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Comorbidity and disease burden in the National Comorbidity Survey Replication (NCS-R)

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Abstract

Background—Disease burden estimates rarely consider comorbidity. Using a recently developed methodology for integrating information about comorbidity into disease burden estimates, we examined the comparative burdens of 9 mental and 10 chronic physical disorders in the National Comorbidity Survey Replication (NCS-R).

Methods—Face-to-face interviews in a national household sample (n = 5,692) assessed associations of disorders with scores on a visual analog scale (VAS) of perceived health. Multiple regression analysis with interactions for comorbidity was used to estimate these associations. Simulation was used to estimate incremental disorder-specific effects adjusting for comorbidity.

Results—74.9% of respondents reported one or more disorders. 73.8–98.2% of respondents with disorders reported having at least one other disorder. The best-fitting model to predict VAS scores included disorder main effects and interactions for number of disorders. Adjustment for comorbidity reduced individual-level disorder-specific burden estimates substantially, but with considerable between-disorder variation (.07–.69 ratios of disorder-specific estimates with and without adjustment for comorbidity). Four of the five most burdensome disorders at the individual level were mental disorders based on *bivariate* analyses (panic/agoraphobia, bipolar disorder, PTSD, major depression) but only two based on *multivariate* analyses, adjusting for comorbidity (panic/agoraphobia, major depression). Neurological disorders, chronic pain conditions, and diabetes were the other most burdensome individual-level disorders. Chronic pain conditions, cardiovascular disorders, arthritis, insomnia, and major depression were the most burdensome societal-level disorders.

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Conclusions—Adjustments for comorbidity substantially influence estimates of disease burden, especially those of mental disorders, underlining the importance of including information about comorbidity in studies of mental disorders.

Keywords

bias; burden of illness; confounding factors; cost of illness; epidemiology; global burden of disease; health valuation; visual analog scale (VAS)

INTRODUCTION

Estimates of comparative disease burden are valuable for health policy planning and decision-making.[1–3] Disease burden is typically estimated using a condition-specific severity weight based on expert ratings of the relative burdens of different conditions.[3, 4] However, this approach does not take comorbidity into account and has been severely criticized for failing to do so.[5] This is a nontrivial issue, as methodological research has shown that condition-specific severity weights vary significantly depending on the presence-absence of comorbidity[6] and epidemiological studies show that comorbidity is a pervasive feature of common chronic mental and physical disorders.[7, 8] A statistical approach that allows comorbidity to be taken into consideration in estimating disease burden was recently developed,[9] but has not up to now been used to derive estimates of comparative disease burden for common mental and physical disorders in the US. Such estimates are presented in the current report based on data collected in the US National Comorbidity Survey Replication (NCS-R).[10]

METHODS

The sample

The NCS-R design has been described elsewhere.[10] In brief, the NCS-R is a national face-to-face household survey of adults (ages 18+) designed to study prevalence and correlates of DSM-IV disorders. The survey was administered 2001–3 and had two parts. Part I included an assessment of core DSM-IV mental disorders administered to all respondents (n = 9,282). Part II included questions about mental disorders of secondary interest, physical disorders, disease burden, and other correlates administered to all Part I respondents who met lifetime criteria for any Part I disorder plus a roughly one-in-three probability sub-sample of other Part I respondents (n = 5,692). The Part I-II response rate was 70.9%. The Part II sample, which is the basis of the current report, was weighted to adjust for differential probabilities of selection and under-sampling of Part I respondents without DSM-IV disorders. A weight was also used to adjust for small discrepancies between sample and population Census data on socio-demographic and geographic variables. Verbal informed consent was obtained from participants and these procedures were approved by the Institutional Review Board of Harvard Medical School. A more detailed discussion of NCS-R sampling and weighting procedures is presented elsewhere.[10]

Measures

Mental disorders—Mental disorders were assessed with Version 3.0 of the WHO Composite International Diagnostic Interview (CIDI), a fully-structured interview designed to generate diagnoses of common mental disorders according to the criteria of both the ICD-10 and DSM-IV systems.[11,12] DSM-IV criteria are used here. The nine mental disorders included here are major depressive episode or dysthymia, bipolar disorder I-II, panic/agoraphobia (either panic disorder or agoraphobia without a history of panic disorder), specific phobia, social phobia, generalized anxiety disorder, post-traumatic stress disorder (PTSD), alcohol abuse with or without dependence (i.e., abuse assessed without taking the presence vs. absence of dependence into consideration), and drug abuse with or without dependence. Most of these were assessed in Part I but some (PTSD and, in some countries, substance use disorders) in Part II. WMH clinical reappraisal studies showed that CIDI diagnoses of these disorders have generally good concordance with diagnoses based on blinded clinician-administered reappraisal interviews.[13] We focus on mental disorders present at some time in the 12 months before interview.

