

Original Contribution

Perceived Stress and Its Relationship With Chronic Medical Conditions and Multimorbidity Among 229,293 Community-Dwelling Adults in 44 Low- and Middle-Income Countries

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In this study, we assessed the association of chronic medical conditions and multimorbidity with perceived stress among community-dwelling adults in 44 low- and middle-income countries. Data from the World Health Survey (2002–2004), including 229,293 adults, were analyzed. A perceived stress score (range, 0 (lowest stress)–100 (highest stress)) was computed on the basis of 2 questions from the Perceived Stress Scale. Eleven chronic conditions were assessed. Multivariable linear regression analyses were conducted to explore the associations. All chronic conditions were associated with significantly higher mean perceived stress scores, with the exception of edentulism. The associations were particularly strong for depression ($\beta = 14.71$, 95% confidence interval (CI): 13.68, 15.74), visual impairment ($\beta = 10.66$, 95% CI: 8.09, 13.23), and schizophrenia ($\beta = 9.98$, 95% CI: 7.71, 12.24). Compared with no chronic conditions, the β coefficients for perceived stress with the presence of 1, 2, 3, and ≥ 4 chronic conditions were 5.58 (95% CI: 4.94, 6.23), 9.58 (95% CI: 8.67, 10.49), 14.15 (95% CI: 12.63, 15.67), and 20.17 (95% CI: 18.29, 22.05), respectively. The associations with perceived stress were significantly stronger among the poorest individuals for arthritis, asthma, diabetes, edentulism, and ≥ 4 chronic conditions. Our data suggest that a range of chronic conditions and multimorbidity are associated with greatly increased perceived stress among people in low- and middle-income countries, and that the poorest persons may be a particularly vulnerable group.

chronic conditions; low- and middle-income countries; multimorbidity; perceived stress; poverty

Abbreviations: CI, confidence interval; LMICs, low- and middle-income countries.

Multimorbidity is typically defined as the presence of 2 or more chronic medical conditions, and recent estimates have suggested that up to 72% of the general population has multimorbidity (1). The high prevalence of multimorbidity is predominantly attributed to the growing incidence of chronic conditions (2) coupled with increasing life expectancy, and it is without a doubt one of the most significant challenges faced by health-care providers and policy-makers (3, 4). Multimorbidity is associated with increased use of health-care services (5), a lower quality of life (6), and a higher risk of premature mortality (7). Large-scale studies from single countries have demonstrated a clear socioeconomic pattern, with a higher prevalence of multimorbidity being observed in socioeconomically vulnerable settings (4).

This global evolving disease burden, along with a growing understanding of multimorbidity and its risk factors, requires the development of systems that integrate all aspects of health care, including the management of the psychological burden of chronic diseases (8), such as perceived stress. Perceived stress can be defined as feelings or thoughts people have about how much stress they are under, as well as feelings about the uncontrollability and unpredictability of one's life, how often one has to deal with irritating hassles, how much change is occurring in one's life, and confidence in one's ability to deal with problems or difficulties (9). Chronic conditions may cause stress as a consequence of their symptoms, long-term prognosis, and other related issues such as treatment and its costs. Among people with chronic

conditions, such as asthma, arthritis, or diabetes, stress can intensify the effect of illness by increasing pain, functional limitations, and disability and decreasing adherence to medical treatment protocols, all of which may lead to psychological distress (i.e., a state of emotional suffering characterized by symptoms of depression and anxiety (10)), poorer health outcomes, and increased risks of severe and chronic psychiatric and somatic complications (11–13). Moreover, perceived stress contributes significantly to higher mortality rates in a dose-response pattern (14), with even more stress-associated deaths being evident among people with multimorbidity (15). These findings clearly suggest that people with multimorbidity are a particularly susceptible group for increased perceived stress.

However, to date, most of the research investigating associations between stress and chronic conditions or multimorbidity has focused on stress within the context of psychological distress in high-income countries. For example, in a US study including 110,455 adult participants, Swartz et al. (16) found that more psychological distress and mental illness were associated with higher probabilities of developing many chronic medical conditions but not multimorbidity, although the association of psychological distress with mental illness and multimorbidity strengthened as the number of chronic medical conditions increased. To the best of our knowledge, there have been no multinational representative population studies investigating associations between perceived stress, chronic conditions, and multimorbidity. In addition, there is an absence of such data from low- and middle-income countries (LMICs). This is an important research gap given the rapid increase in noncommunicable diseases, mainly due to changes in lifestyles in these countries (17). Furthermore, the associations between chronic conditions or multimorbidity and perceived stress may differ in LMICs due to different disease profiles, limited treatment options and suboptimal treatment, or the high costs associated with treatment, which may even lead to catastrophic expenditures, especially in poor households (18).

