Depression, chronic diseases, and decrements in health: results from the World Health Surveys

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Summary

Background Depressed is an important public-health problem, and one of the leading causes of disease burden worldwide. Depression is often comorbid with other chronic diseases and can worsen their associated health outcomes. Few studies have explored the effect of depression, alone or as a comorbidity, on overall health status.

Methods The WHO World Health Survey (WHS) studied adults aged 18 years and older to obtain data for health, health-related outcomes, and their determinants. Prevalence of depression in respondents based on ICD-10 criteria was estimated. Prevalence values for four chronic physical diseases—angina, arthritis, asthma, and diabetes—were also estimated using algorithms derived via a Diagnostic Item Probability Study. Mean health scores were constructed using factor analysis and compared across different disease states and demographic variables. The relation of these disease states to mean health scores was determined through regression modelling.

Findings Observations were available for 245 404 participants from 60 countries in all regions of the world. Overall, 1-year prevalence for ICD-10 depressive episode alone was 3.2% (95% CI 3.0–3.5); for angina 4.5% (4.3–4.8); for arthritis 4.1% (3.8–4.3); for asthma 3.3% (2.9–3.6); and for diabetes 2.0% (1.8–2.2). An average of between 9.3% and 23.0% of participants with one or more chronic physical disease had comorbid depression. This result was significantly higher than the likelihood of having depression in the absence of a chronic physical disease (p<0.0001). After adjustment for socioeconomic factors and health conditions, depression had the largest effect on worsening mean health scores compared with the other chronic conditions. Consistently across countries and different demographic characteristics, respondents with depression comorbid with one or more chronic diseases had the worst health scores of all the disease states.

Interpretation Depression produces the greatest decrement in health compared with the chronic diseases angina, arthritis, asthma, and diabetes. The comorbid state of depression incrementally worsens health compared with depression alone, with any of the chronic diseases alone, and with any combination of chronic diseases without depression. These results indicate the urgency of addressing depression as a public-health priority to reduce disease burden and disability, and to improve the overall health of populations.

Introduction Depression is an important global public-health issue, both because of the relatively high lifetime prevalence ranging from 2% to 15% and because it is associated with substantial disability. Rated as the fourth leading cause of disease burden in 2000, depression accounted for 4.4% of total disability adjusted life years (DALYs). It is also responsible for the greatest proportion of disease burden attributable to non-fatal health outcomes, accounting for almost 12% of total years lived with disability worldwide. Without treatment, depression has the tendency to assume a chronic course, be recurrent, and over time to be associated with increasing disability.

The comorbidity of depression with chronic physical diseases such as arthritis and diabetes is well recognised in developed countries. Several studies have shown that there is an increased risk of having major depression in people with one or more chronic diseases. The degree to which these comorbid states exist at the global level has not been shown. With a growing elderly population, and the associated increase in prevalence of chronic medical conditions, a concomitant rise in the prevalence of depression is to be expected. In fact, projections indicate that after heart disease, depression is expected to become the second leading cause of disease burden by the year 2020.

The increasing prevalence of chronic physical diseases and depression leads to the question of how these disorders compare in terms of their effect on overall individual health. The presence of self-reported chronic physical diseases such as angina, arthritis, asthma, and diabetes has been associated with reduced health-related quality of life scores. Lower health status has been reported in depressed patients than in those without depression, and this state is unequally distributed across population groups. Effects of depressive episodes have also been studied with regard to loss in productivity and poor health-related quality of life. Despite this evidence, depression, like other mental disorders, is often not deemed to be on a par with other chronic physical health conditions in terms of its effect on overall health. This view is perhaps one of the underlying reasons behind the lack of parity between mental and physical disorders in terms of access to health care.

To our knowledge, there has been no worldwide
comparison of depression with other chronic diseases and their effect, either individually or comorbid, on health.