Chronic physical disorders—Physical disorders were assessed with a standard chronic conditions checklist based on the list in the US National Health Interview Survey.[14,15] Respondents were asked to report whether they ever had a series of symptom-based conditions (e.g., chronic headaches) and whether a health professional ever told them they had a series of silent conditions (e.g., hypertension) and whether episodic conditions were still present in the 12 months before interview. Methodological research has shown that checklists like this yield more accurate reports than estimates derived from responses to open-ended questions.[16,17] In addition, methodological studies in the US and UK have documented good concordance between such condition reports and medical records.[18–20] The reports were grouped into ten categories to maximize comparability with previous studies[3]: arthritis, cancer, cardiovascular disorders (heart attack, heart disease, hypertension, stroke), chronic pain conditions (chronic back or neck pain, other chronic pain conditions), diabetes, frequent or severe headaches or migraines, chronic insomnia, neurological disorders (multiple sclerosis, Parkinson's, epilepsy, seizure disorders), digestive disorders (stomach or intestinal ulcer, irritable bowel disorder), and respiratory disorders (seasonal allergies, asthma, COPD, emphysema). We focus on disorders present at any time in the 12 months before interview.

Health valuations—Respondents were asked to make a health valuation after all physical and mental disorders had been assessed by using a 0-to-100 visual analog scale (VAS), where 0 represents *the worst possible health a person can have* and 100 represents *perfect health*. The rating task was to rate their own overall health (combining physical and mental health into a single summary evaluation) during the past 30 days. The recall period for the VAS (30-days) is different from the recall period for disorders (12-months) because we wanted to include effects not only of active disorders but also of recent disorders that might still have important effects on health valuations (e.g., a recent heart attack). Previous research has reported high levels of reliability and validity for VAS measures in health valuation studies.[21–24]

Analysis methods

It is important to recognize that health valuation analyses are designed to estimate presumed causal effects of disorders. This is typically done using causal modeling techniques, but based on the realization that it is never possible to justify causal assertions about such effects unequivocally from the non-experimental data that are necessarily used as the basis of such evaluations. Provisional estimates of this sort are nonetheless useful as guides to policymakers in making resource allocation decisions. With that caveat in mind, a series of regression models was used to estimate joint predictive associations of disorders with VAS scores controlling for age and sex.

As the sample was too small to allow each of the logically possible multivariate disorder profiles to be a separate predictor, models necessarily made simplifying assumptions about the appropriate predictors to include in the model to describe comorbidity. The first multivariate model (M1) assumed additivity by including a separate predictor for each disorder without interactions. M2 included a series of predictors for number of disorders (e.g., one predictor for having exactly one disorder, another for exactly two, etc.) without terms for types of disorders. M3 included 19 predictors for types of disorders (i.e., one for each of the 9 mental and 10 physical disorders) in addition to predictors for overall number of disorders. The number-of-disorders dummies in M3 represented aggregate patterns of comorbidity assumed to be independent of types. M4 allowed the effects of type to vary as a linear function of number of other disorders (i.e., 19 dummies for the main effects of disorders, additional dummies for number of disorders, and 19 interaction terms between type and a continuous measure of number of disorders).