Given the aforementioned gaps within the literature, we set out to assess whether chronic conditions and multimorbidity were associated with higher perceived stress levels among community-dwelling adults in 44 LMICs and to assess whether this association was stronger among poorer individuals. We hypothesized that higher stress scores would be associated with each chronic condition as well as with higher numbers of chronic conditions, and that these associations would be stronger among the poorest people.

METHODS

Procedure

The World Health Survey was a cross-sectional, community-based study undertaken in 2002–2004 in 70 countries worldwide. Single-stage random sampling and stratified multistage random cluster sampling were conducted in 10 countries and 60 countries, respectively. Stratification was conducted by sex, age, and residential area (rural/urban). Enumeration areas and households were also used as stratification units in the majority of countries. The detailed methodology of the survey has been described elsewhere (19). Briefly, persons aged ≥ 18 years with a valid home address were eligible to participate. Through the use of Kish tables, all members of a household had equal probabilities of being selected.

The same questionnaire was used for data collection in all countries, with some countries using a shorter version. The individual response rate (ratio of completed interviews among selected respondents after excluding ineligible respondents from the denominator) ranged from 63% (Israel) to 99% (Philippines) (20). Ethical approval for conducting this survey was obtained from ethical boards at each study site. Sampling weights were generated to adjust for the population distribution reported by the United Nations Statistical Division, and final poststratification corrections were made to the sampling weights to account for nonresponse. Informed consent was obtained from all participants.

Chronic medical conditions

We assessed all chronic conditions for which information was available in the World Health Survey (i.e., 11 chronic conditions). Arthritis, asthma, and diabetes were based on self-reported lifetime diagnosis. For angina, in addition to a self-reported diagnosis, a symptom-based diagnosis based on the Rose questionnaire was also used (21). Chronic back pain was defined as having had back pain (including disc problems) every day during the last 30 days. Visual impairment was defined as having extreme difficulty in seeing and recognizing a person that one knows from across the road (i.e., from a distance about 20 m) (22). A validity study showed that this response is likely to correspond to World Health Organization definitions of visual impairment (23). The participant was considered to have hearing problems if the interviewer observed this condition at the end of the survey. Edentulism was assessed by means of the question, “Have you lost all your natural teeth?”. Persons who responded affirmatively were considered to have edentulism. A tuberculosis diagnosis was based on past-12-month symptoms and was defined as: 1) having had a cough that lasted for 3 weeks or longer and 2) having had blood in phlegm or having coughed up blood (23). Depression was defined using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, algorithm and was based on duration and persistence of depressive symptoms in the past 12 months, using the same algorithms as in previous World Health Survey publications (24, 25). Finally, participants were asked whether they had ever been diagnosed with schizophrenia or psychosis. Those who answered affirmatively were considered to have schizophrenia. While this question did not refer specifically to schizophrenia, for the sake of brevity, we use the term “schizophrenia” throughout the text. We also calculated the total number of these conditions and classified it as 0, 1, 2, 3, or ≥ 4 .

Perceived stress

In accordance with a previous World Health Survey publication (26), we assessed perceived stress in the last month with the use of 2 questions taken from the Perceived Stress Scale (27). The Perceived Stress Scale is widely used to measure stress sensitivity. The 2 questions from the scale have been validated and applied in many settings worldwide, including LMICs (26). The questions asked in the scale include: “How often have you felt that you were unable to control the important things in your life?” and “How often have you found that you could not cope with all the things that you had to do?”. The answer options were never (score = 1), almost never (score = 2), sometimes (score = 3), fairly often (score = 4), and very often (score = 5). Since these answer

options were on an ordered categorical scale, as in previous World Health Survey studies, we conducted factor analysis with polychoric correlations to incorporate the covariance structure of the answers provided for individual questions measuring a similar construct (28). The principal component method was used for factor extraction, while factor scores were obtained using the regression scoring method. These factor scores were later converted to scores ranging from 0 to 100 (29), with higher values representing higher levels of perceived stress. The mean score on this scale was 36.0 (standard deviation, 27.4; skewness, 0.38; kurtosis, 2.34).

Other variables

Data on sex, age (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, or ≥80 years), highest level of education achieved (no formal education, primary education, completion of secondary or high school, or completion of tertiary education), and countrywise individual-level wealth quintiles were also used in the analysis. The wealth quintiles were created using principal component analysis based on 15–20 assets, including country-specific items for some countries.

