible subsequent disability. Ankle-arm index (AAI) is a very convenient and non-invasive method to detect peripheral arterial disease (PAD). Electrocardiogram (ECG) provides information on several major and minor abnormalities with the heart. In the last few years, carotid artery ultrasound has shown to be an important identifier of carotid atherosclerosis and a good predictor of generalized artery wall thickness [66]. A composite measure of these non-invasive examinations provides with a very sensitive and specific estimate of presence of subclinical CVD [65]. Regular use of AAI or carotid artery ultrasound is not very common in India, especially in research. With growing prevalence of CVD in India, there is an urgent need to understand the burden of subclinical disease and risk factors. Risk factor modification may not only prevent cardiovascular events and mortality, but also can have an impact on reduction and delay in disability and improve quality of life in older adults. Studies have shown association of subclinical PAD with mobility impairment and lower physical function in elderly with subclinical disease [67-69]. Timely detection of subclinical disease may allow for early treatment opportunities leading to improved survival, lower disability and better quality of life in older population.

1.4.1 Importance of objective measures of disease and disability

One of the biggest challenges in measuring health status in most Asian countries and particularly India is the unreliability on participant self-report [11]. Self-reported data has several limitations even in more developed countries, which has led to the introduction of biomarkers in the measurement protocols of most of the European and North American studies and surveys. Health awareness in India is very poor, especially in the rural older population that is mostly illiterate and has inadequate healthcare access. This population is characterized by widespread undiagnosed disease, including easily diagnosable diseases like hypertension and diabetes [9]. Moreover, objectively measured data may indicate preclinical or subclinical disease (e.g. pre-hypertension, pre-diabetes, decline in performance measures, mild cognitive impairment, etc.) that can be used to educate the participants about preventive measures and treatments.

1.4.2 Aging studies in India

To our knowledge, there are three large cross-national efforts that have emerged in the past 10 years to provide data to address some of the health concerns in older adults. These include a Survey of Health and Retirement in Europe (SHARE), modeled on English Longitudinal Study of Ageing (ELSA) and the US Health and Retirement study (US HRS) [70]. SHARE is designed to include all 27 members of the EU in 2008. These projects include surveys of health and disability, but focus on socioeconomic factors related to retirement. The INDEPTH project, International Network for the Demographic Evaluation of Populations and their Health, includes 37 sites in Africa, Asia and Latin American and is designed to provide adult mortality data that is otherwise lacking [71]. The WHO recently launched the Study of Global AGEing and Adult Health (SAGE) in 6 countries, including China, Ghana, India, Mexico, Russia and South Africa. It is modeled on the SHARE project and will also link to INDEPTH [72]. These studies will provide demographic data but are not designed for in depth study of disease prevalence, causes of disability or explore mechanisms.

Another study, the Longitudinal Aging Study in India (LASI), an investigation of the economic, physical and social well-being of India's growing elderly population was started recently, and is a joint effort of the Harvard School of Public Health, the International Institute for Population Sciences and the RAND Corporation [73]. A pilot study was carried out in 2010 and enrolled 1683 subjects, age >45 years from 4 states in India. The long-term goal is to enroll nationally representative sample of 30,000 individuals into a longitudinal survey on aging, health and retirement. The data collection consists of a household survey, household finances, assets, debts and living conditions, with information on demographics, family and social networks, health, health care utilization, work and employment pensions and retirement. The clinical examination in LASI is limited to measurements of blood pressure, blood spot storage, anthropometrics, gait speed, grip strength, balance, lung function and vision [11].

Table 8: Major epidemiologic studies for outcomes of mobility disability in older adults

Study and authors	Study population	Functional assessments	Main conclusions
The Einstein Aging study, Verghese et al. 2006 [62]	488 70 to 99 years old men and women	Predictor – gait disorders Outcome – institutionalization and death	Incidence and prevalence of gait disorders are high in community-residing older adults and are associated with greater risk of institutionalization and death.
Established Populations for Epidemiologic Studies of the Elderly (EPESE), Guralnik et al. 1994 [28]	5174 71 years and older men and women	Predictor – SPPB, ADLs Outcome – nursing home admissions, short-term mortality	Strong association between performance measures and self-reported disability. Both tests were independent predictors of mortality and nursing home admissions.
Established Populations for Epidemiologic Studies of the Elderly (EPESE), Guralnik et al. 1995 [60]	1122 71 years and older, non-disabled men and women	Predictor – SPPB at baseline Outcome – future disability	SPPB was highly predictive of subsequent disability. It may identify elderly with a preclinical stage of disability who may benefit from interventions to prevent the development of frank disability.
Established Populations for Epidemiologic Studies of the Elderly (EPESE) and Hispanic EPESE, Guralnik et al. 2000 [43]	4,588 initially nondisabled older persons in EPESE and 1,946 initially nondisabled persons in Hispanic EPESE	Predictor – SPPB Outcome – ADLs and mobility-related disability	SPPB accurately predict disability across diverse populations. Summary score and the gait speed alone allow for the estimation of risk of disability in community-dwelling populations.
Honolulu Heart Program, Rantanen et al. 1999 [74]	6089 45 to 68 year old Japanese-American men	Predictor – maximum hand grip strength Outcomes – gait speed, chair stand, self-report	Hand grip strength was highly predictive of functional limitations and disability 25 years later.
Longitudinal Study of Aging, Miller et al. 2000 [75]	5151 70 years and older US men and women	Predictors – physical activity, comorbid conditions, levels of functional limitations Outcome – ADL/IADL disability	Past physical activity is important in delaying the onset of disability, regardless of severity of functional limitations
AgeD in HOme Care project, Landi et al. 2007 [37]	2005 65 years and older European men and women admitted to home care programs	Predictor – physical activity Outcome – ADL	Physical activity has an independent effect on functional autonomy among frail and old people
Randomized control trial, Brach et al. 2003 [57]	229 50 to 65 years old women at baseline	Intervention – walking Outcomes – self report, physical performance test, gait speed	Significant relation between physical activity during a 14-year period and current functional status

Table 8 continued

Women's Health and Aging Study, Simonsick et al. 1998 [76]	1002 65 years and older moderately to severely disabled women	Predictor – Social interaction Outcome – disability	Physical disability is not necessarily socially disabling.
Evergreen Project, Hirvensalo et al. 2000 [56]	1109 65 to 84 year old Finnish men and women	Predictor – physical exercise, mobility Outcomes – mortality, dependence	Mobility impairments predicted mortality and dependence
Health, Aging and Body Composition Study, Cesari et al. 2005 [47]	3047 70 to 79 years old, well-functioning men and women at baseline	Predictor – usual gait speed Outcomes – lower extremity limitation, death, hospitalization	Usual gait speed of less than 1 m/s identifies persons at high risk of health-related outcomes in well-functioning older people.
Health, Aging and Body Composition Study, Cesari et al. 2009 [77]	3024 70 to 79 years old, well-functioning men and women at baseline	Predictor – usual gait speed Outcomes – lower extremity limitation, death, hospitalization	Chair stand and standing balance performance may be adequate substitutes when gait speed is unavailable.
Health, Aging and Body Composition Study, Newman et al. 2006 [78]	3075 70 to 79 years old, well-functioning men and women at baseline	Predictors – Ability to complete long-distance corridor walk and total performance time Outcomes – Total mortality, incident cardiovascular disease, incident mobility limitation, and mobility disability	Ability to do the test and performance were important prognostic factors for total mortality, cardiovascular disease, mobility limitation, and mobility disability
Health, Aging and Body Composition Study, Simonsick et al. 2008 [23]	3056 70 to 79 years old, well-functioning men and women at baseline	Predictors – long-distance corridor walk time Outcomes – new self-recognition of mobility limitation within 2 years	A sizable proportion of elders who report no walking difficulty have observable deficits in walking performance that precede and predict their recognition of mobility limitation.
Health, Aging and Body Composition Study, Inzitari et al. 2007 [30]	2776 70 to 79 years old, well-functioning men and women at baseline	Predictors – usual gait speed Outcomes – Digit Symbol Substitution Test (DSST)	Gait speed independently predicts a decline in DSST after 5 years.
Cohort study using data from two health care systems, Perera et al. 2005 [79]	439 65 years and older men and women	Predictor – SPPB Outcome – death, mortality	A decline in gait speed of 0.1 m/s or 1 point in the Short Physical Performance Battery within 1 year increased the subsequent 5-year mortality rate.
Estudio de Evaluacion Funcional del Anciano	102 75 years an older well-	Predictor – activities of daily living, mobility,	Gait velocity measurement may allow detection of healthy

Table 8 continued

(EFA) study, Manuel Montero-Odasso et al. 2004 [80]	functioning men and women	usual gait velocity Outcome – hospitalization, caregiver requirement, incident falls	elderly people at risk for adverse events. Assessment of gait velocity is enough to predict adverse events.
Pooled analysis from 9 cohort studies, Studenski et al. 2011 [16]	34485 65 years and older men and women	Predictor – usual gait speed Outcome – survival rates and life expectancy	Survival increased across the full range of gait speeds, with significant increments per 0.1 m/s.
Systematic review of 27 articles from 1994 to 2009, Gabor et al. 2009 [61]	65 years and older men and women from several different studies	Predictor – usual gait speed Outcome – disability, cognitive impairment, institutionalization, falls, and/or mortality	Gait speed at usual pace was a consistent risk factor for disability, cognitive impairment, institutionalization, falls, and/or mortality.

2.0 DISSERTATION GOALS

Even though a majority of Indian older adults live in rural areas, their health needs have been neglected. The burden of chronic disease and disability has not been estimated using objective measures in this population, which may have led to introduction of biases to these assessments. The Mobility and Independent Living in Elders Study (MILES) was established to determine the prevalence of chronic disease and disability and to identify their risk factors in older rural Indians.

The main goals for this dissertation are to describe the concept and design features of MILES and to determine the prevalence and risk factors for cardiovascular disease and mobility disability in this population.

Manuscript 1: The design of Mobility and Independent Living in Elders Study (MILES): a rural aging cohort in India

Aim for manuscript 1: The main aim of this manuscript was to describe the concept and design features of MILES.

Manuscript 2: Prevalence and risk factors of cardiovascular disease in rural older Indians: The Mobility and Independent Living in Elders Study (MILES)

Aims for manuscript 2: The first aim of this report was to estimate the prevalence of CVD in rural older Indians from the Mobility and Independent Living in Elders Study (MILES), using the self-reported history of CVD, major ECG abnormality, PAD and a combined measure of all three measures. The second aim was to examine the relationship of CVD with traditional risk factors.

Manuscript 3: Prevalence and risk factors for mobility disability in rural older Indians: Mobility and Independent Living in Elders Study (MILES)

Aims for manuscript 3: The first aim of the present study was to estimate the prevalence of mobility disability in a rural Indian population aged >=60 years from the Mobility and Independent Living in Elders Study (MILES), using the 400-meter usual paced walk as the measure of mobility disability. The second aim of this study was to determine the risk factors for mobility disability in this population and its association with cardiovascular disease.

3.0 MANUSCRIPT 1: THE DESIGN OF MOBILITY AND INDEPENDENT LIVING IN ELDERS STUDY (MILES): A RURAL AGING COHORT IN INDIA

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3.1 Abstract

Background: Demographic increase in the older population is most rapid in developing countries and will have major impact on public health. Indian population is not well described, but evidence suggests that the current demographic transition provides a unique opportunity to better understand future disability. To accomplish this, we established a longitudinal cohort study – MILES, in a rural population of older Indians.

Methods: We enrolled a random sample of 564 men and women aged 60+ from Medchal Mandal region in Andhra Pradesh state. Baseline visit consisted of two separate clinic visits for measurements of blood pressure, anthropometry, short physical performance battery, 400-meter walk, grip strength, ankle-arm index, cognitive examination, peripheral quantitative computerized tomography, knee x-ray, carotid ultrasound, blood draw and a comprehensive interview. Annual follow-up visits are planned to collect information on incident disability and disease.

Results: According to data from the first clinic visit, median age of the participants was 66 years (60-92); median body mass index, 21.7 kg/m^2; median gait speed, 0.67 m/s and median grip strength 17 kg; 55% self-reported their health status as fair or poor and 13% reported falling $\geq$1 times in past 12 months.

Conclusion: Data suggest a much frailer population in this cohort compared to US subjects age 66 years. MILES will provide estimates of global burden of disease and disability and their risk factors in older adults, and findings from the study will be used to identify potential interventions to prevent disability appropriate in this rural population of Indians.

3.2 Why was the cohort set up?

Most developed countries already have relatively high proportions (15% – 22%) of individuals $\geq$65 years of age, but the most rapid increases in the older population are in the developing world. Birth rates are rapidly declining in many countries, including developing countries like India, further accelerating the shift toward an aging society [1]. In 1950, about 5% of the world's population was $\geq$65 years of age while 13% was $<$5 years of age. By 2020, individuals who are $\geq$65 years of age will outnumber children who are $<$5 years of age [3, 4]. This projected increase will be equivalent to a 10-fold increase in the 60+ population and a 27-fold increase in the 80+ population globally.

India is the second most populous country in the world with 1.21 billion people in its 2011 census [5]. In 2011, the 60+ population accounted for 8% of India population (93 million people). By the year 2050, the 60+ population will climb and account for 19% (323 million people) of the population [3]. The increase in the 60+ population in India is due to combined effects of fertility decline and increased life expectancy [4]. These trends may lead to increases in the burden of physical and cognitive disability and non-communicable diseases, notably osteoarthritis, cardiovascular disease (CVD) and diabetes. Developing countries like India are ill-equipped to address most of these issues associated with this dramatic change in demographics. There is a great need for more detailed data on the prevalence of these diseases, their risk factors and consequences, particularly with respect to disability and death in developing countries like India.

The current demographic transition in the Indian population provides a unique opportunity to better understand and identify the prevalence, risk factors and develop interventions to prevent the onslaught of disability that accompanies non-communicable diseases. We recruited a random sample of older adults from a rural region in India to establish a longitudinal cohort study – Mobility and Independent Living in Elders Study (MILES), to define the prevalence, incidence and risk factors for disability and age-related disease. The main study objectives were to: 1. determine the prevalence of age-related chronic disease in older adults; 2. determine the prevalence of socioeconomic, psychosocial, behavioral, dietary and environmental risk factors for age-related chronic disease and disability using examinations and non-invasive testing; 3. determine which conditions are most strongly associated with mobility disability, both cross-sectionally and longitudinally. The rationale for the measures chosen was based on a comprehensive model of major common chronic disease and disability, assessed with objective measures. This is the description of the concept and design features of the study.

3.3 Setting and sampling frame

3.3.1 SHARE INDIA/MediCiti Institute of Medical Science (MIMS)

SHARE India Research Foundation (Science Health Allied Research & Education) is an established research institution in Andhra Pradesh, India. It is affiliated with a 500-bed teaching hospital – MediCiti Institute of Medical Sciences. One significant research undertaking by SHARE India has been the REACH project (Rural Effective Affordable Health Care), established in the year 1995. REACH provides health education, immunizations, antenatal care and offers primary to tertiary care for a population of about 43,270 in 7405 households in 40 villages in the Ranga Reddy district on the northern outskirts of Hyderabad, Andhra Pradesh [81, 82]. The REACH Project has enumerated all households in the region and mapped each dwelling by GPS. Household information was collected, including self-reported age of the residents in the area. This annually updated census was used for the MILES sampling frame.

3.4 Who is in the cohort?

3.4.1 Study design and methods

We designed a 5-year prospective longitudinal cohort study of a representative sample of approximately 550 men and women (275 each) aged 60 and above from Medchal Mandal region near Hyderabad in Andhra Pradesh state in south-central India.

3.4.1.1 Sample size and power

The sample size of 550 was chosen to accurately estimate the prevalence of common chronic health conditions and disability, which are likely to range from 10 – 40%. Additionally, we estimated that we would have >80% power to determine risk factors for incidence of mobility disability, defined as inability to complete a usual paced 400-meter walk, if 400 participants of 550 were free of disability at the baseline examination, thus at risk for an incident event.

3.4.1.2 Sampling Methodology

We sampled 10 of 31 villages, and a random sample of households with at least one person aged 60 years or over in each village. Recruitment continued in each village from a random ordered list until the goal for men and women was reached.

There are 40 villages in the Medchal mandal (similar to a county) with a total population of 49,792. Of these, 6737 persons were of age $\geq$60 years, as of July 2, 2011 (source REACH database). Seven villages in which the age eligible population was less than 30 were excluded. Two villages that were used for an Indian Council of Medical Research (ICMR) funded research project on older adults were also excluded. Thus, the final sampling frame consisted of 31 villages. Ten villages were selected by probability proportion to population size method at the first stage. The number of respondents to be recruited from each of the 10 villages was calculated as proportional to the number of adults age 60 and above in the village.