We analysed data from the WHO World Health Survey (WHS) to address the following questions: how does the decrement in health state associated with depression compare with the decrement associated with other common chronic physical conditions; and what is the added effect on decrements in health of suffering from depression, over and above a chronic physical condition?34

Methods
Sample
Countries from the WHS were selected to represent all regions of the world, with 26 countries from the European region, 15 from the African region, six from the Americas, four from the eastern Mediterranean region, five from the southeast Asia region, and four from the western Pacific region, giving a total of 60 countries. The countries included in the survey programme represent those countries that were willing and able to participate in the survey. Countries with samples that were nationally representative, probabilistically selected, and which had sampling weights information available, were used in the analysis for this paper. To adjust for the population distribution as represented by the UN Statistical Division and for non-response, post-stratification corrections were made to the sampling weights.

Procedures
All respondents used in the analysis were interviewed with the standardised WHS survey, which included questions on sociodemographic and economic factors, a series of questions on health status, and questions related to whether the individual had ever been diagnosed with depression, asthma, arthritis, angina, and diabetes, whether the person had ever received or was currently on treatment for these conditions, and, with the exception of diabetes, a series of symptom questions related to each condition. All surveys were implemented as face-to-face interviews with the exception of Luxembourg and Israel, which were implemented as telephone interviews. All questionnaires were translated and back-translated using a standard WHO protocol. The quality of translations was independently verified by bilingual experts before field implementation. Informed consent was obtained from all respondents and the study was cleared by the ethics review committees at each site.

The health status measure presented in this analysis was developed by WHO based on its framework for measuring health. WHO assesses an individual’s state of health as a vector of capacities in multiple domains.34 For measurement in surveys, this information needs to be reduced to a parsimonious set of domains that are clearly defined and measured with reliable self-report questions. After an extensive review of existing survey questionnaires, none were deemed able to match the exact ideas or have the information needed to measure the distribution of health in the general population. Hence, a new measure was developed where the valuation could be estimated—ie, the relative disability weight assigned to different patterns of the health states, thus allowing for cross-country comparability.

The measure was based on 18 health-related questions, where the responses were recorded on a five point scale ranging from “no difficulty or problem” to “extreme difficulty/inability”. Two of the questions assessed general health: one asking overall self-reported health, and the other asking how much difficulty the respondent had in working or doing household activities during the past 30 days. These two items were analysed individually. The remaining 16 questions were grouped into the following eight health domains: vision, mobility, self care, cognition, interpersonal activities, pain and discomfort, sleep and energy, and affect. These domains are included in many commonly used health outcome measures such as the Short Form 36 (SF36), the Health Utilities Index Mark 3 (HUI 3), and the Euroqol 5D.35–37

The health measure had been extensively tested as part of a similar survey done between 2000 and 2001, the Multi-Country Survey Study.38 The internal consistency of the health measure as assessed using Cronbach’s alpha was 0.91. The test-retest reliability of individual items, measured by the weighted Kappa, ranged from 0.48–0.62. Missing data for individual items ranged from 1.3% to 5.8%. Construct validity was also assessed, and respondents who were older or had a chronic condition reported worse health, whereas respondents with higher socioeconomic status and countries with higher life expectancies on average reported better health.34

A composite health status score was derived from the 16 self-reported health questions. Since the item responses were based on a five-point ordered categorical scale, a factor analysis using polychoric correlations was done to take into account the covariance structure of the responses to individual questions. The choice of a one factor solution was justified by the high eigenvalue of the first factor (8.79, 74% as a cumulative percentage of the variance explained) and the high communalities of the original variables (between 0.43 and 0.69). We used the principal component method for factor extraction and the regression scoring method to obtain the factor scores. The factor score was transformed to a 0–100 scale, with 0 indicating worst health and 100 indicating best health.