The skewed distribution of VAS scores made ordinary least squares (OLS) regression both biased and inefficient. We addressed this problem in two ways. First, a two-part modeling approach[25] was used where a Part I logistic regression equation[26] predicted having a VAS score of 100 versus 0–99 in the total sample and a Part II linear regression equation then predicted scores in the 0–99 range. Individual-level predicted scores were estimated by multiplying predicted values based on the two equations. A problem with this approach is that non-random variance in prediction errors can lead to bias even when sophisticated transformation methods are used.[27] A second approach, generalized linear models (GLMs), addressed that problem by pre-specifying functional forms of associations and error structures in one-part models. Such models can sometimes fit highly skewed data better than two-part models.[28–30]

A number of different one-part and two-part models were considered. We selected the best one using standard empirical model comparison procedures.[31] The GLMs with (i) a square root functional form and independent error structure and (ii) a linear functional form and independent error structure were the two best-fitting models. (Results are not reported, but are available on request.) Due to the simpler interpretation of the linear specification, that was the one used in further analyses. M4, the model that allowed the effects of comorbidity to vary by type of disorder, was the best-fitting model among those considered. This is a model of intermediate complexity in that it allows interactions to vary across disorders but not across particular pairs or higher numbers of disorders. Although this is unlikely to be the optimal interaction model one would arrive at in analyzing a sample of immense size, the

fact that it provides the best fit across the range of models considered here suggests that it is a useful first approximation.

A complication in this model, though, is that the coefficients associated with individual disorders have no intuitive interpretation in the presence of interactions. We addressed this problem with a commonly-used simulation approach for models of this sort. This approach began by generating two estimates of predicted VAS scores for each respondent for each simulation. The first estimate was based on the coefficients of the predictors in M4, while the second estimate was based on a revision of this approach that assumed that one particular focal disorder was absent for all respondents. The first estimate of predicted VAS was then subtracted from the second and the sum of differences across respondents was divided by the number of respondents with the focal disorder to estimate the average incremental (i.e., net of all other disorders) individual-level change in VAS scores associated with that disorder. This difference was then interpreted as the incremental effect of the focal disorder (i.e., the effect holding all other disorders constant) in predicting the outcome. The individual-level disorder-specific estimate was then projected to the societal level (i.e., the effect on the mean VAS score) by multiplying it by the disorder prevalence estimate. This process was then repeated for each disorder. This approach generated a single burden estimate for each disorder even when that disorder was involved in a number of significant comorbidity interactions, thus resolving the problem of obtaining unitary disorder-specific estimates of comparative burden in the presence of comorbidity.

Two technical aspects of the model estimation process are noteworthy. First, the simulation approach treats the VAS as an interval scale. This assumption has been called into question[32,33] and nonlinear monotonic transformations have been proposed to approximate interval scale properties.[34] However, strong linear associations have been found between health state values based on VAS scores and ordinal[35] or partially-metric[36] scaling methods. As a result, and given that we explored a number of different nonlinear transformations of the VAS in the GLMs, we treated the VAS as an interval scale in the current analysis. Second, because the NCS-R sample design featured weighting and clustering, all regression analyses used the Taylor series linearization method[37] implemented in the SUDAAN software system[38] to generate design-based standard errors. Standard errors of simulated estimates were obtained using the method of Jackknife Repeated Replications[37] implemented in a SAS macro.[39] Statistical significance was consistently evaluated using two-sided .05 level tests.

RESULTS

Prevalence of disorders and comorbidity

The majority of respondents (74.9%) reported having one or more disorders in the 12 months before interview. Comorbidity was found to be the norm for both mental and physical disorders, as shown by the fact that 73.8–98.2% of respondents with any given disorder reported having at least one other disorder. (Table 1) Co-occurrence of three or more disorders is the typical pattern, as the mean number of additional disorders among respondents with any given disorder is in the range 2.0–4.6. Broad patterns of comorbidity are fairly similar for mental and physical disorders, with medians and inter-quartile ranges

(IQR; 25th–75th percentiles) of the percent of cases with comorbidity equal to 93.5% (90.9–95.6%) for mental and 90.3% (85.6–92.1%) for physical disorders. Comparable statistics for mean numbers of other disorders are 3.6 (3.3–4.5) for mental and 2.8 (2.4–3.1) for physical disorders.

We examined bivariate comorbidity with cross-tabulations. Of the 171 (i.e., 19x18/2) pairs of disorders, 87.7% are positive (median OR = 2.3, range of OR = 1.0–32.0) and 75.3% of these are statistically significant. (Detailed results are not shown, but are available on request.) One-third of the negative associations (median OR = 0.8, range of OR = 0.1–0.9) are statistically significant, virtually all of them involving associations of alcohol-drug abuse with physical disorders.

