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Estimating the true global burden of mental illness

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Abstract/Summary

We argue that the global burden of mental illness is underestimated and examine the reasons for under-estimation to identify five main causes: (i) overlap between psychiatric and neurological disorders; (ii) the grouping of suicide and self-harm as a separate category; (iii) conflation of all chronic pain syndromes with musculoskeletal disorders; (iv) exclusion of personality disorders from disease burden calculations; and (v) inadequate consideration of the contribution of severe mental illness to mortality from associated causes. Using published data, we estimate the disease burden for mental illness to show that the global burden of mental illness accounts for 32·42% of years lived with disability (YLDs) and 13·03% of disability adjusted life years (DALYs), instead of the earlier estimates suggesting 21·2% of YLDs and 7·07% of DALYs.

Currently used approaches underestimate the burden of mental illness by more than a third. Our estimates place mental illness a distant first in global burden of disease in terms of YLDs, and level with cardiovascular and circulatory diseases in terms of DALYs. The unacceptable apathy of governments and funders of global health must be overcome to mitigate the human, social, and economic costs of mental illness.

Introduction

Mental health is defined by the WHO as “a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community”.¹ This state, however, is disrupted in one of every three individuals –or more– during their lifetimes.^{2,3}

Worldwide the magnitude of mental illness has been highlighted by studies on the global burden of disease.⁴ Yet, in spite of the very considerable burden and their associated adverse human, economic and social impacts, global policy makers and funders have so far failed to prioritise treatment and care of people with mental illness.^{5,6} Consequently, people with mental illness worldwide are largely neglected.⁶ Pervasive stigma and discrimination^{7,8} contributes, at least in part, to the imbalance between the global burden of disease attributable to mental disorders, and the attention these conditions receive. Stigma, embodied in discriminatory social structures, policy and legislation, produces a disparity between services geared to physical health and mental health, with lower availability, accessibility and quality of services for the latter.⁹

Globally, rapid economic, demographic, and epidemiological transitions mean a growth in populations that are living longer, but with greater morbidity and disability.¹⁰⁻¹³ Mental disorders are a major driver of the growth of overall morbidity and disability globally.^{14,15}

Five types of mental illness appear in the top 20 causes of global burden of disease (GBD): major depression (2nd), anxiety disorders (7th), schizophrenia (11th), dysthymia (16th), and bipolar disorder (17th) were leading causes of years lived with disability in 2013.¹¹ In this context, this paper aims to: offer a constructive critique of current estimates of GBD related to mental illness; argue that in aggregate mental illness is underestimated; and explore an alternative approach to produce more realistic GBD estimates of mental disorders worldwide. We do not propose a different nosology of

disorders, but aim to better gauge the disease burden of mental illness. An important benefit of a new GBD estimation is to inform prioritisation of health needs and resource allocation, so our aim is to provide decision makers, who rely on specialists to design and implement policies, with a new set of assumptions and tools to produce more accurate estimations using existing data.

Burden of mental illness: measurement challenges

We argue that the burden of mental illness has been underestimated due to five reasons: (i) the overlap between psychiatric and neurological disorders; (ii) the grouping of suicide and behaviours associated with self-injury as a separate category outside the boundary of mental illness; (iii) the conflation of all chronic pain syndromes with musculoskeletal disorders; (iv) the exclusion of personality disorders in mental illness disease burden calculations; and (v) inadequate consideration of the contribution of severe mental illness to mortality from associated causes.

We discuss each of these measurement issues and methodological considerations. Diagnostic classifications such as the ICD-10 system present challenges: they need to consider both the clinical syndrome and the aetiology of each disorder, with the goal of providing a system that is meaningful at the individual explanatory and therapeutic levels, considering the presentation of the illness as well as its natural history. Further, ICD-11, which is currently under development and is due to be approved by the World Health Assembly, is identified by the Advisory Group for ICD-11 as a better tool for reducing burden of mental illness, but without specific mention of improvements in the estimation of global disease burden related to mental disorders as a goal for the revision.¹⁶

The GBD estimation framework uses a comprehensive, mutually exclusive hierarchical list of disorders based on the ICD-10 classification mainly for two reasons: (a) to take advantage of a common nosologic language, and (b) to account for 100% of the disease

burden without double counting (see Appendix Box 1). But GBD differs from nosologic systems: instead of the individual level, it is mainly concerned with the population level; and instead of informing individual aetiology and therapy, it needs to allow for a better understanding of disease distribution and transitions, in order to guide prioritization of population health needs and organization of health services.

The actual grouping of disorders used by the GBD – a hierarchical cause list comprising four levels of aggregation – is sometimes based on clinical grounds (such as with Cardiovascular and Circulatory conditions, a level 2 aggregation), and sometimes on a mix of disease or anatomical criteria (such as Diabetes, Urogenital, Blood and Endocrine disorders, also level 2).¹⁷ Consideration of more pertinent criteria for aggregation is warranted (Appendix Box 1).

The psychiatric-neurological interface

Traditionally, disorders both affecting the central nervous system and producing mental disorders were divided between psychiatric and neurologic conditions: if the syndrome had a clear neuroanatomical or neurophysiological basis it was considered *neurologic*; if not, it was deemed *psychiatric*. This dual distinction, however, has more to do with professional areas of competence than scientific logic. For example, schizophrenia, considered a *psychiatric* disorder, affects the brain's anatomy and physiology, and secondarily produces the cognitive, affective, and behavioral symptoms that constitute the mental syndrome. On the other hand, epilepsy, typically considered a *neurological* disorder, includes conditions such as temporal epilepsy, in which a clearly identifiable psychiatric syndrome is frequently accompanied by an absence of electroencephalographic abnormalities. Given that the nosologic classification for these disorders is in flux and the division between them is arbitrary, other criteria should be used when aggregating diseases for measuring burden. In this respect, in addition to their presentation as psychiatric syndromes, these disorders pose a common challenge at the primary care level, particularly in low and middle income countries, and a common grouping would make this more visible to planners and funders.