To validate the use of symptom questions for diagnosing chronic diseases, WHO implemented in 2003 a diagnostic item probability study in seven countries. Patients were selected from clinics if they were positive for any of the specific disease conditions based on a gold standard diagnostic test, and these patients were considered to be true positives for that particular condition. The patients were then traced back to their homes and asked, for all
disease conditions, the same symptomatic questions as respondents from the WHS. Additionally, a sample of respondents matched by sex, age, and country of origin was drawn from the WHS if they had negative responses to all the self-reported diagnosis questions for depression, asthma, arthritis, angina, and diabetes. These respondents were considered to be the true negatives for the study. The individual response rates, calculated as the ratio of completed interviews in selected respondents in the sample, excluding ineligible respondents from the denominator, ranged from 63% in Israel to 99% in the Philippines (detailed response rates available on request).

The diagnosis of depression was based on the International Classification of Diseases tenth revision (ICD-10) diagnostic criteria for research for depressive episodes, and was derived from an algorithm that took into account respondents reporting symptoms of depression during the past 12 months. The individual questions used to assess these symptoms were based on the World Mental Health Survey version of the Composite International Diagnostic Interview.

The diagnosis for angina was based on the algorithm derived from the Rose questionnaire. For asthma and arthritis, the sensitivity and specificity of all potential combinations of answers to these symptomatic questions were checked based on responses from the diagnostic item probability study. The combination of answers that produced the best result based on the Receiver Operator Characteristic analysis was used to apply a diagnosis for each respondent in all 60 countries of the WHS sample. Respondents were regarded as positive for diabetes if they reported ever being diagnosed with diabetes. Questions about diabetes were asked in only 46 of the countries that implemented the long version of the questionnaire. All diagnoses of these chronic physical diseases applied to the past 12 months from the date of interview. For most of the analysis, respondents were grouped on the basis of their disease status into one of the following: respondents having none of the aforementioned health conditions, respondents having any of the single conditions alone, respondents having any of the chronic physical diseases alone in conjunction with depression, respondents having two or more comorbidities without depression, and respondents having two or more comorbidities with depression.

Analysis
The prevalence of each chronic physical disease was estimated, first alone—ie, without any of the other conditions present—then comorbid with depression but without any additional conditions present, and then two or more comorbid conditions with or without depression. The prevalence of depression in respondents who had any one of the conditions was also estimated. All these estimates were calculated using post-stratified probability weights. To make valid comparisons across countries, age and sex standardisations were done using WHO’s World Standard Population for age and the UN Statistical Division for sex ratio.

The mean of the health score was calculated using probability weights for the entire sample after stratification by sex, age, education, and income quintile, as well as respondents’ disease status. To test the statistical difference of health scores between each pair of disease groups, a one-way analysis of variance using a Scheffe test was done to adjust for multiple comparisons. Linear regression analysis was used on the pooled dataset of 46 countries to model the relation between respondents’ health state and whether they had depression, a chronic physical disease, or a combination thereof, after controlling for country of origin, sex, age, education, marital status, occupational status, income level, and any interaction between sex with the other demographic variables. To establish whether cultural differences in countries affected the relation between disease state and overall health state, interaction terms between marital status, education, and income quintile with the country variable were included in the model.

Responses to some health domains such as sleep and affect are likely to be influenced by whether the respondent is clinically depressed, which could lead to spurious conclusions about the decrements in health associated with depression. To test for this possibility, we did two further analyses. The first analysis explored the association of disease states with each of the two questions of health measure which assess overall health and do not include any symptoms of depression. Second, we used a recursive regression technique to model the effect of depression when the dependent variable, the health score, contained only two domains—mobility and vision. Then, progressively, other domains were added to estimate the health score. The effect of depression on each successive health score was assessed at each marginal addition of a domain by evaluating changes in the regression coefficient. This regression analysis was repeated until all eight health domains were included and their coefficients for depression compared. Minimum differences in the coefficient for each successive regression would corroborate the effects of depression on decrements in health as genuine and not the result of a systematic reporting bias. All analysis was coded and done using STATA version 9.2.

