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Original Article

The Prevalence and Correlates of Frailty in Urban and Rural Populations in Latin America, China, and India: A 10/66 Population-Based Survey

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A B S T R A C T

Background: There have been few cross-national studies of the prevalence of the frailty phenotype conducted among low or middle income countries. We aimed to study the variation in prevalence and correlates of frailty in rural and urban sites in Latin America, India, and China.
Methods: Cross-sectional population-based catchment area surveys conducted in 8 urban and 4 rural catchment areas in 8 countries; Cuba, Dominican Republic, Puerto Rico, Venezuela, Peru, Mexico, China, and India. We assessed weight loss, exhaustion, slow walking speed, and low energy consumption, but not hand grip strength. Therefore, frailty phenotype was defined on 2 or more of 4 of the usual 5 criteria.
Results: We surveyed 17,031 adults aged 65 years and over. Overall frailty prevalence was 15.2% (95% confidence inteval 14.6%–15.7%). Prevalence was low in rural (5.4%) and urban China (9.1%) and varied between 12.6% and 21.5% in other sites. A similar pattern of variation was apparent after direct standardization for age and sex. Cross-site variation in prevalence of frailty indicators varied across the 4 indicators. Controlling for age, sex, and education, frailty was positively associated with older age, female sex, lower socioeconomic status, physical impairments, stroke, depression, dementia, disability and dependence, and high healthcare costs.
Discussion: There was substantial variation in the prevalence of frailty and its indicators across sites in Latin America, India, and China. Culture and other contextual factors may impact significantly on the assessment of frailty using questionnaire and physical performance-based measures, and achieving cross-cultural measurement invariance remains a challenge.

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Conclusions: A consistent pattern of correlates was identified, suggesting that in all sites, the frailty screen could identify older adults with multiple physical, mental, and cognitive morbidities, disability and needs for care, compounded by socioeconomic disadvantage and catastrophic healthcare spending.

According to a 2012 systematic review, prevalence of frailty in high income countries varies substantially among studies, with different operational definitions of frailty contributing to heterogeneity.[1] When restricted to studies using the frailty phenotype,[2] weighted average prevalence was 9.9% [95% confidence interval (CI) 9.6–10.2]. In the Survey of Health, Aging and Retirement in Europe, overall prevalence for those aged 65 years and over, according to a modified Fried phenotype was 17.0%, ranging from 5.8% to 27.3% by country, and increasing from Northern to Southern Europe.[3] Excluding those with difficulties in performing activities of daily living, prevalence ranged from 3.9% to 21.0%. Until recently, there have been few studies of frailty in low- and middle-income countries. However, a 2016 review of studies from Latin America and the Caribbean identified 21 publications,[4] with an overall frailty prevalence of 19.6% (95% CI 15.4%–24.3%). Studies from the multicountry Survey on Health, Well-Being, and Aging in Latin America and the Caribbean (SABE) project,[5] Mexico,[6] Costa Rica,[7] and Peru[8] all suggest a higher prevalence in Latin America than has been observed in high-income countries, consistent with studies of Hispanic populations in the United States.[9] Conversely, findings from the nationally representative Chinese Health and Retirement Longitudinal Study suggest a lower prevalence of frailty (7.0% of those aged 60 years and over), higher in rural regions, and in the economically disadvantaged North West of China.[10] Studies from high-income countries in north America and Europe suggest an increasing prevalence of frailty with older age,[2,3,11] a higher prevalence in women compared with men,[1–3] and an inverse socioeconomic gradient,[2] with similar findings from studies from Latin America,[5,6,8] and China.[10]

There have been few cross-national studies of the prevalence of frailty and its indicators using common standardized assessments in all settings. The validity of comparisons across separate studies conducted in different countries is doubtful, given the variable operationalization of the frailty phenotype.[12,13] We, therefore, set out to present prevalence data from rural and urban catchment area sites in 6 countries in Latin America, and in India and China, where 4 of the 5 frailty phenotype indicators were applied using a uniform methodology and consistent training of research workers. We explore cross-site variation in prevalence after standardizing for age and sex, and in the sociodemographic and health correlates of frailty. We examine the independent association of frailty with healthcare spending and costs. We have previously published on the predictive validity of the frailty phenotype and its indicators in these sites, which, other than exhaustion, reliably predicted the onset of dependence and mortality independent of sociodemographic variables, diagnoses, and disability.[14]

Methods

Settings and Study Design

We conducted catchment area surveys of participants aged 65 years and older in urban sites in Cuba (Havana and Matanzas), Dominican Republic (Santo Domingo), Puerto Rico (Bayamon), Venezuela (Caracas), and urban and rural sites in Peru (Lima and Canete), Mexico (Mexico City and Morelos state), China (Xicheng and Daxing), and India (Chennai and Vellore). For convenience, these sites are referred to subsequently by their country and urban or rural location. The protocols for the 1-phase surveys, comprising; a clinical interview; a health, medical history, healthcare utilization and lifestyle interview; a cognitive assessment; a physical examination; and an informant interview are detailed elsewhere.[15,16] Recruitment was by signed informed consent. Studies were approved by local ethical committees, and the King's College London Research Ethics Committee.

Measures

Full details are available elsewhere.[15] Here we summarize the measures directly relevant to the analyses presented in this article.

Frailty

The physical frailty phenotype proposes 5 frailty indicators (exhaustion, weight loss, weak grip strength, slow walking speed, and low energy expenditure). Individuals are frail if they meet 3 or more of the 5 criteria, prefrail if they meet one or 2, and nonfrail if they meet none of the 5 criteria.[2] We assessed 4 of the 5 indicators of frailty, but using a slightly different operationalization to those originally proposed[2] for exhaustion, weight loss, and energy consumption, and omitting hand grip strength. Exhaustion was assessed using an item (Q.48.1) from the Geriatric Mental Status (GMS) structured clinical interview[17]; those reporting feeling worn out or exhausted were considered to have this frailty. Self-reported weight loss was assessed using item (Q53.1) from the GMS, those reporting weight loss of 10 lbs (4.5 kg) or more in the last 3 months were considered to have this frailty. Slow walking speed was assessed using a timed walking test (5 meters at usual speed, turn, and return to the starting point) with the slowest fifth in each catchment area subpopulation within each sex and height stratum (divided by median height for sex) considered to have a slow walking speed. For sensitivity analyses, we used an alternative population independent approach, applying the same cutpoint of 16 seconds or longer to complete the task across all sites, allowing 3 seconds to make the turn; this corresponds to a walking speed of $<$0.8 m/s. Those who rated themselves as "not at all physically active" in response to the question "Taking into account both work and leisure, would you say that you are; very, fairly, not very, or not at all physically active?" were considered to have low energy expenditure. As handgrip strength was not measured we considered participants frail if they fulfilled 2 or more of the 4 frailty indicators; for the overall frailty criterion, the effect is the same as imputing a value of 1 for handgrip strength.

Healthcare utilization and costs

Details of healthcare cost estimations are provided elsewhere.[18] Participants were asked about contacts with primary healthcare professionals, public hospital doctors, other publically provided professionals, and private healthcare services (private doctors, dentists, and traditional healers). For each service, participants were asked how often they had used it in the last 3 months, the duration of the consultation, and fees for the service. Travel costs were also elicited. Lengths of stay and out of pocket costs for hospital admissions, and total costs of medication paid out-of-pocket for any of these services were also recorded. Out-of-pocket costs comprised the total annualized payments made by healthcare service users. Total costs from a public perspective reflect the actual cost to the provider, regardless of financing, including staff salaries, facilities

and equipment, and overheads. Lacking appropriate local unit costs in each country, these were (1) derived from United Kingdom (UK) unit costs,[19] (2) converted to international dollars (purchasing power parity), and (3) adjusted by the ratio for healthcare costs between the UK and each project country based upon the World Health Organization (WHO)- Choosing Interventions that are Cost-Effective (CHOICE) database. Where UK unit costs were not available (private doctor, dentist, traditional healer, and medication), out of pocket payments were used instead because these services are generally not publicly funded and are subject to market forces. Given the positively skewed distribution of healthcare costs, both out-of-pocket costs and total costs were dichotomized at the 90th centile of the distribution in each site to reflect catastrophic healthcare spending and high total healthcare costs, respectively.

Covariates—sociodemographic circumstances, morbidity, disability, and dependence

Age was ascertained from participant and informant reports, and documented age, or an event calendar. Education level was ascertained, and coded as; no education, did not complete primary, and completed primary, secondary, or tertiary education. Wealth was assessed by enumerating 7 household assets and amenities, and categorized into quarters within each site. Food insecurity was defined as reporting going hungry in the last 1 month because of inadequate resources to purchase food. We assessed physical, mental, and cognitive morbidity through measures of stroke, physical impairments, dementia and depression, the main contributors to disability and dependence.[20,21] Dementia was diagnosed according to the cross-culturally developed, calibrated and validated 10/66 dementia diagnosis algorithm.[22] Stroke was self-reported, but confirmed by the interviewer as having characteristic symptoms lasting for more than 24 hours.[23] Physical multimorbidity was defined as 3 or more of 9 self-reported limiting physical impairments (arthritis; persistent cough; breathlessness, difficulty breathing or asthma; high blood pressure; heart trouble or angina; stomach or intestine problems; faints or blackouts; paralysis, limb weakness or loss; skin disorders such as pressure sores, leg ulcers or severe burns). *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (ICD-10) depressive episode was diagnosed using a computerized algorithm applied to the GMS structured clinical interview.[17] Disability was assessed by the WHO Disability Assessment Schedule (WHODAS) 2.0 scale, developed by the WHO as a culture-fair assessment tool for use in cross-cultural comparative epidemiologic and health services research.[24,25] Dependence (needs for care) was identified through a series of open-ended questions to a key informant, and a detailed assessment of caregiving roles.[21]

Analyses

We report prevalence of frailty by age and sex with robust standard errors and 95% CIs, accounting for household clustering. We estimate the prevalence of frailty by site, both including and excluding those who already have needs for care. We compare site-specific prevalence of frailty and its indicators after direct standardization for age and sex, with the whole survey sample as the standard population. The cutpoints for the walking speed indicator were normed for each site with no cross-site variation in prevalence of those considered to have the deficit; therefore, for this indicator we present instead the marginal adjusted mean time in seconds to complete the task, adjusted for age, sex, and height. We then estimated Spearman correlation of site rank orders of standardized prevalence or marginal adjusted means, between the 4 frailty phenotype indicators.

