On Burden: A Study of the Population-Level Health-Effects of Mental Illness

ON BURDEN: A STUDY OF THE POPULATION-LEVEL HEALTH-EFFECTS OF MENTAL ILLNESS

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Abstract

The burden of disease framework provides a unique tool for rational health systems planning. However, due to methodological constraints it systematically underestimates the burden of mental disorders. I develop a constructive critique of the burden of disease methodology, and a framework to partially correct current estimates. This framework is then applied at different levels -province, country, continent, and globally- with the goal of: (a) adequately informing mental health prioritization and intervention by governments and organizations; (b) detecting disease distribution patterns in countries belonging to different sub-regions and income-levels; (c) understanding the ecological association of group-level poverty and specific mental disorders; (c) quantifying the imbalance between disease burden and government spending on mental health; and (d) making the case for considering the adequate care for mental disorders a global health and development priority. This study of the burden of mental disorders puts it at the top of the disability ranking -and second in the combined ranking of disability and mortality- globally and in the Americas, and provides actionable needs-assessments for governments, multilateral organizations, and non-profits. It provides a life-course perspective on how the epidemiologic transition shapes disease distribution across country-income levels, finds a direct association of the percentage of the population in poverty with group-level depression disability, an inverse association with schizophrenia disability -which can be ascribed to increased lethality in low-income settings-, and a direct effect -controlling for

group-level poverty- of disability due to depression in women of child-bearing age on under-five burden due to communicable, perinatal, and nutritional disorders. Also, it finds that the imbalance between burden and spending on mental health -factoring in allocative efficiency- is inversely associated with country income-level in the Americas: poorer countries spend a lower fraction of their health expenditures on mental health and allocate it less efficiently. Finally, I argue that in order to make mental health a global health and development priority, a governance and advocacy effort is required, including the creation of a specific organizational setting of global reach capable of engaging key partners that have so far been elusive, such as Governments, global donors, and economic actors.

Contents

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Introduction

Illness and injuries have always imposed, through premature death and disability, major constraints on humanity's potential. Before the advent of science and its transformative impact on public health and medical care, human life was severely interfered by illnesses and injuries, and much shorter. Furthermore, normal life-cycle events and situations, such as birth, infancy, pregnancy, and older age presented humans with stark odds of death and disability. For most of mankind's existence these odds were largely attributable to communicable diseases, injuries, and maternal or child conditions and disorders. The past century saw a dramatic shift on the toll imposed by disease and injury on human life. Between 1800 and 1900, life expectancy rose around 12% from 28.5 to 32 years.(1) Between 1900 and 2000, however, it more than doubled, reaching 71.4 in 2016 according to WHO.(2) In 50 more years global life expectancy at birth will reach 80 years old.(3) This dramatic change in the landscape of death and disease has not been homogeneous. The seminal paper by Samuel Preston -and the thereafter famous *Preston curve*- inextricably linked economic development and health: the hypothesis that increased country-level income led to improved health outcomes resulting in increased life-expectancy -with the most gains to be made at the bottom of the income pyramid- helped broaden the discussion on what influences health outcomes, to include income and, more broadly, social determinants of health. This correlation -between income and health- can have, however, different causal explanations. Indeed, several authors pointed out that it is not merely income that begets health: it is by way of improved nutrition, education, and, most notably, advances in public health and medical care.(4–7) Indeed, before the 1900's health outcomes were more equitably distributed -i.e.: similarly dismal- between the rich and the poor, with the exception of injuries and diseases resulting from

the differential exposure of the poor and dispossessed to human-imposed hardships and the resulting human-made catastrophes -such as war, slavery, bondage, and inhumane labor conditions-.

In addition to the recent changes in mortality, it is important to highlight a similarly consequential shift in morbidity: whereas in the past -and to some extent in present day societies without access to adequate nutrition, education and health services- illness frequently led to death, today most diseases result in prolonged periods of treated illness with varying degrees of dysfunction. The classic epidemiologic approach to measuring population level morbidity is through incidence and prevalence, which provide respectively the number of emergent cases and the number of total cases in a given population and time period. So, the incidence, prevalence, and mortality of a given disorder give us a partial idea of its impact. However, they do not allow for a ready comparison across disorders. Diseases A and B can both have a 12-month prevalence of 500 per 100,000 persons, and they can have a similar cause-specific death rate. However, similar prevalence and similar mortality by no means results in similar impact: disease A can be mildly incapacitating and affect mostly people who have already surpassed their life expectancy at birth, while disease B can strike during youth, be highly incapacitating, and result in premature death. Schizophrenia would be an example of disease B. The societal impact of these diseases is clearly different.