Role of the funding source
This study was funded by WHO. The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.
Results

The prevalence for depression alone, each chronic disease alone, depression with each chronic physical disease, and having multiple chronic conditions with or without depression for 60 countries was estimated with CIs (results not shown, available on request). At the worldwide level, the prevalence for having any one condition alone did not exceed 5·0%. The prevalence of having diabetes alone had the lowest overall prevalence of 2·0% (1·8–2·2). However, since diabetes prevalence was based on self-report, the role of reporting bias that possibly underestimates the true prevalence cannot be ruled out. Depression alone had the next lowest overall prevalence at 3·2% (3·0–3·5). Asthma alone had an overall prevalence of 3·3% (2·9–3·6), prevalence of arthritis alone was 4·1% (3·8–4·3), and angina alone 4·5% (4·3–4·8). There were variations across countries, but the range of differences in prevalence of any one condition did not exceed eight percentage points.

A significant percentage of respondents with any one of the chronic physical conditions also had depression. For respondents with diabetes, at a worldwide level, 9·3% (7·3–11·3) also had depression, 10·7% (9·1–12·3) with arthritis also had depression, 15·0% (12·9–17·2) with angina, and respondents with asthma had the highest prevalence of depression at 18·1% (15·9–20·3). For the 7·1% (6·6–7·6) of respondents who had comorbidity of two or more chronic physical conditions, nearly a quarter (23%) also had depression in addition to their existing comorbid conditions. Thus, the prevalence of depression in respondents with chronic diseases is significantly higher than in respondents without chronic diseases (3·2%, p<0·0001).

The figure shows the mean health score and the 95% CIs for each disease. Respondents without any of the chronic diseases or depression had the highest health score, 90·6—i.e., reported having the best health. Respondents with asthma, angina, arthritis, or diabetes alone, had mean health scores of 80·3, 79·6, 79·3, and 78·9, respectively, which were significantly different from having no disease but not from each other. Respondents with depression had the lowest health score among all the chronic disease conditions, 72·9 (p<0·0001). Respondents who had depression comorbid with another chronic condition had much lower mean health scores than respondents who had the chronic condition alone (p<0·01). For respondents who had two or more chronic conditions excluding depression, their mean health score was 71·8, lower than any of the disease conditions alone but higher than any disease state comorbid with depression. The lowest overall mean health score was for respondents with two or more chronic conditions comorbid with depression (56·1). These results show that comorbid depression is significantly associated with lower health states in respondents with chronic conditions in comparison to having chronic conditions, including multiple chronic conditions, without depression (p<0·0001).

We examined mean health scores by disease state in more detail by looking across sociodemographic variables (results not shown). The patterns are consistent, and for depression alone the mean health score is lower than for other chronic conditions alone, across all socioeconomic variables. For all comorbid depression, the mean health score is lower across all socioeconomic variables than for any of the chronic conditions alone or for depression alone. Thus, having depression comorbid with another chronic physical disease lowers health status substantially, irrespective of a respondent’s age, sex, and other demographic variables.

The coefficients of a regression model in the table summarises the relation between overall health and the different disease states and the sociodemographic determinants of sex, age, education, employment status, income quintile, and marital status. We also controlled for country of residence, interaction of country with education, marital status and income quintile, and interaction of sex with education, employment status, and income quintile (results not shown).

The results from the model indicate that lower coefficient values are associated with lower health scores. Results of the model show that being older is indicative of decreased health status, as is having less education, having lower income, and being unemployed. Women had a lower overall health score, and the decrements in health were greater for women who were unemployed, less educated, or widowed as indicated by the significant coefficients for the interaction terms of sex with these demographic variables (results not shown). There does not seem to be a significant difference in health status between being married and
never having been married or cohabitating. However, being separated, divorced, or widowed is associated with lower health scores.