The distribution of VAS scores

Consistent with previous general population surveys,[40,41] VAS scores are highly skewed. (Detailed results are not reported, but are available on request.) The mean on the 0–100 scale is 82.3 and the standard deviation is 17.5. Fewer than 5% of respondents have VAS scores below 50, while 12.3% have scores of 100 and an additional 12.5% have scores in the range 91–100. The median (IQR) among respondents with scores less than 100 is 85 (75–90).

The individual-level predictive associations of conditions with VAS scores

Bivariate regression models (M0) find all 19 conditions are associated with decrements in perceived health. (Table 2) Four of the five disorders with the strongest associations are mental disorders (panic/agoraphobia, bipolar disorder, PTSD, and major depression), with decrements in VAS scores of 14.0–16.5. The one physical disorder in the top five is digestive disorders, with a decrement of 14.1.

All coefficients become weaker in the multivariate additive model (M1), but this is especially true for bipolar disorder and PTSD, which are associated with among the highest VAS scores in bivariate models but not in the multivariate model. Further analysis (detailed results are not reported, but are available on request) showed that these extreme reductions for bipolar disorder and PTSD are largely due to strong comorbidities with major depression and panic disorder. Major depression is the only mental disorder that remains among those with the largest decrements in VAS scores (5.9), although panic/agoraphobia has nearly as large a decrement (5.8). Neurological disorders (8.6), chronic pain conditions (6.7), insomnia (6.2), and diabetes (5.9) are the other disorders in the top five. The model that considers only number of disorders (M2) shows a strong monotic association between number of disorders and decrease in VAS scores. However, this model fits the data less well than the additive model that considers only types of disorders (M1) ($\chi^2_{19} = 1784.7$, $p < .001$, AIC = 48,789.9 for M1 vs. $\chi^2_4 = 399.2$, $p < .001$, AIC = 49,077.6 for M2), a result that is consistent with the fact that an evaluation of slope differences in M1 shows the assumption of equal slopes across disorders implicit in M2 to be inconsistent with the data ($\chi^2_{18} = 344.4$, $p < .001$).

The coefficients associated with number of disorders are no longer significant individually, but are as a set ($\chi^2_3 = 10.6$, $p = .014$), in the model that includes information about both number and types of disorders (M3). A more complex model found that linear interactions

between types and number of disorders are significant as a set ($\chi^2_{18} = 112.5$, $p < .001$), making this the best-fitting model among those considered here (AIC = 48,752.3 vs. 48,777.9–49,077.6 for the other models). However, only three disorder-specific interactions were individually significant out of 18 (associations of arthritis and panic/agoraphobia with VAS increasing in the presence of comorbidity and the association of insomnia with VAS decreasing in the presence of comorbidity). (Detailed results are not reported, but are available on request.) Based on the fact that the vast majority of disorder-specific interactions were not significant in M4, we focused on M3 as our preferred model.

Given the presence of interactions in M3, the coefficients associated with types of disorders in that model have to be interpreted as the associations of *pure* disorders (i.e., disorders occurring to respondents with no other disorders) with VAS scores (compared to scores of respondents with no disorders). It is instructive to compare these coefficients to those in the bivariate models (M0), as this shows that the associations involving pure disorders are less than half as large as those involving overall disorders for all mental disorders and five physical disorders. These results indicate that comorbidity accounts for the major part of the associations with VAS scores for most disorders considered here. Only one of the five pure disorders with the strongest associations is a mental disorder – major depression, with a VAS decrement of 5.5 – while panic/agoraphobia has a somewhat lower decrement (5.3). The pure physical disorders in the top five are neurological disorders (8.2), chronic pain conditions (6.2), insomnia (5.6), and diabetes (5.5).

The coefficients associated with number of disorders in M3 can be interpreted as non-additive effects of comorbidity. Comorbid clusters made up of exactly two disorders are estimated to have VAS decrements 1.3 less than the sum of the pure-disorder decrements, while the VAS decrements associated with comorbid clusters made up of exactly three disorders are estimated to be 0.3 less than the sum of the pure-disorder decrements. By far the largest non-additive effects of comorbidity, though, are associated with clusters of four or more comorbid disorders, where the decrements are estimated to be 2.5 more than the sum of the pure-disorder decrements. This is referred to as a *super-additive interaction*. As noted above, these three number-of-disorders coefficients are significant as a set even though none of them is significant individually.