The burden of disease framework emerged precisely to provide a single composite metric to understand and compare population level disability plus mortality outcomes across disorders, regions, and sub-populations such as women and men, young and old, etc. These metrics serve not only a descriptive purpose, but also a pragmatic goal: given the fact that income determines health outcomes partially through health interventions, the rational allocation of resources in

order to achieve the best possible health outcomes is of the highest societal importance. This is not only a question of economic efficiency, but also an ethical imperative. The burden of disease framework addresses only a fraction of this complex issue: it provides a composite metric of mortality and disability that can be used in cost-effectiveness analyses and health prioritization exercises. Like any complex metric, it is not only imbued with consequential technical assumptions, but also laden with value judgements that need to be taken into account in order to use them wisely. Mechanistic use of these metrics -which is the norm rather than the exception- can actually yield the wrong conclusion, and provide -under the guise of a rational hierarchy of interventions- an unethical or misinformed allocation of resources. This thesis' main focus is on the applicability of this framework and these metrics to the field of mental health. Furthermore, I will limit my scope to:

- understanding how the model's technical assumptions affect the disability and mortality estimates for mental health
- proposing a modified framework to improve said estimations
- applying the modified framework at different levels: province, country, continent, and global level

An additional area of focus for this thesis is the relation of country-level income and mental illness, which I explore from different perspectives:

  - In the context of the Americas, studying how disease distribution varies sub-regionally and how mental health funding and allocation vary by income-level

- In the global context, studying how disease distribution varies with respect to multi-dimensional poverty in the countries where the poorest billion people live

In summary, the goal of this thesis is to develop a needs-assessment framework based on the estimation of disease burden, and to build such assessment from the ground up, including:

1. Developing a critique of the usual GBD framework for estimating mental illness disease burden, and proposing an alternative framework (Chapter 1)
2. Developing a framework to produce locally grounded prevalence and disability estimates for mental disorders, and producing improved disease burden estimates integrating available data; also, analyzing variations and identifying patterns of disease distribution across countries (Chapter 2)
3. Producing improved continent-level disease burden estimates for mental disorders in the Americas, and analyze variations of disease distribution by sub-regions and by country income level (Chapter 3)
4. Studying the correlation between disease burden attributable to mental illness and government effective spending on mental health (Chapter 4)
5. Produce updated and improved global disease burden estimates for mental disorders, and study how disease distribution varies globally in relation to multidimensional poverty, including sub-group analyses by sex and gender (Chapter 5)

Finally, after attempting to provide an improved estimation of the global disease burden attributable to mental illness, an improved understanding of the spending gap affecting mental health services, and an improved understanding of the relation of poverty with disease distribution, I will devote the last section to studying the governance challenge involved in

prioritizing mental health not only from a global health perspective but also as an issue of global development (Epilogue).

Analytical Platform

Chapter 1. General methodological approach

The burden of disease framework

As a result of the need to assess health outcomes, evaluate interventions, and rationally allocate resources, a series of summary population health metrics -that became known collectively as health-adjusted life-years- began to be developed during the mid-20th century. The first to gain traction was the quality-adjusted life-year (QALY) -created in the 1960s-, a summary assessment of the quality of life related to a number of health states -between 0 and 1, representing respectively death and full health- which, factoring in the number of years spent in each health state, provided an overall measure of health-adjusted life-years. Of note, the QALY was not related to specific disorders, and represented what's known as a *health expectancy* measure, that is a *good* to be maximized -as opposed to a *health gap* measure, a *bad* to be averted-. It was developed by economists for the purpose of cost-effectiveness analysis and was firmly grounded in the conceptual framework of economic welfare and expected utility theory.(8) One of the caveats in response to the QALY framework emerged from the complexity of validly and reliably measuring general health states. Several functionality scales were used by different researchers or policy-makers, with each instrument measuring a different sub-set of domains, threatening the validity of the construct. An added concern was the fact that QALYs were not grounded on specific disorders, which made them unsuitable for assessing disorder specific health states.

A collaboration between the World Bank (WB), the World Health Organization (WHO), and researchers from the Harvard School of Public Health (HSPH) yielded a different approach to

measuring health-adjusted life-years: instead of a *health expectancy* measure, a *health gap* measure; and instead of a general health state assessment, a disorder specific assessment of health loss. In the intervening years, the DALY has largely dominated the heath policy debate. A tempting hypothesis is that a health gap measure -a metric of what is lost in terms of health, rather than a metric of what is gained, such as the QALY and other health expectancy metrics- lends itself better to what prospect theory and behavioral economics have found time and again: that "losses loom larger than gains".(9) The process of decision-making under risk seems to be systematically biased by the fact that the psychological pain of loss is larger than the reward of gain; and what is population-level health decision-making, if not a process of selecting population exposure to some losses -rather than others-, resulting from the discretional -allegedly rational- allocation of scarce resources? In the rest of this section we will delve deeper into this methodology, highlight some of its limitations and propose specific improvements for the mental health field.