Statistical analysis

Data were publicly available for 69 countries. The data were nationally representative for all countries except China, Comoros, the Republic of Congo, Ivory Coast, India, and Russia. Countries without any sampling information (10 countries—Austria, Belgium, Denmark, Germany, Greece, Guatemala, Italy, the Netherlands, Slovenia, and the United Kingdom) were excluded. Furthermore, 10 high-income countries (Finland, France, Ireland, Israel, Luxembourg, Norway, Portugal, Sweden, Spain, and United Arab Emirates) were excluded because the focus of our study was on LMICs. Of the remaining LMICs, Brazil, Hungary, Turkey, and Zimbabwe were omitted because information on perceived stress was not collected. Furthermore, Georgia was also excluded due to a negative correlation between the 2 questions on perceived stress (26). Thus, the final analytical sample consisted of 229,293 people from a total of 44 countries. According to the World Bank classification in 2003, these countries corresponded to 20 low-income countries and 24 middle-income countries.

The statistical analysis was performed with Stata 14.1 (Stata-Corp LP, College Station, Texas). Information on perceived stress was missing from 7.2% of the sample, while data on chronic conditions were missing from 5.6% (angina) to 18.4% (tuberculosis). We conducted multiple imputation of missing values using the *mi* commands in Stata by means of chained equations (20 imputations). The variables included in the imputation model were the outcome and all other covariates. The difference in mean perceived stress score according to the sample characteristic was tested by Student's *t* test and 1-way analysis of variance for variables with 2 categories and variables with 3 or more categories, respectively. We conducted multivariable linear regression analysis to assess the association between each of the 11 chronic conditions or number of chronic conditions (exposure variables) and perceived stress score (outcome), while adjusting for sex, age, education, individual-level wealth, and country. For the analyses on the individual chronic conditions, we also adjusted for the presence of other illnesses in an attempt to obtain estimates that were

less likely to be confounded by comorbid conditions. The variable on other illnesses was a binary variable (yes/no) and included information on whether the individual had any other chronic conditions, apart from the chronic condition in question. A total of 12 separate models were constructed: 1 for each of the 11 chronic conditions and 1 for number of chronic conditions. In order to assess whether there was an interaction effect by individual-level poverty in the association between chronic conditions or number of chronic conditions and perceived stress, we also conducted interaction analysis by including an interaction term in the models (chronic condition (or total number of chronic conditions) × poverty (defined as the lowest individual-level wealth quintile)). These analyses were adjusted for sex, age, education, other illnesses, and country.

All variables were included in the models as categorical variables, with the exception of the perceived stress score (continuous variable). We adjusted for country by including dummy variables in the models, as in previous World Health Survey publications (28, 29). The sample weighting and the complex study design were taken into account in all analyses with the use of the *svy* command in Stata, which uses the Taylor linearization method for robust variance estimation. We also conducted sensitivity analysis based on complete cases. The results obtained from the imputed and nonimputed data sets were very similar (data not shown). Results from the linear regression models are presented as β coefficients with 95% confidence intervals. The level of statistical significance was set at $P < 0.05$.

RESULTS

The overall mean age of the analytical sample was 38.3 years, and 50.8% of the sample was female (Table 1). The full list of the included countries and their sample sizes can be found in Appendix Table 1. The prevalence of ≥2 chronic conditions was 15.0%, with angina (15.1%) and arthritis (13.5%) being the most common chronic conditions. Female sex, older age, and lower levels of education and individual-level wealth were significantly associated with higher perceived stress scores, and so were all of the 11 chronic conditions and higher numbers of chronic conditions. Higher stress scores were associated with an increase in the prevalence of all 11 chronic conditions and multimorbidity. Between perceived stress scores of <20 and 80–100, the prevalence of multimorbidity increased from 7.8% to 33.8% (see Web Figure 1, available at <https://academic.oup.com/aje>). Perceived stress increased with incremental numbers of chronic conditions; we observed a clear pattern of heightened perceived stress scores associated with lower levels of individual wealth, regardless of the number of chronic conditions, especially when the lowest and highest levels of individual wealth were compared (Figure 1).