We describe, for each site, associations between frailty and demographic and socioeconomic factors; age (per 5-year band), sex (male vs female), education (per level), assets (per quarter), food insecurity, and living alone; and health-related factors; limiting physical impairments, stroke, ICD-10 depressive episode, dementia, disability (per point on the WHODAS 2.0 disability scale) and dependence. Prevalence ratios were obtained using Poisson regression models adjusted for age, sex, and education.

We estimate associations between frailty and 2 healthcare cost outcomes: (1) catastrophic out-of-pocket healthcare spending and (2) high total healthcare costs, using Poisson regression to generate prevalence ratios adjusted for age, sex, and education (base model), then further adjusted for morbidity (physical impairments, stroke, dementia, and depression—fully adjusted model).

Poisson models were estimated with robust standard errors accounting for household clustering. We ran the models in each site, and then used a fixed effects meta-analysis to combine them. Higgins I^2 estimates the proportion of between-site variability in the prevalence ratios accounted for by heterogeneity, as opposed to sampling error; up to 40% heterogeneity is conventionally considered negligible, while up to 60% may reflect moderate heterogeneity.[26]

Results

Sample Characteristics

In all, 17,031 participants were surveyed in the 12 sites in 8 countries, and 16,886 (99.1%) provided sufficient data to establish frailty phenotype. Mean ages varied between 71.3 and 76.3 years, higher in urban than rural and in more than less developed sites (Table 1). Most participants (62.4%) were female. Education levels varied widely among sites, with between 14.4% and 90.7% completed primary education, lowest in rural sites in India, Mexico, and China and in the Dominican Republic, and highest in urban Peru, Puerto Rico, and Cuba. Food insecurity was the most common in urban (20.8%) and rural India (14.1%), in rural Peru (13.5%), and Dominican Republic (12.1%). Overall, 16.1% reported 3 or more physical impairments, 6.7% had a past history of stroke, 5.5% met criteria for ICD-10 Depressive Episode in the last 1 month, and 9.3% for 10/66 dementia diagnosis. Physical impairments and stroke were less frequently reported in rural and less developed sites, and depression was rarely identified in China.

Prevalence of Frailty and Variation among Sites

The overall crude prevalence of frailty phenotype was 15.2%. The lowest prevalences were recorded in urban China (9.1%) and rural China (5.4%), and the highest in Dominican Republic (21.5%) and urban Peru (20.1%). Prevalences in other sites varied between 12.6% and 16.8% (Table 1). For the sensitivity analysis, applying a single walking speed cutpoint to all sites, the overall prevalence was 17.1%, but with a range from 7.7% to 35.0% (Supplementary Tables, available online). In most sites between one-quarter and one-third of those who were frail already had needs for care, rising to 48% in rural China and 80% in urban China (Figure 1). Restricting the frailty definition to those who remained independent, prevalence was only 1.8% in urban China and 2.8% in rural China, varying between 8.4% and 15.2% in other sites, with a similar pattern to that for total prevalence. The distribution of WHODAS 2.0 disability scores for frailty phenotype cases was similar among most sites, but markedly higher in urban and rural China, and lower in rural Peru and urban India (Figure 2). After direct standardization for age and sex, there was considerable residual variation among sites in the prevalence of frailty and the prevalence or distribution of the 4 frailty indicators (Table 2). However, the pattern of variation was inconsistent across indicators. Participants in the China sites were relatively unlikely to report weight loss or exhaustion, while there was a high prevalence of

Table 1
Sociodemographic and Health Characteristics of Participants by Country

	Cuba	Dominican Republic	Puerto Rico	Peru (Urban)	Peru (Rural)	Venezuela	Mexico (Urban)	Mexico (Rural)	China (Urban)	China (Rural)	India (Urban)	India (Rural)	All Centers
N	2944	2011	2009	1381	552	1965	1003	1000	1160	1002	1005	999	17,031
Sociodemographic exposures													
Age (y) Mean (SD)	75.1 (7.0) MV = 7	75.3 (7.5)	76.3 (7.4)	75.0 (7.4) MV = 1	74.2 (7.3)	72.3 (6.9) MV = 4	74.5 (6.6) MV = 1	74.1 (6.7)	73.9 (6.2)	72.4 (6.0)	71.3 (6.1) MV = 4	72.6 (5.8)	74.2 (7.0) MV = 17
Female sex (%)	1913 (65.0)	1325 (66.0) MV = 2	1347 (67.3) MV = 7	888 (64.3)	295 (53.4)	1252 (63.7)	666 (66.4)	602 (60.2)	661 (57.0)	556 (55.5)	571 (57.7) MV = 15	545 (54.6)	10621 (62.5) MV = 24
Education level: Did not complete primary (%)	730 (24.9) MV = 8	1414 (71.0) MV = 19	461 (23.1)	127 (9.3) MV = 8	225 (41.3) MV = 8	601 (31.2) MV = 40	581 (58.1) MV = 2	837 (83.7)	385 (33.2)	693 (69.2)	662 (66.0) MV = 2	855 (85.6)	7571 (44.7) MV = 97
Living alone (%)	261 (8.9)	254 (12.6)	472 (23.5)	45 (3.3)	44 (8.0)	61 (3.1)	106 (10.6)	112 (11.2)	54 (4.7)	49 (4.9)	44 (4.4)	120 (12.0)	1622 (9.5)
Socioeconomic indicators													
Food insecurity (%)	140 (4.8) MV = 11	240 (12.1) MV = 22	32 (1.6) MV = 14	63 (4.6) MV = 16	74 (13.5) MV = 5	111 (6.0) MV = 103	39 (3.9) MV = 4	85 (8.6) MV = 7	0 (0.0)	12 (1.2)	207 (20.8) MV = 10	141 (14.1)	1144 (6.8) MV = 192
Assets Median (interquartile range)	6 (5–6) MV = 8	5 (4–6) MV = 5	7 (6-7)	6 (6–6)	5 (4–6)	6 (6–7)	6 (6–7)	4 (3–6)	5 (5–6) MV = 1	6 (5–7)	4 (3–5) MV = 4	3 (2–4)	4 (3–5) MV = 18
Health status													
3 or more physical impairments	292 (9.9) MV = 6	465 (23.1) MV = 2	429 (21.4) MV = 7	224 (16.2) MV = 1	40 (7.2) MV = 1	489 (25.3) MV = 33	158 (15.8)	185 (18.5)	208 (17.9)	39 (3.9)	41 (4.1) MV = 1	168 (16.8)	2738 (16.1) MV = 51
Any ICD 10 depressive episode	144 (4.9) MV = 3	278 (13.8)	47 (2.3) MV = 1	87 (6.3) MV = 2	16 (2.9)	107 (5.5) MV = 1	47 (4.7)	45 (4.5)	3 (0.3)	7 (0.7)	39 (3.9)	126 (12.6)	946 (5.5) MV = 7
10/66 dementia (%)	316 (10.8) MV = 13	235 (11.7)	233 (11.7) MV = 11	129 (9.4) MV = 2	36 (6.5)	140 (7.1) MV = 1	86 (8.6)	85 (8.5)	81 (7.0)	56 (5.6)	75 (7.5)	106 (10.6)	1578 (9.3) MV = 27
Past history of stroke	230 (7.8) MV = 9	175 (8.7%) MV = 6	168 (8.4) MV = 8	112 (8.2) MV = 8	20 (3.6) MV = 2	135 (7.0) MV = 45	67 (6.7)	74 (7.4)	109 (9.4)	18 (1.8)	20 (2.0) MV = 1	11 (1.1)	1139 (6.7) MV = 79
Frailty phenotype	437 (14.9) MV = 2	431 (21.5) MV = 5	293 (14.6) MV = 70	277 (20.1) MV = 2	93 (16.8)	243 (12.6) MV = 34	157 (15.7) MV = 4	156 (15.7) MV = 8	195 (9.1)	54 (5.4) MV = 4	164 (16.3) MV = 1	154 (15.4)	2564 (15.2) MV = 130
Dependence (any needs for care)	261 (10.0) MV = 348	237 (11.8) MV = 4	288 (14.4) MV = 7	135 (9.8)	26 (4.7) MV = 2	209 (10.6) MV = 2	114 (11.4)	82 (8.2)	183 (15.8)	54 (5.4)	29 (2.9)	85 (8.5)	1703 (10.2) MV = 381
WHODAS 2.0 disability scale score, mean (SD)	13.4 (20.0) MV = 11	16.5 (20.3) MV = 15	16.6 (22.8) MV = 9	13.1 (20.6) MV = 10	10.4 (14.6) MV = 2	10.7 (16.3) MV = 96	10.0 (17.3) MV = 3	11.1 (19.1) MV = 0	8.1 (20.1) MV = 10	8.0 (20.1) MV = 2	10.5 (15.4) MV = 4	28.3 (18.3) MV = 0	13.4 (19.7) MV = 162

MV, number of participants with missing values; SD, standard deviation.

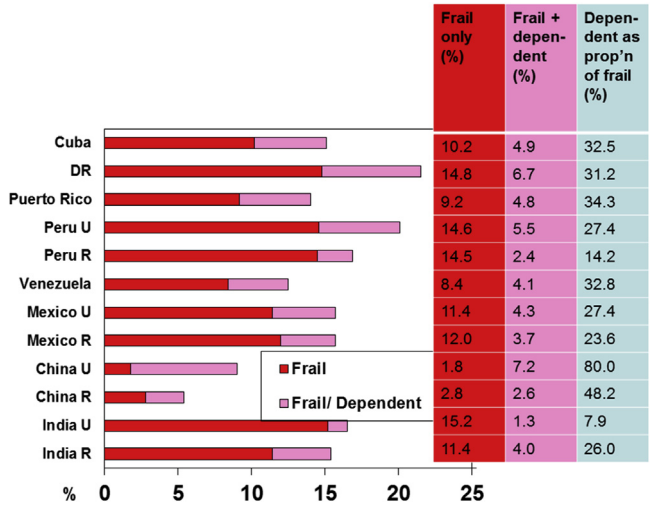

Fig. 1. Prevalence of frailty, with and without established needs for care, by site.

exhaustion in Latin American sites and urban India. Mean walking speeds were fastest in sites in Mexico and India and slowest in Dominican Republic, rural China, and Cuba. Low energy expenditure was most commonly reported in China and the Caribbean sites, and least commonly reported in rural Peru and rural India. Site rank orders for standardized prevalences were modestly positively correlated between weight loss and exhaustion (+0.31), and slow walking speed and low energy consumption (+0.43). However, the rank orders for prevalence of weight loss and low energy consumption (−0.83), and exhaustion and slow walking speed (−0.36) were negatively correlated.