The disability adjusted life-year: years lived with disability plus years of life lost

The burden of disease methodology was developed in the 90s to provide measures of mortality, disability, and a composite measure of both, that would allow for comparison of burden across diseases and regions, as well as for cost-effectiveness analyses. The goal is to capture not only the lethality of a disease and its non-lethal headcount impact -traditionally captured by the cause-specific mortality and prevalence rates- but the actual loss in terms of healthy life associated with each disorder. The methodology has evolved over time in response to the scientific community's input, and estimates of global and local disability adjusted life years (DALYs) are provided yearly, along with the DALY's building blocks: the years of life lost (YLLs) due to premature mortality, plus the years lived with disability (YLDs) produced by most human disorders.(10)

Currently, YLLs are a mortality measure weighted by normative life expectancy: death will produce a number of YLLs equivalent to standard life expectancy at the time of death. Normative life tables -with a life expectancy at birth of 86- were developed integrating the lowest death rate for each age-group observed in countries of more than 5 million people. Also, age-discounting previously applied to calculation of YLLs -intended to reflect social preference for years saved now rather than in the future- was dropped. We can appreciate in the current configuration of YLLs the value-laden technical assumptions we mentioned earlier: YLLs are calculated using a normative life table artificially created to reflect the best life-expectancy achievable anywhere in the world by each age-group, instead of using the locally available life tables. The implication is that when we say that suicide produced 1237 YLLs per 100,000 persons in Lesotho in 2015, we are not considering the estimated life-expectancy for Lesotho -which is 47 years old-, but the years that would be lost to suicide if Lesotho had a life-expectancy more similar Japan's -86 years old for females-. The reason for this consequential methodological decision is that, should we use local life-tables, we would necessarily conclude that a similarly cost-effective intervention in terms of deaths-by-suicide averted, would be much more beneficial in terms of YLLs averted if applied in Japan than in Lesotho. We can see how an ethical consideration -estimating the burden *potentially* saved ceteris paribus -if all other health-determinants were equal- takes precedence over an also defensible realistic consideration -providing a precise estimation of the burden actually averted in any specific country-. This apparently technical decision involves a highly meaningful ethical stand: in true Rawlsian fashion, it forces decision-makers to act *under a veil of ignorance* with respect to the differential life-expectancy between developed and developing countries.

The YLD provides a similarly rich picture of ethical positioning under the guise of technical decisions. It is useful to do a brief historical overview of the YLD: it started as a composite measure of incidence, duration of illness, and expert judgement on how disabling each disorder is. Two major changes took place leading to YLD's current form: *incidence times average duration of illness* was replaced by *prevalence* -they are equivalent for relatively infrequent disorders-, and expert input was replaced by an empirical determination of the general public's opinion about how disabling the different health states are. So, current YLDs are a measure of prevalence weighted by the general public's perception -a value judgement- of the impairment resulting from all health states resulting from disease. Surveys were conducted in different stages -which at this point include 60890 respondents- including: a globally accessible online survey (n=16328); face-to-face or telephone interviews in five countries from different world regions (America, Asia and Africa; n=13902); and a web-based survey in four European countries (n=30660). Surveys asked respondents to conduct paired comparisons between two randomly selected health states (i.e.: asking which of the two was considered healthier), and probit regression analysis produced a disability weight between 0 –perfect health- and 1 –equivalent to death-. The resulting disability weight is multiplied by the prevalence of each of the health states associated with each disorder in order to produce the final disorder-specific YLDs.(11,12)

As was mentioned before, each disorder produces one or several health states or sequelae, each carrying its own specific disability weight. This framework accounts for the clinical fact that the same disease can manifest itself differently in different patients -some patients have a severe form of depression while others have a milder syndrome-, and that it might affect the same patient differently across time -a patient might be asymptomatic for a large part of the year and then

suffer a month-long moderate mood episode; or she can suffer acute psychosis that then recedes into a chronic residual state-. This clinical heterogeneity translates directly to the aggregate level, and the population distribution of the continuum between asymptomatic and severe presentations, phases or states needs to be accounted for. As described in Burstein et al 2015,(13) individual level functionality data -from three representative population level surveys in high income countries- was mapped to 62 health states -representing the full spectrum of disability- and the functionality data from the population surveys were translated into values representing total disability for each individual. A cumulative disability weight multiplicative function allowed for retrieving the specific weights for each condition combination, and a mixed-effects model allowed estimation of the marginal effect of the condition of interest, yielding the condition-specific disability net of the effects of all comorbid conditions and providing a severity distribution for each condition, including an asymptomatic fraction.