Overall, disease status has a greater association with reported health scores than do sociodemographic characteristics. Controlling for all other factors, having depression is associated with the lowest health scores, either alone or comorbid with other chronic diseases \( p<0.0001 \). The coefficient values from the model show that the comorbid state of depression with diabetes causes even greater decrements in health than the addition of the two conditions separately. This finding is suggestive of an interactive effect between depression and diabetes that causes an extra negative effect on health beyond the simple addition of each of the two conditions. Having more than two chronic diseases without depression \( \text{(coefficient } -11.97) \), although associated with a lower health score than having any one chronic disease, has much less of a negative association with health than does having depression alone \( \text{(coefficient } -13.89) \), or depression comorbid with one of the chronic diseases \( \text{(coefficients range from } -16.77 \text{ to } -23.43) \). Respondents with two or more chronic diseases in addition to having depression had the lowest health scores of all the disease groups \( \text{(coefficient } -24.38) \).

Interacting sociodemographic variables with the country variable did not show statistically significant change the coefficients of depression and comorbid depression in the model, which suggests that cultural differences across countries and their interaction with sociodemographic characteristics does not affect the influence of depression on overall health.

To rule out the effects of depression on some of the health domains included in the health measure, we compared the mean scores by disease status for the two general questions on overall self-rated health and difficulties with work and activities \( \text{(results not shown)} \). Although the scores for the difficulties with work question were higher than the overall health question, the pattern across disease states for both questions was quite similar to the pattern seen for the overall mean health score. Respondents who reported no chronic conditions had the highest scores, respondents with depression alone or comorbid with another condition had the lowest scores overall. Even respondents with two or more chronic conditions but no depression scored higher than any respondent with depression alone or comorbid with another condition.

We also did a recursive regression as described in the methods section \( \text{(results not shown)} \). The coefficient for depression in the model with the least-related of the health domains, vision and mobility, had a value of \(-9.93\). Adding a third domain, pain, the coefficient for depression rose slightly to \(-13.67\). With each successive addition of a health domain, the coefficient does not exceed \(-13.9\). The addition of more domains—even those that are likely to be most responsive to the presence of depression such as sleep or energy and affect—did not have an appreciable addition on the average effect of depression on health status. The coefficient remains fairly stable irrespective of the composition of domains that underlie the computation of the health score. These analyses show that our findings are unlikely to indicate a bias due to inclusion of items in the overall health status score that are related to depression.