The association between chronic conditions and perceived stress estimated by multivariable linear regression is illustrated in Figure 2. Compared with persons without the condition, the mean perceived stress score was much higher for depression ($\beta = 14.71$, 95% confidence interval (CI): 13.68, 15.74), visual impairment ($\beta = 10.66$, 95% CI: 8.09, 13.23), and schizophrenia ($\beta = 9.98$, 95% CI: 7.71, 12.24). In comparison with having no chronic conditions, having 1, 2, 3, and ≥4 chronic conditions was associated with mean perceived stress scores that were higher by 5.58 (95% CI: 4.94, 6.23; $P < 0.0001$), 9.58 (95% CI: 8.67,

Table 1. Characteristics of the Study Sample and Mean Perceived Stress Scores by Characteristic, World Health Survey, 2002–2004^a

Characteristic	Unweighted No. of Participants (n = 229,293)	Column %	Perceived Stress Score ^b		P Value ^c
			Mean	95% CI	
Sex					<00001
Male	99,032	49.2	34.7	34.1, 35.2	
Female	121,765	50.8	37.1	36.6, 37.6	
Missing data	8,496				
Age, years					<0.0001
18–29	67,017	37.1	33.1	32.5, 33.7	
30–39	54,332	21.6	35.7	35.1, 36.3	
40–49	40,328	16.9	35.7	35.0, 36.4	
50–59	26,049	11.5	38.3	37.4, 39.2	
60–69	18,248	7.6	40.8	39.7, 41.8	
70–79	10,778	4.2	43.6	42.2, 45.0	
≥80	3,861	1.2	46.7	44.5, 48.9	
Missing data	8,680				
Education					<0.0001
No formal education	51,193	28.7	44.4	43.7, 45.1	
Primary school or less	71,506	29.6	36.8	36.2, 37.4	
Secondary schooling completed	81,123	32.4	29.1	28.5, 29.6	
Tertiary schooling completed	16,087	9.3	30.4	29.2, 31.7	
Missing data	9,384				
Wealth quintile (individual level)					<0.0001
1 (Poorest)	48,930	20.4	39.2	38.3, 40.0	
2	43,685	20.1	37.7	37.0, 38.4	
3	40,307	19.9	36.1	35.4, 36.9	
4	38,230	19.9	34.5	33.8, 35.3	
5 (Richest)	36,175	19.8	31.8	31.0, 32.6	
Missing data	21,966				
Chronic medical conditions					
Angina					<0.0001
No	187,467	84.9	34.2	33.7, 34.7	
Yes	28,919	15.1	45.4	44.6, 46.1	
Missing data	12,907				
Arthritis					<0.0001
No	187,721	86.5	34.5	34.1, 35.0	
Yes	27,284	13.5	44.5	43.7, 45.3	
Missing data	14,288				
Asthma					<0.0001
No	205,798	95.7	35.5	35.1, 36.0	
Yes	9,531	4.3	43.4	42.3, 44.6	
Missing data	13,964				
Chronic back pain					<0.0001
No	188,731	94.0	35.1	34.6, 35.5	
Yes	10,525	6.0	48.8	47.5, 50.1	
Missing data	30,037				

Table continues

Table 1. Continued

Characteristic	Unweighted No. of Participants (n = 229,293)	Column %	Perceived Stress Score ^b		P Value ^c
			Mean	95% CI	
Depression					<0.0001
No	200,977	93.7	34.6	34.1, 35.0	
Yes	12,982	6.3	55.5	54.5, 56.5	
Missing data	15,334				
Diabetes					<0.0001
No	193,410	97.3	35.7	35.3, 36.1	
Yes	5,973	2.7	41.8	40.2, 43.5	
Missing data	29,910				
Edentulism					<0.0001
No	181,212	95.0	35.7	35.2, 36.1	
Yes	11,917	5.0	39.9	38.7, 41.1	
Missing data	36,164				
Hearing problems					<0.0001
No	208,841	96.5	35.5	35.0, 35.9	
Yes	7,084	3.5	47.4	44.9, 49.8	
Missing data	13,368				
Schizophrenia					<0.0001
No	211,934	99.0	35.7	35.3, 36.2	
Yes	2,248	1.0	51.3	48.9, 53.6	
Missing data	15,111				
Tuberculosis					<0.0001
No	183,938	98.3	35.7	35.3, 36.1	
Yes	3,129	1.7	47.5	45.5, 49.5	
Missing data	42,226				
Visual impairment					<0.0001
No	204,300	98.7	35.6	35.2, 36.0	
Yes	2,254	1.3	56.2	53.3, 59.1	
Missing data	22,739				
No. of chronic conditions					<0.0001
0	123,935	63.5	31.6	31.1, 32.1	
1	42,978	21.5	39.8	39.1, 40.4	
2	17,298	9.2	45.5	44.7, 46.4	
3	6,777	3.7	50.6	49.0, 52.1	
≥4	3,443	2.1	57.1	55.3, 59.0	
Missing data	34,862				

Abbreviation: CI, confidence interval.