Demographic and Socioeconomic Correlates of Frailty

Prevalence of frailty was higher in women than men in all sites other than Mexico, and rural China; overall prevalence was 16.4% in females and 13.1% in men (Table 3). There was a clear trend in all sites for prevalence to increase with age; from 9.5% (65–69 years), 11.9% (70–74 years), 16.5% (75–79 years), and 25.5% (80 years and over). These trends were confirmed in a multivariable analysis mutually controlling for age and sex, and educational status (Table 4). The pooled adjusted prevalence ratio (aPR - per 5 year increment in age) was 1.35, 95% CI 1.30–1.39, with marked heterogeneity among sites ($I^2 = 80\%$). The age gradient was most pronounced in China, rural Mexico, and Venezuela. The pooled aPR for sex (male vs female) was 0.86, 95% CI 0.80–0.93, with moderate heterogeneity among sites ($I^2 = 58\%$). Frailty was inversely associated with education level (aPR 0.89, 95% CI 0.86–0.93, $I^2 = 50\%$), and assets (aPR 0.91, 95% CI 0.88–0.95, $I^2 = 67\%$), and positively associated with food insecurity (aPR 1.73, 95% CI 1.55–1.94, $I^2 = 57\%$), all with low to moderate heterogeneity among sites. Those with frailty were less likely to live alone (aPR 0.80, 95% CI 0.70–0.91, $I^2 = 0\%$) with no heterogeneity among sites.

Health Correlates of Frailty

Controlling for age, sex, and education, frailty was more prevalent among those with 3 or more physical impairments (aPR 2.29, 95% CI 2.13–2.47, $I^2 = 78\%$), stroke (aPR 2.31, 95% CI 2.10–2.55, $I^2 = 79\%$), ICD-10 depressive episode (aPR 3.31, 95% CI 3.04–3.59, $I^2 = 85\%$), and 10/66 dementia (aPR 2.23, 95% CI 2.05–2.43, $I^2 = 86\%$), and there were strong positive associations between frailty and both disability score (aPR per 1 point increment 1.029, 95% CI 1.027–1.030, $I^2 = 90\%$) and care dependence (aPR 3.32, 95% CI 3.07–3.60, $I^2 = 87\%$) (Table 5). Although the associations were consistently in the positive direction

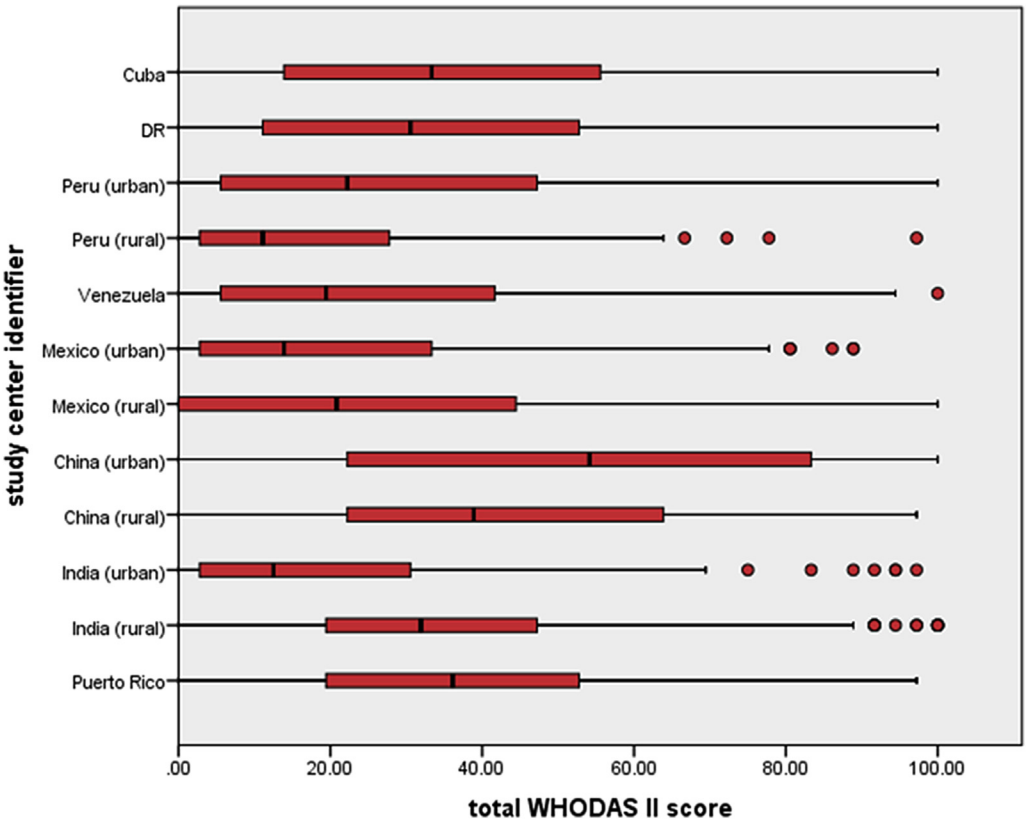

Fig. 2. Boxplot indicating the distribution of WHODAS 2.0 disability scores among frailty cases, by site.

Table 2
Age and Sex Standardized Prevalence of Frailty and Prevalence or Marginal Adjusted Mean of Frailty Indicators (95% CI), by Site, with Rank Orders

	Weight Loss		Exhaustion		Walking Speed		Low Energy Expenditure		Frailty	
	Standardized Prevalence (%)	Rank	Standardized Prevalence (%)	Rank	Marginal Adjusted* Mean (s)	Rank	Standardized Prevalence (%)	Rank	Standardized Prevalence (%)	Rank
Cuba	5.4 (4.6–6.2)	10	26.9 (25.3–28.5)	9	19.4 (18.8–20.1)	3	9.4 (8.4–10.4)	2	14.1 (12.9–15.3)	9
Dominican Republic	12.9 (11.4–14.4)	5	40.8 (38.7–43.0)	5	22.3 (21.5–23.1)	1	8.7 (7.4–9.9)	5	20.5 (18.8–22.2)	1
Puerto Rico	6.3 (5.2–7.4)	8	32.8 (30.6–34.9)	6	11.4 (10.5–12.2)	7	9.1 (7.9–10.3)	4	13.7 (12.1–15.2)	10
Peru (urban)	15.4 (13.5–17.4)	3	42.4 (39.9–45.0)	3	15.1 (14.1–16.0)	4	5.1 (4.0–6.2)	9	19.3 (17.2–21.3)	2
Peru (rural)	18.3 (15.1–21.7)	1	31.7 (27.7–35.6)	7	14.1 (12.7–15.5)	5	2.1 (0.9–3.4)	12	17.2 (4.0–20.3)	4
Venezuela	13.2 (11.6–14.8)	4	29.9 (27.8–32.0)	8	13.1 (12.3–14.0)	6	6.5 (5.3–7.7)	6	14.2 (12.5–15.8)	8
Mexico (urban)	6.7 (5.1–8.3)	7	47.5 (44.3–50.6)	1	8.7 (7.6–9.8)	12	6.2 (4.7–7.7)	7	15.8 (13.4–18.1)	5
Mexico (rural)	6.1 (4.6–7.6)	9	41.9 (38.8–44.9)	4	9.1 (8.0–10.2)	11	5.6 (4.2–7.0)	8	15.5 (13.3–17.7)	7
China (urban)	1.3 (0.7–2.0)	11	9.2 (7.5–11.0)	11	11.1 (10.1–12.1)	8	9.2 (7.6–10.9)	3	9.7 (7.9–11.4)	11
China (rural)	0.4 (0.0–0.8)	12	2.6 (1.6–3.6)	12	21.8 (20.7–22.8)	2	11.7 (9.5–14.0)	1	6.7 (4.9–8.5)	12
India (urban)	8.9 (7.0–10.9)	6	47.4 (44.1–50.7)	2	10.1 (9.0–11.1)	9	4.1 (2.7–5.5)	10	17.5 (14.8–20.1)	3
India (rural)	18.0 (15.5–20.4)	2	15.6 (13.1–18.1)	10	9.5 (8.4–10.6)	10	2.5 (1.3–3.7)	11	15.8 (13.4–18.3)	5

*Adjusted for age, sex, and height.

Table 3
Prevalence (%) of Frailty by Site, Age, and Sex (95% CI) According to Modified Frailty Phenotype Criteria