Categorizing suicide and intentional self-harm

In 2013, mental illness accounted for 21.2% of the YLDs worldwide – higher than any other group of conditions.¹¹ However, using the composite measure DALYs, the burden of mental illness accounted for 7.1%, ranking fifth overall in terms of global burden of disease.^{18,19} The gap between the burden of mental illness as measured by years lived with disability and that measured by disability adjusted life years is explained by the fact that DALYs underestimate mental illness mortality due to suicide, to the disease process itself and to reasons secondary to the mental disorder. Suicide and all forms of self-harm, which are to a large extent imputable to mental disorders, are coded under *injuries*, and are excluded from calculations of the impact of mental illnesses.^{10,20,21}

Ferrari et al. studied mental disorders as risk factors for suicide reviewing existing literature, pooling relative-risk estimates and then estimating which percentage of deaths by suicide could be causally linked to a number of mental disorders (mainly mood and anxiety disorders, substance abuse and schizophrenia). After reviewing the psychological autopsy studies available, the authors assign ceiling values to account for cultural variability in the causal relation between mental illness and suicide, and suggest an addition of 22 million DALYs amounting to 0.9% of total DALYs to the mental illness burden.²¹ These estimates would have been higher if all self-harm (suicide, attempted suicide, and self-injurious behaviour) due to mental illness and sub-syndromal conditions were included. Ferrari et al. reduce the attribution of lethal self-harm to the mental illness burden based on two arguments: (a) the authors put a cap of 68% to suicides attributable to mental illness taking place in China, India and Taiwan, which account for 50.0% of the world's suicides, and of 85.0% to those happening elsewhere, and (b) they don't include suicides in the context of sub-syndromal states (e.g.: impulsive states, which are common in the context of personality disorders, also excluded from the GBD).

From a clinical and public health perspective we have three caveats with the approach used by Ferrari et al.: first, it does not account for non-lethal self-harm, which includes both attempted suicide and self-injurious behavior; second, by excluding suicides in the context of sub-syndromic states and restricting the assessment to specific disorders, it leaves around 25.0% of the world's suicides and 39.0% of suicide burden in the category of injuries, along with traffic accidents, where they clearly don't belong; and third, the assignment of a low ceiling due to cultural considerations in China, India, and Taiwan is questionable as cultural differences could mean that stigma associated with mental illness but not with suicide leads to under-reporting of the causal link. For example, in China, suicide has been established as a frequent outcome in the context of mental syndromes, even in the absence of full diagnostic criteria. Case control studies of non-lethal attempted suicide have shown that cases had significantly higher stress, impulsiveness and aggression, more severe depressive symptoms, and were more likely to meet criteria for a psychiatric diagnosis. Of the psychological factors, severity of depressive symptoms in the two preceding weeks was the most significant, to the extent that suicide in China is linearly related to severity of depression.^{22,23} And the limitations of the psychological autopsy studies on which Ferrari et al. base their rationale for excluding a third of the global self-harm disease burden from mental disorders allow for a very different conclusion: the existence of a psychiatric diagnosis was established indirectly by interviewing family members, and personality disorders were excluded from the assessment, potentially leading to significant under-registry.²⁴ In this context, the attribution of self-harm – lethal or not – to impulsiveness, aggression, and availability of a lethal tool, does not disprove the existence of an underlying mental disorder. The authors highlight these limitations, acknowledging that the conventional wisdom that suicide is almost always the outcome of mental illness will not be altered by their studies.²⁵ In other words, the absence of unequivocal evidence of the causal link is not evidence of absence of a causal link. Hence the decision to allocate disease burden from suicides to *Injuries* or to *Mental Disorders* needs to be carefully considered.

In this context, and with insufficient evidence, what is the preferred choice between different burden estimation methods? The rationale by Ferrari et al. to leave all non-lethal self-harm and a quarter of the world's suicides –therefore more than a third of self-harm DALYs – in the Injuries aggregation doesn't seem justifiable. We find it preferable from a population health perspective to aggregate all self-injuries with the mental health related disease burden, with the caveat that it is likely to incorrectly include the burden of suicides that can be judged to be non-mental health related, such as assisted suicide (producing a much smaller error than the alternative approach).

Chronic pain syndromes

Musculoskeletal conditions were the second major cause of YLDs¹¹ and seventh ranked cause of DALYs in 2013 globally.²⁶ They include anatomically based disorders (such as osteoarthritis and rheumatoid arthritis), and also syndromes and symptoms (e.g. fibromyalgia, low back pain) characterized by pain but without specific anatomical correlates. The allocation of the burden corresponding to these syndromes *in total* to the *musculoskeletal* aggregation is problematic, since (a) a significant proportion of these disorders, which account for up to 6.1% of DALYs globally, should actually be classified as either 'chronic pain syndrome' (currently considered as disorders of the nervous system by the ICD-10 classification but should be considered as mental and behavioural disorders) or 'somatoform disorder' (considered as mental and behavioural disorders in ICD-10), (b) the prevalence of these pain disorders in patients with a major affective, anxiety, or stress related disorder exceeds 30%, and in certain samples with post-traumatic stress disorder reaches 80%, and (c) they converge with chronic mental illness at the therapeutic and service delivery level. These caveats suggest the existence of subpopulations with a common syndrome, which are difficult to classify from a nosologic perspective (see Appendix Box 2). We argue that when estimating disease burden, it is reasonable to attribute a proportion of these conditions to mental illness.