^a All estimates were based on a weighted sample, except for the numbers of participants.

^b The perceived stress score ranged from 0 to 100, with higher scores indicating higher levels of perceived stress.

^c The difference in the perceived stress score according to sample characteristic was tested by means of Student's *t* test and 1-way analysis of variance for characteristics with 2 categories and characteristics with more than 2 categories, respectively.

10.49; $P < 0.0001$), 14.15 (95% CI: 12.63, 15.67; $P < 0.0001$), and 20.17 (95% CI: 18.29, 22.05; $P < 0.0001$) points, respectively (data shown only in text). The effect of interaction between individual-level poverty and chronic conditions or number of chronic conditions on perceived stress is shown in Table 2. The

associations between arthritis, asthma, diabetes, or edentulism and perceived stress were significantly stronger among persons in the poorest individual-level wealth quintile than in wealthier persons. This was also the case for those who had 4 or more chronic conditions.

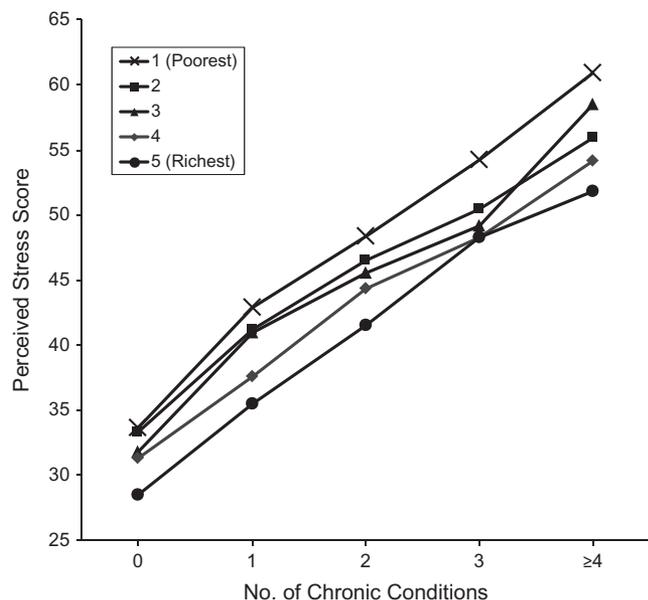


Figure 1. Perceived stress score according to number of chronic medical conditions and quintile of individual-level wealth, World Health Survey, 2002–2004. Estimates were based on a weighted sample. The perceived stress score ranged from 0 to 100, with higher scores indicating higher levels of perceived stress.

DISCUSSION

General findings

To the best of our knowledge, the current study is the first large-scale ($n = 229,293$), multinational (44 LMICs) analysis to show that chronic medical conditions and multimorbidity are associated with higher levels of perceived stress. Interestingly, compared with persons who were not in the poorest quintile, this association was significantly stronger among the poorest individuals for arthritis, asthma, diabetes, edentulism, and ≥ 4 chronic conditions. In addition, higher levels of perceived stress were associated with greater prevalence of chronic conditions and multimorbidity; between perceived stress scores of < 20 and 80 – 100 , the prevalence of ≥ 2 chronic conditions increased from 7.8% to 33.8% . Relatively few large-scale studies have investigated the relationship between perceived stress and multimorbidity. Nonetheless, a recent large-scale study in Denmark (15) demonstrated that perceived stress was associated with an excess number of deaths among people with multimorbidity. Specifically, the authors noted that mortality hazard ratios (highest stress quintile vs. lowest) were 1.51 (95% CI: $1.25, 1.84$) among persons without multimorbidity, 1.39 (95% CI: $1.18, 1.64$) among those with 2 or 3 conditions, and 1.43 (95% CI: $1.18, 1.73$) among those with 4 or more conditions, even after adjustment for lifestyle factors and socioeconomic status. To our knowledge, there have been no specific representative multinational studies investigating perceived stress and multimorbidity in the Western world or LMICs.