Simulated individual-level associations

Simulations of the disorder-specific associations with VAS scores based on M4 show that all disorders considered here other than cancer are associated with decrements in VAS scores. (Table 3) The median (IQR) disorder-specific VAS decrement is 3.7 (2.5–5.8). Two of the disorders with the largest (top 5) VAS decrements are mental disorders: panic/agoraphobia and major depression. The three others are neurological disorders, chronic pain conditions, and diabetes. Of the 171 differences between pairs of 19 disorders, 29.2% are statistically significant at the .05 level. (Detailed results of these comparisons are not shown, but are available on request.)

The effects of comorbidity on these estimates can be seen in the fact that the final condition-specific estimates are, on average, only about one-third as large as the estimates based on the bivariate model, with a median (IQR) ratio of .34 (.24–.49). This reduction is considerably

more pronounced for mental disorders [.26 (.22–.31)] than physical disorders [.48 (.34–.57] with the exceptions of the opposite-sign effect for cancer and an especially low ratio for respiratory disorders (.07). The greater reductions for mental than physical disorders are comparable to the pattern found above in the comparison of pure-disorder coefficients with bivariate coefficients. Indeed, the simulated estimates are very similar to, although typically somewhat higher than, the pure disorder coefficients. That the simulated coefficients are higher, not lower, than the pure-disorder coefficients means that the super-additive interaction involving profiles with four or more comorbid disorders overwhelms the sub-additive interactions involving profiles with two or three comorbid disorders.

Simulated societal-level associations

Societal-level estimates of disorder-specific burden were derived by multiplying simulated individual-level estimates by disorder prevalence to arrive at estimated associations of disorders with changes in mean population-level VAS scores. (Table 4) The median (IQR) value of the population-level estimates is .17 (.08–.55). Major depression is the only mental disorder in the top five population-level estimates (0.6). The other four are chronic pain conditions (1.5), cardiovascular disorders (1.4), arthritis (1.3), and insomnia (0.8). These associations are all less than one-tenth of a standard deviation on the VAS scale (which, as noted above, has a standard deviation of 17.5). The top conditions from a societal perspective are dominated by high-prevalence conditions that have intermediate individual-level burden, although two of the top five, chronic pain conditions and major depression, also have high individual-level burdens.

DISCUSSION

The above results are limited in a number of ways. The first limitation is the one noted above as an inherent feature of the health valuation process: that health valuation analyses are designed to estimate presumed causal effects of disorders even though we recognize that causal assertions about such effects cannot be justified unequivocally from the non-experimental data that are necessarily used as the basis of such evaluations. Implicit causal interpretations consequently have to be recognized as provisional guides rather than definitive documentations.

Within the context of that overarching limitation, four more technical limitations of our analysis are noteworthy. First, only a small set of common disorders was included in the analysis. Second, diagnoses of chronic physical disorders were based on self-reports rather than medical records or objective tests. Third, VAS scores were based on evaluations of respondents' own perceived health, whereas previous studies typically were based on expert VAS ratings of hypothetical illness scenarios. It would be useful for a future study to use parallel methods to obtain ratings based on both self-reports from a representative community sample and independent expert ratings of the illness burdens of that same sample across a wider range of disorders than considered here. For this to be done, though, the expert ratings should rate the disability of the *entire patient* based on a multivariate disorder profile rather than the disability of a particular condition averaged across patients. Such an approach would allow for a methodological evaluation of the effects of self-ratings versus

expert ratings on estimates of disease burden taking comorbidity into consideration. Fourth, information on within-disorder variation in severity was not taken into consideration. The evaluation and analysis of severity are complex issues that lend themselves to no simple solutions, but clearly warrant consideration in future refinements of the methodology of evaluating disease burden.

As noted in the section on assessment, the analysis examined the burdens of 12-month disorders on 30-day health valuations. This discrepancy in time frames was created by design to estimate the current (i.e., past 30 days) effects of recent (i.e., past 12 months) chronic-recurrent conditions that might be either in or out of episode at the time of interview. The extent to which results would have been different if the time frames had been made the same is unclear. The highly skewed distribution of VAS scores and non-additive effects of comorbid conditions might also be seen as limitations in that they could have led to instability of results. Finally, while estimates might be accurate for the overall adult population, comparative ratings might be quite different in particular population subgroups.