Another relevant consideration is that, given the fact that prevalence and mortality data are unavailable in many countries, and that the available data is of different quality, one of the main challenges in calculating the DALY's building blocks -the YLDs and YLLs- is to create a global dataset collating all existing epidemiological evidence, adjusting it for known sources of bias and inconsistencies, and predicting missing data. This is done through the DISMOD-MR software, an integrative meta-regression model described in detail in Flaxman et al.(14) This model has also evolved: from the original and much simpler DISMOD and DISMOD-2, the current model allows for input of diverse sources for each metric (e.g.: several prevalence estimations, several cause-specific death rates, etc.), and given a minimum of three different metrics it provides an adjusted and consistent set of measures, including the prevalence and mortality needed to calculate the

YLDs and YLLs respectively. The result of the burden of disease framework is a summary disability-mortality metric that can contribute to our understanding of population illness and guide our decision-making process to design an appropriate social response. In other words, it provides an actionable assessment of need.

Two final outstanding issues: (a) There are several *burdens* that result from illness: societal burden, economic burden, family burden, and broader individual burdens resulting from decreased quality of life and perturbed social interactions. The burden of disease framework, however, is purposefully restricted to *within the skin* functioning: the disability metric aims at capturing the specific impact of the disorder on bodily functions, senses, cognition, and ambulation, excluding all broader burdens on the individual, family, and community. It does not deny the importance of -for example- the decreased quality of life, the carer's burnout, the economic hardship, but it aims to capture the immediate impairment generated by disease, upon which, arguably, all higher-level burdens subsequently emerge. One of the main risks of this restrictive approach to burden estimation is that it can lead to reductionist approaches to understanding and ameliorating human suffering. Furthermore, it can create (b) the illusion that all suffering captured by the disease burden is of biomedical -or psychological- causation, and is therefore amenable to -and should be provided a- medical solution. There is a well-established literature on social determinants of health that cautions against reductionist biomedical approaches: higher-level social and economic factors such as stigma, violence, poverty, and failing institutions -be them within the health system or in other sectors such as schools and families- can very well lead to death and disability at the population level. The concept of *social suffering* accounts for how these higher-level determinants get *under the skin*, and can emerge to the unaware eye as a biologically determined disease-entity

in need of a biomedical solution.(15) Which may very well be necessary, but keeping in mind that the effective long term answer to such burden will not reside within the health system, but at the higher-level social and economic arrangements that produced them. The health system will, however, systematically bear the initial brunt of these forms of socially determined suffering emerging as disease burden, and it should be prepared to deal with it while recognizing its multidetermined nature.

So, to summarize these two final caveats: (a) the disease burden metrics do not capture the full breadth of burden that emerges from disease -just the *within the skin* impairment-; and (b) not all the disease burden rightly captured by these metrics has biomedical or psychological ultimate causes -or solutions-.

Applying the burden of disease framework to mental illness[i]

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".(16) This state, however, is disrupted in one of every three individuals –or more– during their lifetimes.(17,18) Worldwide the magnitude of mental illness has been highlighted by studies on the global burden of disease.(19) 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 prioritize treatment and care of people with mental illness.(20,21) Consequently, people with mental illness worldwide are

[i] This chapter reflects the work led by the author with the mentorship and collaboration of Prof. Rifat Atun and Prof. Graham Thornicroft (68,69)

largely neglected.(21) Pervasive stigma and discrimination(22,23) 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.(24) Globally, rapid economic, demographic, and epidemiological transitions mean a growth in populations that are living longer, but with greater morbidity and disability.(25–28) Mental disorders are a major driver of the growth of overall morbidity and disability globally.(29,30) 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.(26)

How do the technical decisions and assumptions outlined in the previous section affect the estimation of the disability and mortality attributable to mental illness? There are many aspects of the model that condition its results. For example, the fact that disability weights are calculated based on the public's perception of impairment potentially leads to an estimation that is dependent on stigma: healthy people might assess acute psychosis in the context of schizophrenia as the most severely disabling disorder not out of a rational evaluation of impairment but out of stigma toward patients with schizophrenia. The potential bias of stigma against mental illness in the establishment of disability weights cannot be ruled out, and might for example imply that the disease burden assigned to mental illness is *loaded* with a broader scope of burden -not limited to *within the skin* functioning-, including social discrimination and other forms of structural stigma. My focus will, however, be on other sources of bias, namely those that lead to systematic

underestimation of the burden resulting from mental illness. I will offer a 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.

An important benefit of an improved estimation of burden is to inform prioritization of health needs and resource allocation, so my 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

The disease burden attributable to mental illness has been underestimated due to five main 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 psychiatric 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.