**Table: Regression results for overall health**

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Coefficients (standard error)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex ( \text{(reference category-men)} )</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>(-2.03 (0.07))^*</td>
</tr>
<tr>
<td>Age group ( \text{(reference category=15-19 year olds)} )</td>
<td></td>
</tr>
<tr>
<td>30-44</td>
<td>(-2.20 (0.09))^*</td>
</tr>
<tr>
<td>45-59</td>
<td>(-5.58 (0.11))^*</td>
</tr>
<tr>
<td>60-69</td>
<td>(-9.78 (0.14))^*</td>
</tr>
<tr>
<td>70-79</td>
<td>(-15.30 (0.18))^*</td>
</tr>
<tr>
<td>80+</td>
<td>(-22.19 (0.27))^*</td>
</tr>
<tr>
<td>Marital status ( \text{(reference category-married)} )</td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>(0.02 (0.1))</td>
</tr>
<tr>
<td>Cohabiting</td>
<td>(-0.20 (0.13))</td>
</tr>
<tr>
<td>Separated, divorced, or widowed</td>
<td>(-1.93 (0.11))^*</td>
</tr>
<tr>
<td>Education ( \text{(reference category=no school)} )</td>
<td></td>
</tr>
<tr>
<td>Less than primary</td>
<td>(0.88 (0.12))^*</td>
</tr>
<tr>
<td>Primary completed</td>
<td>(1.77 (0.12))^*</td>
</tr>
<tr>
<td>Secondary completed</td>
<td>(2.20 (0.13))^*</td>
</tr>
<tr>
<td>Greater than secondary</td>
<td>(2.69 (0.14))^*</td>
</tr>
<tr>
<td>Employment status ( \text{(reference-unemployed)} )</td>
<td></td>
</tr>
<tr>
<td>Currently employed</td>
<td>(1.77 (0.08))^*</td>
</tr>
<tr>
<td>Income quintiles ( \text{(reference category-lowest quintile)} )</td>
<td></td>
</tr>
<tr>
<td>Second quintile</td>
<td>(0.77 (0.10))^*</td>
</tr>
<tr>
<td>Third quintile</td>
<td>(1.18 (0.11))^*</td>
</tr>
<tr>
<td>Fourth quintile</td>
<td>(1.73 (0.11))^*</td>
</tr>
<tr>
<td>Highest quintile</td>
<td>(2.41 (0.12))^*</td>
</tr>
<tr>
<td>Disease status ( \text{(reference=no health conditions)} )</td>
<td></td>
</tr>
<tr>
<td>Depression alone</td>
<td>(-13.89 (0.20))^*</td>
</tr>
<tr>
<td>Angina alone</td>
<td>(-6.68 (0.17))^*</td>
</tr>
<tr>
<td>Arthritis alone</td>
<td>(-5.92 (0.16))^*</td>
</tr>
<tr>
<td>Asthma alone</td>
<td>(-6.54 (0.15))^*</td>
</tr>
<tr>
<td>Diabetes</td>
<td>(-3.53 (0.26))^*</td>
</tr>
<tr>
<td>Depression+angina</td>
<td>(-20.47 (0.42))^*</td>
</tr>
<tr>
<td>Depression+arthritis</td>
<td>(-16.77 (0.46))^*</td>
</tr>
<tr>
<td>Depression+asthma</td>
<td>(-19.44 (0.39))^*</td>
</tr>
<tr>
<td>Depression+diabetes</td>
<td>(-23.43 (0.86))^*</td>
</tr>
<tr>
<td>More than one chronic condition without depression</td>
<td>(-11.97 (0.16))^*</td>
</tr>
<tr>
<td>Depression with more than one chronic condition</td>
<td>(-24.38 (0.31))^*</td>
</tr>
</tbody>
</table>