Research on the exact mechanisms underlying associations between perceived stress and several chronic conditions, particularly multimorbidity, is in its infancy, and it is important

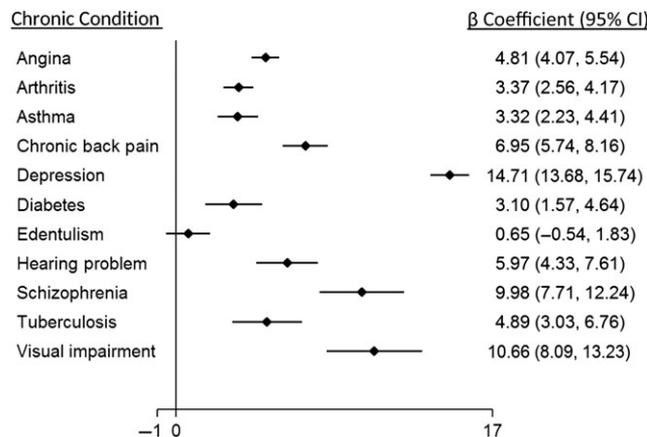


Figure 2. Associations between chronic medical conditions and perceived stress (outcome) as estimated by multivariable linear regression, World Health Survey, 2002–2004. All estimates show the difference in the mean perceived stress score (β) between persons with the specified condition and those without it, and were adjusted for sex, age, education, individual-level wealth, other illnesses, and country. Each chronic condition was assessed individually in a separate model. The perceived stress score ranged from 0 to 100, with higher scores indicating higher levels of perceived stress. $P < 0.001$ for all associations except edentulism ($P = 0.2846$). CI, confidence interval.

that future work attempt to better understand these relationships. There are several hypotheses that may explain these findings. First, the association between higher levels of perceived stress and some chronic conditions, as well as ≥ 4 chronic conditions, was strongest among the poorest people. It may be hypothesized that the poorest subgroup is least able to pay for treatment. Health-related expenditures impoverish an estimated 100 million people in LMICs each year (30). An estimated 50 million more suffer from catastrophic health expenditures, commonly defined as expenditures involving 10% or more of income (30). Moreover, poorer persons spend a higher proportion of their income on health care, which might induce (financial) perceived stress (31), particularly following catastrophic expenditures (32) or high out-of-pocket expenditures in areas with no health insurance (32), although this is not universal in all LMICs (33). Furthermore, treatments costs may increase the likelihood that patients in LMICs forgo needed treatment, particularly when there is a need for multiple medications, which are often prescribed to treat chronic diseases and multimorbidity (34). Untreated chronic conditions may increase the severity of the chronic condition or lead to further complications, which may increase levels of perceived stress. For example, untreated diabetes increases the risk for complications such as neuropathy, retinopathy, and nephropathy, which may further increase the patient's disability level and resultant perceived stress. For edentulism, poorer people may be experiencing more stress due to suboptimal treatment (e.g., lack of dentures or implants). Next, it is also possible that stress precedes the development of chronic conditions. Chronic stress is known to lead to neuroendocrine dysregulation of the hypothalamic-pituitary-adrenal axis, which in turn may cause changes in the immune and inflammation systems and consequently lead to the development of chronic conditions and multimorbidity (35). These processes have been conceptualized as allostatic load (36, 37). Even subclinical perceived stress has been

Table 2. Effect of Interaction Between Individual-Level Poverty^a and Chronic Medical Conditions or Number of Chronic Conditions on Perceived Stress^b, World Health Survey, 2002–2004^c

Chronic Condition	Difference in Perceived Stress Score ^d		P Value	R ²
	β	95% CI		
Angina				0.19
Main effect	4.72	3.84, 5.59	<0.0001	
+ Poverty ^e	2.04	1.11, 2.97	<0.0001	
Interaction ^f	0.80	-0.80, 2.41	0.3263	
Arthritis				0.19
Main effect	2.99	2.09, 3.89	<0.0001	
+ Poverty	1.94	1.04, 2.84	<0.0001	
Interaction	1.86	0.23, 3.49	0.0254	
Asthma				0.19
Main effect	2.73	1.51, 3.94	<0.0001	
+ Poverty	2.14	1.27, 3.01	<0.0001	
Interaction	2.58	0.31, 4.84	0.0261	
Chronic back pain				0.19
Main effect	6.82	5.50, 8.15	<0.0001	
+ Poverty	2.21	1.36, 3.07	<0.0001	
Interaction	0.52	-2.30, 3.34	0.7153	
Diabetes				0.19
Main effect	2.16	0.45, 3.88	0.0134	
+ Poverty	2.18	1.32, 3.03	<0.0001	
Interaction	4.20	0.73, 7.66	0.0179	
Depression				0.20
Main effect	14.60	13.41, 15.79	<0.0001	
+ Poverty	2.12	1.25, 2.98	<0.0001	
Interaction	0.76	-1.41, 2.93	0.4894	
Edentulism				0.19
Main effect	-0.17	-1.53, 1.19	0.8065	
+ Poverty	2.05	1.17, 2.94	<0.0001	
Interaction	3.36	0.78, 5.94	0.0109	
Hearing problems				0.19
Main effect	5.34	3.45, 7.23	<0.0001	
+ Poverty	2.11	1.24, 2.98	<0.0001	
Interaction	2.21	-1.39, 5.82	0.2276	
Schizophrenia				0.19
Main effect	8.86	6.13, 11.59	<0.0001	
+ Poverty	2.20	1.34, 3.05	<0.0001	
Interaction	4.38	-0.29, 9.05	0.0657	
Tuberculosis				0.19
Main effect	4.15	1.76, 6.53	0.0007	
+ Poverty	2.18	1.33, 3.03	<0.0001	
Interaction	2.75	-0.88, 6.38	0.1370	
Visual impairment				0.19
Main effect	9.35	6.17, 12.53	<0.0001	
+ Poverty	2.16	1.29, 3.03	<0.0001	
Interaction	4.20	-0.70, 9.10	0.0928	