Diagnostic classifications such as the ICD-10 system present specific challenges: they need to consider both the clinical syndrome and the etiology 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. (31)

The burden of disease 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. But GBD differs from nosologic systems: instead of the individual level, it is mainly concerned with the population level; and instead of informing individual etiology 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 comprises a hierarchical cause list with four levels of aggregation of 306 diseases and injuries.(10) 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 (DUBE); 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 pain syndromes), 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).

The psychiatric-neurological interface

Traditionally, disorders both affecting the central nervous system and producing mental syndromes 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 electro-encephalographic 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.(26) 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.(32,33) The percentage gap between the burden of mental illness as measured by YLDs, and that measured by DALYs 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.(25,34,35)

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.(35) These estimates would have been higher if all self-harm (suicide, attempted suicide, and self-injurious behaviour) due to mental illness and sub-syndromic

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% of the world's suicides, and of 85% to those happening elsewhere, and (b) they don't include suicides in the context of sub-syndromic 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% of the world's suicides and 39% 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.(36,37) And with respect to potential under-diagnosis, Phillips et al. find that underlying depression prevalence doubles when using culturally appropriate probes.(37) 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.(38) 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.(39) 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).(40)

Psychiatric pain syndromes

Musculoskeletal conditions were the second major cause of YLDs (26) and seventh ranked cause of DALYs in 2013 globally.(41) 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 'chronic pain syndrome' (a disorder of the nervous system by the ICD-10 classification), 'somatoform pain disorder' (a mental/behavioral disorder in ICD-10), or 'somatic symptom disorder with prominent pain' (a psychiatric disorder as per DSM-5); (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.(42,43) These caveats suggest the existence of subpopulations with a common syndrome, which are difficult to classify from a nosologic perspective. 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 is widely contested. It escapes the scope of this thesis 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 Frohlich et al, following strict diagnostic methodology, found that 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).(44) None of these disorders are captured as such in the GBD list of causes, 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 the one piece of consistent evidence we do 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(44)- that painful symptoms are often considered part of the wider mental syndrome.(42,45) Plausibility also suggests that the critical mechanistic level for these conditions is the central nervous system –through a central

dysregulation of pain sensitivity,(46–48) 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 and service delivery level: chronic pain syndromes and mood disorders are treated with the same drugs, accompanied by similar psychotherapies and multidisciplinary psychosocial approaches.(43) 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. 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)(49) 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.(49) However, due to the inconsistent quality of the evidence personality disorders were not explicitly included in GBD estimates.(41) 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.(50) 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 an additional 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 diseases(51) 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.(52–54) 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.(55) Indeed, a recent systematic review estimated that 14.3% of deaths worldwide, or approximately eight million deaths each year, are attributable to mental disorders.(54) 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 throughout the 25 years of GBD measurements. 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 global Disability Adjusted Life Years 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 disorders. 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).

Psychiatric pain syndromes can potentially account for a significant fraction of the 5.4% of DALYs currently attributed to low back and 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 before, 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 pain

syndromes; or (b) which portion of 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 psychiatric pain syndromes, and for the purposes of producing a more accurate estimation, we assume given the limited data(42) 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: 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, 2015(33) 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 psychiatric pain syndrome currently attributed to musculoskeletal disorders should be reattributed to mental disorders

Revising global Years Lived with Disability estimates for mental illness

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.(26) As we have argued above, a significant portion, which we assume to be 5.1 percentage points (see Table 2), potentially corresponds to 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: 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, 2015(26)