Coefficients for country and sociodemographic interactions not shown. \(^*p<0.01\).
Discussion

The worldwide prevalence of depression, asthma, angina, arthritis, and diabetes based on data collected in the World Health Surveys, and used in the analysis presented here, are similar to the data reported by WHO’s Global Burden of Disease study. The data show that comorbidity between chronic physical conditions and depression is common, and that people with chronic diseases are significantly more likely to suffer from depression than those without (p<0.0001). Our data indicate that depression is associated with a decrement in health that is significantly greater than those associated with the other chronic diseases in this study. Though depression has previously been shown to be associated with disability and declines in health-related quality of life, this is the largest scale study to our knowledge that shows this decline using direct comparisons across physical conditions in multiple countries with a common measurement strategy. Furthermore, we have also shown that depression comorbid with other chronic diseases produced significantly greater decrements in health than from one or more chronic diseases, and that this additive effect is substantially amplified in the case of depression comorbid with diabetes. These associations remained evident after adjustment for sociodemographic, country of origin, and economic factors.

Our findings are consistent with earlier studies that have shown a high degree of association between depression and disability. There are, however, few studies that have compared the effect of depression with other chronic diseases. One reason for our findings could be that depression is associated specifically with decrements in mental domains of health, which were included in the composite health score we computed for our analyses. However, in the recursive regression analysis, we showed that adding each health domain serially does not alter the substantive results, since the size of the depression regression coefficient is barely changed. This finding confirms that the measure is not biased towards depression. Another reason for our findings might be that depression is associated with a negative assessment of functioning in all domains and therefore what one is measuring is merely a negative frame of mind that leads to reporting biases. An illustration of such a response bias is shown in the study by Owsley and colleagues, who assessed the effect of depression in elderly individuals on their response to a vision questionnaire. After controlling for demographics, general health, and vision, depression was found to be associated with reduced scores on the questionnaire, suggesting negative reporting as a function of being depressed rather than actual vision ability. To address this bias, the WHS also included vignettes in the survey whereby each respondent was presented with a set of brief descriptions of individuals in a fixed level of health for a particular domain. Five vignettes per domain were presented ranging, for example, from quadriplegia at one extreme of mobility, to a marathon runner at the other extreme. Respondents were asked how they would rate their difficulty in that particular domain if they were the person described in each of the vignettes. The examination of these rating patterns show that respondents with and without depression showed the same pattern of rating, even though they differed in self-report of their own experiences in each domain. This finding suggests that depressed respondents were not reporting things more negatively for the same level of health, and further supports the absence of biased reporting due to depression (results not shown). Our vignette method was possibly not sufficiently sensitive in detecting systematic reporting biases: though we do not believe this to be the case, this possibility needs to be investigated in future studies. Additionally, the reporting of depressive symptoms or diagnosis could vary between countries because of cultural differences in reporting such symptoms. If respondents in some countries underreported their depressive symptoms, leading to an underestimate of the prevalence of depression in these countries, and if this was associated with denial of health problems, it would in fact narrow the difference in the reported decrements in health between those with and without depression. Our results show this situation was not the case, that even after controlling for country effects, the decrements in health due to depression, both in pure and comorbid states, continue to remain significant. So if underestimating of depression prevalence is occurring, it actually strengthens the findings that depression increases decrements in health. Thus, these reporting biases, if they exist, do not detract from our substantive findings.

The WHS was a cross-sectional study and did not include questions on onset and duration of illness, fluctuations in course and details of health-care use such as number and timing of contacts with health-care services, the reasons for contact, and the outcome following contact. Hence, we cannot establish what burden depression, and its comorbidity with other chronic diseases, places on the health system, how depression can modify the course of these disorders, and whether treatment of depression when present with these chronic physical diseases would alter their course. For the estimation of prevalence, the algorithms for the chronic physical conditions were based on a small validation study in a few countries that used negatives drawn from respondents in the WHS who self-reported no chronic diseases. Since these conditions are known to have an average prevalence in the general population of around 5%, the likelihood of these true negative respondents having any one of the above diagnoses is low. Both depression and angina were based on validated algorithms, but the algorithms of asthma and arthritis could benefit from a more comprehensive validation study, since the presence of some false negative respondents cannot be ruled out. The algorithms might
need to be modified if larger validation studies are done in more countries and if the true negatives were also identified on a gold standard test. Diabetes was based on self-report, and the role of reporting bias on the prevalence presented in our study is noted. However, we do not think that the possibility of a small misclassification bias would substantially alter the core message of this study that being sad is bad for one's health.

In conclusion, we report the largest population-based worldwide study to our knowledge that explores the effect of depression in comparison with four other chronic diseases on health state. Our main findings show that depression impairs health state to a substantially greater degree than the other diseases. A significant percentage of respondents have depression in addition to their existing chronic physical conditions, a group that is often unrecognised and untreated.29,48 This finding is of special importance, considering the presence of depression and its treatment is clearly related to the outcome of these chronic diseases.7,46–48 Comorbidity with depression significantly worsens the health state of people with chronic diseases. The need for timely diagnosis and treatment of depressive disorders to reduce the burden on public health is imperative. In many primary care settings, patients presenting with multiple disorders that include depression often don't get diagnosed, and if they do, often treatment is focused towards the other chronic diseases.6 Depression can be treated in primary care or community settings with locally available cost-effective interventions.51 On the basis of our results, addressing the further exacerbation of disability due to depression needs to be a priority of health systems worldwide. Primary care providers must be taught not to ignore the presence of depression when patients present with a chronic physical condition, in view of the marked effect that it has on an individual's health. This goal can be accomplished in part by sending a message which, in addition to reducing the stigma surrounding mental illness, can alert providers and the public at large that depression is a disease at least on a par with physical chronic diseases in damaging health.

Contributors
SM, SC, and TBU contributed to the design of the study. SM, SC, EV, AT, and VP contributed to the analyses. All authors were involved in the development of the manuscript and approved the final version. The views expressed in this paper are those of the authors and do not necessarily represent the views or policies of the Asian Development Bank or the World Health Organization.

Conflict of interest statement
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