A random number generator was used to assign a random number to each household in the village with at least one person age 60 or older. The household list was sorted in order of random number. The recruitment team consecutively went to each household in the ordered list to recruit until they recruited the expected number of respondents from that village. If both husband and wife and any other adult member living in the same household were age eligible, all were recruited for the study. Initial age eligibility was based on reported age in the 2011 REACH census.

3.4.1.3 Recruitment process

A two-member team went to the village in a SHARE vehicle, accompanied by two community health volunteers. Recruitment was conducted 3 days per week (Monday, Thursday and Saturday). The goal was to recruit 4 individuals for each day, 5 days a week (from Monday to Friday). A maximum number of 3 visits were made to each household if the selected household members were not available. Telugu translated and IRB approved consent form, recruitment script and eligibility form were developed. Individuals who were eligible and agreed to participate were scheduled for the MILES clinic visit.

3.4.1.4 Eligibility

Men and women were eligible to participate in MILES if they were aged $\geq$60 years according to the REACH census and lived in a randomly selected household. Eligibility also included ability to give informed consent (functional vision, hearing and cognitive function), no plan to move from the area over the next 5 years and no end-stage diseases, such as terminal cancer.

3.4.1.5 Informed Consent

The protocol and consent form was approved by the MIMS Ethics Committee and the University of Pittsburgh IRB. The consent form was translated into Telugu and back translated into English to ensure comparability. All Indian staff hired to work on MILES were fluent in English and Telugu. All participants provided informed consent. The international collaboration between SHARE INDIA and the University of Pittsburgh researchers was approved by the Indian Council of Medical Research.

3.4.1.6 Data Collection

Baseline assessment for MILES was organized into two clinic visits. The duration of each visit was approximately 5 hours. The first visit consisted of a fasting blood draw, measurements of blood pressure, anthropometry, short physical performance battery, 400 meter walk, grip strength, ankle arm index, ECG, and an interview including questions on demographic information, socio-economic status, health behaviors, and self-reported disease and disability. The second visit consisted of a cognitive function examination, peripheral quantitative computerized tomography (pQCT) of bone and muscle in the upper and lower extremities, knee x-ray, monofilament test for peripheral nerve function, dietary questionnaire, event history questionnaire and a carotid ultrasonography. All forms and protocols were modeled after major global and US aging studies [29, 83-85].

Figure 14 shows the recruitment flowchart for the first baseline visit. **Table 9** demonstrates the mean age of 60+ population in the county, sampled villages, refusals, not-eligible and enrolled participants. The data collection and questionnaire plan are summarized in **Tables 10 and 11.**

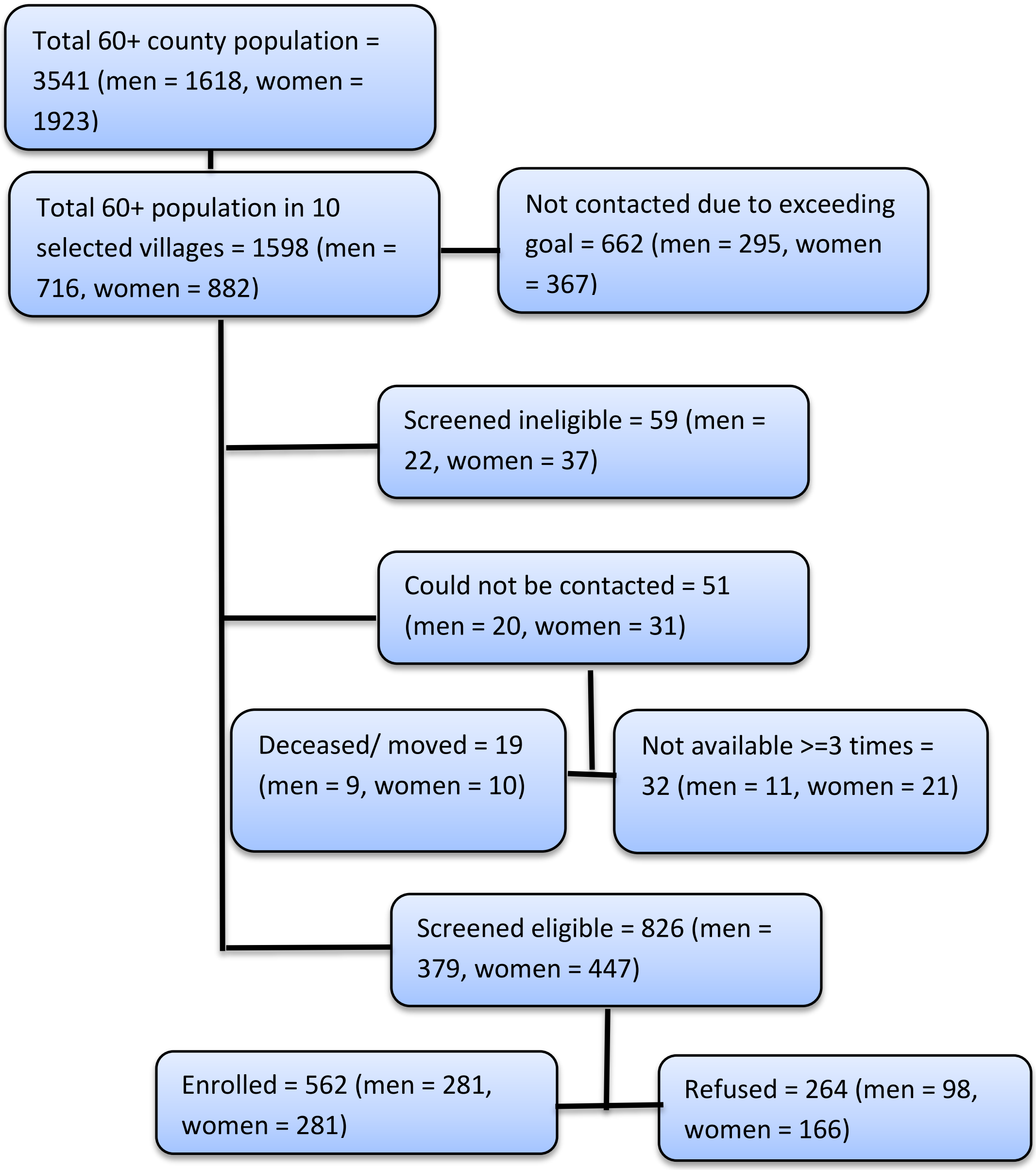

Figure 14: Recruitment flowchart for MILES

Table 9: Mean age of 60+ population in the county, sampled villages, refusals, not-eligible and participants enrolled in the study

Level of Sampling	Mean age (total population>= 60)	Mean age (>= 60 Men)	Mean age (>= 60 Women)
40 villages (total county)	68.6	68.6	68.6
31 villages (sample universe)	68.6	68.6	68.5
10 villages (selected)	68.4	68.4	68.5
Approached individuals	68.2	68.1	68.2
Underwent eligibility	68.2	68.2	68.2
Eligible respondents	67.8	68.0	67.6
Not-eligible respondents	73.7	70.6	75.5
Enrolled respondents	67.6	67.9	67.3
Refused respondents	68.3	68.3	68.3

3.5 What has been measured?

3.5.1 Components of MILES evaluation

Table 10: Components of MILES baseline evaluation

Measurement Category	Data points, procedures and instruments
First clinic visit	
Interviewer administered questionnaires	
General characteristics	• Age, religion, caste
Socioeconomic and lifestyle	• Marital status • Education • Occupation • Work activity • Living arrangement • Household possessions • Income and expenditure • Healthcare access
Medical history (self-report of a health professional's diagnosis of health conditions)	• Osteoarthritis/ Rheumatoid arthritis • Stroke • Hypertension • CABG/ angioplasty • Myocardial infarction • Angina [86] • Rheumatic heart disease • Diabetes • Chronic pulmonary disease, asthma • Depression (Geriatric Depression Scale – GDS) [87]. • Vision problems, cataract • Hearing problems • Number of teeth in the mouth • Falls, fractures and other injuries • Cancer • Cervical cancer and breast cancer screening questions (women) • Urinary incontinence (women) • Prostate health (men) • Infectious conditions
Disability	• Overall health • Problems with work or activity due to physical health • Pain that interfered with normal activities • Problems with memory • Problems with work or activity due to emotions • Sleep and fatigue

Table 10 continued

	• Difficulty with activities of daily living
Tobacco and alcohol use	• Smoking history, type, frequency, quantity and duration • Exposure to tobacco smoke • Chewing tobacco use • Alcohol use history, type, frequency and quantity • Other substance abuse
Weight and weight loss	• Weight and weight loss history
Cooking, water and food security	• Type of cooking fuel • Exposure to smoke from cooking fuel • Source of water used for cooking and drinking • Water storage • Food security
Physical activity	• Walking/ bicycling for daily work/ activities • Exercise frequency and duration • Time spent sitting or reclining
Pain/ stiffness	• Knee pain, back pain or any other joint pain • Joint stiffness or swelling
Medication inventory	• Type, name and duration of physician prescription, non-physician prescription, and over-the-counter medications taken in the last 14 days • Information on alternative medication use, including ayurvedic and homeopathic preparations
Physical examination	
Fasting blood sample	• Lipid Profile (total cholesterol, HDL, LDL, triglycerides) • Fasting blood sugar • Complete blood count, including hemoglobin and hematocrit
Anthropometry	• Height • Weight • Waist and hip circumference
Blood pressure and heart rate	• Resting blood pressure and heart rate measured thrice in seated participants after an initial resting period of 5 minutes using an Omron 705 automatic BP machine (Omron Healthcare, Inc., Lake Forest, IL). • Average of all three measurements was taken for analysis. • Hypertension defined as self-reported and use of anti-hypertensive medication or by the measured blood pressure categorized according to the JNC 7 criteria [88]
Physical performance	
Short Physical Performance Battery (SPPB) [28]	• Balance tests • 4 meter usual paced walk • Chair stands
400-meter walk [85]	
Grip strength [25]	• Hand grip strength was measured to assess upper body skeletal muscle function using Jamar handheld dynamometer (Lafayette Instrument, Lafayette, IN)
Cardiovascular examination	

Table 10 continued

Electrocardiogram (ECG)	• Standard 12-lead resting electrocardiograms were obtained using GE MAC 600 (GE Healthcare) machine and were read by a physician and classified into major and minor ECG abnormalities [89].
Ankle-Brachial Index (ABI)	• ABI is the ratio of ankle to brachial systolic blood pressure and is <0.9 when there is obstruction to blood flow from atherosclerosis. ABI is a sensitive and specific measure of lower extremity peripheral artery disease. A handheld 8-megahertz Doppler probe with built-in speaker, and an OMRON 705 automatic BP machine was used to measure ankle and brachial blood pressure [90].

Second clinic visit

Carotid artery ultrasonography	• Carotid artery ultrasonography was used to measure common carotid intima-media thickness and plaque number and size in the left and right common carotid arteries using Terason T3000 ultrasound machine with a 12L5 probe set to 8 MHz frequency [66, 91].
Cognitive function examination [92]	• Translated version of the Hindi Mental State Examination (HMSE), which is a modified version of the Mini Mental State Examination (MMSE). • Word List Learning, Recall, and Delayed Recognition Tests. • Object Naming Test. • Verbal Fluency Test.
Peripheral quantitative computed tomography (pQCT)	• pQCT uses low intensity radiologic beams to measures bone strength, quality and skeletal muscle area and fat infiltration. • The distal radius and distal tibia were scanned using the STRATEC XCT 2000L machine (Stratec Medizintechnik GmbH, Pforzheim, Germany). • The images will be read by a single center using specialized software. Standard protocols were followed [93].
Bilateral fixed flexion knee radiograph	• Knee osteoarthritis is a very common disease in older adults and is poorly captured by questionnaires. • Radiographs of both right and left knees were acquired using the Osteoarthritis Initiative (OAI) protocol. • Articular cartilage thickness measured indirectly by radiographic joint-space width was used to assess osteoarthritis of the knee. • To reduce variability due to image acquisition, the SynaFlexer (CCBR-Synarc, Newark, CA) positioning frame and phantom were used. • The images were read by a clinical radiologist using a Kellgren-Lawrence scale protocol [94, 95].
Monofilament test	• Monofilaments were used to evaluate the presence or absence of normal light touch sensation, an indicator of the state of peripheral nerve function [96].
Dietary questionnaire	• A mix of closed and open- ended questions were used to capture questions on meal pattern, frequency of consumption,

Table 10 continued

	food intake changes over the last one year, as well as trying to identify symptoms associated with food intake.
Health events questionnaire	• Questions on health events since the last study visit.

Table 11: Components of MILES annual follow-up contact

<u>**Measurement**</u>
Questionnaires
General Health and Function
Physical Activity/Sleep
Health events
Anthropometry
Height
Weight
Blood Pressure
Heart Rate
Short Physical Performance Battery
400 Meter Walk
Grip Strength
Medication Inventory
Blood Draw
Fasting Blood Glucose
Hemoglobin

3.5.2 Training and quality control

Training and certification were required for all MILES staff before the start of the study. MILES staff underwent three weeks of training with clinic staff from the Center for Aging and Population Health, University of Pittsburgh. Training included review of examination protocols, practice with data form completion and instruction in standardized interviewing strategies. Certification required documentation of practice sessions with observation by an expert staff member using a step-by-step checklist. Retraining and recertification was conducted periodically and at least every 6 months. Training and certification for carotid ultrasonography were provided by technicians from the Ultrasound Research Lab (URL) at the University of Pittsburgh.

Data quality was assessed through periodic inter- and intra-technician review for carotid ultrasonography, pQCT and knee x-ray. Annual recertification of all MILES staff was required to ensure that they have not deviated from MILES protocol and MOP, and standardization has been maintained. Quality was also ensured by random checks of data at regular intervals. All equipment was calibrated frequently to ensure proper functioning.

3.6 What has it found? Key findings and publications

Table 12: Demographic characteristics of MILES cohort at baseline

Characteristics	Men (n=281)	Women (n=281)
Age (years), median (range)	66 (60-90)	65 (60-92)
Marital status		
Currently married, N (%)	253 (90.4)	109 (38.8)
Widowed, N (%)	26 (9.3)	169 (60.1)
Divorced/separated/abandoned, N (%)	1 (0.3)	3 (1.1)
Schooling (any level), N (%)	132 (47.1)	24 (8.5)
Currently working, N (%)	123 (43.9)	64 (22.8)

Table 13: Health and function measures of MILES cohort at baseline

Characteristics	Men (n=281)	Women (n=281)
Health status (self-reported)		
Good, N (%)	134 (47.9)	118 (42.0)
Fair, N (%)	144 (51.4)	120 (42.7)
Poor, N (%)	2 (0.7)	43 (15.3)
BMI (kg/m^2), mean (range)	21.4 (13.6-33.1)	23.1 (14.3-43.7)
Fallers (in the last 12 months), N (%)	24 (8.6)	47 (16.7)
Diabetes, N (%) (self-reported)	34 (12.14)	43 (15.30)
Diabetes, N (%) (self-reported and/or FBS>125)	45 (16.07)	65 (23.30)
CVD history, N (%) (self-reported)	28 (10.0)	16 (5.7)
Difficulty in walking short distances (self-reported)	88 (31.4)	167 (59.4)
Difficulty in walking long distances (self-reported)	203 (72.5)	222 (79.0)
Gait speed (m/s), median (IQR)	0.74 (0.59-0.85)	0.61 (0.49-0.72)
Grip strength (kg), median (IQR)	19.5 (16.0-23.5)	12.0 (9.5-16.5)
SPPB score, median (IQR)	9 (7-11)	8 (5-9)

BMI = Body Mass Index; FBS = Fasting Blood Sugar; CVD = Cardiovascular Disease; IQR = Inter quartile range; SPPB = Short Physical Performance Battery

In this cohort of rural older Indians, there were important differences in the health profiles between men and women **(Tables 12 and 13)**. At a similar median age, women had worse function and more chronic health conditions compared to men. More than 90% of the men were married, but the majority (>60%) of the women were widowed. Almost half of the men had some level of schooling, whereas only 8.5% of the women had any formal education. Women were slightly heavier with a mean BMI of 23.1 compared to a BMI of 21.4 in men. Women also had a higher prevalence of diabetes and reported more difficulty in walking short and long distances in comparison with men. Further analysis of this rich dataset will help validate these rates by comparison of self-report to objective measures.

3.7 What are the main strengths and weaknesses?

MILES is novel and important in several ways, most notably in its extensive characterization of health, disease, and physical and cognitive function in a population based random sample of older adults from rural India. The data from the study will enable us to analyze many important health issues facing this neglected population. The study incorporates a mix of subjective and objective measures, which will enable us to assess clinical and subclinical disease, and function in this population. The longitudinal data will provide us with incidence and risk factors for morbidity, disability and mortality in older Indians.