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

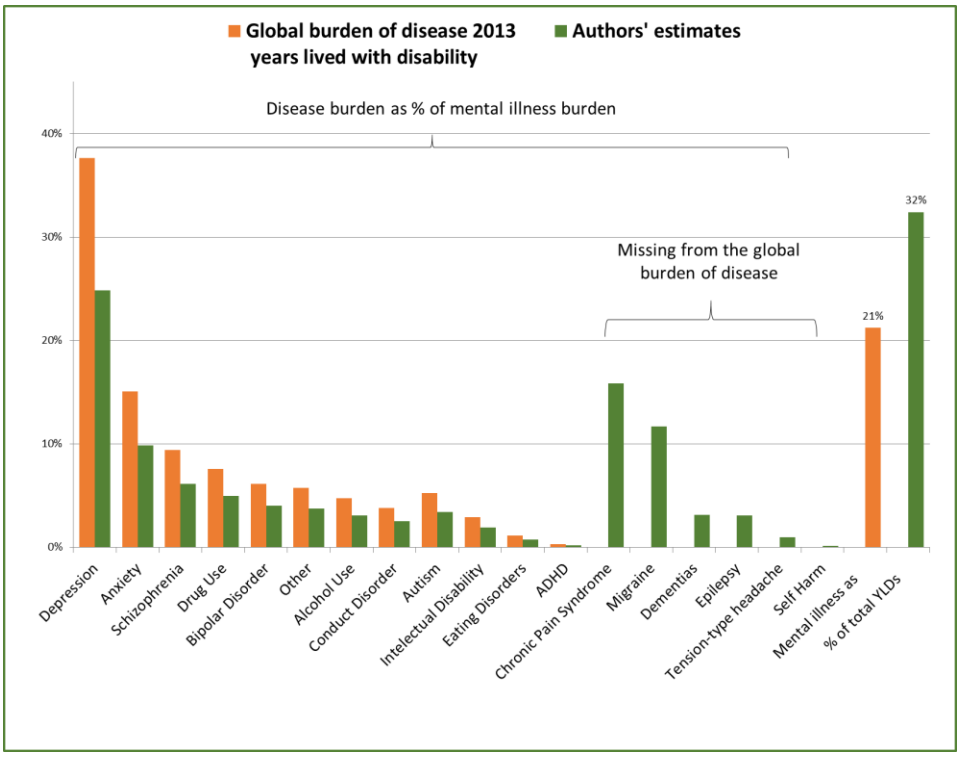
[2]Self-harm repositioned to mental illness: 231600 YLDs

[3] Applying 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)

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 Figure 1 and Figure 2). We also show that mental

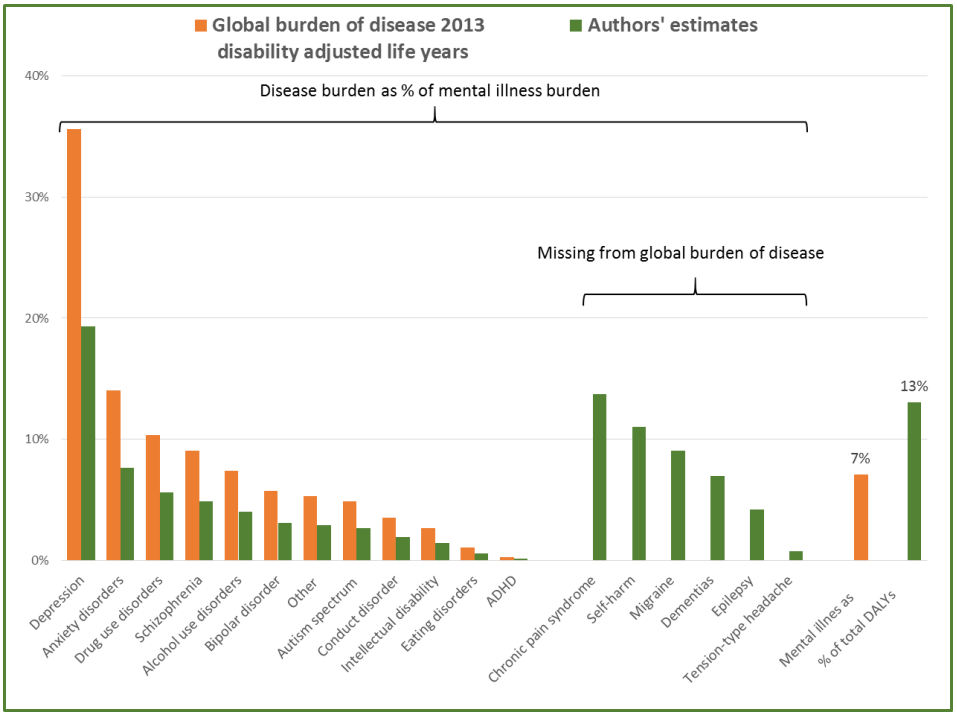
illness accounts for a third of the global disability (Table 2), instead of a fifth, as currently estimated.

Figure 1. Comparison of Global Burden of Disease 2013 years lived with disability with our estimates



Analysis based on data from Vos et al, 2015 (26)

Figure 2. Comparison of Global Burden of Disease 2013 disability adjusted life years with our estimates



Analysis based on data from Murray et al., 2015 (33)

Implications of current underestimation of the burden attributable to mental disorders