Age Groups, y (n)	65–69	70–74	75–79	80+	All Ages
Cuba	n = 760	n = 789	n = 638	n = 748	n = 2935
Female (n = 1908)	7.6 (5.2–10.0)	12.5 (9.5–15.4)	16.4 (12.8–20.0)	26.2 (22.4–30.0)	15.8 (14.2–17.5)
Male (n = 1027)	5.9 (3.1–8.6)	9.2 (5.9–12.6)	12.2 (8.0–16.5)	27.0 (21.3–32.7)	13.0 (10.9–15.1)
Both sexes (n = 2935)	7.0 (5.2–8.8)	11.3 (9.1–13.5)	14.9 (12.2–17.6)	26.5 (23.3–29.6)	14.9 (13.5–16.2)
Dominican Republic	n = 532	n = 519	n = 397	n = 557	n = 2005
Female (n = 1321)	16.0 (12.1–19.9)	21.9 (17.4–26.4)	29.1 (23.6–34.5)	31.4 (26.8–36.1)	24.6 (22.3–27.0)
Male (n = 684)	12.2 (7.5–16.9)	8.7 (4.8–12.7)	17.4 (11.0–23.9)	25.4 (18.9–32.0)	15.5 (12.8–18.2)
Both sexes (n = 2005)	14.6 (11.6–17.6)	17.0 (13.7–20.2)	25.2 (21.0–29.4)	29.6 (25.8–33.4)	21.5 (19.7–23.3)
Puerto Rico	n = 406	n = 448	n = 475	n = 606	n = 1935
Female (n = 1347)	10.4 (7.0–13.8)	8.4 (5.3–11.6)	16.5 (12.4–20.6)	25.3 (21.0–29.6)	15.9 (13.9–17.9)
Male (n = 655)	11.2 (5.2–17.2)	7.9 (3.6–12.2)	12.5 (7.4–17.6)	19.5 (14.2–24.8)	13.6 (10.9–16.2)
Both sexes (n = 2002)	10.5 (7.5–13.5)	8.3 (5.7–10.9)	15.2 (11.9–18.4)	23.2 (19.9–26.6)	15.1 (13.5–16.7)
Peru (urban)	n = 375	n = 352	n = 297	n = 354	n = 1378
Female (n = 885)	14.1 (9.9–18.3)	17.7 (12.7–22.8)	23.3 (17.3–29.3)	35.7 (29.3–42.1)	22.1 (19.4–24.8)
Male (n = 493)	9.8 (4.4–15.3)	12.1 (6.6–17.7)	12.0 (5.9–18.2)	29.1 (21.6–36.5)	16.4 (13.2–19.7)
Both sexes (n = 1378)	12.8 (9.4–16.2)	15.6 (11.9–19.4)	19.2 (14.8–23.6)	33.1 (28.2–37.9)	20.1 (18.0–22.2)
Peru (rural)	n = 179	n = 141	n = 101	n = 131	n = 552
Female (n = 295)	12.0 (5.6–18.4)	10.8 (4.1–17.6)	32.1 (19.5–44.6)	20.3 (10.1–30.6)	16.9 (12.7–21.2)
Male (n = 257)	16.5 (8.3–24.6)	17.2 (7.5–27.0)	10.4 (1.8–19.1)	20.8 (11.5–30.2)	16.7 (12.1–21.4)
Both sexes (n = 552)	14.0 (8.9–19.0)	13.5 (7.9–19.1)	21.8 (13.8–29.8)	20.6 (13.5–27.7)	16.8 (13.6–20.1)
Venezuela	n = 830	n = 465	n = 341	n = 292	n = 1928
Female (n = 1224)	8.9 (6.5–11.4)	9.7 (6.3–13.1)	18.5 (13.3–23.7)	28.9 (22.7–35.1)	14.3 (12.3–16.2)
Male (n = 704)	5.1 (2.6–7.5)	9.1 (4.9–13.4)	11.2 (5.7–16.7)	25.0 (15.9–34.1)	9.7 (7.5–11.8)
Both sexes (n = 1928)	7.5 (5.7–9.2)	9.5 (6.7–12.2)	15.8 (11.9–19.8)	27.7 (22.6–32.9)	12.6 (11.1–14.1)
Mexico (urban)	n = 245	n = 328	n = 204	n = 221	n = 998
Female (n = 666)	9.7 (5.5–14.0)	13.3 (8.7–17.9)	19.2 (12.3–26.1)	22.7 (15.8–29.6)	15.6 (12.8–18.3)
Male (n = 337)	16.7 (7.2–26.1)	13.6 (7.4–19.7)	16.5 (8.3–24.6)	18.8 (10.2–27.3)	16.0 (12.1–20.0)
Both sexes (n = 1003)	11.4 (7.5–15.4)	13.4 (9.7–17.2)	18.1 (12.9–23.4)	21.3 (15.8–26.8)	15.7 (13.4–18.0)
Mexico (rural)	n = 298	n = 251	n = 217	n = 226	n = 992
Female (n = 602)	9.7 (5.5–13.8)	12.1 (6.8–17.3)	15.4 (9.2–21.6)	26.4 (18.6–34.3)	14.9 (12.1–17.8)
Male (n = 398)	4.9 (7.1–9.1)	14.7 (7.8–21.6)	18.4 (10.2–26.5)	29.5 (20.8–38.2)	16.9 (13.2–20.6)
Both sexes (n = 1000)	8.1 (5.0–11.1)	13.1 (9.0–17.3)	16.6 (11.6–21.6)	27.9 (22.1–33.6)	15.7 (13.5–18.0)
China (urban)	n = 316	n = 362	n = 254	n = 228	n = 1160
Female (n = 661)	4.9 (1.9–7.9)	7.0 (3.4–10.5)	8.8 (4.0–13.5)	26.9 (18.9–34.9)	10.3 (8.0–12.6)
Male (n = 449)	2.7 (0.0–5.7)	6.2 (2.5–9.9)	6.8 (2.3–11.4)	14.7 (8.0–21.3)	7.4 (5.1–9.7)
Both sexes (n = 1160)	4.1 (1.8–6.4)	6.6 (4.0–9.3)	7.9 (4.6–11.2)	21.1 (15.8–26.3)	9.1 (7.4–10.7)
China (rural)	n = 383	n = 294	n = 200	n = 121	n = 998
Female (n = 556)	2.1 (0.1–4.1)	5.5 (2.0–9.0)	4.1 (0.6–7.6)	14.7 (6.7–22.7)	5.2 (3.4–7.1)
Male (n = 446)	1.5 (0.0–3.3)	2.3 (0.0–4.9)	16.9 (8.5–25.3)	13.0 (3.3–22.8)	5.6 (3.5–7.7)
Both sexes (n = 1002)	1.8 (0.5–3.2)	4.1 (1.8–6.3)	9.0 (5.1–12.9)	14.0 (7.8–20.3)	5.4 (4.0–6.8)
India (urban)	n = 411	n = 315	n = 142	n = 121	n = 986
Female (n = 571)	15.5 (10.9–20.2)	17.5 (12.0–22.9)	22.7 (13.2–32.1)	19.7 (10.1–29.3)	17.7 (14.5–20.8)
Male (n = 419)	11.6 (6.8–16.3)	14.3 (8.2–20.4)	16.4 (7.5–25.3)	23.1 (11.6–34.5)	14.6 (11.2–17.9)
Both sexes (n = 990)	14.0 (10.6–17.4)	16.0 (12.0–20.1)	19.4 (13.0–25.9)	21.0 (13.8–28.1)	16.3 (14.0–18.7)
India (rural)	n = 331	n = 350	n = 177	n = 141	n = 999
Female (n = 545)	13.0 (8.3–17.8)	17.3 (12.0–22.7)	15.7 (8.1–23.3)	19.1 (9.8–28.5)	15.8 (12.7–18.8)
Male (n = 454)	13.7 (8.0–19.4)	13.0 (7.7–18.3)	15.9 (8.3–23.6)	20.5 (11.3–29.8)	15.0 (11.7–18.3)
Both sexes (n = 999)	13.3 (9.6–17.0)	15.4 (11.7–19.2)	15.8 (10.4–21.2)	19.9 (13.3–26.4)	15.4 (13.2–17.6)
All centers combined	n = 5066	n = 4614	n = 3443	n = 3743	n = 16866
Female (n = 10621)	10.3 (9.3–11.4)	13.1 (11.9–14.4)	18.3 (16.7–19.9)	26.9 (25.2–28.7)	16.4 (15.7–17.2)
Male (n = 6386)	8.1 (6.9–9.4)	10.0 (8.6–11.4)	13.5 (11.7–15.4)	23.2 (21.0–25.4)	13.1 (12.2–13.9)
Both sexes (n = 17007)	9.5 (8.7–10.3)	11.9 (11.0–12.9)	16.5 (15.2–17.7)	25.5 (24.1–26.9)	15.2 (14.6–15.7)

Table 4
Associations between Sociodemographic and Socioeconomic Variables and Modified Frailty Phenotype (Prevalence Ratios and Robust 95% CI) Controlling for Age, Sex, and Education

	Age	Sex (Male vs Female)	Education	Assets	Food Insecurity	Living Alone
Cuba (n = 2944)	1.51 (1.38–1.64)	0.88 (0.73–1.06)	0.90 (0.83–0.99)	0.94 (0.86–1.03)	1.44 (1.06–1.98)	0.71 (0.49–1.02)
Dominican Republic (n = 2011)	1.25 (1.17–1.35)	0.66 (0.54–0.81)	0.96 (0.88–1.05)	0.89 (0.81–0.97)	1.71 (1.39–2.11)	0.81 (0.61–1.08)
Puerto Rico (n = 2009)	1.36 (1.22–1.52)	0.85 (0.67–1.07)	0.88 (0.80–0.96)	0.93 (0.82–1.04)	1.56 (0.83–2.93)	0.75 (0.58–0.98)
Peru (urban) (n = 1381)	1.36 (1.23–1.50)	0.74 (0.59–0.94)	0.87 (0.79–0.97)	0.90 (0.79–1.03)	1.52 (1.04–2.22)	0.59 (0.25–1.38)
Peru (rural) (n = 552)	1.11 (0.94–1.31)	1.09 (0.74–1.60)	0.76 (0.62–0.93)	0.96 (0.80–1.16)	1.35 (0.82–2.20)	0.90 (0.44–1.86)
Venezuela (n = 1904)	1.57 (1.40–1.75)	0.74 (0.57–0.96)	1.04 (0.91–1.20)	0.98 (0.86–1.12)	1.61 (1.07–2.43)	0.39 (0.13–1.17)
Mexico (urban) (n = 1002)	1.19 (1.04–1.36)	1.03 (0.76–1.40)	0.82 (0.72–0.94)	1.05 (0.93–1.20)	0.76 (0.33–1.75)	0.81 (0.49–1.34)
Mexico (rural) (n = 1000)	1.48 (1.29–1.69)	1.06 (0.80–1.41)	0.89 (0.75–1.05)	0.92 (0.80–1.06)	1.19 (0.72–1.96)	0.85 (0.54–1.34)
China (urban) (n = 1160)	1.76 (1.45–2.13)	0.77 (0.50–1.16)	0.84 (0.72–0.98)	1.31 (0.99–1.75)	None exposed	0.55 (0.18–1.66)
China (rural) (n = 1002)	1.89 (1.46–2.44)	1.43 (0.86–2.39)	0.81 (0.59–1.10)	0.94 (0.74–1.19)	No frail exposed	0.38 (0.05–2.66)
India (urban) (n = 1005)	1.16 (1.02–1.33)	0.86 (0.63–1.18)	0.93 (0.82–1.07)	0.66 (0.56–0.77)	2.00 (1.48–2.71)	0.68 (0.29–1.57)
India (rural) (n = 999)	1.10 (0.96–1.26)	1.34 (0.98–1.83)	0.60 (0.45–0.78)	0.79 (0.69–0.90)	1.56 (0.83–2.93)	1.27 (0.84–1.91)
Pooled estimate	1.35 (1.30–1.39)	0.86 (0.80–0.93)	0.89 (0.86–0.93)	0.91 (0.88–0.95)	1.73 (1.55–1.94)	0.80 (0.70–0.91)
I^2	80 (66–88)	58 (21–78)	50 (2–74)	67 (40–82)	57 (13–79)	0 (0–58)

in all sites and statistically significant in almost all sites, effect sizes varied considerably, accounting for high levels of heterogeneity. The effects of physical impairment, stroke and dementia, disability, and dependence were particularly strong in urban and rural China, as were those for depression in rural China and rural India. Excluding China from the meta-analyzed pooled effects reduced heterogeneity among estimates, particularly for physical impairments, stroke, dementia, and dependence.