Including people with personality disorders

Personality disorders are common (4-15% in point prevalence community surveys)²⁷ and when severe impose a significant burden both at personal, family, community, and population levels. People with personality disorders have shorter life expectancy and higher comorbidity with other general and mental illnesses than the general population.²⁷ However, due to the inconsistent quality of the evidence personality disorders were not included in GBD 2013 estimates within the overall category of mental illness.²⁶ A proportion of their disease burden might be currently under the '*Other mental and substance use disorders*' aggregation, but hardly capturing its true relevance and the need to consider them in their own right. Another portion, arguably significant, might be captured under the *Musculoskeletal* aggregation, given that 30% of people diagnosed with chronic pain syndromes also have personality disorder.²⁸ Finally, we have seen that personality traits such as impulsivity and aggression, as well as depressive symptoms, frequently provide the psychological context in which self-harm occurs, providing a rationale to aggregate self-harm under the mental disorder burden. Though our re-allocation of self-harm and a fraction of chronic pain (see below) partially recaptures this burden, there is not enough data to comprehensively account for the burden of personality disorders.

Premature mortality

People with severe mental illness have up to 60% higher chances of dying prematurely, from non-communicable diseases²⁹ that are neglected because of the underlying mental condition. They die 10 to 20 years younger than their peers in high income countries, and 30 years younger in low income countries.³⁰⁻³² Charlson et al. estimate that up to 8% of years of life lost globally corresponded to excess deaths due to mental health related conditions including dementia, epilepsy, and migraine.³³ Indeed, a recent systematic review estimated that 14.3% of deaths worldwide, or approximately eight million deaths each year, are attributable to mental disorders.³² However, mental

disorders appear to only account for 0.5% of total years of life lost, because GBD estimates only reflect deaths directly attributed to mental disorders recorded in death certificates (mostly due to schizophrenia and substance abuse), which leads to zero global deaths attributed to bipolar disorder, depression, and other mental illnesses. The result with current methodology, which does not count excess deaths due to self-harm and increased overall mortality, is that in the case of mental illness, DALYs are basically YLDs. The issue of self-harm can be partially addressed through aggregation (see below), but the issue of increased mortality due to general conditions poses a very complex challenge. GBD methodology is based on zero-sum attribution, which means that if a patient with schizophrenia suffers a fatal myocardial infarction at 55 years old as a result of smoking, for which she is at increased risk, and neglected metabolic syndrome – a likely consequence of antipsychotic medication – then her YLLs will be included in the cardiovascular DALYs. In the context of increasing NCD comorbidities, the tradition of attributing mortality to a single disease should be reassessed, and alternative approaches explored, such as partial attribution of YLLs resulting from a single death to different frequently co-occurring disorders.

Revising Disability Adjusted Life Years (2013) estimates for mental illness

For these reasons set out above we propose that when estimating disease burden, certain *neurologic* syndromes i.e. the dementias, epilepsy, tension-type headache, and migraine should be aggregated within the overall category of mental illness. This adjustment would move the total rank of mental illnesses in the GBD tables from 5th to 3rd place overall, accounting for 9.8% of DALYs globally (Table 1). Repositioning all self-harm related DALYs from the category of *injuries* to *mental health* would increase the number of DALYs from 9.8 to 11.2%, placing it 2nd in the ranking (Table 1).

Chronic pain syndromes can potentially account for a significant fraction of the 5.4% of DALYs currently attributed to low back, neck pain plus *other musculoskeletal*, once we exclude entities for which there is evidence of a musculoskeletal critical mechanistic

level (such as arthritides and gout). As highlighted in Appendix Box 2, a proportion of the burden resulting from these syndromes should be aggregated to the *mental* rather than *musculoskeletal disorder burden*. However, due to a lack of primary disaggregated data it is not possible to gauge with any precision: (a) which portion of the burden of *musculoskeletal disorders* corresponds to these chronic pain syndromes; or (b) which portion of chronic pain syndrome burden corresponds to centrally caused syndromes (and therefore to the mental/neurologic burden as previously defined). Considering that a fraction of *low back, neck pain*, and 50% of *other musculoskeletal* potentially corresponds to chronic pain syndromes, and for the purposes of producing a more accurate estimation and stimulating debate, we assume given the limited data that one third (rather than 0%, as it is now) of the disease burden of these pain syndromes is potentially attributable to mental disorders and explore the effect on mental illness burden calculations: re-allocating 1.8% of global DALYs would increase mental illness burden from 11.2% (with certain neurological disorders and self-harm added) to 13.0% of total, practically tied with all cardiovascular and circulatory disorders, which account for 13.5% (Table 1).

(Table 1 about here)

Revising Years Lived with Disability (2013) estimates for mental illness

In 2013, mental illness accounted for 21.2% of global YLDs, 3.5 times greater than the disability associated with all infectious diseases (6.0% of YLDs), 4 times that for all injuries combined (5.0% of YLDs), 8 times the disability associated with all cardiovascular and circulatory diseases (2.8% of YLDs), and 24 times the disability associated to all cancers (0.9% of YLDs). Musculoskeletal disorders (plus fractures and soft tissue injuries) accounted for 20.8% of total YLDs.¹¹ As we have argued above, a significant portion, which we assume to be 5.1 percentage points (see Table 2), potentially corresponds to chronic pain syndromes that should not be considered *musculoskeletal*, but are rooted

in the central nervous system and therefore better understood as part of the burden of mental illness. Applying our framework, the new YLD estimation of mental health related burden is 32.4%.