State of the art techniques and internationally valid methods were used in MILES to quantify the burden of disease and disability. To our knowledge, 400-meter walk has not been used in studies in India, and the use of carotid intima-media thickness to identify subclinical disease has been very limited. The same is true for peripheral quantitative computerized tomography (pQCT). The addition of the ABI and carotid intima-media thickness (IMT) to make a composite subclinical CVD measure to study the Indian population is novel. Standardized measures used in epidemiological studies worldwide were used in MILES, to enable comparison of these findings from India with other populations in future. To our knowledge, there are no cross-national comparative studies using all these measures in an older Indian population.

There were several limitations in the study. The recruitment for MILES reflected they study goal of recruiting committed individuals who agreed to be followed-up over a period of five years. Therefore, the generalizability of the study was limited in favor of internal validity. Pulmonary function test using spirometry was planned to be included in the study initially, but was not performed due to technical challenges. A food frequency questionnaire was considered but was too time consuming for the study participants at the baseline visit, which was already very long.

Despite the substantial progress in improving our understanding of aging, and age-related disease and disability in the developed world, there is very little known about the disease processes, risk factors and impact of aging and disease on disability and mortality in older Indian population. Yet, the bulk of future disease and disability burden will be in developing countries like India. The scant literature about Indian health comes primarily from urban settings yet 70% of the Indian population is rural [5]. In Asian populations, there are important biological differences in age-related chronic disease with differences in risk factors and potential differences related to genetic factors as well [9]. For example, rates of cardiovascular disease and diabetes in Indians are high, even at lower prevalence of obesity compared to some developed countries. Thus, it is important that each region of the world conduct studies to identify the factors that are unique to that region.

To our knowledge, there are three large cross-national efforts that have emerged in the past 10 years to provide data to address some of the health concerns in older adults. These include a Survey of Health and Retirement in Europe (SHARE), modeled on the English Longitudinal Study of Ageing (ELSA) [97] and the US Health and Retirement study (US HRS) [70]. SHARE is designed to include all 27 members of the EU in 2008. These projects include surveys of health and disability, but focus on socioeconomic factors related to retirement. The INDEPTH project, International Network for the Demographic Evaluation of Populations and their Health, includes 37 sites in 19 countries in Africa, Asia (including India) and Latin American and is designed to provide adult mortality data that is otherwise lacking [71]. The WHO recently launched the Study of Global AGEing and Adult Health (SAGE) in 6 countries, including China, Ghana, India, Mexico, Russia and South Africa. It is modeled on the SHARE project and will also link to INDEPTH [72]. These studies will provide demographic data but are not designed for in depth study of disease prevalence, causes of disability or explore mechanisms.

Another study, the Longitudinal Aging Study in India (LASI), an investigation of the economic, physical and social well-being of India's growing elderly population was started recently, and is a joint effort of the Harvard School of Public Health, the International Institute for Population Sciences and the RAND Corporation [73]. A pilot study was carried out in 2010 and enrolled 1683 subjects, age >45 years from 4 states in India. The long-term goal is to enroll nationally representative sample of 30,000 individuals into a longitudinal survey on aging, health and retirement. The data collection consists of a household survey, household finances, assets, debts and living conditions, with information on demographics, family and social networks, health, health care utilization, work and employment pensions and retirement. The clinical examination in LASI is limited to measurements of blood pressure, blood spot storage, anthropometrics, gait speed, grip strength, balance, lung function and vision [11]. There is no assessment of subclinical disease, e.g. CVD, knee osteoarthritis, or state of the art measures of bone or muscle.

MILES is well positioned to characterize the major contributors to disease and disability with long follow-up. The study will present opportunities for further understanding of disease processes and developing interventions, not only in India, but also in other developing and developed countries. The future plan for MILES is to continue annual visits to capture incident disease and disability in this cohort of rural older Indians.

3.8 Can I get hold of the data? Where can I find out more?

All collected source data are maintained and stored at the study research office, SHARE India. Specific proposals for future collaboration, subject to approval of Indian Council of Medical Research would be welcome. Further information can be found on the research center website: www.sharefoundations.org or through email to P.S. Reddy at reddyps@verizon.net.

4.0 MANUSCRIPT 2: PREVALENCE AND RISK FACTORS OF CARDIOVASCULAR DISEASE IN RURAL OLDER INDIANS: THE MOBILITY AND INDEPENDENT LIVING IN ELDERS STUDY (MILES)

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4.1 Abstract

Background: Cardiovascular disease (CVD) is a major health problem accounting for 30% of deaths globally. Projected increases in the population aged 60+ are greatest in developing countries, including India and will lead to increased CVD burden. Hypertension is the most common risk factor for CVD worldwide. We examined the prevalence of CVD and its relationship with hypertension and other risk factors in a cohort of rural Indians from the Mobility and Independent Living in Elders Study (MILES).

Methods: MILES is an observational cohort study, which enrolled 562 community dwelling men (N=281) and women (N=281), aged 60+ in Andhra Pradesh, India. CVD was defined as a composite of self-reported history of CVD, major ECG abnormality or peripheral artery disease. Logistic regression was used to analyze the association between CVD and risk factors in cross-sectional analyses.

Results: Prevalence of CVD was 24.6% in men and 25.6% in women. In multivariate analyses among men, each standard deviation increase in BMI was associated with 56% increase in the odds of CVD prevalence. Hypertension was associated with more than two-fold and physical inactivity with more than four-fold higher prevalence of CVD in men. Among women, chewing tobacco was associated with almost a three-fold and hypertension and physical inactivity with at least two-fold higher prevalence of CVD. Current alcohol use was associated with 55% lower odds for prevalent CVD. Two hundred and eighty two participants were hypertensive, but only 161 individuals were on treatment and 77 individuals of the treated still had uncontrolled hypertension.

Conclusion: The prevalence of CVD and several key risk factors is substantial among this cohort of older rural Indians. A high proportion of women have hypertension, use chewing tobacco and are physically inactive, and all these factors are independently associated with higher prevalence of CVD. There is low awareness of hypertension and poor treatment optimization in this cohort. These data indicate urgent need for primary prevention measures and increasing availability of treatment to prevent further complications.

4.2 Introduction

Cardiovascular disease (CVD) is a major global health problem and is estimated to account for about one-third of all deaths [98, 99]. According to the World Health Organization (WHO) statistics from 2005, of the 58 million deaths from all causes, there were 17.5 million CVD deaths worldwide. This is three times the number of deaths caused by major infectious diseases, including tuberculosis, HIV/AIDS, and malaria combined [100]. The WHO estimates that by the year 2030, cardiovascular mortality will increase to 23.4 million and chronic disease will account for more than three-fourths of all deaths. This will be an increase of almost 37% compared to rates from 2004 [98]. More specifically, by the year 2030, the leading causes of death globally are predicted to be ischemic heart disease and stroke [98, 99].

Research has shown that CVD has is not confined only to the developed world, but is the leading cause of mortality in developing countries as well. About 80% of cardiovascular deaths occur in developing countries [100]. Similarly, deaths from cerebrovascular events were 5 times higher in developing, compared to developed countries [101]. With a rise of global older population, the burden of chronic disease, including CVD is predicted to increase. The most rapid increases in the older population are in the developing world [1]. This change towards an aging society is unprecedented and will result in even more chronic disease.

India is the second most populous country in the world with 1.21 billion people in its 2011 census [5]. In 2011, the 60+ population accounted for 8% of India's population (93 million people). According to estimates, by the year 2050, the 60+ population will climb and account for 19% (323 million people) of the population [3]. As a result of this demographic shift, India is expected to face a higher burden of chronic disease and disability than any other country in the world over the next few decades. Estimates from the WHO report on global burden of disease showed age-standardized CVD mortality among older adults aged 60 years and above to be 1,978 per 100,000 persons in India, compared to 800 per 100,000 in the United States [102]. With rapidly changing lifestyle and dietary habits of Indians leading to increase in cardiovascular risk factors, these numbers are predicted to rise further in the near future [103, 104].

Several techniques have been developed for the early detection of arterial damage that have provided important insights into patterns and pathogenesis of cardiovascular disease and possible subsequent disability. Ankle-brachial index (ABI) is a very convenient and non-invasive method to detect peripheral artery disease (PAD) [105]. Electrocardiogram (ECG) provides information on several major and minor abnormalities with the heart. These non-invasive examinations can provide a very sensitive and specific estimate of the presence of subclinical CVD [65].

Several research studies have been conducted in the Indian population to determine the prevalence and risk factors for CVD. However, the vulnerable older population has been neglected in most of these studies. Even though as many as two-thirds of elderly persons in India live in rural areas, the research efforts do not represent this population group [106, 107].

The first aim of this report was to estimate the prevalence of CVD in rural older Indians from the Mobility and Independent Living in Elders Study (MILES), using the self-reported history of CVD, major ECG abnormality, PAD and a combined measure of all three measures. The second aim was to examine the relationship of CVD with traditional risk factors. We hypothesized that traditional CVD risk factors would be associated with prevalent disease, independent of potential confounders.

4.3 Methods

4.3.1 Population

The Mobility and Independent Living in Elders Study (MILES) enrolled 562 individuals aged 60 years or above from Medchal Mandal in Andhra Pradesh state, India. Equal number of men and women were randomly selected after conducting door-to-door recruitment in 10 villages from February 2012 to November 2012 to be a part of the study. Age was determined by the self-report from the Rural Effective Affordable Health Care (REACH) 2011 census. Eligibility was determined on participants' ability to give informed consent (functional vision, hearing and cognitive function), physical ability to travel to the study clinic in a hospital vehicle, no plan to move from the area over the next 5 years and no end-stage diseases, such as terminal cancer. Eligible participants were scheduled for a clinic visit where a written informed consent was obtained and comprehensive interview and clinical examination were conducted. A detailed description of the study has been published elsewhere (REF – MILES study design paper – Manuscript #1).

4.3.2 Cardiovascular disease

History of cardiovascular disease was defined as a self-report of a health professional's diagnosis of myocardial infarction or stroke, or a history of angiography or coronary artery bypass graft.

Standard 12-lead resting electrocardiograms were obtained using GE MAC 600 (GE Healthcare) machine and were read by a physician and classified into major and minor ECG abnormalities [89]. Major ECG abnormality was defined to include major Q or QS abnormalities, left ventricular hypertension (LVH), isolated major ST-T wave abnormality, atrial fibrillation, first degree atrioventricular block, left bundle branch block (LBBB), right bindle branch block (RBBB) and intraventricular block of indeterminate type.

Ankle brachial index (ABI) is the ratio of ankle to brachial systolic blood pressure and is <0.9 when there is obstruction to blood flow from atherosclerosis. ABI is a sensitive and specific measure of lower extremity peripheral artery disease. A handheld 8-megahertz Doppler probe with built-in speaker, and an OMRON 705 automatic BP machine was used to measure ankle and brachial blood pressure [90]. Peripheral artery disease was defined as an ABI of <0.9 or inability to find pulse in the lower extremities.

Combined cardiovascular disease was defined as a composite of self-reported history of CVD, major ECG abnormality or PAD.

4.3.3 Measurement of risk factors

Age, male sex, body mass index (BMI), smoking, chewing tobacco, alcohol, total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, diabetes, hypertension and physical inactivity were considered as traditional risk factors.

Seca 214 Stadiometer (Seca, Hanover, MD) was used to measure height in centimeters (cm) to the nearest millimeter; Seca 813 Digital Scale (Seca, Hanover, MD) was used to measure weight in kilograms (kg); and Gulick II tape measure was used to measure the waist circumference in centimeters. Body mass index (BMI), calculated as $kg/meter^2$ and waist circumference were examined as continuous variables in the analyses.

Smoking was classified as current, past, or never. Current use of any type of chewing tobacco and alcohol was recorded.

Participants were asked to fast overnight or for at least 10 hours before the clinic visit. This was confirmed by collecting information for the time of last meal at the time of the clinic visit. Blood was obtained from fasting participants to measure blood sugar, lipids and complete blood count.

Participants were asked to bring all prescription and non-prescription medications they had taken in the last 14 days. Dosage, frequency and duration were recorded and medications were categorized into classes.

Diabetes was defined as self-report of a health professional's diagnosis, use of antidiabetic medication or a fasting blood glucose level greater than or equal to 126 mg/dL.

Resting blood pressure was measured thrice in seated participants after an initial resting period of 5 minutes using an Omron 705 automatic BP machine (Omron Healthcare, Inc., Lake Forest, IL). Average of all three measurements was taken for analysis. Hypertension was defined as a self-report of a health professional's diagnosis confirmed by the use of anti-hypertensive medication or by the measured blood pressure categorized according to the JNC 7 criteria [88].

Physical inactivity was defined as a self-report of not walking 10 minutes or more continuously every day.

4.3.4 Measurement of potential confounders

Caste, religion, marital status, and schooling or reading ability were examined as potential confounders. Number of years of schooling was determined by self-report and reading ability was assessed in individuals with 1-5 years of schooling. Information about caste, marital status, religion and current working status were collected from the participants.

4.3.5 Statistical analyses

Descriptive analyses were conducted for all variables to assess proportions, means, standard deviations, normality, etc. Participant characteristics were compared for men and women using chi-square tests for categorical variables and t-tests for continuous variables.

Prevalence of cardiovascular disease was calculated in the overall sample and in men and women separately. Characteristics were compared for individuals with and without cardiovascular disease. Bivariate associations between cardiovascular disease and risk factors, including potential confounders were examined. Continuous variables were analyzed using standard deviation as a unit. Variables that were significant ($p<0.25$) in the bivariate analyses were included in the multivariate logistic regression model in stepwise logistic regression, along with variables that were determined a priori to be important based on previously published literature. The final multivariate model included significant ($p<0.05$) and a priori determined variables. All analyses were conducted for the total sample and men and women separately. Data were analyzed using Stata 12.

4.4 Results

4.4.1 Population characteristics

Descriptive characteristics for the total sample are shown in **Table 14**. A total of 562 individuals (281 men and women each) completed the baseline clinic visit in the study. The median age in men was 66 years (range 60-90) and in women 65 years (range 60-92). More than 90% of the individuals were Hindu and a small number were Muslims and Christians. More than 90% of the men were currently married; however, less than half of the women were married. Men and women both had very low level of education with 91.5% of the women having had no schooling and only 26.5% of men having either more than or equal to 6 years of schooling or reading ability. Most women and men were not currently working. Women were mostly non-smokers, but more than half used chewing tobacco; however, nearly half the men were current smokers and one-third were past smokers. More than half the women, but only 6% of the men used chewing tobacco. A majority of the men and women were current alcohol drinkers. The median BMI was low in both men (21.2 kg/m^2) and women (22.5 kg/m^2). Even though not significantly different, diabetes was more prevalent in women (23.3%) than men (17.9%). More women (43.8%) than men (26.4%) were not physically active. About half of both men and women were hypertensive.

4.4.2 Cardiovascular disease

Table 15 shows the prevalence of cardiovascular disease in men and women. About a quarter of both men and women had prevalent cardiovascular disease. Self-reported history of CVD was 10% in men and 5.7% in women. Equal proportion of men and women (15.7% each) had major ECG abnormality, even though the prevalence of abnormality subcategories was different. More than one-third of total ECG abnormalities in men were major Q/QS changes and about one-fourth were due to major ST-T wave abnormality. Among women, major ST-T wave changes contributed to almost half of the total ECG abnormalities, and about a quarter were because of left ventricular hypertrophy. The prevalence of PAD was 6.1% in men and 7.1% in women.

Tables 16, 17 and 18 compare the characteristics of the total sample, men and women with respect to prevalent cardiovascular disease. Among men, BMI and systolic blood pressure (SBP) were significantly higher in individuals with prevalent CVD compared to the individuals without CVD. The proportion of hypertensive, diabetic and physically inactive men were also higher in the group with prevalent CVD. Women with prevalent CVD were more likely to have higher SBP, chewed tobacco and were hypertensive and physically inactive compared to the group without prevalent CVD.

4.4.3 Bivariate and multivariate analyses

Tables 19, 20 and 21 show the results of bivariate logistic regression analyses between prevalent CVD and other variables in the total sample, men and women respectively. Among men, higher BMI, greater waist circumference, not currently working, diabetes, greater number of depressive symptoms, physical inactivity and hypertension were associated with higher prevalence of CVD in bivariate analyses. In women, chewing tobacco, not being physically active and being hypertensive were associated with higher prevalence of CVD.

Multivariate logistic regression analyses were conducted to ascertain the strength of relationship between prevalent CVD and risk factors after adjustments for potential confounders. The final multivariate models for the total sample, men and women are shown in **tables 22, 23 and 24**. In men, each standard deviation increase in BMI was associated with 56% increase in the odds of CVD prevalence. Hypertension was associated with more than two-fold and physical inactivity with more than four-fold higher prevalence of CVD in men. Among women, chewing tobacco was associated with almost a three-fold and hypertension and physical inactivity with at least two-fold higher prevalence of CVD. Current alcohol use was associated with 55% lower odds for prevalent CVD in women. Age, smoking, and lipids were not associated with prevalent CVD in bivariate and multivariate analyses for either men or women.