Associations of Frailty with Healthcare Costs

In the base model, adjusting for age, sex and education, catastrophic out-of-pocket healthcare spending was significantly associated with frailty in most sites, with negligible heterogeneity (aPR 1.75, 95% CI 1.57–1.96, $I^2 = 40\%$) (Table 6). After controlling also for physical, mental, and cognitive morbidities, associations were attenuated but remained statistically significant when pooled, with no heterogeneity (aPR 1.46, 95% CI 1.30–1.64). Associations with total healthcare costs from a public perspective were of similar magnitude for the base model (aPR 1.76, 95% CI 1.56–1.98, $I^2 = 63\%$) and fully adjusted model (aPR 1.51, 95% CI 1.33–1.72, $I^2 = 62\%$), the moderate heterogeneity accounted for mainly by null associations in urban and rural India.

Discussion

In a cross-sectional population-based catchment area survey of rural and urban sites in Latin America, India, and China, the prevalence of frailty according to a modified frailty phenotype, and its 4 indicators, varied substantially after direct standardization for age and sex. Frailty phenotype prevalence was generally higher in sites in Latin America and lower in sites in China. The cross-site variation in the frailty deficits differed for the 4 indicators (weight loss, exhaustion, slow walking speed, and low energy consumption). Despite these measurement anomalies, frailty was quite consistently associated with older age, female sex, lower socioeconomic status, physical impairments, stroke, depression, dementia, disability and dependence, and high healthcare costs. Effect sizes, rather than the direction of the effect did vary considerably among sites, with associations in sites in China often among the outliers.

The main strengths of this study include the large population-based samples with a high proportion of responders and modest missing data. The diverse countries and settings, across 3 continents, allowed us to study and explore variation in the context of a common study protocol, with detailed assessment of physical, mental, and cognitive comorbidities, and healthcare utilization and costs. The main weakness of the study is that we had not included assessment of handgrip strength, and, in common with many other studies, had operationalized some of the other indicators in slightly different ways from those originally suggested.[13] Reviews have noted a tendency for a higher prevalence of frailty when frailty phenotype criteria are modified.[1,4] The prevalences we report, based upon 2 or more of the 4 indicators studied, are the maximum possible if all those meeting exactly 2 other criteria would also have been among the 20% in their site with the weakest hand grip strength. We have, therefore, likely

Table 5
Associations between Health Variables and Modified Frailty Phenotype Controlling for Age, Sex, and Education—aPRs with 95% CIs

	Physical Impairments	Stroke	ICD-10 Depressive Episode	10/66 Dementia	Disability	Dependence
Cuba (n = 2944)	2.19 (1.84–2.60)	2.14 (1.72–2.66)	2.75 (2.19–3.45)	2.31 (1.89–2.83)	1.029 (1.027–1.032)	3.25 (2.69–3.93)
Dominican Republic (n = 2011)	1.92 (1.62–2.27)	1.98 (1.61–2.43)	2.53 (2.13–3.00)	1.78 (1.45–2.17)	1.028 (1.025–1.031)	2.95 (2.48–3.51)
Puerto Rico (n = 2009)	2.37 (1.92–2.94)	2.14 (1.63–2.81)	4.01 (3.10–5.18)	2.09 (1.61–2.71)	1.034 (1.031–1.038)	3.09 (2.45–3.91)
Peru (urban) (n = 1381)	1.94 (1.55–2.44)	2.12 (1.64–2.73)	2.87 (2.29–3.58)	2.02 (1.58–2.59)	1.023 (1.020–1.025)	2.88 (2.28–3.64)
Peru (rural) (n = 552)	0.99 (0.47–2.08)	1.55 (0.68–3.52)	3.30 (1.97–5.52)	1.78 (1.00–3.15)	1.024 (1.017–1.031)	2.80 (1.70–4.59)
Venezuela (n = 1904)	2.69 (2.11–3.42)	2.11 (1.55–2.87)	2.75 (1.98–3.81)	2.11 (1.53–2.90)	1.028 (1.023–1.032)	3.41 (2.61–3.59)
Mexico (urban) (n = 1002)	2.18 (1.61–2.96)	2.77 (1.95–3.92)	2.31 (1.51–3.52)	2.21 (1.52–3.22)	1.025 (1.021–1.030)	2.61 (1.90–3.59)
Mexico (rural) (n = 1000)	1.91 (1.41–2.59)	1.50 (0.92–2.46)	3.22 (2.36–4.39)	1.97 (1.42–2.73)	1.026 (1.022–1.030)	3.30 (2.45–4.43)
China (urban) (n = 1160)	6.03 (4.24–8.59)	5.66 (3.99–8.03)	4.08 (1.42–11.72)	9.46 (6.44–13.90)	1.039 (1.035–1.043)	18.86 (11.73–30.32)
China (rural) (n = 1002)	6.53 (3.03–14.08)	11.73 (6.54–24.83)	16.20 (9.34–28.08)	7.09 (3.79–13.28)	1.049 (1.043–1.056)	12.62 (7.35–21.68)
India (urban) (n = 1005)	2.25 (1.66–3.05)	1.39 (0.56–3.42)	4.13 (3.01–5.68)	2.02 (1.38–2.96)	1.023 (1.018–1.028)	2.61 (1.64–4.16)
India (rural) (n = 999)	2.72 (2.04–2.47)	2.56 (2.10–2.55)	6.03 (4.66–7.82)	1.63 (1.11–2.38)	1.020 (1.014–1.027)	3.38 (2.52–4.53)
Pooled estimate (all sites)	2.29 (2.13–2.47)	2.31 (2.10–2.55)	3.31 (3.04–3.59)	2.23 (2.05–2.43)	1.029 (1.027–1.030)	3.32 (3.07–3.60)
I^2 (%)	78 (64–88)	79 (65–88)	85 (76–91)	86 (77–91)	90 (85–94)	87 (78–92)
Pooled estimate (excluding China)	2.17 (2.01–2.34)	2.09 (1.89–2.31)	3.18 (2.92–3.46)	2.01 (1.84–2.20)	1.027 (1.026–1.028)	3.07 (2.83–3.33)
I^2 (%)	36 (0–70)	0 (0–62)	78 (60–88)	0 (0–62)	76 (56–87)	0 (0–62)

Table 6
Associations between Modified Frailty Phenotype and Catastrophic Out of Pocket Healthcare Spending, and High Total Healthcare Costs—aPRs with 95% CIs

	Catastrophic Out of Pocket Healthcare Spending* (above 90th Centile for Site)		High Total Healthcare Costs† (Above 90th Centile for Site)	
	Base Model‡	Fully Adjusted§	Base Model‡	Fully Adjusted§
Cuba (n = 2944)	1.73 (1.34–2.24)	1.43 (1.10–1.87)	1.53 (1.17–2.01)	1.38 (1.04–1.84)
Dominican Republic (n = 2011)	1.64 (1.22–2.19)	1.47 (1.08–2.01)	1.96 (1.49–2.59)	1.76 (1.30–2.39)
Puerto Rico (n = 2009)	1.96 (1.42–2.69)	1.56 (1.10–2.21)	Data not available	Data not available
Peru (urban) (n = 1381)	1.27 (0.84–1.91)	1.24 (0.82–1.87)	2.10 (1.49–2.96)	1.90 (1.31–2.76)
Peru (rural) (n = 552)	1.50 (0.82–2.75)	1.35 (0.71–2.54)	2.31 (1.34–3.98)	2.06 (1.15–3.68)
Venezuela (n = 1904)	1.78 (1.25–2.54)	1.42 (0.98–2.07)	1.54 (1.09–2.17)	1.23 (0.86–1.74)
Mexico (urban) (n = 1002)	1.83 (1.21–2.77)	1.55 (1.02–2.36)	1.74 (1.13–2.67)	1.55 (1.00–2.41)
Mexico (rural) (n = 1000)	1.68 (1.06–2.68)	1.68 (1.04–2.69)	1.47 (0.93–3.06)	1.42 (0.90–2.25)
China (urban) (n = 1160)	2.59 (1.67–4.01)	1.78 (1.05–3.01)	2.85 (1.92–4.22)	2.17 (1.32–3.57)
China (rural) (n = 1002)	3.43 (2.11–5.57)	2.47 (1.27–4.78)	3.30 (1.67–6.49)	3.72 (1.63–8.46)
India(urban) (n = 1005)	1.05 (0.64–1.74)	0.88 (0.52–1.50)	0.68 (0.37–1.25)	0.48 (0.26–0.91)
India (rural) (n = 999)	1.48 (0.93–2.36)	1.39 (0.80–2.42)	1.09 (0.66–1.79)	1.04 (0.58–1.85)
Pooled estimates (all sites)	1.75 (1.57–1.96)	1.46 (1.30–1.64)	1.76 (1.56–1.98)	1.51 (1.33–1.72)
I^2 (%)	40 (0–70)	0 (0–58)	63 (28–81)	62 (26–80)

*Out of pocket payments for consultations, medications, hospital admissions, and travel.
†Total healthcare costs from a public perspective.
‡Adjusted for age, sex, and education.
§Adjusted for age, sex, education, physical impairments, stroke, dementia, and depression.

somewhat overestimated prevalence. On the other hand, we underestimated the prevalence of the weight indicator, because our question required 4.5 kg weight loss in the last 3 months, as opposed to 1 year for the frailty phenotype criterion. The modification in operationalization, applied consistently across our sites, means that we are much better placed to make valid comparisons between our study sites, than externally, with other studies that have applied different criteria.