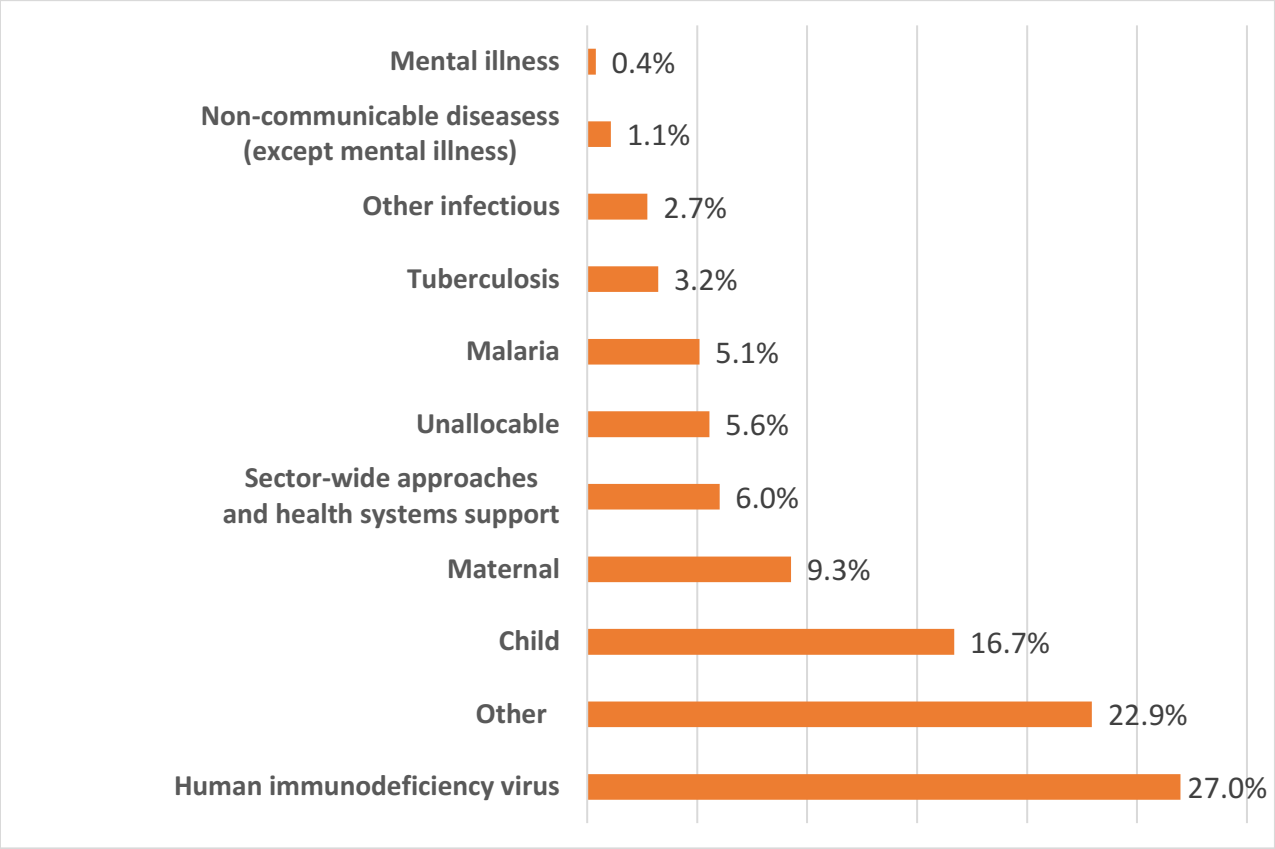
Disproportionately weak global response to mental illness

Mental disorders – in various forms and intensities – affect a majority of the population in their lifetime.(17,18) 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 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 appropriately design health systems in proportion to the nature and the scale of these challenges and effectively allocate resources.

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)(56) 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,(32) and attracted the vast majority of DAH reaching 68.0% of the $35.9 billion disbursed in 2014.(57,58) Despite the changing burden of disease, characterized by multi-morbidity and disability,(27) from 2000 to 2014 only 1.5% of DAH was invested globally in NCDs (combined, accounting for 82.0% of YLDs) (see Figure 3),(57,59) while none of the MDGs referred to mental illness, which received 0.40% of DAH despite accounting for 32.4% of YLDs.