Table continues

Table 2. Continued

Chronic Condition	Difference in Perceived Stress Score ^d		P Value	R ²
	β	95% CI		
No. of chronic conditions				
Main effect				0.19
0	1.00			
1	5.38	4.63, 6.12	<0.0001	
2	9.39	8.35, 10.44	<0.0001	
3	13.46	11.79, 15.13	<0.0001	
≥ 4	19.01	16.67, 21.35	<0.0001	
+ Poverty	1.45	0.35, 2.56	0.0101	
Interaction				
1	1.30	-0.17, 2.78	0.0826	
2	1.15	-0.83, 3.14	0.2552	
3	2.98	-0.61, 6.57	0.1029	
≥ 4	4.45	0.69, 8.21	0.0206	

Abbreviation: CI, confidence interval.

^a Poverty was defined as being in the lowest countrywise individual-level wealth quintile.^b The perceived stress score ranged from 0 to 100, with higher scores indicating higher levels of perceived stress.^c All estimates were adjusted for sex, age, education, other illnesses, and country.^d Difference in the mean perceived stress score between persons with the specified condition and those without it.^e Addition of poverty to the model.^f Interaction with poverty.

linked to changes in cortisol levels, immune system response, and cortical reactivity (38). There is also evidence to suggest that perceived stress is a core feature of several mental illnesses. For instance, the relationship between perceived stress and depression has been observed previously (39). One should therefore consider that the strong relationship between depression and stress may in part be accounted for by some overlap in core symptoms (39). Finally, perceived stress may also lead to unhealthy behaviors, such as smoking, alcohol consumption, unhealthy dietary choices (40, 41), and a sedentary lifestyle (42), which might also be implicated in the development of chronic conditions. Notably, it was not possible to adjust for some of these important lifestyle factors, which may have influenced the relationships that we observed between stress and chronic conditions and multimorbidity. Therefore, additional research will be required to better understand the impact of lifestyle on the trajectory of the stress–chronic condition relationship.

Practical implications and future research

Our data indicate that existing health-care models need to adapt to the increasing rates of multimorbidity and chronic conditions, particularly among the poor. This is especially relevant in LMICs, where all levels of care must be carefully planned in the context of economic restraints. The Innovative Care for Chronic Conditions framework developed by the World

Health Organization provides a road map for coping with chronic conditions in developing countries, but there is still a need to fully incorporate multimorbidity and the assessment of perceived stress within primary and mental health care settings (43). First of all, there is a clear need to increase awareness of the importance of considering chronic conditions and perceived stress among primary and mental health care providers in LMICs, particularly in socioeconomically vulnerable groups (i.e., the poorest). Future research could explore the efficacy and effectiveness of a dual strategy in which both a smaller group of master trainers/supervisors and researchers and a larger group of practitioners (e.g., nurses, occupational therapists) trained in the basics of cognitive behavioral coping strategies and who are supported by regular supervision are involved. This method has been successfully employed for treating depression and psychosis in LMICs in clinical trials (44, 45). Within this stepped-care approach, patients start with self-help. Then, if they do not recover, they progress to working with manualized approaches from a nonspecialist worker (e.g., nurses, occupational therapists) who is supervised, and they are referred to a specialist (e.g., a psychologist or psychiatrist) only if there is no improvement as a result of this intervention. However, as stated, careful consideration of which intervention models would be most effective and further research into the therapeutic effectiveness of this stepped-care approach is essential to determine whether there is a need to further develop this therapy for LMICs. Outcomes research including levels of perceived stress but also more distal outcomes, such as the risk of chronic conditions and multimorbidity, could usefully compare such an approach with more indigenous models of alleviating perceived stress. Longitudinal research is also needed to establish causal associations between common chronic disorders, multimorbidity, perceived stress, and poverty; such studies may help identify the specific factors that are associated with the risk of chronic disorders and multimorbidity, and conversely, the factors that help reduce the risk in persons who face severe economic or social adversity. One should note that the participants included in our sample were generally quite young (mean age = 38.3 years). It is evident that chronic conditions and multimorbidity typically increase with age, in LMICs as well as in other countries (46). Therefore, our finding of a strong relationship between stress and chronic conditions among younger adults in LMICs is concerning. It might be hypothesized that this relationship between stress and chronic conditions becomes stronger with increasing age in LMICs, and future research is required to explore this in the context of LMICs.