In line with previous studies, our results show that comorbidity is the norm among chronic conditions[7, 8, 42, 43] and that the vast majority of the mental and physical disorders considered here are associated with decrements in perceived health.[9] A possible explanation for cancer being the exception is that psychological adaptation might have occurred for individuals with cancer, leading to a recalibration of internal standards for perceived health.[44, 45] We also went beyond previous studies and found that adjusting for comorbidity had an enormous effect on estimates of disorder burden. Indeed, disorder-specific decrements on VAS scores were, on average, only about one-third as large after than before adjusting for comorbidity. Furthermore, the joint effects of comorbid conditions on VAS scores were significantly non-additive, which means that simple linear regression models would have been inappropriate to control for the effects of comorbid conditions in interpreting the coefficients associated with specific disorders. Both of these results are consistent with the cross-national findings of Alonso *et al.*[9] Although a small number of previous studies also examined effects of comorbidity,[46–48] they focused largely on comorbidity between pairs of disorders. We found, in comparison, that super-additive effects of comorbidity were limited to comorbid clusters involving sets of at least four disorders. Based on this result, future research on comorbidity and illness burden should be especially concerned with this kind of high comorbidity, which has been referred to elsewhere as *multimorbidity*.[49]

At the individual level, neurological disorders, chronic pain conditions, panic/agoraphobia, major depression, and diabetes were estimated to be associated with the greatest decrements in VAS scores after adjusting for comorbidity. Three of these five (neurological, panic/agoraphobia, major depression) were in the top five across all developed countries in the Alonso *et al.* analysis,[9] but the other two (i.e., chronic pain conditions and diabetes) are higher in the US than in other developed countries, while two conditions in the top five in the Alonso *et al.* analysis (insomnia and digestive disorders) were not in the top five in the NCS-R. The neurological disorders considered here included epilepsy and seizure disorders, Parkinson's disease, and multiple sclerosis, all of which have been associated with high disability in previous studies.[50, 51] Chronic pain conditions, panic/agoraphobia, and major

depression have also been associated with high disability in previous studies.[52, 53] The evidence in previous studies is more mixed, though, regarding the burden of diabetes on functioning, which is sometimes estimated to be relatively low[54] and at least partially explained by comorbid mental disorders.[55] It is consequently striking that the results of the current study, which arguably included more thorough controls for comorbidity than any previous study of diabetes, found diabetes to be associated with among the highest decrements in VAS at the individual level. This is especially true in light of evidence that the prevalence of diabetes has reached epidemic proportions in many countries.[56]

With regard to societal-level burdens, the rank-ordering of disorders found here was close to the one found in a range of developed countries by Alonso *et al*.[9] Indeed, the three disorders ranked as the most severe at the societal level (chronic pain conditions, cardiovascular disorders, and arthritis) were ranked in exactly the same order in both studies. As in previous studies that compared the rank-ordering of individual-level and societal-level estimates,[57–59] the disorders estimated to be most burdensome at the societal level were dominated by high-prevalence conditions with intermediate individual-level severities, although two of the five disorders with the highest societal-level burdens (chronic pain conditions and major depression) also had high individual-level coefficients.

These results underscore the importance of including information about comorbidity in studies of the burden of common mental and physical disorders. This was found to be especially true, though, for mental disorders, arguing against a focus on pure disorders in epidemiological studies designed to evaluate the effects of mental disorders on functioning as well as in studies designed to evaluate the effects of treatment in reducing the impairments associated with mental disorders. Our results also highlight the importance of panic/agoraphobia and major depression as especially important components of the burden of common mental disorders, suggesting that assessments of these syndromes should be included routinely in clinical and epidemiological studies of other mental disorders.