4.4.4 Hypertension medication use and management

Given a strong association of hypertension with prevalent cardiovascular disease, separate analyses were conducted exploring the management of hypertension among individuals on antihypertensive medication. Two hundred and eighty two participants were hypertensive, but only 161 individuals were on treatment and 77 individuals of the treated still had uncontrolled hypertension **(Figure 15**). According to the blood pressure measured in MILES clinic, 218 (38.8%) individuals in the full cohort either had stage 1 (SBP: 140-159 or DBP: 90-99) or stage 2 (SBP>=160 or DBP>=100) hypertension.

4.5 Discussion

In this study of rural older Indians, a quarter of the participants were found to have prevalent cardiovascular disease and the prevalence was similar in men and women. Self-reported prevalence of CVD history was 10% in men and 5.7% in women. These estimates are similar to other studies in India, where the self-reported prevalence varies from 2.7% to 15.7% in different studies, settings and age groups [108].

Most major studies have shown men to have higher prevalence of CVD compared to women [109-111]. The similar rate of disease in men and women in this study might represent a survival advantage for women, with men more likely to have died from coronary heart disease. This possibility is supported by observing a much higher proportion of widowed women (60%) compared to men (9%) in the sample. The high prevalence of CVD in women can also be due to a two-fold higher rate of non-specific ST-T wave abnormality in women compared to men. Similar results have been shown in other major studies in older adults [89], but are not fully explained. Previous studies have shown ST-T wave abnormalities to be associated with higher risk for future coronary heart disease and mortality in both men and women [112, 113]. Men reported higher rates of CVD events in the past and this might explain the higher prevalence of Q/QS abnormality in men. These changes may also reflect higher prevalence of unrecognized heart disease in men or failure to seek medical care in presence of symptoms.

In this study, the prevalence of peripheral artery disease was 6.1% in men and 7.1% in women. These estimates are slightly lower than estimates from other studies in low-and middle-income countries, which show a prevalence of 5.5-21.5% in men and 8.9-18.7% in women aged 60-99 years [114]. Studies have shown association of subclinical PAD with mobility impairment and lower physical function in elderly [67, 68, 115]. Timely detection of subclinical disease may allow for early treatment opportunities leading to improved survival and mobility, lower disability and better quality of life in older population.

Age was not associated with CVD in this study. Smoking is an established risk factor for CVD. However, in these analyses smoking was not associated with CVD. A majority of the women were using chewing tobacco and its use was associated with higher prevalence of CVD. Previous studies have shown similar associations of the use of smokeless tobacco with cardiovascular morbidity and mortality [116].

In this study, almost half of the participants were hypertensive. This is consistent with other studies of hypertension in India [117]. The relationship of hypertension with future cardiovascular disease and mortality has been established in studies all over the world previously. However, this study showed a low awareness of hypertension, with about half of the hypertensive individuals on medication. Furthermore, of these, only half had their hypertension under control. These numbers are better than the proportion of treated or controlled hypertensive individuals from several low- and middle-income countries, but not as good as some developed countries [118].

Physical inactivity, another established risk factor for CVD, was associated with higher prevalence of CVD in this population. To our knowledge, there are no published studies analyzing the relationship between physical activity and CVD in older adults in India. Physical activity is an important modifiable risk factor for CVD [119] and more effort is needed to increase awareness about regular physical activity in this population.

Cardiovascular disease is the leading cause of mortality in the Indian population. Cardiovascular mortality has declined in most developed countries in the last few years [120]. However, with an increase in life expectancy and higher number of older adults, the cardiovascular mortality has increased in several Asian countries, including India [120]. Most of the global decline in cardiovascular mortality can be attributed improved treatment and management and reduction of risk factors, including hypertension, smoking, and cholesterol [120].

This study has several strengths. Older Indian rural population has a high burden of cardiovascular morbidity and mortality, but there is very limited research conducted in this neglected population. Most studies conducted to estimate the prevalence of CVD in this population have used self-report as a measure of prevalent disease. Self-reports of diagnosed medical conditions depend on health awareness and access to health care, and therefore, can conceal undiagnosed conditions [11, 73, 121]. In developing countries like India where access to health care is limited, particularly in rural areas, the prevalence of undiagnosed diseases is expected to be higher compared to urban areas or developed countries. The addition of objectively measured PAD and ECG to estimate the prevalence of CVD is novel in this population and enabled us to have a better estimate of disease. The addition and use of objective measures enabled us to eliminate self-report biases that may be differentially associated with health awareness or health care access. These objective measures provide additional insights into true disease prevalence as well as the extent of undiagnosed and subclinical disease in this population.

There are a few limitations of the study. The data analyzed in this effort are cross-sectional and causal relationships cannot be inferred. This can be particularly true for the relationship between low physical activity and CVD where low activity may be a consequence of disease.

In this study, there is a clear relationship of some of the well-known risk factors for CVD with prevalent disease. With growing prevalence of CVD in India, there is an urgent need to understand the burden of clinical as well as subclinical disease and risk factors using studies conducted in India. Risk factor modification may not only prevent cardiovascular events and mortality, but also can have an impact on reduction and delay in disability and improve quality of life in older adults. Strong public health policies are required to not only restrict use of smoking, but also chewing tobacco. Physical activity needs to be promoted, particularly among older adults. Improved access to health care, and inexpensive but effective medication, is required to combat disease and risk factors, including hypertension. Better optimization of treatment is needed for management of diagnosed disease. Good incidence data is needed to have better understanding of disease processes in this population, particularly in women.

4.6 CVD tables and figure

Table 14: Descriptive characteristics of all MILES participants at baseline

Characteristics	Men (N=281)	Women (N=281)	p-value
Age (years), median (range)	66 (60-90)	65 (60-92)	0.163
Marital status			**<0.001**
Currently married, N (%)	**253 (90.4)**	**109 (38.8)**	
Widowed, N (%)	**26 (9.3)**	**169 (60.1)**	
Divorced/separated/abandoned, N (%)	**1 (0.3)**	**3 (1.1)**	
Religion			0.514
Hindu, N (%)	258 (92.1)	253 (90.0)	
Muslim, N (%)	11 (3.9)	17 (6.1)	
Christian, N (%)	11 (3.9)	11 (3.9)	
Caste			0.598
Scheduled caste, N (%)	37 (13.2)	48 (17.1)	
Scheduled tribe, N (%)	17 (6.1)	16 (5.7)	
Backward caste, N (%)	157 (56.1)	146 (52.0)	
Other, N (%)	69 (24.6)	71 (25.3)	
Schooling and reading ability, N (%)			**<0.001**
No schooling, N (%)	**148 (53.1)**	**257 (91.5)**	
<6 years of schooling and not able to read, N (%)	**57 (20.4)**	**11 (3.9)**	
>=6 years of schooling or able to read	**74 (26.5)**	**13 (4.6)**	
Currently not working, N (%)	**157 (56.1)**	**217 (77.2)**	**<0.001**
Health status (self-reported)			0.163
Good, N (%)	134 (47.9)	118 (42.0)	
Fair, N (%)	144 (51.4)	120 (42.7)	
Poor, N (%)	2 (0.7)	43 (15.3)	
Weight (kg), median (range)	**54.7 (28.9-92.2)**	**49.4 (28.3-108.7)**	**<0.001**
Height (cm), median (range)	**161.2 (141.3-177.7)**	**147.4 (128.0-162.9)**	**<0.001**
BMI (kg/m^2), median (range)	**21.2 (13.6-33.1)**	**22.5 (14.3-43.7)**	**<0.001**
Waist circumference (cm), median (range)	**83.0 (52.9-112.3)**	**78.8 (54.7-132.6)**	**0.004**

Table 14 continued

Smoking			**<0.001**
Current, N (%)	**121 (43.1)**	**1 (0.4)**	
Past, N (%)	**91 (32.4)**	**6 (2.1)**	
Never, N (%)	**69 (24.6)**	**274 (97.5)**	
Chewing tobacco, N (%)	**17 (6.1)**	**145 (51.6)**	**<0.001**
Alcohol, N (%)	**199 (71.1)**	**161 (57.3)**	**0.001**
Fasting blood sugar (FBS) (mg/dL), median (IQR)	95 (84-112)	100 (87-116)	0.047
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	50 (17.9)	65 (23.30)	0.112
Hemoglobin (g/dL), median (IQR)	**13.9 (12.4-15.1)**	**12.4 (11.5-13.1)**	**<0.001**
Total cholesterol (mg/dL), median (IQR)	**171.0 (144.5-199.0)**	**195.0 (168.0-224.0)**	**<0.001**
LDL cholesterol (mg/dL), median (IQR)	**100.0 (77.0-126.0)**	**117.5 (96.0-145.0)**	**<0.001**
HDL cholesterol (mg/dL), median (IQR)	**45.5 (38.0-54.5)**	**46.0 (40.0-56.0)**	**0.026**
Systolic blood pressure (SBP) mmHg, median (IQR)	133.7 (118.0-153.0)	130.0 (115.0-145.3)	0.021
Diastolic blood pressure (DBP) mmHg, median (IQR)	72.0 (64.7-80.3)	72.3 (65.7-79.7)	0.834
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	137 (48.8)	143 (50.9)	0.613
Physically inactive (not walking 10 minutes continuously every day), N (%)	**74 (26.43)**	**123 (43.77)**	**<0.001**

Table 15: Prevalence of cardiovascular disease in men and women at baseline

	Men (N=281)	Women (N=281)	p-value
CVD history (self-reported), N (%)	**28 (10.0)**	**16 (5.7)**	**0.058**
Peripheral artery disease, N (%)	**17 (6.1)**	**20 (7.1)**	**0.626**
ECG abnormality, N (%)	**44 (15.7)**	**44 (15.7)**	**1.000**
Major Q/QS abnormality, N (%)	15 (5.3)	5 (1.8)	0.023
LVH, N (%)	5 (1.8)	10 (3.6)	0.191
Major ST-T wave abnormality, N (%)	10 (3.6)	20 (7.1)	0.061
Atrial fibrillation, N (%)	2 (0.7)	1 (0.4)	0.563
First degree AV block, N (%)	5 (1.8)	3 (1.1)	0.476
LBBB, N (%)	2 (0.7)	2 (0.7)	1.000
RBBB, N (%)	9 (3.2)	1 (0.4)	0.011
Intraventricular block (indeterminate), N (%)	1 (0.4)	2 (0.7)	0.563
Combined cardiovascular disease, N (%)	**69 (24.6)**	**72 (25.6)**	**0.770**

Table 16: Characteristics of all MILES participants by combined cardiovascular disease

Characteristics	With combined CVD (N=141)	Without combined CVD (N=421)	p-value
Age (years), mean (SD)	68.4 (6.8)	67.3 (6.3)	0.076
Male sex, N (%)	69 (48.9)	212 (50.4)	0.770
Not currently married, N (%)	47 (33.6)	152 (36.1)	0.587
Schooling and reading ability, N (%)			0.940
No schooling, N (%)	100 (71.9)	305 (72.5)	
<6 years of schooling and not able to read, N (%)	18 (12.6)	50 (11.9)	
>=6 years of schooling or able to read	21 (15.1)	66 (15.7)	
BMI (kg/m^2), mean (SD)	22.7 (4.7)	22.1 (4.5)	0.210
Smoking			0.521
Never, N (%)	86 (61.0)	257 (61.1)	
Past, N (%)	28 (19.9)	69 (16.4)	
Current, N (%)	27 (19.2)	95 (22.6)	
Chewing tobacco	**53 (37.9)**	**109 (25.9)**	**0.007**
Alcohol	**80 (57.1)**	**280 (66.5)**	**0.045**
Total cholesterol (mg/dL), mean (SD)	189.0 (48.4)	184.8 (43.2)	0.334
LDL cholesterol (mg/dL), mean (SD)	112.9 (36.3)	114.2 (49.3)	0.785
HDL cholesterol (mg/dL), mean (SD)	49.0 (14.4)	47.5 (12.1)	0.205
Systolic blood pressure (SBP), mean (SD)	**141.7 (24.8)**	**132.0 (23.0)**	**<0.001**
Diastolic blood pressure (DBP), mean (SD)	74.2 (11.2)	72.6 (11.9)	0.153
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	**91 (64.5)**	**191 (45.4)**	**<0.001**
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	36 (25.7)	79 (18.9)	0.082
Physically inactive (not walking 10 minutes continuously every day), N (%)	**76 (54.3)**	**121 (28.7)**	**<0.001**

Table 17: Characteristics of men by combined cardiovascular disease

Characteristics	With combined CVD (N=69)	Without combined CVD (N=212)	p-value
Age (years), mean (SD)	68.7 (7.3)	67.7 (6.4)	0.276
Not currently married, N (%)	4 (5.9)	23 (10.9)	0.227
Schooling and reading ability, N (%)			0.439
No schooling, N (%)	31 (46.3)	117 (55.2)	
<6 years of schooling and not able to read, N (%)	16 (23.9)	41 (19.3)	
>=6 years of schooling or able to read	20 (29.9)	54 (25.5)	
BMI (kg/m^2), mean (SD)	**22.6 (4.0)**	**21.0 (3.8)**	**0.004**
Smoking			0.552
Never, N (%)	16 (23.2)	53 (25.0)	
Past, N (%)	26 (37.7)	65 (30.7)	
Current, N (%)	27 (39.1)	94 (44.3)	
Alcohol	45 (66.2)	154 (72.6)	0.306
Total cholesterol (mg/dL), mean (SD)	176.3 (40.0)	172.3 (38.4)	0.461
LDL cholesterol (mg/dL), mean (SD)	106.0 (36.2)	105.8 (55.6)	0.985
HDL cholesterol (mg/dL), mean (SD)	47.6 (13.4)	46.3 (11.8)	0.446
Systolic blood pressure (SBP) mmHg, median (IQR)	**146.0 (26.1)**	**133.8 (23.6)**	**<0.001**
Diastolic blood pressure (DBP) mmHg, median (IQR)	74.6 (12.1)	72.6 (12.4)	0.253
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	**47 (68.1)**	**97 (45.8)**	**0.001**
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	**18 (26.5)**	**32 (15.1)**	**0.033**
Physically inactive (not walking 10 minutes continuously every day), N (%)	**34 (50.0)**	**40 (18.9)**	**<0.001**

Table 18: Characteristics of women by combined cardiovascular disease

Characteristics	With combined CVD (N=72)	Without combined CVD (N=209)	p-value
Age (years), mean (SD)	68.1 (6.2)	66.9 (6.2)	0.146
Not currently married, N (%)	43 (59.7)	129 (61.7)	0.764
BMI (kg/m^2), mean (SD)	22.8 (5.2)	23.3 (4.8)	0.455
Chewing tobacco	**47 (65.3)**	**98 (46.9)**	**0.007**
Alcohol	35 (48.6)	126 (60.3)	0.084
Total cholesterol (mg/dL), mean (SD)	201.1 (52.7)	197.7 (44.2)	0.591
LDL cholesterol (mg/dL), mean (SD)	119.4 (35.3)	122.7 (40.2)	0.531
HDL cholesterol (mg/dL), mean (SD)	50.3 (15.2)	48.6 (12.4)	0.333
Systolic blood pressure (SBP) mmHg, median (IQR)	**137.6 (22.8)**	**130.3 (22.3)**	**0.018**
Diastolic blood pressure (DBP) mmHg, median (IQR)	73.9 (10.4)	72.6 (11.5)	0.384
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	**44 (61.1)**	**94 (45.0)**	**0.018**
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	18 (25.0)	47 (22.7)	0.692
Physically inactive (not walking 10 minutes continuously every day), N (%)	**42 (58.3)**	**81 (38.8)**	**0.004**

Table 19: Bivariate logistic regression analyses of combined CVD with the total sample