(Table 2 about here)

Our estimations of disability alone (YLDs) and combined with mortality (DALYs) indicate that by excluding certain conditions from the mental illness burden current assessments underestimate both YLDs and DALYs by more than a third (see Figures 1 and 2). We also show that mental illness accounts for a third of the global disability (Table 2), instead of a fifth, as currently estimated.

Disproportionately weak global response to mental illness

The global development assistance for health (DAH) allocated to mental illness is far below the levels warranted by the impact of these disorders. The Millennium Development Goals (MDGs)³⁴ prioritised child health (MDG 4), maternal health (MDG 5), and communicable diseases (MDG 6), which collectively accounted for 46.9% of DALYs 25 years ago,¹⁸ and attracted the vast majority of DAH reaching 68.0% of the \$35.9 billion disbursed in 2014.^{35,36} Despite the changing burden of disease, characterized by multi-morbidity and disability,¹² from 2000 to 2014 only 1.5% of DAH was invested globally in NCDs (combined, accounting for 82.0% of YLDs) (see Table 3),^{35,37} while none of the MDGs referred to mental illness, which received 0.40% of DAH despite accounting for 32.4% of YLDs.

(Table 3 about here)

The imbalance between disease burden, financing, and service access is observed in countries of different income levels (Appendix Table1): global median spending in mental health stands at 2.8% of total health spending, more than two thirds of which

are on average allocated to neuropsychiatric hospitals in spite of international evidence-based recommendations for community based services.³⁸

Low income countries spend a very modest 0.5% of national health budgets on mental health, with up to 90.0% going to stand-alone psychiatric institutions that provide, in population terms, very low rates of treatment (contact) coverage. Although high income countries provide adequate services, there are variations in accessibility and coverage for geographic and socio-economic groups.^{39–41}

Discussion

The recent GBD (DALY and YLD) estimates produce an under-estimate of the true impact of mental disorders on populations due to (i) the overlap between psychiatric and neurological disorders; (ii) the grouping of suicide and behaviours associated with self-injury as a separate category outside the boundary of mental illness; (iii) the conflation of all chronic pain syndromes with musculoskeletal disorders; (iv) the exclusion of personality disorders in mental illness disease burden calculations; and (v) inadequate consideration of the contribution of severe mental illness to mortality from associated causes. Using the currently available evidence and specified assumptions to correct (i), (ii), and (iii), we provide a more accurate picture of mental illnesses as a leading cause of global disease burden.

Why are these findings important?

Mental disorders – in various forms and intensities – affect a majority of the population in their lifetime.^{2,3} In most cases people experiencing mild episodes of depression or anxiety deal with them in ways that allow them to continue living a productive life. A significant minority of the population, however, experience more disabling conditions such as schizophrenia, Alzheimer’s disease, bipolar disorder type I, severe recurrent depression, and severe personality disorders. Whereas *common mild disorders* are

amenable to self-management and relatively simple educational or support measures, *severe mental illness* demands complex, multi-level care that may require a longer-term engagement with the individual, and with the family. Hence a more nuanced and accurate picture of mental health related burden is critical to effectively allocate resources and appropriately design health systems in proportion to the nature and the scale of these challenges.

Why are these findings important now?

Universal Health Coverage, identified as a Sustainable Development Goal⁴², offers opportunities for addressing the neglect for mental illnesses, which constitute, along with all cardiovascular plus circulatory disorders (13·0% and 13·5% respectively), the leading causes of global disease burden. Of particular importance is the inclusion of the mental health indicators proposed in the 2015 Global Reference List of Core Health Indicators⁴³ (see Appendix Box 3).

Limitations of this approach

The main limitation of this study is the difficulty of quantifying the disease burden associated with: (1) personality disorders, (2) excess all-cause mortality secondary to mental illness, and (3) chronic pain syndrome burden as part of the mental illness burden. Regarding 1 and 2, data for further evidence-based assumptions is required, so their contribution remains to be determined. Regarding chronic pain syndromes, there is partial evidence to make a scientifically informed assumption that in our view provides a better estimate than the current hypothesis of 0% attribution. However, the speculative nature of the portion of the chronic pain burden considered by the authors to be related to mental health –one third- remains hypothetical.

Time for Global Action

Globally, achieving effective coverage will demand concerted global stewardship to increase funding for mental illness, better allocate resources, and improve integration of mental illness with other health services.

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Table 1: The effect of reallocating disability adjusted life years (DALYs) of neurological disorders, self-harm and a fraction of chronic pain syndrome

| Rank | Global burden of disease 2013 | DALYs (%) | Reallocating neurological disorders ¹ | DALYs (%) | Reallocating self harm ² | DALYs (%) | Reallocating chronic pain syndrome ³ | DALYs (%) |
|------|-------------------------------|-----------|--|-----------|-------------------------------------|-----------|---|-----------|
| 1 | Cardiovascular disease | 13.5 | Cardiovascular disease | 13.5 | Cardiovascular disease | 13.5 | Cardiovascular disease | 13.5 |
| 2 | Common infections | 10.2 | Common infections | 10.2 | Mental illness | 11.2 | Mental illness | 13.0 |
| 3 | Cancer | 8.1 | Mental illness | 9.8 | Common infections | 10.2 | Common infections | 10.2 |
| 4 | Neo-natal | 7.7 | Cancer | 8.1 | Cancer | 8.1 | Cancer | 8.1 |
| 5 | Mental illness | 7.1 | Neo-natal | 7.7 | Neo-natal | 7.7 | Neo-natal | 7.7 |

Analysis based on data from Murray et al, 2015¹⁹ and from: <http://ghdx.healthdata.org/global-burden-disease-study-2013-gbd-2013-data-downloads>, Sept 26, 2015.