The reasons for the large variations in prevalence of frailty phenotype and its indicators among sites are likely to be complex. True variation is one possibility, but other explanations must be considered. The results of our study suggest an ascertainment bias in sites in China toward identification of those only with more marked advanced frailty, given the low prevalence of frailty, the relatively high levels of disability of those identified as frail, and the stronger associations with older age, physical impairments, stroke, and dementia. Research workers, in all sites, were carefully trained to a common protocol with particular focus on the GMS structured clinical interview and physical examinations that provide the data for the frailty indicators. Training videos illustrated the correct assessment procedures. Nevetheless, site-specific variation in administering and rating the questions and assessments cannot be excluded. Cultural variation is a particularly plausible explanation for the very low endorsement in China sites of the weight loss and exhaustion indicators, and the high prevalence of self-reported exhaustion in the Latin America sites. Responses will depend upon normative reference points, and rely upon recall and summarizing of recent experiences; the wording of the questions is important, and sensitive to cultural effects when translated into different languages.[12] Although walking speed is considered an objective test of physical performance, international research has identified cultural, economic, and climatic influences at country level on normal walking speed in healthy adults.[27] Our decision, for the main analyses, to norm walking speed cutpoints for each catchment area is justifiable to the extent that any residual variation between populations, after standardizing for sex and height, is explained by extraneous factors of this nature, and/or variability in test administration. However, inconveniently for cross-cultural research, it removes all variation between populations other than that arising from compositional differences in height and sex, including the effects of any population differences in processes fundamentally related to frailty. For this reason, we also performed sensitivity analyses, in which we applied a population independent cutpoint of 16 seconds to complete the walking task; the cross-site variation in the prevalence of frailty was naturally much greater, and the effect of sex more prominent. However, there was very little effect on associations with other covariates (Supplementary Tables, available online).

As a common metric applied across cultures, the frailty phenotype indicators as assessed in our study are problematic. The correlation of rank orders of indicator prevalence suggests that they are unlikely to meet basic criteria for cross-cultural measurement invariance. A more psychometric approach to the selection of appropriate indicators may be indicated. Culture, individual subjectivity, and extraneous individual characteristics may impact upon questionnaire responses and performance assessment. Indicators based upon relevant biomarkers may reduce these influences on the assessment of the structural and physiological aging-related changes that underpin the frailty phenotype conceptual model.[12] Cross-cultural studies of trajectories of change in these biomarkers with age, and their relationship to adverse outcomes would help to define appropriate thresholds, and to ascertain whether these were population dependent.

These limitations notwithstanding, the construct validity of the modified frailty phenotype used in this study is supported by the pattern of independent associations observed with hypothesized correlates. Our study provides additional strong and quite consistent evidence from a range of middle-income countries supporting associations with low education, less wealth, and food insecurity (a robust indicator of current absolute poverty). The health inequalities that predispose to frailty may begin in early life and operate across the life course.[5] However, direction of causality cannot be determined in a cross-sectional study, and associations with physical impairment, stroke, depression, and dementia are particularly difficult to interpret.[28] Limited evidence from systematic reviews supports a prospective association between depression and the incidence of frailty, perhaps linked to depression induced weakness, underactivity, and fatigue.[28,29] There is also overlap beween frailty indicators and symptoms and sequelae of depression and dementia, for example weight loss and exhaustion. These conditions may affect a person's motivation to apply effort to a physical performance task, or even prevent them from carrying it out. The physical frailty phenotype may, therefore, be to some extent confounded with these conditions.[28]

The findings of our research support the conceptual strength and universal applicability of the frailty phenotype, while also indicating the need for more work on its operationalization into measurements

appropriate for cross-cultural research. The main value of the cross-sectional associations observed in our study is to emphasize that those identified as physically frail according to simple and practical screening approaches are likely to have a high prevalence of multimorbidity, including with mental and cognitive disorders, often giving rise to needs for care. They will include many who are vulnerable by dint of socioeconomic and educational disadvantage, and who face high healthcare costs. They are, therefore, an appropriate target group for multidimensional community and home-based assessment and care,[30] particularly in settings where access to healthcare is inequal.[31] A critical issue in defining frailty for screening purposes is the extent to which interventions may still be effective in those with established disability and needs for care.[12] This question has yet to be answered satisfactorily, particularly in low- and middle-income countries, where little attention has been given to optimizing health and functioning in older adults needing long-term care.

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Appendix. Supplementary Tables

Juan J. Llibre Rodriguez, et al Sensitivity analyses applying an independent criterion (>16 seconds to complete 10-meter walking task) to all sites, for slow walking speed in estimation of frailty phenotype.

Supplementary Table 1
Sociodemographic and Health Characteristics of Participants by Country

	Cuba	Dominican Republic	Puerto Rico	Peru (Urban)	Peru (Rural)	Venezuela	Mexico (Urban)	Mexico (Rural)	China (Urban)	China (Rural)	India (Urban)	India (Rural)	All Centers
n	2944	2011	2009	1381	552	1965	1003	1000	1160	1002	1005	999	17031
Sociodemographic exposure													
Age (y) Mean (SD)	75.1 (7.0) MV = 7	75.3 (7.5)	76.3 (7.4)	75.0 (7.4) MV = 1	74.2 (7.3)	72.3 (6.9) MV = 4	74.5 (6.6) MV = 1	74.1 (6.7)	73.9 (6.2)	72.4 (6.0)	71.3 (6.1) MV = 4	72.6 (5.8)	74.2 (7.0) MV = 17
Female sex (%)	1913 (65.0)	1325 (66.0) MV = 2	1347 (67.3) MV = 7	888 (64.3)	295 (53.4)	1252 (63.7)	666 (66.4)	602 (60.2)	661 (57.0)	556 (55.5)	571 (57.7) MV = 15	545 (54.6)	10621 (62.5) MV = 24
Education level Did not complete primary (%)	730 (24.9) MV = 8	1414 (71.0) MV = 19	461 (23.1)	127 (9.3) MV = 8	225 (41.3) MV = 8	601 (31.2) MV = 40	581 (58.1) MV = 2	837 (83.7)	385 (33.2)	693 (69.2)	662 (66.0) MV = 2	855 (85.6)	7571 (44.7) MV = 97
Living alone	261 (8.9)	254 (12.6)	472 (23.5)	45 (3.3)	44 (8.0)	61 (3.1)	106 (10.6)	112 (11.2)	54 (4.7)	49 (4.9)	44 (4.4)	120 (12.0)	1622 (9.5)
Socioeconomic indication													
Food insecurity (%)	140 (4.8) MV = 11	240 (12.1) MV = 22	32 (1.6) MV = 14	63 (4.6) MV = 16	74 (13.5) MV = 5	111 (6.0) MV = 103	39 (3.9) MV = 4	85 (8.6) MV = 7	0 (0.0)	12 (1.2)	207 (20.8) MV = 10	141 (14.1)	1144 (6.8) MV = 192
Assets Median (interquartile range)	6 (5–6) MV = 8	5 (4–6) MV = 5	7 (6–7)	6 (6–6)	5 (4–6)	6 (6–7)	6 (6–7)	4 (3–6)	5 (5–6) MV = 1	6 (5–7)	4 (3–5) MV = 4	3 (2–4)	4 (3–5) MV = 18
Health status													
3 or more physical impairments	292 (9.9) MV = 6	465 (23.1) MV = 2	429 (21.4) MV = 7	224 (16.2) MV = 1	40 (7.2) MV = 1	489 (25.3) MV = 33	158 (15.8)	185 (18.5)	208 (17.9)	39 (3.9)	41 (4.1) MV = 1	168 (16.8)	2738 (16.1) MV = 51
Any ICD- 10 depressive episode	144 (4.9) MV = 3	278 (13.8)	47 (2.3) MV = 1	87 (6.3) MV = 2	16 (2.9)	107 (5.5) MV = 1	47 (4.7)	45 (4.5)	3 (0.3)	7 (0.7)	39 (3.9)	126 (12.6)	946 (5.5) MV = 7
10/66 dementia (%)	316 (10.8) MV = 13	235 (11.7)	233 (11.7) MV = 11	129 (9.4) MV = 2	36 (6.5)	140 (7.1) MV = 1	86 (8.6)	85 (8.5)	81 (7.0)	56 (5.6)	75 (7.5)	106 (10.6)	1578 (9.3) MV = 27
Past history of stroke	230 (7.8) MV = 9	175 (8.7%) MV = 6	168 (8.4) MV = 8	112 (8.2) MV = 8	20 (3.6) MV = 2	135 (7.0) MV = 45	67 (6.7)	74 (7.4)	109 (9.4)	18 (1.8)	20 (2.0) MV = 1	11 (1.1)	1139 (6.7) MV = 79
Frailty phenotype	613 (20.8) MV = 2	703 (35.0) MV = 5	273 (14.1) MV = 70	355 (25.7) MV = 2	96 (17.4)	244 (12.4) MV = 34	108 (10.8) MV = 4	94 (9.5) MV = 8	89 (7.7)	87 (8.7) MV = 4	123 (12.3) MV = 1	113 (11.3)	2898 (17.1) MV = 130
Dependence (any needs for care)	261 (10.0) MV = 348	237 (11.8) MV = 4	288 (14.4) MV = 7	135 (9.8)	26 (4.7) MV = 2	209 (10.6) MV = 2	114 (11.4)	82 (8.2)	183 (15.8)	54 (5.4)	29 (2.9)	85 (8.5)	1703 (10.2) MV = 381
WHODAS 2.0 disability scale score, mean (SD)	13.4 (20.0) MV = 11	16.5 (20.3) MV = 15	16.6 (22.8) MV = 9	13.1 (20.6) MV = 10	10.4 (14.6) MV = 2	10.7 (16.3) MV = 96	10.0 (17.3) MV = 3	11.1 (19.1) MV = 0	8.1 (20.1) MV = 10	8.0 (20.1) MV = 2	10.5 (154) MV = 4	28.3 (18.3) MV = 0	13.4 (19.7) MV = 162

MV, number of participants with missing values; SD, standard deviation.