	Odds Ratio	95% confidence interval	p-value
Age	1.03	1.00–1.06	0.077
Male sex	0.94	0.65–1.38	0.770
Caste			
Others	1.00 (ref)	1.00 (ref)	1.00 (ref)
Backward caste	0.75	0.47–1.18	0.217
Scheduled caste/Scheduled tribe	1.01	0.58–1.74	0.984
Not currently married	0.89	0.60–1.34	0.587
Schooling and reading ability			
No schooling	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 years of school & inability to read	1.10	0.61–1.97	0.754
>=6 years of school or able to read	0.97	0.57–1.67	0.913
BMI (per SD)	1.13	0.93–1.36	0.211
Waist circumference (per SD)	1.15	0.95–1.39	0.151
Smoking			
Never smoked	1.00 (ref)	1.00 (ref)	1.00 (ref)
Past smoking	1.21	0.73–2.00	0.452
Current smoking	0.85	0.52–1.39	0.516
Chewing tobacco	**1.74**	**1.16–2.61**	**0.007**
Alcohol	**0.67**	**0.45–0.99**	**0.046**
Not working	**1.78**	**1.15–2.75**	**0.009**
Total cholesterol (per SD)	1.10	0.91–1.33	0.333
LDL cholesterol (per SD)	0.97	0.80–1.18	0.784
HDL cholesterol (per SD)	1.13	0.94–1.36	0.206
Hypertension (BP>=140/90 and/or self-reported AND medication use)	**2.19**	**1.48–3.25**	**<0.001**
Diabetes	1.49	0.95–2.34	0.083
Not physically active (not walking 10 minutes continuously every day)	**2.94**	**1.99–4.37**	**<0.001**

Table 20: Bivariate logistic regression analyses of combined CVD for men

	Odds Ratio	95% confidence interval	p-value
Age	1.02	0.98–1.06	0.276
Caste			
Others	1.00 (ref)	1.00 (ref)	1.00 (ref)
Backward caste	0.75	0.39–1.44	0.395
Scheduled caste/Scheduled tribe	0.92	0.41–2.06	0.841
Not currently married	0.51	0.17–1.54	0.235
Schooling and reading ability			
No schooling	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 years of school & inability to read	1.47	0.73–2.97	0.279
>=6 years of school or able to read	1.40	0.73–2.67	0.311
BMI (per SD)	**1.59**	**1.16–2.19**	**0.004**
Waist circumference (per SD)	**1.58**	**1.16–2.14**	**0.003**
Smoking			
Never smoked	1.00 (ref)	1.00 (ref)	1.00 (ref)
Past smoking	1.33	0.64–2.72	0.444
Current smoking	0.95	0.47–1.92	0.890
Chewing tobacco	1.77	0.63–4.98	0.280
Alcohol	0.74	0.41–1.32	0.307
Not working	**2.08**	**1.16–3.71**	**0.014**
Total cholesterol (per SD)	1.13	0.82–1.54	0.460
LDL cholesterol (per SD)	1.00	0.78–1.28	0.985
HDL cholesterol (per SD)	1.11	0.84–1.48	0.445
Hypertension (BP>=140/90 and/or self-reported AND medication use)	**2.53**	**1.43–4.50**	**0.002**
Diabetes	**2.03**	**1.05–3.91**	**0.035**
Not physically active (not walking 10 minutes continuously every day)	**4.30**	**2.39–7.73**	**<0.001**

Table 21: Bivariate logistic regression analyses of combined CVD for women

	Odds Ratio	95% confidence interval	p-value
Age	1.03	0.99–1.08	0.147
Caste			
Others	1.00 (ref)	1.00 (ref)	1.00 (ref)
Backward caste	0.74	0.39–1.42	0.371
Scheduled caste/Scheduled tribe	1.08	0.51–2.27	0.846
Not currently married	0.92	0.53–1.59	0.764
Schooling and reading ability			
No schooling	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 years of school & inability to read	0.61	0.13–2.87	0.528
>=6 years of school or able to read	0.23	0.03–1.78	0.158
BMI (per SD)	0.91	0.70–1.17	0.454
Waist circumference (per SD)	0.92	0.71–1.19	0.538
Chewing tobacco	**2.13**	**1.22–3.71**	**0.008**
Alcohol	0.62	0.36–1.07	0.085
Not working	1.46	0.74–2.89	0.270
Total cholesterol (per SD)	1.07	0.83–1.38	0.590
LDL cholesterol (per SD)	0.90	0.65–1.24	0.530
HDL cholesterol (per SD)	1.13	0.88–1.46	0.332
Hypertension (BP>=140/90 and/or self-reported AND medication use)	**1.92**	**1.11–3.32**	**0.019**
Diabetes	1.13	0.61–2.12	0.692
Not physically active (not walking 10 minutes continuously every day)	**2.21**	**1.28–3.82**	**0.004**

Table 22: Multivariate logistic regression analyses of combined CVD with the total sample

	Odds Ratio	95% confidence interval	p-value
Age	1.02	0.98–1.05	0.311
Male sex	1.63	0.81–3.30	0.172
BMI (per SD)	1.07	0.85–1.34	0.579
Smoking			
Never smoked	1.00 (ref)	1.00 (ref)	1.00 (ref)
Past smoking	1.18	0.58–2.40	0.647
Current smoking	1.04	0.49–2.20	0.912
Chewing tobacco	**2.19**	**1.28–3.75**	**0.004**
Alcohol	**0.63**	**0.41–0.97**	**0.036**
Total cholesterol (per SD)	1.39	0.86–2.25	0.179
LDL cholesterol (per SD)	0.66	0.38–1.16	0.148
HDL cholesterol (per SD)	1.03	0.81–1.32	0.797
Diabetes	1.38	0.82–2.34	0.225
Hypertension (BP>=140/90 and/or self-reported AND medication use)	**2.06**	**1.34–3.15**	**0.001**
Physically inactive (not walking 10 minutes continuously every day)	**2.78**	**1.83–4.23**	**<0.001**

Table 23: Multivariate logistic regression analyses of combined CVD for men

	Odds Ratio	95% confidence interval	p-value
Age	1.03	0.98–1.08	0.249
BMI (per SD)	**1.56**	**1.06–2.30**	**0.024**
Smoking			
Never smoked	1.00 (ref)	1.00 (ref)	1.00 (ref)
Past smoking	1.38	0.60–3.16	0.450
Current smoking	1.25	0.54–2.90	0.609
Chewing tobacco	1.65	0.48–5.71	0.431
Alcohol	0.94	0.47–1.86	0.855
Total cholesterol (per SD)	0.86	0.52–1.41	0.551
LDL cholesterol (per SD)	1.06	0.71–1.57	0.783
HDL cholesterol (per SD)	1.10	0.79–1.52	0.576
Diabetes	1.66	0.74–3.70	0.216
Hypertension (BP>=140/90 and/or self-reported AND medication use)	**2.09**	**1.11–3.93**	**0.023**
Physically inactive (not walking 10 minutes continuously every day)	**4.03**	**2.14–7.60**	**<0.001**

Table 24: Multivariate logistic regression analyses of combined CVD for women

Variable	Odds Ratio	95% confidence interval	p-value
Age	1.01	0.96–1.06	0.749
BMI (per SD)	0.91	0.67–1.25	0.570
Chewing tobacco	**2.71**	**1.40–5.23**	**0.003**
Alcohol	**0.45**	**0.24–0.82**	**0.010**
Total cholesterol (per SD)	**1.94**	**1.03–3.67**	**0.040**
LDL cholesterol (per SD)	**0.44**	**0.21–0.94**	**0.033**
HDL cholesterol (per SD)	0.98	0.71–1.36	0.920
Diabetes	1.34	0.64–2.79	0.442
Hypertension (BP>=140/90 and/or self-reported AND medication use)	**2.03**	**1.12–3.70**	**0.020**
Physically inactive (not walking 10 minutes continuously every day)	**2.05**	**1.15–3.65**	**0.015**

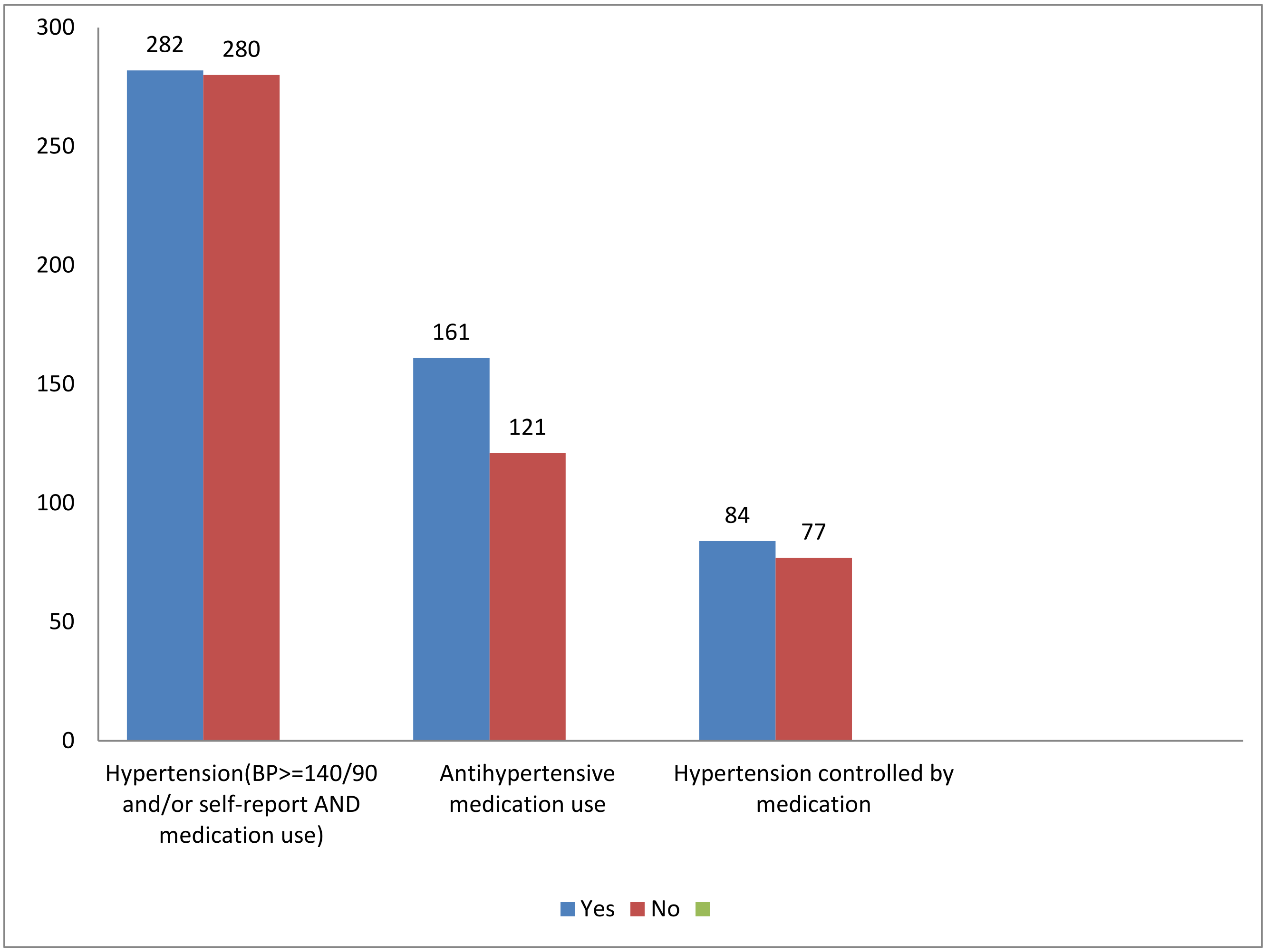

Figure 15: Number of individuals with hypertension, using antihypertensive medication and with controlled hypertension

5.0 MANUSCRIPT 3: PREVALENCE AND RISK FACTORS FOR MOBILITY DISABILITY IN RURAL OLDER INDIANS: MOBILITY AND INDEPENDENT LIVING IN ELDERS STUDY

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5.1 Abstract

Background and Objective: Older population is predicted to increase globally and this increase is most rapid in developing countries. Mobility disability is a serious health problem encountered in the elderly, causing loss of independence and higher rates of morbidity and mortality. However, there is insufficient research from developing countries determining the prevalence of objectively measured mobility disability. The purpose of this study was to estimate the prevalence and risk factors for mobility disability in a rural Indian population aged >=60 years from the Mobility and Independent Living in Elders Study (MILES).

Methods: MILES is an observational cohort study, which enrolled 562 community dwelling men (N=281) and women (N=281), aged >=60 years in rural India. Mobility disability was defined as inability to attempt or complete a 400-meter usual paced walk. Logistic regression was used to analyze the association between mobility disability and risk factors in cross-sectional analyses. Additional analyses were conducted for participants who completed the 400-meter walk, to examine the relationship between walk time and risk factors for mobility disability.

Results: Median age of women (65 years) and men (66 years) were similar. Mobility disability prevalence was much higher in women (43.8%) compared to men (27.9%). In men, knee pain, fair vision and chronic lung disease were associated with >3-fold higher mobility disability. Each standard deviation (SD) increase in depressive symptoms was associated with an 81% increase in the odds of mobility disability. Among women, knee pain was associated with almost two-fold, poor or very poor vision with more than three-fold, CVD history with a five-fold and PAD with more than ten-fold higher mobility disability. Each SD increase in waist circumference and depressive symptoms was associated with approximately 60% increased odds of mobility disability. Mean walking times were high in those men (435 seconds) and women (503 seconds) who completed the walk. Higher walking times were associated with higher waist circumference, knee pain and use of a walking aid in both men and women.

Conclusion: In this cohort of community dwelling rural older Indians, the prevalence of mobility disability was high, particularly in women. Poor vision, knee pain and depression were the major risk factors. Potential targets for intervention include earlier diagnosis and better management of chronic disease and depression. Long-term follow-up of this population will provide an opportunity to understand the influence of mobility disability on incident morbidity and mortality.

5.2 Introduction

Almost all nations in the world are now experiencing a growth in the number of older adults, though there is considerable variability. The most rapid increases in the older population are in the developing world [1]. This change towards an aging society is unprecedented and will result in increased disability and disease.

India is the second most populous country in the world with 1.21 billion people in its 2011 census [5]. In 2011, the 60+ population accounted for 8% of India population (93 million people). According to estimates, by the year 2050, the 60+ population will climb and account for 19% (323 million people) of the population [3]. As a result of this demographic shift, India is expected to face a higher burden of chronic disease and disability than any other country in the world over the next few decades.

Mobility disability is a serious health problem encountered in the elderly, causing loss of independence and higher rates of morbidity and mortality. However, there is insufficient research from developing countries, including India, determining the prevalence of objectively measured mobility disability. Most of the research on disability from developing countries, including India has been recognized to be limited and of poor quality [122]. Nearly all estimates on aging, chronic disease and disability in India have been projected from small surveys conducted in specific sub-populations, causing concern that most of the data do not indicate the true measure of the problem [123]. Most current research has been done in urban older adults, even though more than two-third of the older adults in India live in rural areas [124-126]. Moreover, the estimates of disability have been assessed using self-reported diagnostic history or problems in activities of daily living, which may introduce biases to the estimates.

The first aim of the present study was to estimate the prevalence of mobility disability in a rural Indian population aged >=60 years from the Mobility and Independent Living in Elders Study (MILES), using the 400-meter usual paced walk as the measure of mobility disability. The ability or inability to walk 400 meters has been shown to predict future disability in self-care and mortality [13, 23, 45, 48-50]. It has been proposed that inability to walk 400 meters is an important threshold for classifying older adults as mobility disabled [127].

The second aim of this study was to determine the risk factors for mobility disability in this population and its association with cardiovascular disease. We hypothesize that major mobility disability risk factors would be associated with prevalent mobility disability, independent of potential confounders.

5.3 Methods

5.3.1 Population

The Mobility and Independent Living in Elders Study (MILES) enrolled 562 individuals aged 60 years or above from Medchal Mandal in Andhra Pradesh state, India. Equal number of men and women were randomly selected after conducting door-to-door recruitment in 10 villages from February 2012 to November 2012. Age was determined by the self-report from the Rural Effective Affordable Health Care (REACH) 2011 census. Eligibility was determined on participants' ability to give informed consent (functional vision, hearing and cognitive function), physical ability to travel to the study clinic in a hospital vehicle, no plan to move from the area over the next 5 years and no end-stage diseases, such as terminal cancer, etc. Eligible participants were scheduled for a clinic visit where a written informed consent was obtained and comprehensive interview and clinical examination were conducted. A detailed description of the study has been published elsewhere (REF – MILES study design paper – Manuscript #1).

5.3.2 Mobility disability

Ability to walk 400 meters at usual pace was assessed on a 20-meter course (10 laps) in an open corridor. Exclusion criteria were resting heart rate <40 or >135 beats per minute, systolic blood pressure >200 mmHg or a diastolic blood pressure >110 mmHg. Participants were asked about their ability and willingness to complete or attempt the walk and the test was conducted only for participants who felt comfortable to make an attempt to walk the course. Criteria for termination of the test were chest pain, tightness or pressure in the chest, shortness of breath, dizziness, lightheadedness or significant leg pain. Time taken to complete the course or partial laps, number of rest stops taken and reasons for failure or no attempt were recorded for all participants [85]. Mobility disability was defined as inability to attempt or complete the 400-meter walk.