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Table 1

Twelve-month prevalence estimates of physical and mental disorders in the Part II NCS-R (n = 5,692)

	Prevalence		% with at least one other disorder		Mean number of other disorders among those with any	
	%	(SE)	%	(SE)	Est	(SE)
I. Physical						
Arthritis	27.3	(0.9)	87.8	(1.1)	2.4	(0.1)
Cancer	6.6	(0.5)	90.6	(1.8)	2.6	(0.1)
Cardiovascular disorders	23.8	(0.6)	84.2	(1.6)	2.3	(0.1)
Chronic pain conditions	22.5	(0.9)	91.9	(1.0)	2.8	(0.1)
Diabetes	6.1	(0.4)	92.8	(2.2)	2.8	(0.2)
Digestive disorders	3.3	(0.2)	94.8	(1.6)	3.9	(0.2)
Headaches or migraines	12.7	(0.6)	89.9	(1.5)	3.1	(0.1)
Insomnia	14.0	(0.6)	92.1	(1.5)	3.2	(0.1)
Neurological disorders	1.8	(0.2)	85.6	(5.7)	2.8	(0.3)
Respiratory disorders	33.7	(1.2)	73.8	(1.4)	2.0	(0.1)
II. Mental						
Alcohol abuse[a]	3.1	(0.3)	83.6	(2.6)	2.7	(0.2)
Bipolar disorder	2.4	(0.2)	94.6	(1.3)	4.6	(0.2)
Drug abuse[a]	1.4	(0.2)	91.4	(4.3)	3.1	(0.3)
Generalized anxiety disorder	2.7	(0.2)	98.2	(0.9)	3.8	(0.2)
Major depressive episode	8.9	(0.4)	93.5	(1.0)	3.6	(0.2)
Panic disorder/agoraphobia	3.7	(0.2)	93.7	(2.7)	4.5	(0.2)
Post-traumatic stress disorder	3.6	(0.3)	96.5	(1.2)	4.4	(0.2)
Social phobia	7.2	(0.3)	90.4	(1.3)	3.5	(0.1)
Specific phobia	9.2	(0.5)	91.4	(1.3)	3.4	(0.1)

[a]With or without dependence

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Table 2

Bivariate and multivariate associations of type-number of disorders with VAS scores (n = 5,692)

	M0 Bivariate[a]		M1 Multivariate types of disorders[b]		M2 Multivariate number of disorders[c]		M3 Multivariate types and number of disorders[d]	
	Est	(SE)	Est	(SE)	Est	(SE)	Est	(SE)
I. Physical								
Arthritis	−9.4*	(0.8)	−4.5*	(0.7)			−4.2*	(0.9)
Cancer	−1.4	(1.4)	1.0	(1.0)			1.3	(1.0)
Cardiovascular disorders	−9.2*	(0.9)	−5.4*	(0.8)			−5.2*	(1.0)
Chronic pain conditions	−12.1*	(1.0)	−6.7*	(0.8)			−6.2*	(0.8)
Diabetes	−10.3*	(2.3)	−5.9*	(1.8)			−5.5*	(1.7)
Digestive disorders	−14.1*	(2.6)	−5.0	(2.6)			−4.3	(2.6)
Headaches or migraines	−10.8*	(0.8)	−3.7*	(0.7)			−3.3*	(0.7)
Insomnia	−12.7*	(1.3)	−6.2*	(1.2)			−5.6*	(1.1)
Neurological disorders	−12.4*	(3.4)	−8.6*	(2.5)			−8.2*	(2.6)
Respiratory disorders	−3.2*	(0.8)	−0.4	(0.7)			−0.2	(0.7)
II. Mental								
Alcohol abuse[e]	−7.3*	(1.1)	−1.9	(1.2)			−1.6	(1.4)
Bipolar disorder	−16.3*	(1.5)	−3.8*	(1.6)			−3.2*	(1.6)
Drug abuse[e]	−9.7*	(1.8)	−3.1	(1.9)			−2.9	(1.9)
Generalized anxiety disorder	−11.3*	(0.9)	−3.2*	(1.3)			−2.6	(1.5)
Major depressive episode	−14.0*	(1.1)	−5.9*	(0.8)			−5.5*	(0.8)
Panic disorder/agoraphobia	−16.5*	(1.4)	−5.8*	(1.3)			−5.3*	(1.4)
Post-traumatic stress disorder	−15.0*	(1.4)	−3.6*	(1.2)			−3.0*	(1.3)
Social phobia	−10.7*	(1.1)	−2.5*	(1.2)			−2.1	(1.4)
Specific phobia	−9.8*	(0.8)	−2.4*	(0.8)			−2.0*	(1.0)
III. Number of disorders								

	M0 Bivariate[a]		M1 Multivariate types of disorders[b]		M2 Multivariate number of disorders[c]		M3 Multivariate types and number of disorders[d]	
	Est	(SE)	Est	(SE)	Est	(SE)	Est	(SE)
Exactly 1					−2.4*	(0.5)		
Exactly 2					−5.3*	(0.9)	1.3	(1.1)
Exactly 3					−10.3*	(0.7)	0.3	(1.2)
4 or more					−21.8*	(1.3)	−2.5	(2.3)

*Significant at the .05 level, two-sided test.