¹ Neurological disorders repositioned to mental illness: Dementias, epilepsy, migraine, “tension-type” headache (66872300 DALYs)

² Self-harm repositioned to mental illness: 35170400 DALYs

³ Considering a third of the 131697900 DALYs (1.8%) of potential chronic pain syndrome currently attributed to musculoskeletal disorders should be reattributed to mental disorders

Table 2: The effect of reallocating years lived with disability (YLDs) of neurological disorders, self-harm and chronic pain syndrome

| Rank | Global burden of disease 2013 | YLDs (%) | Reallocating neurological disorders ¹ | YLDs (%) | Reallocating self-harm ² | YLDs (%) | Reallocating Chronic Pain Syndrome ³ | YLDs (%) |
|------|-------------------------------|----------|--|----------|-------------------------------------|----------|---|----------|
| 1 | Mental illness | 21·2 | Mental illness | 27·2 | Mental illness | 27·3 | Mental illness | 32·4 |
| 2 | Musculoskeletal | 20·9 | Musculoskeletal | 20·9 | Musculoskeletal | 20·9 | Musculoskeletal | 15·7 |

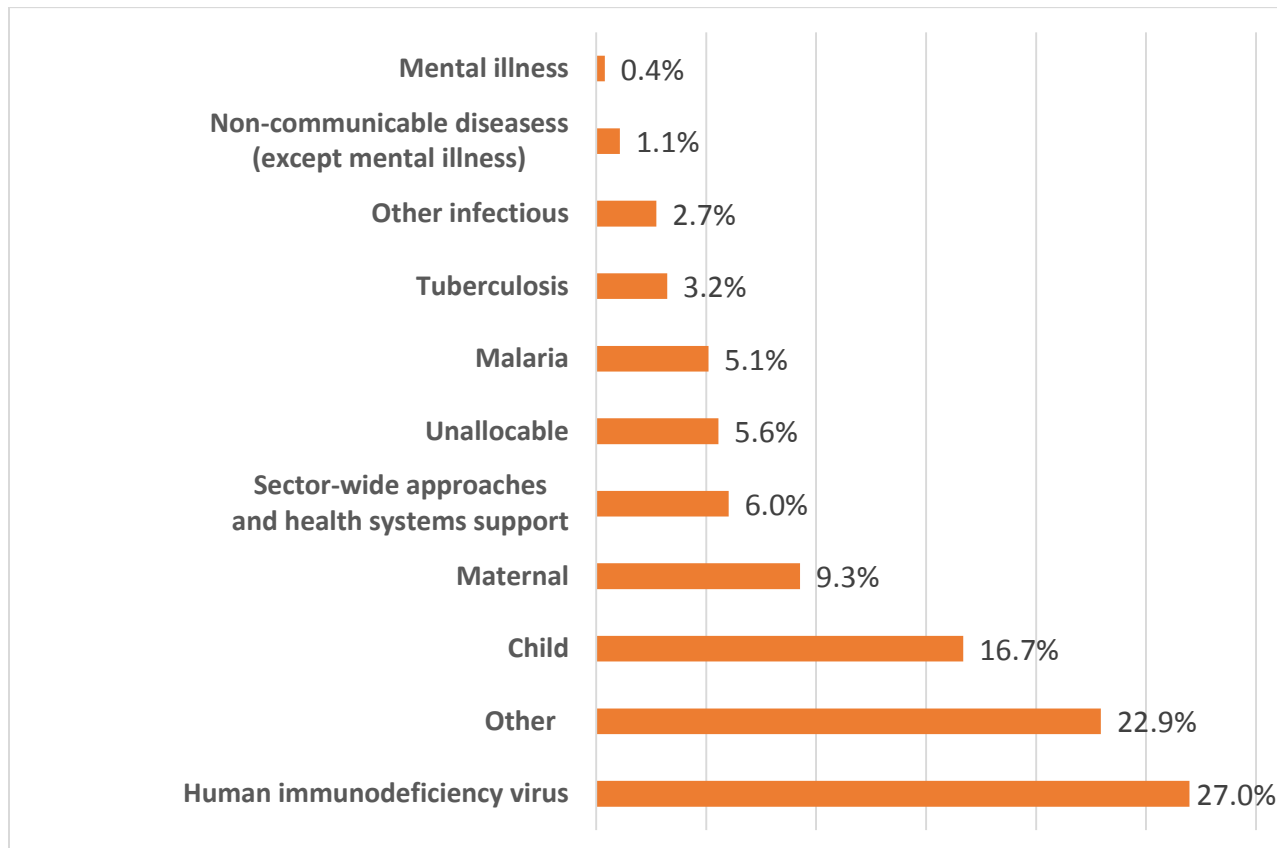
Analysis based on data from Vos et al, 2015¹¹

¹Neurological disorders repositioned to mental illness: Dementias, epilepsy, migraine and tension-type headache (46579100 YLDs)