Strengths and limitations

Strengths of the present study include the use of a very large multinational data set focused on LMICs, countries that are underrepresented in the existing research literature. The primary limitation was the use of cross-sectional data, which made it difficult to infer the direction of causality between poverty, heightened perceived stress, and higher risks of chronic conditions and multimorbidity. Whereas it is plausible to speculate that the cross-sectional relationships can be best interpreted in the context of poverty's being a risk factor for increased perceived stress and consequently chronic disorders and multimorbidity, reverse causality can be a consideration, because chronic conditions and multimorbidity are known to produce disability, stress, and

increased health-care costs. In any event, it is more likely that poverty, stress, and chronic conditions and multimorbidity interact with one another in setting up, among vulnerable individuals, a vicious cycle. Second, the self-reported measurement of all chronic conditions and multimorbidity may have led to a bias in the diagnosis of the medical conditions, particularly among older subjects. In addition, while we included 11 medical conditions (all that were available in the data set), other medical conditions which are frequently reported in multimorbidity indices (47), such as stroke and hypertension, may have been present and not identified in the study. Third, it is likely that the sample included in our study suffered from an element of selection bias, in that people with more severe stress or mental or physical health problems may have been less likely to participate. Therefore, our study findings may actually represent underestimates of the associations observed. Therefore, in future research, investigators should attempt to include people with more pronounced stress and worse health. Fourth, due to lack of information, we were unable to adjust for factors which have been associated with both stress sensitivity and chronic conditions, such as previously experienced trauma (48). Thus, residual confounding may exist. Fifth, for the purposes of this study, we used an abridged version of the Perceived Stress Scale, which may mean that there is some variation in the validity and reliability of our findings in comparison with the original complete scale, and there may also be some psychometric variation across cultures.

In conclusion, our data demonstrate that perceived stress is high among people with chronic conditions and multimorbidity in LMICs. Since perceived stress and chronic conditions are collectively associated with worse health outcomes (including increased mortality rates), there is a pressing need to address this issue. Although this may be related to the symptoms of the chronic conditions, the fact that the association was stronger among the poorest individuals points to the possibility that financial factors may also play a role. This may imply that a multidisciplinary approach involving social workers, psychologists, physiotherapists, and physicians is needed to decrease stress levels among persons with chronic conditions, and this may ultimately lead to better clinical outcomes. Further studies designed to understand the underlying causes of stress in chronic conditions are warranted.

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(Appendix follows)

Appendix Table 1. Countries Included in an Analysis of Perceived Stress and Chronic Disease and Their Sample Sizes

Country	Unweighted No. of Participants (<i>n</i> = 229,293)
Bangladesh	5,942
Bosnia-Herzegovina	1,031
Burkina Faso	4,948
Chad	4,870
China	3,994
Comoros	1,836
Croatia	993
Czech Republic	949
Dominican Republic	5,027
Ecuador	5,675
Estonia	1,020
Ethiopia	5,089
Ghana	4,165
India	10,687
Ivory Coast	3,251
Kazakhstan	4,499
Kenya	4,640
Laos	4,988
Latvia	929
Malawi	5,551
Malaysia	6,145
Mali	4,886
Mauritania	3,902
Mauritius	3,968
Mexico	38,746
Morocco	5,000
Myanmar	6,045
Namibia	4,379
Nepal	8,820
Pakistan	6,501
Paraguay	5,288
Philippines	10,083
Republic of Congo	3,075
Russia	4,427
Senegal	3,461
Slovakia	2,535
South Africa	2,629
Sri Lanka	6,805
Swaziland	3,117
Tunisia	5,202
Ukraine	2,860
Uruguay	2,996
Vietnam	4,174
Zambia	4,165