Supplementary Table 2
Age and Sex Standardized Prevalence (%) of Frailty and Frailty Indicators, by Site, with Rank Orders

	Weight Loss		Exhaustion		Slow Walking Speed		Low Energy Expenditure		Frailty	
	Prevalence	Rank	Prevalence	Rank	Prevalence	Rank	Prevalence	Rank	Prevalence	Rank
Cuba	5.4 (4.6–6.2)	10	26.9 (25.3–28.5)	9	39.6 (37.9–41.3)	3	9.4 (8.4–10.4)	2	19.7 (18.4–21.1)	3
Dominican Republic	12.9 (11.4–14.4)	5	40.8 (38.7–43.0)	5	55.9 (53.8–58.1)	2	8.7 (7.4–9.9)	5	33.8 (31.8–35.8)	1
Puerto Rico	6.3 (5.2–7.4)	8	32.8 (30.6–34.9)	6	13.4 (11.9–14.9)	7	9.1 (7.9–10.3)	4	12.6 (11.1–14.0)	7
Peru (urban)	15.4 (13.5–17.4)	3	42.4 (39.9–45.0)	3	33.4 (31.0–35.7)	4	5.1 (4.0–6.2)	9	24.8 (22.6–27.0)	2
Peru (rural)	18.3 (15.1–21.7)	1	31.7 (27.7–35.6)	7	25.6 (21.9–29.3)	5	2.1 (0.9–3.4)	12	17.9 (14.6–21.1)	4
Venezuela	13.2 (11.6–14.8)	4	29.9 (27.8–32.0)	8	18.5 (16.7–20.3)	6	6.5 (5.3–7.7)	6	14.2 (12.5–15.8)	5
Mexico (urban)	6.7 (5.1–8.3)	7	47.5 (44.3–50.6)	1	7.7 (6.0–9.3)	12	6.2 (4.7–7.7)	7	10.7 (8.7–12.7)	9
Mexico (rural)	6.1 (4.6–7.6)	9	41.9 (38.8–44.9)	4	8.6 (6.8–10.3)	11	5.6 (4.2–7.0)	8	9.4 (7.6–11.2)	11
China (urban)	1.3 (0.7–2.0)	11	9.2 (7.5–11.0)	11	12.7 (10.8–14.6)	8	9.2 (7.6–10.9)	3	8.2 (6.6–9.8)	12
China (rural)	0.4 (0.0–0.8)	12	2.6 (1.6–3.6)	12	69.3 (66.4–72.1)	1	11.7 (9.5–14.0)	1	10.7 (8.5–12.8)	9
India (urban)	8.9 (7.0–10.9)	6	47.4 (44.1–50.7)	2	10.4 (8.2–12.6)	10	4.1 (2.7–5.5)	10	13.1 (10.8–15.4)	6
India (rural)	18.0 (15.5–20.4)	2	15.6 (13.1–18.1)	10	11.1 (8.9–13.3)	9	2.5 (1.3–3.7)	11	11.9 (9.8–14.1)	8

Supplementary Table 3
Prevalence (%) of Frailty by Site, Age, and Sex (95% CI) according to Modified Frailty Phenotype Criteria

Age Groups, y (n)	65–69	70–74	75–79	80+	All Ages
Cuba	n = 760	n = 789	n = 638	n = 748	n = 2935
Female (n = 1908)	14.8 (11.6–17.9)	20.9 (17.3–24.5)	25.7 (21.4–29.9)	35.9 (31.7–40.1)	24.5 (22.6–26.5)
Male (n = 1027)	6.2 (3.4–9.1)	11.0 (7.4–14.5)	12.2 (8.0–16.5)	28.8 (22.9–34.6)	14.0 (11.9–16.1)
Both sexes (n = 2935)	11.7 (9.4–14.0)	17.2 (14.6–19.9)	20.8 (17.7–24.0)	33.7 (30.3–37.1)	20.8 (19.3–22.3)
Dominican Republic	n = 532	n = 519	n = 397	n = 557	n = 2005
Female (n = 1321)	34.3 (29.3–39.3)	36.1 (30.9–41.3)	44.5 (38.5–50.5)	48.2 (43.2–53.2)	40.9 (38.2–43.6)
Male (n = 684)	16.5 (11.2–21.8)	16.9 (11.7–22.2)	31.1 (23.2–39.0)	34.3 (27.1–41.5)	23.8 (20.6–27.0)
Both sexes (n = 2005)	28.0 (24.1–31.8)	28.9 (25.0–32.8)	40.1 (35.2–44.9)	44.0 (39.8–48.2)	35.0 (32.9–37.2)
Puerto Rico	n = 406	n = 448	n = 475	n = 606	n = 1935
Female (n = 1347)	9.4 (6.1–12.7)	8.1 (5.0–11.2)	15.9 (11.8–19.9)	24.8 (20.5–29.1)	15.3 (13.4–17.2)
Male (n = 655)	9.3 (3.8–14.9)	6.6 (2.6–10.5)	10.0 (5.4–14.6)	17.7 (12.6–22.8)	11.7 (9.2–14.2)
Both sexes (n = 2002)	9.3 (6.5–12.1)	7.6 (5.2–10.0)	13.9 (10.8–17.0)	22.2 (18.9–25.5)	14.1 (12.5–15.6)
Peru (urban)	n = 375	n = 352	n = 297	n = 354	n = 1378
Female (n = 885)	22.4 (17.4–27.5)	25.5 (19.7–31.2)	33.9 (27.2–40.5)	40.8 (34.3–47.4)	30.0 (27.0–22.8)
Male (n = 493)	10.7 (5.0–16.4)	12.9 (7.2–18.6)	16.7 (9.6–23.7)	29.8 (22.3–37.3)	18.1 (14.7–21.4)
Both sexes (n = 1378)	18.9 (14.9–22.9)	20.7 (16.5–25.0)	27.6 (22.5–32.8)	36.4 (31.5–41.4)	25.7 (23.4–28.1)
Peru (rural)	n = 179	n = 141	n = 101	n = 131	n = 552
Female (n = 295)	12.0 (5.6–18.4)	10.8 (4.1–17.6)	34.0 (21.2–46.7)	23.7 (12.9–34.6)	18.0 (13.6–22.4)
Male (n = 257)	16.5 (8.3–24.6)	17.2 (7.5–27.0)	10.4 (1.8–19.1)	20.8 (11.5–30.2)	16.7 (12.1–21.4)
Both sexes (n = 552)	14.0 (8.9–19.0)	13.5 (7.9–19.1)	22.8 (14.7–30.9)	22.1 (14.9–29.4)	17.4 (14.1–20.6)
Venezuela	n = 830	n = 465	n = 341	n = 292	n = 1928
Female (n = 1224)	9.3 (6.8–11.9)	10.0 (6.5–13.5)	18.5 (13.3–23.7)	31.4 (25.0–37.7)	14.9 (12.9–16.9)
Male (n = 704)	4.4 (2.2–6.7)	7.4 (3.6–11.3)	11.2 (5.7–16.7)	22.7 (13.9–31.5)	8.7 (6.6–10.7)
Both sexes (n = 1928)	7.5 (5.7–9.2)	9.0 (6.3–11.7)	15.8 (11.9–19.8)	28.8 (23.5–34.0)	12.6 (11.1–14.1)
Mexico (urban)	n = 245	n = 328	n = 204	n = 221	n = 998
Female (n = 666)	7.6 (3.8–11.4)	10.0 (6.0–14.0)	13.6 (7.6–19.6)	14.9 (9.0–20.8)	11.2 (8.8–13.6)
Male (n = 337)	10.0 (2.4–17.6)	10.2 (4.7–15.6)	10.1 (3.5–16.8)	10.0 (3.4–16.6)	10.1 (6.9–13.3)
Both sexes (n = 1003)	8.2 (4.7–11.6)	10.1 (6.8–13.3)	12.3 (7.7–16.8)	13.1 (8.5–17.7)	10.8 (8.8–12.8)
Mexico (rural)	n = 298	n = 251	n = 217	n = 226	n = 992
Female (n = 602)	4.1 (1.3–6.9)	6.7 (2.7–10.7)	11.5 (6.0–17.0)	18.2 (11.3–25.1)	9.2 (6.9–11.5)
Male (n = 398)	3.9 (0.2–7.7)	9.8 (4.0–15.6)	9.2 (3.1–15.3)	16.2 (9.1–23.2)	9.8 (6.9–12.8)
Both sexes (n = 1000)	4.0 (1.8–6.3)	8.0 (4.6–11.3)	10.6 (6.4–14.8)	17.3 (12.3–22.2)	9.5 (7.6–11.3)
China (urban)	n = 316	n = 362	n = 254	n = 228	n = 1160
Female (n = 661)	4.4 (1.6–7.2)	5.5 (2.3–8.6)	5.8 (1.9–9.8)	23.5 (15.9–31.2)	8.5 (6.4–10.6)
Male (n = 449)	2.7 (0.0–5.7)	5.6 (2.0–9.1)	6.0 (1.7–10.3)	12.8 (6.6–19.1)	6.6 (4.4–8.8)
Both sexes (n = 1160)	3.8 (1.5–6.1)	5.5 (3.2–7.9)	5.9 (3.0–8.8)	18.4 (13.3–23.5)	7.7 (6.1–9.2)
China (rural)	n = 383	n = 294	n = 200	n = 121	n = 998
Female (n = 556)	6.3 (2.9–9.7)	9.8 (5.2–14.3)	9.8 (4.5–15.0)	20.0 (10.9–29.1)	9.9 (7.5–12.4)
Male (n = 446)	2.1 (0.1–4.1)	3.1 (0.1–6.0)	16.9 (8.5–25.3)	23.9 (11.6–36.2)	7.2 (4.8–9.6)
Both sexes (n = 1002)	4.2 (2.2–6.2)	6.8 (4.0–9.6)	12.5 (8.0–17.0)	21.5 (14.1–28.8)	8.7 (7.0–10.4)
India (urban)	n = 411	n = 315	n = 142	n = 121	n = 986
Female (n = 571)	12.6 (8.4–16.8)	12.2 (7.5–16.8)	18.7 (9.8–27.5)	15.2 (6.5–23.8)	13.5 (10.7–16.3)
Male (n = 419)	9.2 (4.9–13.6)	9.5 (4.4–14.6)	13.4 (5.3–21.6)	13.5 (4.2–22.7)	10.5 (7.6–13.4)
Both sexes (n = 990)	11.4 (8.2–14.5)	11.0 (7.6–14.5)	16.0 (10.0–22.0)	14.5 (8.3–20.7)	12.3 (10.1–14.3)
India (rural)	n = 331	n = 350	n = 177	n = 141	n = 999
Female (n = 545)	9.9 (5.7–14.1)	13.3 (8.5–18.0)	11.2 (4.7–17.8)	17.6 (8.6–26.7)	12.3 (9.5–15.1)
Male (n = 454)	9.4 (4.5–14.2)	8.4 (4.1–12.8)	10.2 (3.9–16.6)	15.1 (6.9–23.3)	10.1 (7.4–12.9)
Both sexes (n = 999)	9.7 (6.5–12.9)	11.1 (7.8–14.4)	10.7 (6.2–15.3)	16.3 (10.3–22.4)	11.3 (9.4–13.3)
All centers combined	n = 5066	n = 4614	n = 3443	n = 3743	n = 16866
Female (n = 10621)	13.4 (12.2–14.5)	15.8 (14.5–17.2)	22.2 (20.4–23.9)	31.4 (29.6–33.3)	19.9 (19.1–20.7)
Male (n = 6386)	7.7 (6.5–8.9)	9.7 (8.4–11.1)	13.4 (11.5–15.2)	22.3 (20.1–24.5)	12.6 (11.8–13.4)
Both sexes (n = 17007)	11.3 (10.4–12.2)	13.5 (12.5–14.4)	18.8 (17.5–20.1)	28.0 (26.6–29.5)	17.1 (16.6–17.7)