²Self-harm repositioned to mental illness: 231600 YLDs

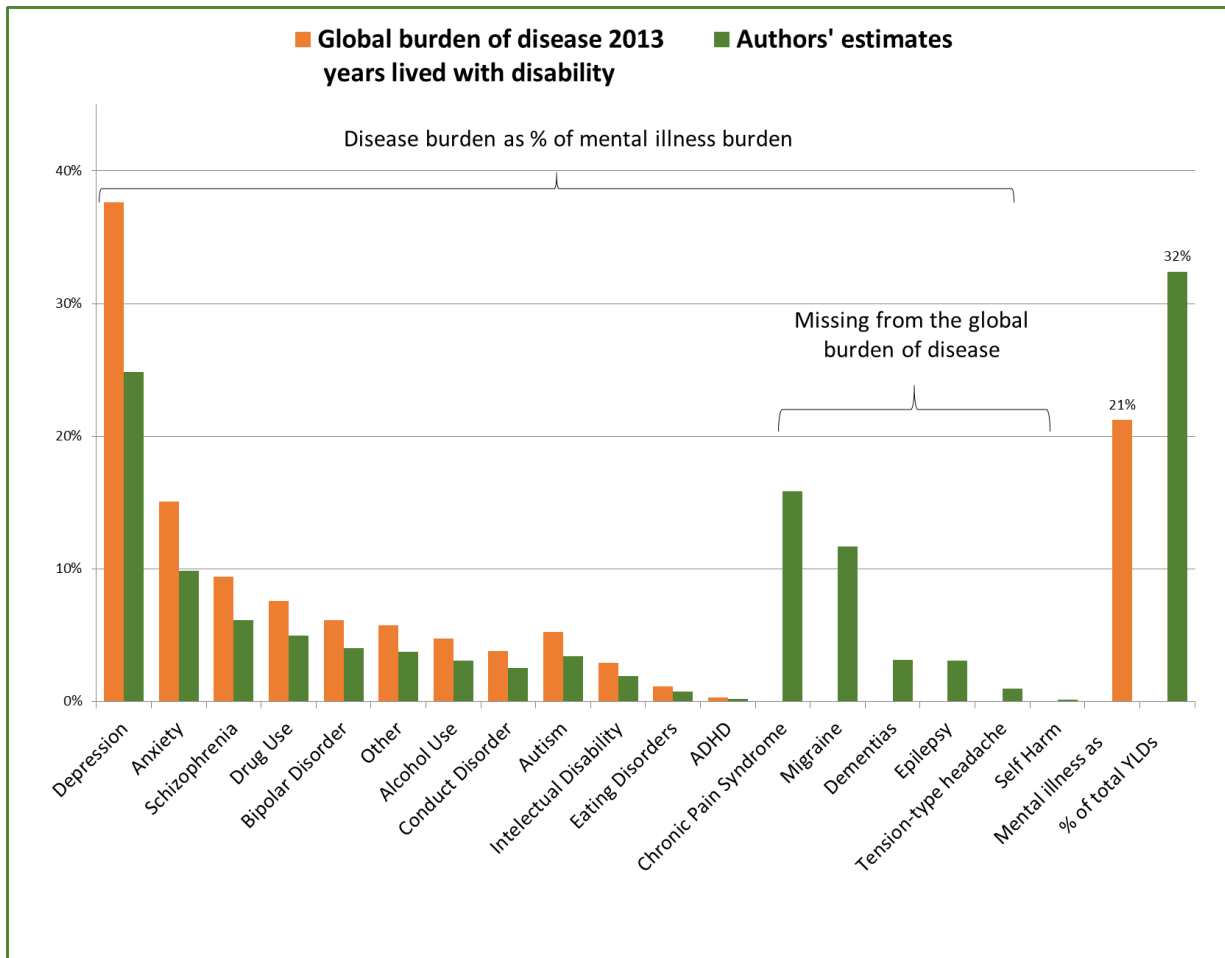
³Applying the same rationale and repositioning the same proportion as in Table 1 from musculoskeletal to mental illness (5·1 percentage points –a third- of 15·4%, which are the YLDs attributable to chronic pain syndromes and other musculoskeletal disorders, excluding anatomically based lesions)

Table 3. Development assistance for health per area, 2000 to 2014



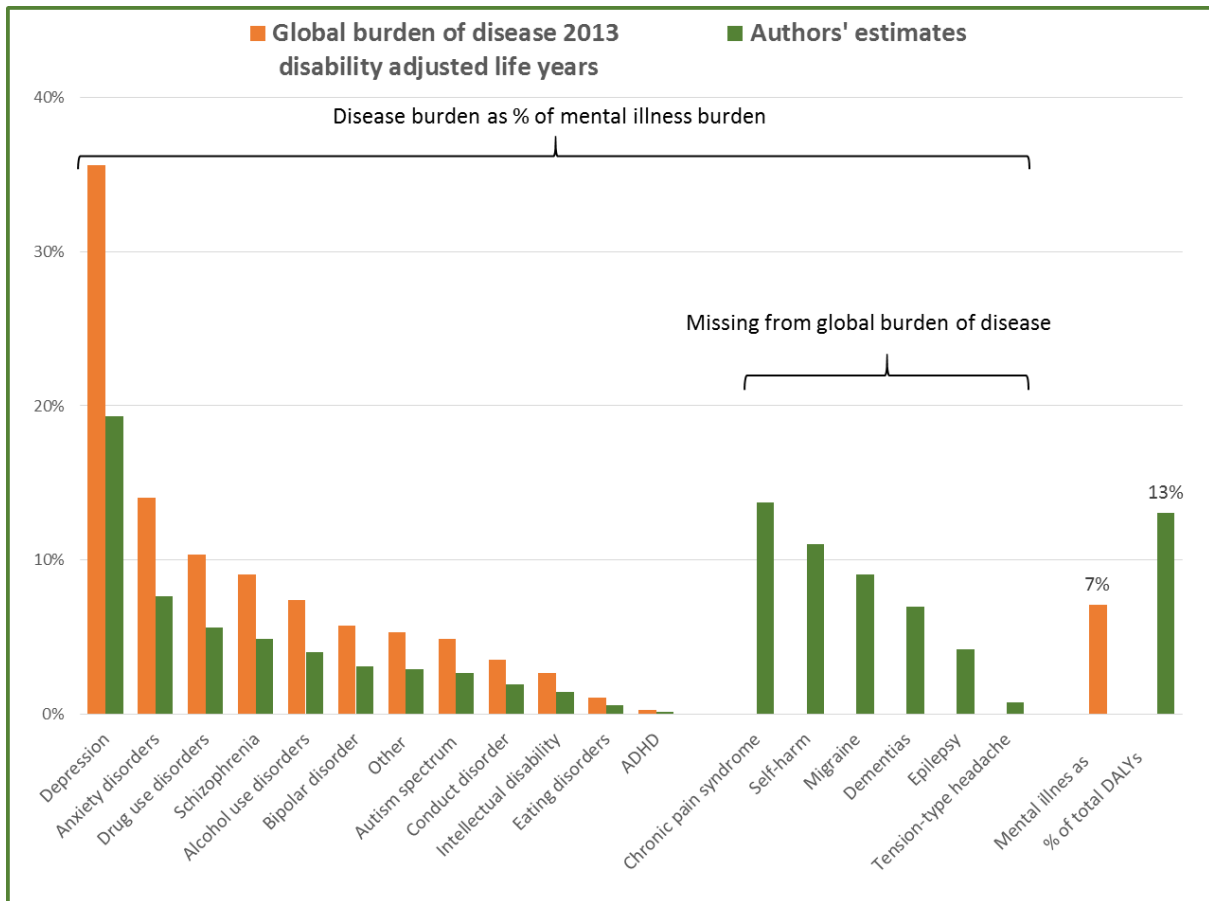
Analysis based on data from Institute for Health Metrics and Evaluation, 2015. Reference 35.