5.3.3 Measurements of risk factors and potential confounders

Age, weight, waist circumference, poor vision, joint pain, joint stiffness, knee pain, hypertension, chronic lung disease, arthritis, depressive symptoms, self-reported cardiovascular disease and major ECG abnormality diabetes and peripheral artery disease were considered as risk factors for mobility disability. Sex, caste, religion, marital status, schooling or reading ability and smoking were examined as potential confounders.

Information about caste, marital status and religion were collected from the participants. Number of years of schooling was determined by self-report and reading ability was assessed in individuals with 1-5 years of schooling.

Seca 813 Digital Scale (Seca, Hanover, MD) was used to measure weight in kilograms (kg); and Gulick II tape measure was used to measure the waist circumference in centimeters.

Smoking was classified as current, past, or never. Participants were asked about history of joint pain, stiffness or swelling lasting more than a month in the last 12 months, joint stiffness in the morning or after long periods of inactivity and knee pain lasting more than a month.

Vision was rated and categorized by self-report as good, fair, poor or very poor. Arthritis was defined as a health professional's diagnosis of osteoarthritis or rheumatoid arthritis. Depressive symptoms were assessed on the basis of 15-item Geriatric Depression Scale (GDS) [87, 128], which was translated to the local language (Telugu) and back translated to ensure accuracy.

Participants were asked to fast overnight or for at least 10 hours before the clinic visit. Blood was obtained from fasting participants to measure blood sugar. Participants were asked to bring all prescription and non-prescription medications they had taken in the last 14 days. Dosage, frequency and duration were recorded and medications were categorized into classes. Diabetes was defined as self-report of a health professional's diagnosis, use of antidiabetic medication or a fasting blood glucose level greater than or equal to 126 mg/dL.

Resting blood pressure was measured thrice in seated participants after an initial resting period of 5 minutes using an Omron 705 automatic BP machine (Omron Healthcare, Inc., Lake Forest, IL). Average of all three measurements was taken for analysis. Hypertension was defined as a self-report of a health professional's diagnosis confirmed by the use of anti-hypertensive medication or by the measured blood pressure categorized according to the JNC 7 criteria [88].

History of cardiovascular disease was defined as a self-report of a health professional's diagnosis of myocardial infarction or stroke, or a history of angiography or coronary artery bypass graft.

Standard 12-lead resting electrocardiograms were obtained using GE MAC 600 (GE Healthcare) machine and were read by a physician and classified into major and minor ECG abnormalities [89]. Major ECG abnormality was defined to include major Q or QS abnormalities, left ventricular hypertension (LVH), isolated major ST-T wave abnormality, atrial fibrillation, first degree atrioventricular block, left bundle branch block (LBBB), right bindle branch block (RBBB) and intraventricular block of indeterminate type.

Ankle brachial index (ABI) is the ratio of ankle to brachial systolic blood pressure and is <0.9 when there is obstruction to blood flow from atherosclerosis. ABI is a sensitive and specific measure of lower extremity peripheral artery disease. A handheld 8-megahertz Doppler probe with built-in speaker, and an OMRON 705 automatic BP machine was used to measure ankle and brachial blood pressure [90]. Peripheral artery disease was defined as an ABI of <0.9 or inability to find pulse in the lower extremities.

5.3.4 Statistical analyses

Descriptive analyses were conducted for all variables to assess proportions, means, standard deviations, normality, etc. Participant characteristics were compared for men and women using chi-square tests for categorical variables and t-tests for continuous variables.

Prevalence of mobility disability was calculated in the overall sample and in men and women separately. Characteristics were compared for individuals with and without mobility disability. Bivariate associations between mobility disability and risk factors, including potential confounders were examined. Continuous variables were analyzed using standard deviation as a unit. Variables that were significant (p<0.25) in the bivariate analyses were included in the multivariate logistic regression model in stepwise logistic regression, along with variables that were determined a priori to be important based on previously published literature. The final multivariate model included significant (p<0.05) and a priori determined variables. All analyses were conducted for the total sample and men and women separately.

Linear regression was used to determine associations with 400-meter walk time in those who completed the walk. Bivariate and multivariate models were generated for men and women separately to identify predictors for 400-meter walk time. Use of walking aid was added as a predictor for walk time. Data were analyzed using Stata 12.

5.4 Results

5.4.1 Population characteristics

Descriptive characteristics for the total sample are shown in **Table 25**. A total of 562 individuals (281 men and women each) completed the baseline clinic visit in the study. The median age of men was 66 years (range 60-90) and in women 65 years (range 60-92). More than 90% of the individuals were Hindu and a small number were Muslims and Christians. More than 90% of the men were currently married; however, less than half of the women were married. Men and women both had very low level of education with 91.5% of the women having had no schooling and only 26.5% of men having either more than or equal to 6 years of schooling or reading ability. Women were mostly non-smokers; however, nearly half the men were current smokers and one-third were past smokers. The median weight was low in both men (54.7 kg) and women (49.4 kg). Almost half of the men and women complained of knee pain lasting at least a month. Majority of the men and women had either fair or poor vision. Almost 40% of the women and 10% of the men had depressive symptoms suggestive of mild or severe depression. About a quarter of women and 14% of the men had diagnosed arthritis. Ten percent of men and women had a history of chronic lung disease. Even though not significantly different, diabetes was more prevalent in women (23.3%) than men (17.9%). About half of both men and women were hypertensive.

5.4.2 Mobility disability

Table 26 shows the prevalence of mobility disability in men and women. The prevalence of mobility disability was much higher in women (43.8%) compared to men (27.9%). Of the individuals who did not complete the 400-meter walk, 6.8% of the men and 5.7% of the women did not attempt the walk.

Tables 27, 28 and 29 compare the characteristics of the total sample, men and women with respect to mobility disability. Men, who were unable to complete the walk were more likely to have a history of knee pain, fair or poor vision, chronic lung disease and greater number of depressive symptoms. Among women with mobility disability, waist circumference was higher and they were more likely to have history of knee pain, poor vision, arthritis, greater number of depressive symptoms, history of CVD and peripheral artery disease compared to the group without mobility disability.

5.4.3 Bivariate and multivariate analyses

Tables 30, 31 and 32 show the bivariate logistic regression analyses between mobility disability and risk factors in the total sample, men and women separately. Among men, knee pain, fair vision, chronic lung disease and greater number of depressive symptoms were associated with mobility disability in bivariate analyses. Ability to read or six years or more of schooling was associated with lower odds of mobility disability. In women, higher waist circumference, joint pain, joint stiffness, knee pain, fair or poor vision, hypertension, arthritis, greater number of depressive symptoms, CVD history and PAD were associated with mobility disability. Age was not significantly associated with mobility disability in ether men or women.

Multivariate logistic regression analyses were conducted to ascertain the strength of relationship between mobility disability and risk factors after adjustments for potential confounders. The final multivariate models for the total sample, men and women are shown in **tables 33, 34 and 35**. Age was not associated with mobility disability in either men or women. In men, history of knee pain lasting at least a month, fair vision and chronic lung disease were associated independently with more than three-fold higher mobility disability. Each standard deviation increase in depressive symptoms was associated with an 81% increase in the odds of mobility disability. Among women, history of knee pain was associated with almost two-fold, poor or very poor vision with more than three-fold, CVD history with a five-fold and PAD with more than ten-fold higher mobility disability. Each standard deviation increase in waist circumference and depressive symptoms was associated with approximately 60% increased odds of mobility disability.

5.4.4 Time to complete 400-meter walk in those who completed the walk

In the analyses for time to walk 400 meters, the median walking time was significantly higher in women (503 seconds) compared to men (435 seconds) **(Table 36)**. Among the 360 participants who completed the walk, walking times were available for 353 individuals. Nine men out of 197 and 8 women out of 156 used a walking aid **(Table 37).**

Tables 38, 39 and 40 show the results of bivariate linear regression analyses between walking time and other variables in the total sample, men and women respectively. In men, age, joint pain, knee pain, arthritis, greater number of depressive symptoms, CVD history and use of a walking aid were associated with greater walking time. Among women, bivariate linear regression analyses showed associations of age, joint pain, joint stiffness, knee pain, chronic lung disease, greater number of depressive symptoms, and use of a walking aid with increased walking time. Greater height was associated with lower walking times.

Tables 41, 42 and 43 show multivariate linear regression analyses for walking time for the total sample, men and women. Among men, each year increase in age and each centimeter increase in waist circumference were associated with a slight increase in walking times. History of knee pain was associated with a 26 seconds increase, and use of walking aid was associated with a more than 100 seconds increase in walking time. Among women, each kilogram increase in weight was associated with slightly lower walking time and each centimeter increase in waist circumference was with slightly higher walking times. History of knee pain was associated with a 38 seconds increase, and use of walking aid was associated with a more than 120 seconds increase in walking time.

5.5 Discussion

In this cohort of community dwelling rural Indians aged 60 years and above, the prevalence of mobility disability, identified by inability to complete or attempt a 400-meter walk was high. Almost 45% of the women and more than a quarter of the men had mobility disability. In men, mobility disability was associated with a history of knee pain, chronic lung disease, poor vision and greater number of depressive symptoms. In women, mobility disability was associated with higher waist circumference, history of knee pain, poor vision greater number of depressive symptoms, history of CVD and peripheral artery disease.

It has been shown in previous literature that even though progress has been made by India in extending the life span of its residents, this success has not been carried over to better health care provision or management of disability for older adults [129, 130]. As there is no reliable monitoring and reporting for health and disability related condition, most of the data and generalizations about prevalence are from small samples [131]. Most studies have depended upon data released by the National Sample Survey Organization (NSSO) or smaller studies with limited generalizability or survey style data collection. As a result, the estimates of mobility disability vary widely between studies. According to NSSO, approximately 5% of elderly in rural and urban India were immobile or unable to move without help and older women had more physical health issues [132]. In another study, 45% of the older participants complained of problems in walking and 26% of rural women needed help with at least one activity of daily living [130]. A study in rural older Indians aged 60 and above estimated the prevalence of self-reported agility disability (defined as functional limitation in locomotion, walking, climbing stairs, body movement and dexterity) to be 30% in men and 35% in women [133].

In our analyses, age was not associated with mobility disability in MILES participants. This could be because of the inaccuracy of the reported age, as majority of the population did not have birth certificates and had difficulty reporting their correct age.

Most studies, including ours have shown higher prevalence of disability in older women compared to men [23, 56, 134]. Several explanations have been proposed to understand these differences. The prevalence of mobility disability was more than 50% higher in women compared to men and such difference might represent a survival effect for women. Other theories to explain this difference include greater perception of functional impairment in women compared with men [135] and higher rates of comorbidity or chronic health conditions in women, including depression, dementia and osteoarthritis [136]. This was also true in MILES where we saw higher prevalence of chronic conditions in women and their relationship with mobility disability. Another recent study by Tseng et al. found poorer physical function in women related to their higher fat mass compared to men, and by other body composition differences [137]. They found that higher proportion of body fat in women may put them at significant biomechanical disadvantage for greater disability in old age [137]. Furthermore, as results from MILES and other previous studies have shown, older women in rural India are likely to be illiterate or poorly educated and unlikely to hold a remunerative job. As a result of this, they are dependent on others for economic needs [129]. This might lead to women having poor health awareness and access to health care, increasing disease and disability, particularly in the older age groups. Moreover, policymakers and health care advisors have ignored this vulnerable group, and very little funding is allotted to the health needs of the older women in India [129].

Greater number of depressive symptoms was associated with mobility disability in both men and women. Several studies of older adults across rural and urban parts of India have shown geriatric depression to be highly prevalent. The estimates have varied between 6% and 43%, with higher proportion of women being affected [130, 138, 139][140]. In a study of inpatients in geriatric ward, Shah et al. detected depressive symptoms in 40% of the patients [129]. Depression was shown to be associated with mobility disability in several cross-sectional studies and as predictor of future mobility disability in older adults [141-143]. Even though almost half of the participants reported depressive symptoms in our study, none of them were on antidepressant treatment. Undiagnosed and untreated depression may lead to increased disability in this already highly disabled population.

Problems with vision was another factor that was independently associated with mobility disability in men as well as women. More than 50% of the participants reported having fair or poor vision in MILES. Similar results have been observed in previous studies in older Indians [129, 130]. Poor vision was associated with mobility disability and poor physical function in several epidemiological studies [144, 145].

Several other chronic conditions and diseases, including history of knee pain, lung disease, CVD and PAD were also associated with mobility disability. These conditions were associated with prevalent and incident mobility disability and poor physical performance in other cohorts of older adults [38, 60, 67-69, 78, 146]. There was high prevalence of these chronic conditions in MILES participants. Chronic diseases, including cardiovascular disease have been a major health problem in developed countries for a long time, but their presence in developing countries has been escalating only in the last few years. There are numerous factors contributing to this rise, including demographic shifts with altered age profiles, lifestyle and diet changes related to rapid urbanization, among several others [147, 148]. With advances in health care in developing countries, the population suffering from chronic disease is living to be older than ever before and this has led to an increase in disability due to these conditions in the older age groups.

In this study, more than 6% participants did not attempt the walk and almost 38% of the women and 21% men started the walk, but could not complete it. Of those who completed the walk, the mean walking time was 435 seconds for men and 503 seconds for women. By comparison, in a study of well-functioning older American men and women aged 70-79 years, mean walking time was 320 seconds in a 400-meter walk protocol demanding faster walk [54]. Another study of Italian older adults aged 65-91 year showed the mean 400-meter walking time to be 331 seconds [48]. Data from a physical activity clinical trial in American elderly participants aged 70-85 years showed similar walking time as MILES participants [149].

Greater walking times were associated with higher waist circumference, knee pain and use of a walking aid in both men and women. Greater number of depressive symptoms was associated with increased walking times for the total sample, but lost significance when analyzing men and women separately. Sample sizes are much smaller for this subset of participants who completed the walk, particularly when analyzing men and women separately.

There are several strengths to this study. To our knowledge, this is the first study in Indian older adults to identify mobility disability by using the participants' ability to complete a 400-meter walk. As self-report can give biased estimates, the objective measurement of mobility presents a more accurate prevalence. Moreover, most self-report questionnaires identify an advanced stage of disability, and do not discriminate at the level of high physical function. They have low sensitivity, provide very little information about the physical function of higher functioning individuals (ceiling effect) and identify persons whose ability to perform basic functions has already been impaired.

There were a few limitation of this study. The data analyzed in this effort are cross-sectional and causal relationships cannot be inferred, in particular for the relationship between depression and mobility disability. Also, because the study enrollment demanded that participants be physically able to at least walk a few steps and travel in a hospital vehicle to reach the clinic, severely disabled individuals could not be included in the study. Some information on risk factors was based on a health professional's diagnosis of that disease and may have been underestimated because of undiagnosed disease, poor health awareness and limited health care access in this population. Despite these limitations, MILES provides much needed estimates for prevalence and risk factors of mobility disability and offers novel opportunities for further research in this critical health issues in older adults.

Understanding the burden of mobility disability is crucial in this rapidly aging population. Mobility disability is shown to be risk factor for several geriatric conditions, including falls, fractures, cognitive decline, dementia and functional decline. Decreased mobility due to impaired mobility leads to further increase in health problems in older adults, including loss of muscle mass and strength, and deterioration of other chronic conditions, increasing the risk of institutionalization and death [16, 43, 47, 58, 61, 62].

The high prevalence of depressive symptoms observed among older adults indicates an urgent need, both for greater awareness of depression among community members and to ensure availability and accessibility of appropriate health care services to manage depression. At the same time, it is important to increase community support and create networks for better geriatric care. These results suggest that prevention or reduction of depressed mood could play a role in reducing functional decline in older persons. Improvement in vision is a very important modifiable risk factor for mobility disability and more effort is needed to provide access to corrective surgery and prosthetic aids to neglected and vulnerable populations. Timely detection of subclinical disease may allow for early treatment opportunities leading to improved survival and lowering disability in older population. Earlier diagnosis and better management of chronic conditions may delay the development of mobility disability and related morbidity. Risk factor modification may not only prevent disability, but can also have an impact on improving quality of life in older adults.