Supplementary Table 4
Associations between Sociodemographic and Socioeconomic Variables and Modified Frailty Phenotype (Prevalence Ratios and Robust 95% CI) Controlling for Age, Sex, and Education

	Age	Sex (Male vs Female)	Education	Assets	Food Insecurity	Living Alone
Cuba (n = 2944)	1.37 (1.28–1.46)	0.60 (0.51–0.71)	0.92 (0.86–0.98)	0.98 (0.91–1.06)	1.23 (0.92–1.64)	0.80 (0.61–1.05)
Dominican Republic (n = 2011)	1.16 (1.10–1.22)	0.61 (0.49–0.75)	0.93 (0.88–1.00)	0.91 (0.86–0.97)	1.47 (1.27–1.70)	1.00 (0.83–1.20)
Puerto Rico (n = 2009)	1.42 (1.26–1.59)	0.75 (0.58–0.96)	0.90 (0.82–0.99)	0.93 (0.82–1.04)	1.47 (0.75–2.88)	0.74 (0.57–0.98)
Peru (urban) (n = 1381)	1.24 (1.14–1.35)	0.61 (0.49–0.75)	0.88 (0.81–0.97)	0.97 (0.87–1.08)	1.82 (1.38–2.41)	0.52 (0.24–1.12)
Peru (rural) (n = 552)	1.14 (1.00–1.34)	1.03 (0.71–1.50)	0.74 (0.60–0.90)	0.98 (0.82–1.17)	1.31 (0.80–2.14)	1.00 (0.52–1.94)
Venezuela (n = 1904)	1.58 (1.42–1.76)	0.63 (0.48–0.83)	1.03 (0.90–1.18)	0.96 (0.84–1.10)	1.76 (1.20–2.57)	0.51 (0.20–1.29)
Mexico (urban) (n = 1002)	1.12 (0.95–1.32)	0.92 (0.63–1.35)	0.82 (0.70–0.97)	1.09 (0.93–1.27)	0.66 (0.22–1.98)	0.76 (0.39–1.46)
Mexico (rural) (n = 1000)	1.57 (1.31–1.87)	0.99 (0.67–1.45)	0.94 (0.75–1.19)	0.86 (0.72–1.04)	1.20 (0.61–2.36)	0.81 (0.44–1.52)
China (urban) (n = 1160)	1.75 (1.40–2.17)	0.84 (0.53–1.33)	0.83 (0.70–0.99)	1.35 (0.99–1.84)	None exposed	0.44 (0.11–1.71)
China (rural) (n = 1002)	1.66 (1.36–2.03)	0.95 (0.62–1.46)	0.81 (0.62–1.05)	0.93 (0.78–1.11)	2.11 (0.63–7.12)	0.71 (0.23–2.22)
India (urban) (n = 1005)	1.12 (0.96–1.32)	0.80 (0.55–1.16)	0.95 (0.82–1.10)	0.62 (0.51–0.75)	2.00 (1.39–2.88)	0.53 (0.18–1.59)
India (rural) (n = 999)	1.13 (0.96–1.34)	1.27 (0.87–1.85)	0.49 (0.33–0.75)	0.80 (0.68–0.94)	3.26 (2.33–4.56)	1.22 (0.75–2.00)
Pooled estimate	1.28 (1.24–1.32)	0.70 (0.65–0.75)	0.91 (0.88–0.94)	0.93 (0.90–0.96)	2.28 (2.12–2.46)	0.87 (0.77–0.97)
I^2	83 (72–90)	64 (34–81)	46 (0–72)	67 (40–82)	65 (33–82)	0 (0–58)

Supplementary Table 5
Associations between Health Variables and Modified Frailty Phenotype Controlling for Age, Sex, and Education– aPRs with 95% CIs

	Physical Impairments	Stroke	ICD-10 Depressive Episode	10/66 Dementia	Disability	Dependence
Cuba (n = 2944)	2.21 (1.89–2.58)	1.94 (1.62–2.32)	2.42 (2.03–2.89)	1.94 (1.65–2.28)	1.025 (1.023–1.027)	2.37 (2.03–2.78)
Dominican Republic (n = 2011)	1.93 (1.72–2.16)	1.49 (1.27–1.75)	2.03 (1.81–2.28)	1.32 (1.13–1.54)	1.019 (1.017–1.022)	1.92 (1.69–2.19)
Puerto Rico (n = 2009)	3.15 (2.53–3.91)	2.21 (1.66–2.94)	4.06 (3.13–5.27)	2.17 (1.66–2.83)	1.035 (1.031–1.039)	3.30 (2.59–4.21)
Peru (urban) (n = 1381)	2.07 (1.74–2.45)	1.94 (1.56–2.42)	2.48 (2.05–2.99)	1.73 (1.38–2.16)	1.019 (1.017–1.022)	2.34 (1.90–2.88)
Peru (rural) (n = 552)	2.55 (1.67–3.89)	1.50 (0.65–3.44)	3.16 (1.87–5.34)	1.65 (0.93–2.93)	1.023 (1.016–1.031)	2.63 (1.59–4.33)
Venezuela (n = 1904)	1.83 (1.44–2.33)	2.02 (1.48–2.75)	2.68 (1.93–3.73)	2.04 (1.48–2.81)	1.028 (1.023–1.032)	3.35 (2.55–4.40)
Mexico (urban) (n = 1002)	2.09 (1.41–3.11)	3.08 (1.96–4.83)	3.32 (2.12–5.20)	2.29 (1.38–3.78)	1.033 (1.027–1.038)	2.88 (1.93–4.30)
Mexico (rural) (n = 1000)	2.09 (1.41–3.08)	1.94 (1.10–3.43)	3.67 (2.43–5.52)	2.22 (1.42–3.48)	1.034 (1.030–1.039)	5.40 (3.69–7.91)
China (urban) (n = 1160)	2.90 (2.00–4.22)	6.53 (4.41–9.66)	2.46 (0.55–10.92)	13.21 (8.62–20.24)	1.043 (1.039–1.048)	31.77 (17.42–57.93)
China (rural) (n = 1002)	5.25 (3.31–8.34)	7.46 (4.01–13.90)	11.63 (6.85–19.73)	7.85 (5.17–11.93)	1.041 (1.036–1.046)	6.78 (4.50–10.21)
India(urban) (n = 1005)	1.61 (0.83–3.11)	1.90 (0.77–4.69)	4.97 (3.43–7.21)	2.54 (1.66–3.90)	1.027 (1.022–1.033)	3.77 (2.35–6.07)
India (rural) (n = 999)	2.21 (1.54–3.16)	3.50 (1.51–8.12)	6.09 (4.45–8.35)	1.97 (1.29–3.02)	1.025 (1.019–1.032)	3.61 (2.54–5.13)
Pooled estimate (all sites)	2.18 (2.04–2.33)	2.03 (1.86–2.21)	2.70 (2.52–2.91)	2.00 (1.84–2.16)	1.026 (1.025–1.027)	2.68 (2.49–2.88)
I^2 (%)	69 (43–83)	85 (75–91)	89 (83–93)	93 (89–95)	94 (92–96)	92 (88–95)
Pooled estimate (excluding China)	2.12 (1.98–2.27)	1.86 (1.70–2.03)	2.63 (2.45–2.83)	1.76 (1.62–1.92)	1.024 (1.023–1.025)	2.50 (2.33–2.69)
I^2 (%)	52 (1–76)	45 (0–74)	88 (79–93)	61 (23–81)	91 (85–94)	82 (68–90)

Supplementary Table 6
Associations between Modified Frailty Phenotype and Catastrophic Out of Pocket Healthcare Spending, and High Total Healthcare Costs—aPRs with 95% CIs

	Catastrophic Out of Pocket Healthcare Spending* (above 90th Centile for Site)		High Total Healthcare Costs† (above 90th Centile for Site)	
	Base Model‡	Fully Adjusted§	Base Model‡	Fully Adjusted§
Cuba (n = 2944)	1.49 (1.17–1.90)	1.20 (0.92–1.56)	1.42 (1.10–1.83)	1.34 (1.02–1.77)
Dominican Republic (n = 2011)	1.67 (1.26–2.20)	1.36 (1.01–1.84)	1.78 (1.36–2.33)	1.43 (1.07–1.92)
Puerto Rico (n = 2009)	1.88 (1.36–2.60)	1.35 (0.93–1.95)	Data not available	Data not available
Peru (urban) (n = 1381)	1.49 (1.04–2.14)	1.38 (0.93–2.02)	2.16 (1.54–3.02)	1.90 (1.30–2.78)
Peru (rural) (n = 552)	1.45 (0.79–2.67)	1.21 (0.64–2.31)	2.24 (1.29–3.88)	1.84 (1.02–3.31)
Venezuela (n = 1904)	1.79 (1.25–2.55)	1.43 (0.98–2.10)	1.43 (1.00–2.03)	1.16 (0.81–1.65)
Mexico (urban) (n = 1002)	2.24 (1.44–3.46)	1.95 (1.26–3.01)	2.02 (1.27–3.21)	1.76 (1.09–2.83)
Mexico (rural) (n = 1000)	1.81 (1.07–3.07)	1.85 (1.08–3.14)	1.86 (1.12–3.06)	1.74 (1.07–2.81)
China (urban) (n = 1160)	2.76 (1.75–4.34)	2.02 (1.12–3.64)	3.07 (2.05–4.60)	2.47 (1.50–4.09)
China (rural) (n = 1002)	3.08 (1.97–4.82)	1.94 (1.00–3.73)	2.69 (1.44–5.02)	1.87 (0.81–4.32)
India (urban) (n = 1005)	1.26 (0.74–2.13)	1.15 (0.67–1.99)	0.95 (0.52–1.73)	0.71 (0.38–1.33)
India (rural) (n = 999)	1.88 (1.36–2.60)	1.05 (0.56–1.97)	0.84 (0.45–1.56)	0.61 (0.30–1.65)
Pooled estimate (all sites)	1.76 (1.58–1.96)	1.40 (1.24–1.58)	1.75 (1.55–1.97)	1.45 (1.28–1.65)
I^2 (%)	32 (0–66)	0 (0–58)	60 (23–80)	52 (6–76)

*Out of pocket payments for consultations, medications, hospital admissions, and travel.
†Total healthcare costs from a public perspective.
‡Adjusted for age, sex, and education.
§Adjusted for age, sex, education, physical impairments, stroke, dementia, and depression.