Figure 1. Comparison of Global Burden of Disease 2013 years lived with disability with the authors' estimates



Analysis based on data from Vos et al, 2015¹¹

Figure 2. Comparison of Global Burden of Disease 2013 disability adjusted life years with the authors' estimates



Analysis based on data from Murray et al., 2015¹⁹

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Appendix

Box 1: 25 years estimating the Global Burden of Disease: DALYs, YLLs, and YLDs revisited

The GBD methodology was developed in 1990 as an attempt to provide a composite measure comprising mortality and disability, and allowing for comparison of burden across diseases and across countries. The scope of the collaboration has grown and the basic methodology has evolved over time in response to the scientific community's input. The staple is still the measure Disability Adjusted Life Years (DALY), which is the sum of the Years of Life Lost (YLLs) due to premature mortality and the Years Lived with Disability (YLDs) produced by a given disorder –or group of disorders- in a given country, region, or globally.

The YLL can be understood as a mortality measure weighted by *normative* life expectancy: death will produce a number of YLLs equivalent to life expectancy minus age of death. The normative life tables, with a life expectancy at birth of 86, were developed to reflect the lowest death rate for each age group observed in countries of more than 5 million people.(1)

The YLD can be understood as a measurement of disability weighted by the general public's perception of different health states resulting from disease. This was achieved through empiric assessment: a survey was conducted in five countries from different regions (n=13902) and online (n=16328), eliciting paired comparisons between two random health states (i.e.: asking which of the two was regarded as *healthier*), and producing a disability weight between 0 –perfect health- and 1 –equivalent to death-. The YLD is the result of multiplying the disability weight by the prevalence of the disorder.(2)

To classify diseases, the GBD produces a list of 306 diseases and injuries –from the ICD-10 nosology-, aggregated in four hierarchical levels. There are three categories in the first level: *communicable, maternal, neonatal and nutritional disorders; non-communicable disorders (NCDs); and injuries*. In the second level we find 21 mutually exclusive and collectively exhaustive aggregations, among them: *mental and substance use disorders; musculoskeletal disorders; cardiovascular and circulatory disorders; diabetes, urogenital, blood and endocrine; self-harm and interpersonal violence*. The third level presents lower levels of aggregation, such as *depressive disorders, low-back and neck pain, and self-harm* (with no lower aggregations for *self-harm*). The fourth level contains individual diseases, such as *major depressive disorder and low-back pain*, or the lowest level of aggregation available, such as *Alzheimer's disease and other dementias*. This is a dynamic hierarchical list, in which several factors –such as quality of evidence, perceived burden, or policy interest- influence the decision of whether to include a specific disorder. Some aggregations follow clinically related syndromes (such as *depressive disorders* for *major depression* and *dysthymia*, sometimes they follow epidemiologic considerations

(such as *NCDs*), and sometimes they are laundry-lists (*DUBE*). Given these considerations, it is legitimate –and even desirable– to explore different aggregations ex-post (such as we propose for some *neurological disorders*, *self-harm*, and a fraction of *chronic pain syndrome*), to better inform specific estimates. This kind of repositioning, aimed at a more nuanced understanding in the light of insufficient data, respects the *zero-sum* criterion. More challenging is the correction of estimates of excess death resulting from multi-morbidity without double counting (*see Premature mortality*).

Box 2. The nosologic conundrum of pain syndromes

Painful syndromes highlight the frequently arbitrary nature of diagnostic classifications, particularly when etiology is unclear. Most mental disorders are syndromes – collections of symptoms and signs – which based on the existing evidence are believed to be causally related to underlying disease entities. This relation – between the syndrome we diagnose and the underlying disease – is not transparent, and in some cases widely contested. It escapes the scope of this article to review psychiatric nosology, but it is necessary to bear in mind that nosologic classifications should be based on the best existing evidence. And in the absence of nosologic clarity, GBD aggregation decisions should contemplate population health needs and service delivery considerations.

As was mentioned before, standard GBD methodology is based on strictly following ICD criteria, which warrants comprehensive burden allocation without double counting. The tradeoff is that results can be misleading, particularly when they compound nosologic limitations. They need to be qualified and contextualized so that they are useful to inform population health interventions.