5.6 Mobility disability tables

Table 25: Descriptive characteristics of all MILES participants at baseline

Characteristic	Men (N=281)	Women (N=281)	p-value
Age (years), median (range)	66 (60-90)	65 (60-92)	0.163
Marital status			**<0.001**
Currently married, N (%)	**253 (90.4)**	**109 (38.8)**	
Widowed, N (%)	**26 (9.3)**	**169 (60.1)**	
Divorced/abandoned, N (%)	**1 (0.3)**	**3 (1.1)**	
Religion			0.514
Hindu, N (%)	258 (92.1)	253 (90.0)	
Muslim, N (%)	11 (3.9)	17 (6.1)	
Christian, N (%)	11 (3.9)	11 (3.9)	
Caste			0.598
Scheduled caste, N (%)	37 (13.2)	48 (17.1)	
Scheduled tribe, N (%)	17 (6.1)	16 (5.7)	
Backward caste, N (%)	157 (56.1)	146 (52.0)	
Other, N (%)	69 (24.6)	71 (25.3)	
Schooling and reading ability, N (%)			**<0.001**
No schooling, N (%)	**148 (53.1)**	**257 (91.5)**	
<6 years of schooling and not able to read, N (%)	**57 (20.4)**	**11 (3.9)**	
>=6 years of schooling or able to read	**74 (26.5)**	**13 (4.6)**	
Currently not working, N (%)	**157 (56.1)**	**217 (77.2)**	**<0.001**
Health status (self-reported)			0.163
Good, N (%)	134 (47.9)	118 (42.0)	
Fair, N (%)	144 (51.4)	120 (42.7)	
Poor, N (%)	2 (0.7)	43 (15.3)	
Weight (kg), median (range)	**54.7 (28.9-92.2)**	**49.4 (28.3-108.7)**	**<0.001**
Height (cm), median (range)	**161.2 (141.3-177.7)**	**147.4 (128.0-162.9)**	**<0.001**
BMI (kg/m^2), median (range)	**21.2 (13.6-33.1)**	**22.5 (14.3-43.7)**	**<0.001**
Waist circumference (cm), median (range)	**83.0 (52.9-112.3)**	**78.8 (54.7-132.6)**	**0.004**
Smoking			**<0.001**

Table 25 continued

Current, N (%)	**121 (43.1)**	**1 (0.4)**	
Past, N (%)	**91 (32.4)**	**6 (2.1)**	
Never, N (%)	**69 (24.6)**	**274 (97.5)**	
Alcohol, N (%)	**199 (71.1)**	**161 (57.3)**	**0.001**
Hemoglobin (g/dL), median (IQR)	**13.9 (12.4-15.1)**	**12.4 (11.5-13.1)**	**<0.001**
Joint pain, stiffness, swelling lasting >1 month in last 12 months, N (%)	**93 (33.2)**	**61 (21.7)**	**0.002**
Joint stiffness in morning/ after inactivity, N (%)	**92 (32.9)**	**161 (57.3)**	**<0.001**
Knee pain lasting >1 month, N (%)	136 (48.6)	133 (47.3)	0.769
Not physically active (not walking 10 minutes continuously every day), N (%)	**74 (26.4)**	**123 (43.8)**	**<0.001**
Difficulty in walking short distances (self-reported), N (%)	**88 (31.4)**	**167 (59.4)**	**<0.001**
Difficulty in walking long distances (self-reported), N (%)	203 (72.5)	222 (79.0)	0.072
Vision (self-reported)			**<0.001**
Good, N (%)	**114 (40.7)**	**98 (34.9)**	
Fair, N (%)	**163 (58.2)**	**97 (34.5)**	
Poor/very poor, N (%)	**3 (1.1)**	**86 (30.6)**	
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	137 (48.8)	143 (50.9)	0.613
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	50 (17.9)	65 (23.30)	0.112
Depression categories (15-item GDS)			**<0.001**
No depression (<=5 depressive answers), N (%)	**247 (89.2)**	**170 (60.7)**	
Mild depression (6-10 depressive items), N (%)	**21 (7.6)**	**66 (23.6)**	
Severe depression (>10 depressive answers), N (%)	**9 (3.3)**	**44 (15.7)**	
Arthritis (self-reported), N (%)	**40 (14.3)**	**67 (23.8)**	**0.004**
Chronic lung disease (self-reported), N (%)	27 (9.6)	29 (10.3)	0.789
CVD history (self-reported), N (%)	**28 (10.0)**	**16 (5.7)**	**0.058**
ECG abnormality, N (%)	**44 (15.7)**	**44 (15.7)**	**1.000**
Peripheral artery disease, N (%)	**17 (6.1)**	**20 (7.1)**	**0.626**

Table 26: Prevalence of mobility disability (non-completion of 400 meter walk) in men and women

	Men (N=280)	Women (N=280)	p-value
400 meter walk (non-completers), N (%)	**78 (27.9)**	**123 (43.8)**	**<0.001**
400 meter walk status			**<0.001**
Not attempted, N (%)	19 (6.8)	17 (5.7)	
Attempted, but not completed, N (%)	59 (21.1)	106 (37.9)	
Completed, N (%)	202 (72.1)	158 (56.4)	

Table 27: Characteristics of all MILES participants by mobility disability (400 meter walk not completed)

Characteristic	With mobility disability (N=201)	Without mobility disability (N=360)	p-value
Age (years), mean (SD)	68.2 (6.2)	67.2 (6.6)	0.087
Male sex, N (%)	**78 (38.8)**	**202 (56.1)**	**<0.001**
Not currently married, N (%)	**90 (44.8)**	**109 (30.3)**	**0.001**
Schooling and reading ability, N (%)			**<0.001**
No schooling, N (%)	**159 (79.5)**	**246 (68.3)**	
<6 years of schooling and not able to read, N (%)	**26 (13.0)**	**42 (11.7)**	
>=6 years of schooling or able to read	**15 (7.5)**	**72 (20.0)**	
BMI (kg/m^2), mean (SD)	22.7 (5.1)	22.0 (4.2)	0.08
Waist circumference (cm), mean (SD)	81.4 (14.1)	80.3 (12.6)	0.318
Smoking			0.078
Never, N (%)	135 (67.2)	207 (57.5)	
Past, N (%)	30 (14.9)	67 (18.6)	
Current, N (%)	36 (17.9)	86 (23.9)	
Joint pain, stiffness, swelling lasting >1 month in last 12 months, N (%)	63 (31.3)	91 (25.3)	0.123
Joint stiffness in morning/ after inactivity, N (%)	**109 (54.2)**	**144 (40.0)**	**0.001**
Knee pain lasting >1 month, N (%)	**127 (63.2)**	**142 (39.4)**	**<0.001**
Difficulty in walking short distances (self-reported), N (%)	**152 (75.6)**	**103 (28.6)**	**<0.001**
Difficulty in walking long distances (self-reported), N (%)	**192 (95.5)**	**233 (64.7)**	**<0.001**
Vision (self-reported)			**<0.001**
Good, N (%)	**44 (21.9)**	**168 (46.7)**	
Fair, N (%)	**105 (52.2)**	**155 (43.1)**	
Poor/very poor, N (%)	**52 (25.9)**	**37 (10.3)**	
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	111 (55.2)	170 (47.2)	0.069
Chronic lung disease (self-reported), N (%)	**28 (13.9)**	**28 (7.8)**	**0.020**
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	**50 (25.1)**	**65 (18.1)**	**0.048**
Arthritis (self-reported), N (%)	**53 (26.4)**	**54 (15.0)**	**0.001**
Depression categories (15-item GDS)			**<0.001**
No depression (<=5 depressive	**118 (59.6)**	**299 (83.3)**	

Table 27 continued

answers), N (%)			
Mild depression (6-10 depressive answers), N (%)	**44 (22.2)**	**43 (12.0)**	
Severe depression (>10 depressive answers), N (%)	**36 (18.2)**	**17 (4.7)**	
CVD history (self-reported), N (%)	**23 (11.4)**	**21 (5.8)**	**0.018**
ECG abnormality, N (%)	**41 (20.4)**	**46 (12.8)**	**0.017**
Peripheral artery disease, N (%)	**24 (12.0)**	**13 (3.6)**	**<0.001**

Table 28: Characteristics of men by mobility disability (400 meter walk not completed)

Characteristic	With mobility disability (N=78)	Without mobility disability (N=202)	p-value
Age (years), mean (SD)	68.6 (6.3)	67.7 (6.7)	0.332
Not currently married, N (%)	8 (10.3)	19 (9.4)	0.829
Schooling and reading ability, N (%)			**0.011**
No schooling, N (%)	**45 (58.4)**	**103 (51.0)**	
<6 years of schooling and not able to read, N (%)	**21 (27.3)**	**36 (17.8)**	
>=6 years of schooling or able to read	**11 (14.3)**	**63 (31.2)**	
BMI (kg/m^2), mean (SD)	21.2 (3.8)	21.5 (4.0)	0.512
Waist circumference (cm), mean (SD)	82.2 (11.7)	82.3 (12.5)	0.918
Smoking			0.472
Never, N (%)	15 (19.2)	53 (26.2)	
Past, N (%)	27 (34.6)	64 (31.7)	
Current, N (%)	36 (46.2)	85 (42.1)	
Joint pain, stiffness, swelling lasting >1 month in last 12 months, N (%)	28 (35.9)	65 (32.2)	0.554
Joint stiffness in morning/ after inactivity, N (%)	30 (38.5)	62 (30.7)	0.215
Knee pain lasting >1 month, N (%)	**54 (69.2)**	**82 (40.6)**	**<0.001**
Difficulty in walking short distances (self-reported), N (%)	**52 (66.7)**	**36 (17.8)**	**<0.001**
Difficulty in walking long distances (self-reported), N (%)	**76 (97.4)**	**127 (62.9)**	**<0.001**
Vision (self-reported)			**<0.001**
Good, N (%)	**14 (18.0)**	**100 (49.5)**	
Fair, N (%)	**61 (78.2)**	**102 (50.5)**	
Poor/very poor, N (%)	**3 (3.9)**	**0 (0.0)**	
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	42 (53.9)	101 (50.0)	0.564
Chronic lung disease (self-reported), N (%)	**14 (18.0)**	**13 (6.4)**	**0.003**
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	16 (20.5)	34 (16.8)	0.471
Arthritis (self-reported), N (%)	13 (16.7)	27 (13.4)	0.479
Depression categories (15-item GDS)			**0.001**
No depression (<=5 depressive answers), N (%)	**60 (80.0)**	**187 (92.6)**	
Mild depression (6-10 depressive items), N (%)	**8 (10.7)**	**13 (6.4)**	

Table 28 continued

Severe depression (>10 depressive answers), N (%)	**7 (9.3)**	**2 (1.0)**	
CVD history (self-reported), N (%)	11 (14.1)	17 (8.4)	0.155
ECG abnormality, N (%)	17 (21.8)	26 (12.9)	0.063
Peripheral artery disease, N (%)	8 (10.4)	9 (4.5)	0.064

Table 29: Characteristics of women by mobility disability (400 meter walk not completed)

Characteristic	With mobility disability (N=123)	Without mobility disability (N=158)	p-value
Age (years), mean (SD)	68.0 (6.1)	66.6 (6.3)	0.071
Not currently married, N (%)	82 (66.7)	90 (57.0)	0.098
BMI (kg/m^2), mean (SD)	23.7 (5.5)	22.7 (4.4)	0.083
Waist circumference (cm), mean (SD)	**81.0 (15.4)**	**77.6 (12.3)**	**0.045**
Joint pain, stiffness, swelling lasting >1 month in last 12 months, N (%)	**35 (28.5)**	**26 (16.5)**	**0.015**
Joint stiffness in morning/ after inactivity, N (%)	**79 (64.2)**	**82 (51.9)**	**0.038**
Knee pain lasting >1 month, N (%)	**73 (59.4)**	**60 (38.0)**	**<0.001**
Difficulty in walking short distances (self-reported), N (%)	**100 (81.3)**	**67 (42.4)**	**<0.001**
Difficulty in walking long distances (self-reported), N (%)	**116 (94.3)**	**106 (67.1)**	**<0.001**
Vision (self-reported)			**0.001**
Good, N (%)	**30 (24.4)**	**68 (43.0)**	
Fair, N (%)	**44 (35.8)**	**53 (33.5)**	
Poor/very poor, N (%)	**49 (39.8)**	**37 (23.4)**	
Hypertension (BP>=140/90 and/or self-reported AND medication use), N (%)	**69 (56.1)**	**69 (43.7)**	**0.039**
Chronic lung disease (self-reported), N (%)	14 (11.4)	15 (9.5)	0.606
Diabetes, N (%) (self-reported and/or FBS>=126 and/or medication use)	34 (28.1)	31 (19.6)	0.097
Arthritis (self-reported), N (%)	**40 (32.5)**	**27 (17.1)**	**0.003**
Depression categories (15-item GDS)			**0.001**
No depression (<=5 depressive answers), N (%)	**58 (47.2)**	**112 (71.3)**	
Mild depression (6-10 depressive items), N (%)	**36 (29.3)**	**30 (19.1)**	
Severe depression (>10 depressive answers), N (%)	**29 (23.6)**	**15 (9.6)**	
CVD history (self-reported), N (%)	**12 (9.8)**	**4 (2.5)**	**0.010**
ECG abnormality, N (%)	24 (19.5)	20 (12.7)	0.117
Peripheral artery disease, N (%)	**16 (13.0)**	**4 (2.5)**	**0.001**

Table 30: Bivariate logistic regression analyses of mobility disability (400 meter walk not completed) for the total sample

	Odds Ratio	95% confidence interval	p-value
Age	1.02	1.00–1.05	0.088
Male sex	**0.50**	**0.35–0.71**	**<0.001**
Caste			
Other	1.00 (ref)	1.00 (ref)	1.00 (ref)
Backward caste	0.90	0.59–1.37	0.617
Scheduled caste/Scheduled tribe	1.16	0.70–1.91	0.575
Not currently married	**1.87**	**1.31–2.67**	**0.001**
Schooling and reading ability			
No schooling	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 years of school & inability to read	**0.96**	**0.56–1.62**	**0.873**
>=6 years of school or able to read	**0.32**	**0.18–0.58**	**<0.001**
BMI (per SD)	1.16	0.98–1.38	0.081
Waist circumference (per SD)	1.09	0.92–1.30	0.318
Smoking			
Never smoked	1.00 (ref)	1.00 (ref)	1.00 (ref)
Past smoking	0.69	0.42–1.11	0.126
Current smoking	0.64	0.41–1.00	0.051
Chewing tobacco	1.45	0.99–2.11	0.054
Joint pain, stiffness, swelling	1.35	0.92–1.98	0.123
Joint stiffness in morning/ after inactivity	**1.78**	**1.25–2.52**	**0.001**
Knee pain lasting >1 month	**2.63**	**1.85–3.76**	**<0.001**
Vision (self-reported)			
Good	**1.00 (ref)**	**1.00 (ref)**	**1.00 (ref)**
Fair	**2.59**	**1.71–3.91**	**<0.001**
Poor/very poor	**5.37**	**3.14–9.18**	**<0.001**
Hypertension (BP>=140/90 and/or self-reported AND medication use)	1.38	0.97–1.95	0.070
Chronic lung disease	**1.92**	**1.10–3.34**	**0.021**
Diabetes	**1.52**	**1.00–2.31**	**0.049**
Arthritis	**2.03**	**1.32–3.11**	**0.001**
Depression score (per SD)	**1.94**	**1.61–2.33**	**<0.001**
CVD history (self-reported)	**2.09**	**1.12–3.87**	**0.020**
ECG abnormality	**1.75**	**1.10–2.78**	**0.018**
Peripheral artery disease	**3.64**	**1.81–7.32**	**<0.001**

Table 31: Bivariate logistic regression analyses of mobility disability (400 meter walk not completed) for men

	Odds Ratio	95% confidence interval	p-value
Age	1.02	0.98–1.06	0.331
Caste			
Other	1.00 (ref)	1.00 (ref)	1.00 (ref)
Backward caste	0.73	0.39–1.37	0.327
Scheduled caste/Scheduled tribe	1.24	0.58–2.65	0.577
Not currently married	1.10	0.46–2.63	0.829
Schooling and reading ability			
No schooling	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 years of school & inability to read	**1.34**	**0.70–2.54**	**0.378**
>=6 years of school or able to read	**0.40**	**0.19–0.83**	**0.014**
BMI (per SD)	0.90	0.67–1.22	0.510
Waist circumference (per SD)	0.99	0.74–1.30	0.918
Smoking			
Never smoked	1.00 (ref)	1.00 (ref)	1.00 (ref)
Past smoking	1.49	0.72–3.09	0.283
Current smoking	1.50	0.75–2.99	0.254
Chewing tobacco	0.33	0.07–1.47	0.145
Joint pain, stiffness, swelling	1.18	0.68–2.04	0.554
Joint stiffness in morning/ after inactivity	1.41	0.82–2.43	0.216
Knee pain lasting >1 month	**3.29**	**1.89–5.75**	**<0.001**
Vision (self-reported)			
Good	**1.00 (ref)**	**1.00 (ref)**	**1.00 (ref)**
Fair	**4.27**	**2.25–8.13**	**<0.001**
Poor/very poor (omitted)			
Hypertension (BP>=140/90 and/or self-reported AND medication use)	1.17	0.69–1.97	0.564
Chronic lung disease	**2.10**	**1.13–3.91**	**0.019**
Diabetes	1.28	0.66–2.47	0.472
Arthritis	1.30	0.63–2.66	0.480
Depression score (per SD)	**1.98**	**1.40–2.81**	**<0.001**
CVD history (self-reported)	1.79	0.80–4.01	0.159
ECG abnormality	1.89	0.96–3.71	0.066
Peripheral artery disease	2.49	0.92–6.70	0.072