[a]Nineteen models were estimated with one condition at a time.

[b]A separate dummy variable predictor for each of the 19 conditions.

[c]A separate dummy variable predictor for having exactly one of the 19 conditions, exactly two of the 19 conditions, etc.

[d]The predictors in M3 include all those in M1 and M2 with the exception that the predictor for having exactly one disorder is omitted. As a result of this omission, the 19 coefficients associated with types of disorders should be interpreted as applying to *pure* disorders (i.e., respondents with exactly one disorder compared to those with no disorders).

[e]With or without dependence

Table 3

Simulated individual-level condition-specific estimates based on the best-fitting regression model

	Simulated estimate[a]		Simulated estimate/ Bivariate estimate[b]
	Est	(SE)	Est
I. Physical			
Arthritis	−4.9*	(0.7)	0.52
Cancer	0.9	(1.0)	−0.64
Cardiovascular	−5.7*	(0.8)	0.62
Chronic pain	−6.8*	(0.9)	0.57
Diabetes	−5.8*	(1.7)	0.56
Digestive	−4.8	(2.5)	0.34
Headache or migraine	−3.7*	(0.7)	0.34
Insomnia	−5.7*	(1.2)	0.44
Neurological	−8.5*	(2.4)	0.69
Respiratory disease	−0.2	(0.7)	0.07
II. Mental			
Alcohol abuse[c]	−1.9	(1.1)	0.26
Bipolar disorder	−3.3	(1.8)	0.20
Drug abuse[c]	−3.0	(1.8)	0.31
Generalized anxiety disorder	−2.9*	(1.4)	0.26
Major depressive episode	−6.2*	(1.0)	0.45
Panic disorder/agoraphobia	−6.6*	(1.5)	0.40
Posttraumatic stress disorder	−3.3*	(1.3)	0.22
Social phobia	−2.4*	(1.3)	0.22
Specific phobia	−2.5*	(0.8)	0.25

*Significant at the .05 level, two-sided test

[a]Association of the disorder with mean change in VAS scores among respondents with the disorder net of the other disorders.

[b]The ratio of the estimate in the first column divided by the M0 estimate in Table 2.

[c]With or without dependence

Table 4

Simulated societal-level condition-specific estimates of burden based on the best-fitting regression model (n = 5,692)

	Simulated estimate[a]	
	Est	(SE)
I. Physical		
Arthritis	−1.3*	(0.2)
Cancer	0.1	(0.1)
Cardiovascular disorders	−1.4*	(0.2)
Chronic pain conditions	−1.5*	(0.2)
Diabetes	−0.4*	(0.1)
Digestive disorders	−0.2	(0.1)
Headaches or migraines	−0.5*	(0.1)
Insomnia	−0.8*	(0.2)
Neurological disorders	−0.2*	(0.1)
Respiratory disorders	−0.1	(0.3)
II. Mental		
Alcohol abuse[b]	−0.1	(0.0)
Bipolar disorder	−0.1	(0.0)
Drug abuse[b]	−0.0	(0.0)
Generalized anxiety disorder	−0.1	(0.0)
Major depressive episode	−0.6*	(0.1)
Panic disorder/agoraphobia	−0.2*	(0.1)
Posttraumatic stress disorder	−0.1*	(0.1)
Social phobia	−0.2	(0.1)
Specific phobia	−0.2*	(0.1)
III. Any condition		
Physical disorders	−5.5*	(0.5)
Mental disorders	−1.6*	(0.1)
Any disorder	−7.0*	(0.5)

*Significant at the .05 level, two-sided test

[a]Estimated change in the population-level VAS mean associated with eradication of the disorder net of other disorders.

[b]With or without dependence