The case of painful syndromes is an example of how dualistic thinking muddles nosology: ICD-10 includes chronic pain syndrome and persistent somatoform pain, while DSMIV offers pain syndrome, and DSM5 settles for somatic symptom disorder with predominant pain. Despite the lack of nosologic clarity, these are highly prevalent disorders: for example in Germany, following strict diagnostic methodology, pain disorder stood out as the most prevalent psychiatric disorder in the general population, with an 8% yearly prevalence (11% for women and 4% for men).(3) None of these disorders are captured as such in the GBD list of causes,(4) arguably because of the scarcity of quality evidence at the global level. Given GBD methodology, this sub-group of complex patients are in all likelihood included in the *low-back, neck, and other painful syndromes* aggregations. Mechanically aggregating them to the *musculoskeletal disorder burden* ignores a piece of consistent evidence we actually have: what characterizes a sub-group of these patients is the lack of an anatomical musculoskeletal correlate to their clinical syndrome, and a growing body of evidence actually points in the direction of these pain syndromes being related to neurologic or psychiatric disorders. They are frequent conditions -8% yearly prevalence-, so highly co-morbid with mental disorders -53% have concurrent mood or anxiety disorders(3)- that painful symptoms are often considered part of the wider mental syndrome.(5,6) Plausibility also suggests that the critical mechanistic level for these conditions is the central nervous system -through a central dysregulation of pain sensitivity(7-9)-, rather than the musculoskeletal

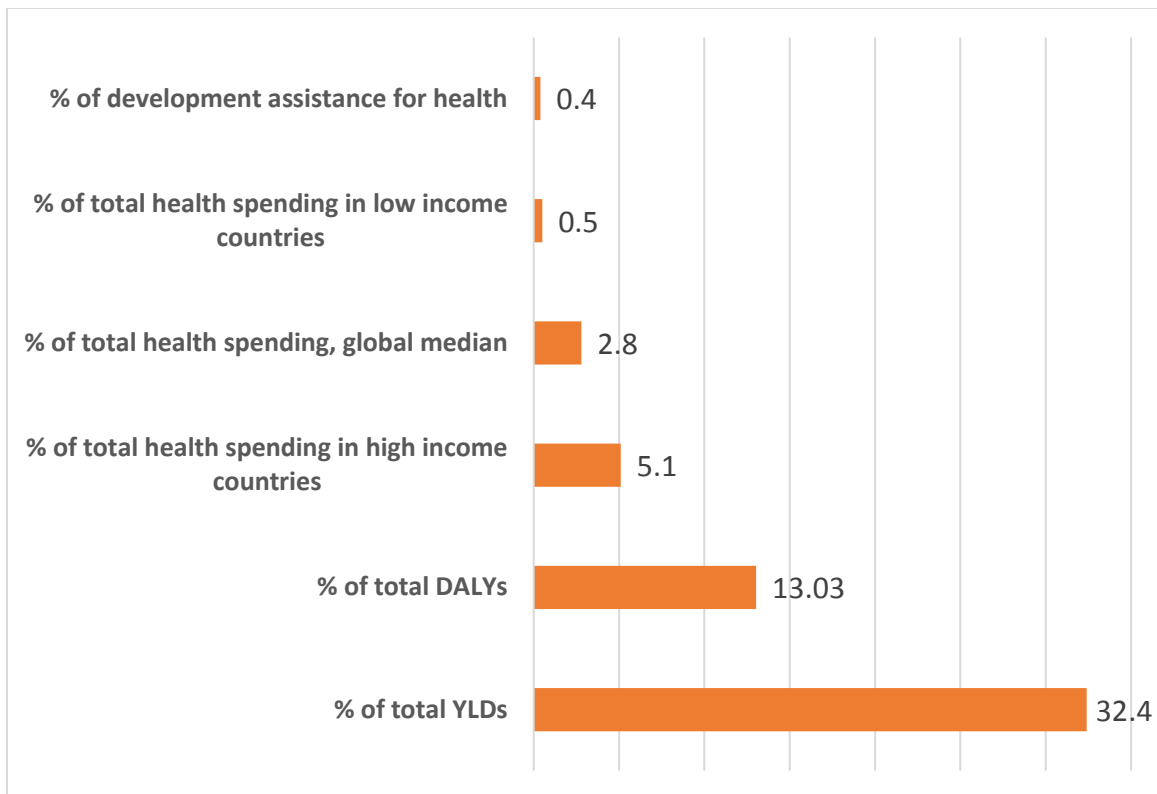
system, where by definition there is nothing specific to be found. In addition to the arguments related to nosology and plausibility, we also find convergence at the therapeutic service delivery level: chronic pain syndromes are most frequently treated with antidepressants and anticonvulsants, which are the only types of drugs that have yielded consistent evidence of partial efficacy, plus a variety of psychotherapeutic and psychosocial approaches, just like chronic mental disorders.(10) So if we were to be guided by the evidence, we should conclude that a significant sub-group of these patients, difficult to identify nosologically with current tools, suffer from a disease burden that is better placed in the *mental* than in the *musculoskeletal* aggregation.

Box 3: Indicators for mental health to track the 2015 Sustainable Development Goals

Indicator 23: Probability of dying between exact ages 30 and 70 from any of cardiovascular disease, cancer, diabetes, chronic respiratory disease, or suicide

Indicator 28: Proportion of persons with a severe mental disorder (psychosis, bipolar affective disorder, or moderate-severe depression) who are using services

Appendix Table 1: Spending on mental illness as a proportion of development assistance for health, of total health expenditure by country income level, and burden of mental illness as a proportion of global disease burden



Analysis based on data from Institute for Health Metrics and Evaluation. References 11 and 12.

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