Table 32: Bivariate logistic regression analyses of mobility disability (400 meter walk not completed) for women

	Odds Ratio	95% confidence interval	p-value
Age	1.04	1.00–1.08	0.073
Caste			
Other	1.00 (ref)	1.00 (ref)	1.00 (ref)
Backward caste	1.10	0.62–1.94	0.752
Scheduled caste/Scheduled tribe	1.06	0.54–2.10	0.861
Not currently married	1.51	0.93–2.47	0.098
Schooling and reading ability			
No schooling	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 years of school & inability to read	1.05	0.31–3.51	0.943
>=6 years of school or able to read	0.56	0.17–1.86	0.341
BMI (per SD)	1.21	0.97–1.51	0.084
Waist circumference (per SD)	**1.26**	**1.01–1.58**	**0.046**
Chewing tobacco	1.16	0.72–1.86	0.543
Joint pain, stiffness, swelling	**2.02**	**1.14–3.59**	**0.017**
Joint stiffness in morning/ after inactivity	**1.66**	**1.03–2.70**	**0.039**
Knee pain lasting >1 month	**2.38**	**1.47–3.86**	**<0.001**
Vision (self-reported)			
Good			
Fair	**1.88**	**1.05–3.38**	**0.035**
Poor/very poor	**3.00**	**1.64–5.50**	**<0.001**
Chronic lung disease	1.22	0.57–2.64	0.606
Hypertension (BP>=140/90 and/or self-reported AND medication use)	**1.65**	**1.02–2.65**	**0.039**
Diabetes	1.60	0.92–2.80	0.098
Arthritis	**2.34**	**1.34–4.09**	**0.003**
Depression score (per SD)	**1.78**	**1.39–2.28**	**<0.001**
CVD history (self-reported)	**4.16**	**1.31–13.25**	**0.016**
ECG abnormality	1.67	0.88–3.19	0.119
Peripheral artery disease	**5.76**	**1.87–17.70**	**0.002**

Table 33: Multivariate logistic regression analyses of mobility disability (400 meter walk not completed) for the total sample

	Odds Ratio	**95% confidence interval**	**p-value**
Age	1.02	0.99–1.05	0.177
Male sex	0.71	0.43–1.15	0.160
Waist circumference (per SD)	**1.29**	**1.05–1.59**	**0.016**
Knee pain lasting >1 month	**2.39**	**1.58–3.59**	**<0.001**
Vision (self-reported)			
Good	**1.00 (ref)**	**1.00 (ref)**	**1.00 (ref)**
Fair	**2.45**	**1.55–3.88**	**<0.001**
Poor/very poor	**4.23**	**2.29–7.85**	**<0.001**
Depression score (per SD)	**1.60**	**1.28–2.00**	**<0.001**
CVD history (self-reported)	**2.06**	**1.01–4.18**	**0.047**
Peripheral artery disease	**4.59**	**2.05–10.26**	**<0.001**

Table 34: Multivariate logistic regression analyses of mobility disability (400 meter walk not completed) for men

	Odds Ratio	95% confidence interval	p-value
Age	1.00	0.95–1.05	0.988
Waist circumference (per SD)	1.22	0.85–1.73	0.275
Smoking			
Never smoked	1.00 (ref)	1.00 (ref)	1.00 (ref)
Past smoking	1.22	0.52–2.87	0.651
Current smoking	1.50	0.65–3.45	0.346
Knee pain lasting >1 month	**3.28**	**1.68–6.40**	**0.001**
Vision (self-reported)			
Good	**1.00 (ref)**	**1.00 (ref)**	**1.00 (ref)**
Fair	**3.87**	**1.87–7.98**	**<0.001**
Poor/very poor (Omitted)			
Chronic lung disease	**3.01**	**1.09–8.33**	**0.034**
Diabetes	1.17	0.50–2.72	0.717
Arthritis	0.74	0.29–1.87	0.525
Depression score (per SD)	**1.81**	**1.18–2.77**	**0.006**
Peripheral artery disease	2.22	0.66–7.45	0.199

Table 35: Multivariate logistic regression analyses of mobility disability (400 meter walk not completed) for women

	Odds Ratio	95% confidence interval	p-value
Age	1.04	1.00–1.09	0.066
Waist circumference (per SD)	**1.58**	**1.16–2.16**	**0.004**
Knee pain lasting >1 month	**1.94**	**1.07–3.52**	**0.029**
Vision (self-reported)			
Good	**1.00 (ref)**	**1.00 (ref)**	**1.00 (ref)**
Fair	**1.79**	**0.91–3.52**	**0.093**
Poor/very poor	**3.41**	**1.67–6.94**	**0.001**
Chronic lung disease	0.49	0.19–1.26	0.139
Diabetes	1.20	0.61–2.38	0.596
Arthritis	1.75	0.90–3.39	0.100
Depression score (per SD)	**1.63**	**1.20–2.21**	**0.002**
CVD history (self-reported)	**5.07**	**1.36–18.95**	**0.016**
Peripheral artery disease	**10.47**	**2.72–40.26**	**0.001**

Table 36: Time taken (seconds) to complete 400 meters walk for completers

	Men (N=197)	Women (N=156)	p-value
400 meter walk time (seconds), mean (IQR)	435 (385–470)	503 (448–542)	**<0.001**

Table 37: Use of walking aid for 400 meter walk for completers and non-completers

	Men	Women
Walking aid used in all 400 meter walk attempters (Total **N=525**), N (%)	30 (11.5)	31 (11.7)
Walking aid used in completers (Total **N=360**), N (%)	9 (4.5)	8 (5.0)
Walking aid used in non-completers (Total **N=165**), N (%)	21 (35.6)	23 (21.5)

Table 38: Bivariate linear regression analyses of time to complete 400 meter walk (in seconds) for the total sample

Variables	Beta coefficient	95% confidence interval	p-value
Age	**1.90**	**0.54, 3.26**	**0.006**
Male sex	**-68.52**	**-85.14, -51.89**	**<0.001**
Not currently married	**47.21**	**28.22, 66.20**	**<0.001**
Weight	**-0.90**	**-1.66, -0.14**	**0.021**
Height	**-3.61**	**-4.59, -2.63**	**<0.001**
Waist circumference	-0.18	-0.89, 0.53	0.623
Joint pain, stiffness, swelling	**21.83**	**1.39, 42.27**	**0.036**
Joint stiffness in morning/ after inactivity	**37.52**	**19.57, 55.46**	**<0.001**
Knee pain lasting >1 month	**34.80**	**16.72, 52.87**	**<0.001**
Vision (self-reported)			
Good	**1.00 (ref)**	**1.00 (ref)**	**1.00 (ref)**
Fair	**13.72**	**-5.07, 32.50**	**0.152**
Poor/very poor	**47.48**	**16.79, 78.17**	**0.003**
Chronic lung disease	**55.52**	**22.74, 88.30**	**0.001**
Diabetes	-1.23	-24.73, 22.27	0.918
Arthritis	**30.83**	**6.05, 55.62**	**0.015**
Depressive symptoms	**9.59**	**6.98–12.20**	**<0.001**
CVD history (self-reported)	3.96	-34.08, 41.99	0.838
Peripheral artery disease	-19.64	-67.37, 28.09	0.419
Use of walking aid	**122.91**	**82.88, 162.95**	**<0.001**

Table 39: Bivariate linear regression analyses of time to complete 400 meter walk (in seconds) for men

Variables	Beta coefficient	95% confidence interval	p-value
Age	**2.40**	**0.85, 3.94**	**0.003**
Not currently married	5.20	-31.70, 42.11	0.781
Weight	0.31	-0.60, 1.22	0.498
Height	-0.37	-2.31, 1.57	0.705
Waist circumference	0.59	-0.25, 1.44	0.167
Joint pain, stiffness, swelling	**32.25**	**10.09, 54.41**	**0.005**
Joint stiffness in morning/ after inactivity	18.41	-4.45, 41.27	0.114
Knee pain lasting >1 month	**29.08**	**7.82, 50.35**	**0.008**
Vision (self-reported)			
Good	1.00 (ref)	1.00 (ref)	1.00 (ref)
Fair	15.14	-6.02, 36.31	0.160
Poor/very poor (omitted)			
Chronic lung disease	36.79	-5.74, 79.32	0.090
Diabetes	-20.07	-48.77, 8.63	0.169
Arthritis	**42.91**	**12.58, 73.23**	**0.006**
Depressive symptoms	**7.08**	**2.50, 11.67**	**0.003**
CVD history (self-reported)	**38.75**	**1.26, 76.23**	**0.043**
Peripheral artery disease	-8.78	-59.71, 42.14	0.734
Use of walking aid	**109.43**	**60.76, 158.09**	**<0.001**

Table 40: Bivariate linear regression analyses of time to complete 400 meter walk (in seconds) for women

Variables	Beta coefficient	95% confidence interval	p-value
Age	**2.33**	**0.27–4.39**	**0.027**
Not currently married	15.56	-10.88, 41.99	0.247
Weight	-0.91	-2.10, 0.28	0.132
Height	**-2.62**	**-4.85, -0.38**	**0.022**
Waist circumference	-0.07	-1.13, 1.00	0.898
Joint pain, stiffness, swelling	**48.18**	**13.70, 82.67**	**0.006**
Joint stiffness in morning/ after inactivity	**30.52**	**4.63, 56.41**	**0.021**
Knee pain lasting >1 month	**47.96**	**21.81, 74.11**	**<0.001**
Vision (self-reported)			
Good	1.00 (ref)	1.00 (ref)	1.00 (ref)
Fair	22.66	-7.51, 52.84	0.140
Poor/very poor	7.97	-25.79, 52.84	0.642
Chronic lung disease	**59.34**	**15.69, 102.99**	**0.008**
Diabetes	10.38	-22.57, 43.33	0.535
Arthritis	8.77	-26.00, 43.54	0.619
Depressive symptoms	**5.59**	**1.98, 9.20**	**0.003**
CVD history (self-reported)	-41.55	-124.58, 41.48	0.324
Peripheral artery disease	-13.07	-96.33, 70.20	0.757
Use of walking aid	**134.02**	**78.27, 189.76**	**<0.001**

Table 41: Multivariate linear regression analyses of time to complete 400 meter walk (in seconds) for the total sample

Variables	Beta coefficient	95% confidence interval	p-value
Age	1.39	0.22, 2.55	0.020
Male sex	-58.41	-75.29, -41.54	<0.001
Weight	-2.85	-4.38, -1.32	<0.001
Waist circumference	3.13	1.74, 4.53	<0.001
Knee pain lasting >1 month	32.98	17.71, 48.24	<0.001
Depressive symptoms	3.61	1.01, 6.22	0.007
Use of walking aid	111.52	76.06, 146.97	<0.001

Table 42: Multivariate linear regression analyses of time to complete 400 meter walk (in seconds) for men

Variables	Beta coefficient	95% confidence interval	p-value
Age	**1.72**	**0.23, 3.20**	**0.024**
Weight	-2.71	-5.51, 0.10	0.058
Height	0.38	-1.90, 2.65	0.744
Waist circumference	**3.24**	**0.82, 5.66**	**0.009**
Knee pain lasting >1 month	**26.24**	**5.73, 46.76**	**0.012**
Diabetes	-12.18	-39.91, 15.54	0.387
Arthritis	23.97	-5.82, 53.77	0.114
Depressive symptoms	2.84	-1.69, 7.37	0.218
Peripheral artery disease	-7.43	-54.73, 39.87	0.757
Use of walking aid	**100.54**	**51.64, 149.44**	**<0.001**

Table 43: Multivariate linear regression analyses of time to complete 400 meter walk (in seconds) for women

Variables	**Beta coefficient**	**95% confidence interval**	**p-value**
Age	0.82	-1.24, 2.88	0.431
Weight	**-2.80**	**-5.33, -0.27**	**0.031**
Height	-0.90	-3.36, 1.56	0.471
Waist circumference	**2.71**	**0.71, 4.72**	**0.008**
Knee pain lasting >1 month	**37.50**	**12.06, 62.95**	**0.004**
Diabetes	12.32	-20.45, 45.09	0.459
Arthritis	-2.78	-34.39, 28.83	0.862
Depressive symptoms	3.20	-0.40, 6.81	0.081
Peripheral artery disease	16.05	-59.56, 91.66	0.675
Use of walking aid	**122.85**	**66.76, 178.94**	**<0.001**

6.0 SUMMARY AND PUBLIC HEALTH SIGNIFICANCE

We are living in a rapidly aging world. Almost all nations in the world are now experiencing a growth in the number of older adults. However, the most rapid increases in the older population are in the developing world. As a result, developing countries will have less time to adjust to the consequences of this change in population restructuring. Developing countries have not encountered such high numbers of older adults in their population and are not fully equipped to handle the challenges presented by this change. Additionally, population aging in developing countries is taking place at much lower levels of socioeconomic development compared to developed countries, leading to further complications.

India is the second most populous country in the world with 1.21 billion people in its 2011 census, and has the second largest population of older adults. More than two-third of the elderly live in rural areas and suffer from several socioeconomic and health challenges. Less than 10% of the population has health insurance. Trends of a shift to an aging society will lead to increases in the burden of physical and cognitive disability and non-communicable diseases, notably osteoarthritis, cardiovascular disease (CVD) and diabetes. Indian health system is poorly equipped to address most of these issues associated with this dramatic change in demographics. There is dearth of health data on older adults in India, which is essential to analyze population aging and formulate mid- and long-term policies.

The Mobility and Independent Living in Elders Study (MILES) was established to define the prevalence, incidence and risk factors for disability and age-related disease in rural older Indians. With this study we were able to fill several gaps in prior literature and made several observations for future directions.

Analyses from MILES showed high prevalence of previously undiagnosed cardiovascular disease and risk factors. There was a clear relationship of some of the well-known risk factors for CVD with prevalent disease. Most of the estimates for global burden of disease, including CVD are from models filled by data from developed countries. With growing prevalence of CVD in India, there is an urgent need to understand the burden of clinical as well as subclinical disease and risk factors using studies conducted in India. Strong public health policies are required to not only restrict use of smoking, but also chewing tobacco. Physical activity needs to be promoted, particularly among older adults. Improved access to health care and inexpensive, but effective medication is required to combat disease and risk factors, including hypertension. Better optimization of treatment is needed for management of diagnosed disease. Good incidence data is needed to have better understanding of disease processes in this population, particularly in women.

The high prevalence of depressive symptoms observed among older adults indicates an urgent need, both for greater awareness of depression among community members and to ensure availability and accessibility of appropriate health care services to manage it. At the same time, it is important to increase community support and create networks for better geriatric care. These results suggest that prevention or reduction of depressed mood could play a role in reducing functional decline in older persons.

Problems with vision were highly prevalent in both men and women. Improvement in vision is a very important modifiable risk factor for mobility disability and more effort is needed to provide access to corrective surgery and prosthetic aids to neglected and vulnerable populations. Increased screening for visual impairment can be an inexpensive, but very effective was tool to improve quality of life in this population.

Timely detection of subclinical disease may allow for early treatment opportunities leading to improved survival and lowering disability in older population. Earlier diagnosis and better management of chronic conditions may delay the development of mobility disability and related morbidity. Risk factor modification may not only prevent disability, but can also have an impact on improving quality of life in older adults.

Mobility disability was highly prevalent in this population, particularly in women. Understanding the burden of mobility disability is crucial in this rapidly aging population. Mobility disability is shown to be risk factor for several geriatric conditions, including falls, fractures, cognitive decline, dementia and functional decline. Decreased mobility due to impaired mobility leads to further increase in health problems in older adults, including loss of muscle mass and strength, and deterioration of other chronic conditions, increasing the risk of institutionalization and death. Even though we could not attribute unidirectional causality between risk factors and mobility disability in this study, we were able to identify factors that were independently associated with mobility disability.

There are several barriers for the mobility disabled population, particularly in developing countries. There are inadequate policies and standards for people with disabilities, or lack of enforcement of existing policies. These include lack of standards and policies for improving accessibility in physical environment and transport systems suitable for disabled, making this already neglected population more isolated. In persons identified as disabled, low priority is given to rehabilitation. Other issues, including negative attitudes toward disabled, lack of provision of services, lack of funding and last but not least, lack of data and evidence, further impeding understanding and action on these issues.

More research using objective measures is urgently needed in older population in developing countries to estimate the burden of disease and disability with more certainty. Improvement in data quality is required by ensuring strict quality controls in research, expanding collaborative efforts and creating comparable data. Development of quality disability and disease data may be a long term effort, but it is required to provide essential support for better monitoring and development of strategies to improve functioning in this population.

MILES is a longitudinal study and we will continue to follow participants for a total of five years. This will provide valuable knowledge about incident disease, disability and mortality.

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