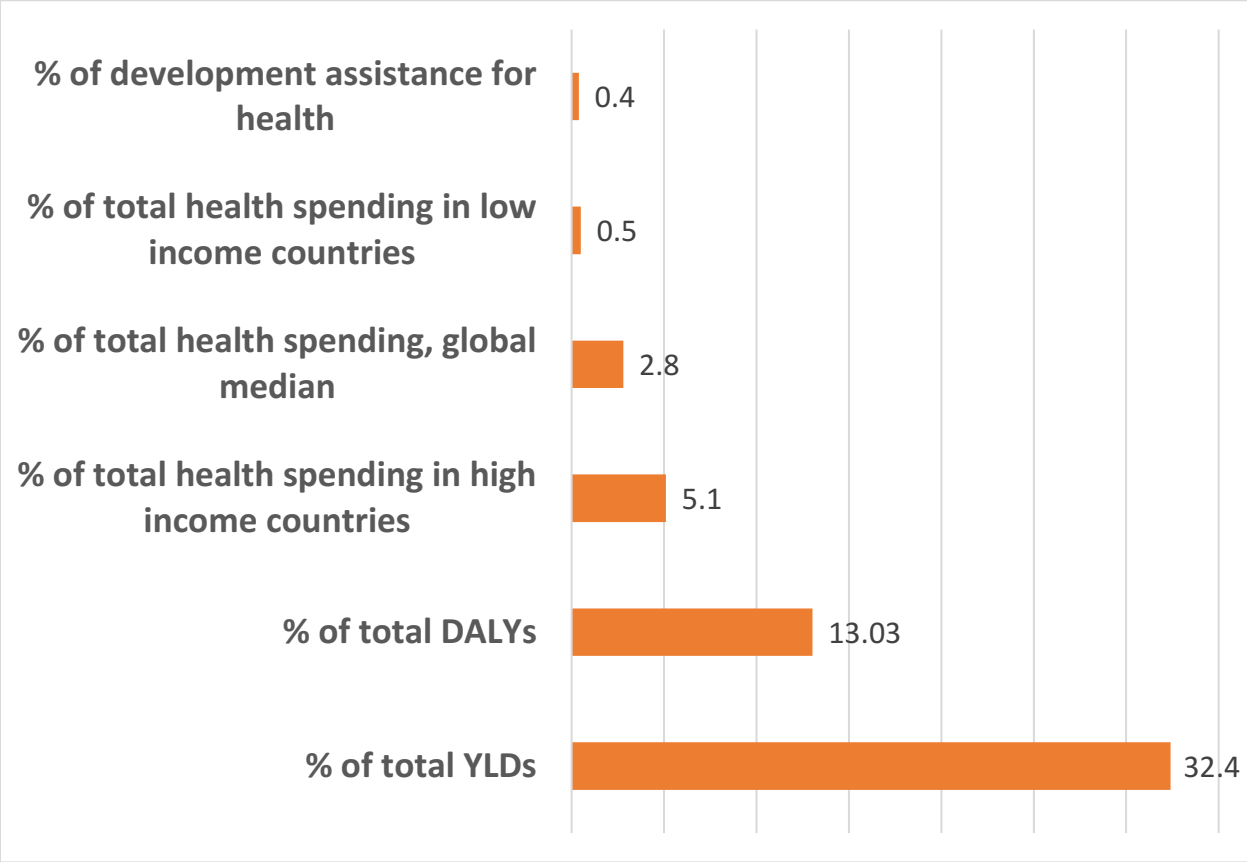
Figure 3: Development assistance for health per area, 2000 to 2014



Analysis based on data from Institute for Health Metrics and Evaluation, 2015. (57)

The imbalance between disease burden, financing, and service access is observed in countries of different income levels (Figure 4): global median spending in mental health stands at 2.8% of total government 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.(60)

Figure 4: Spending on mental illness as a proportion of development assistance for health, of total government 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 (57) and(61).

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.(62–64)

The Sustainable Development Goals and the need to prioritize mental health

Universal Health Coverage, identified as a Sustainable Development Goal,(65) 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[ii]. Of particular importance is the inclusion of the mental health indicators proposed in the 2015 Global Reference List of Core Health Indicators(66):

- 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

Limitations of this approach

A general limitation of the burden of disease framework is that, though useful to establish needs and priorities, it is not sufficient. Any prioritization exercise must include other variables, such as (among others):

- The non-disease burden, which occurs at the individual, family, and community level: loss of quality of life, impairment of social interactions, stigma and discrimination, carer burden, economic burden, and social suffering

[ii] The estimates in this chapter are based on 2013 data. See Chapter 3 for an update to 2015 estimates.

- Ethical considerations, which for example indicate that an infrequent illness producing relatively little population level burden should nevertheless be prioritized given the catastrophic toll it may take at the individual level
- Local priorities and resources

A specific 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) pain syndrome burden as part of the mental illness burden. Regarding 1 and 2, data for further evidence-based assumptions is required, so their overall contribution remains to be determined. Our approach partially captures excess mortality by including self-harm; and personality disorders indirectly through self-harm and pain disorders. Regarding 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 pain burden without musculoskeletal correlate considered to be related to mental health – one third- remains hypothetical.

Section summary

The GBD framework provides a unique starting point to conduct adequate needs-assessments geared towards informing health policy and decision-making. With respect to mental disorders, a number of methodological features lead to significant underestimation of the mortality and disability resulting from mental disorders 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 an improved framework to estimate the disease burden of mental disorders, and a set of more accurate global estimates that establish mental illness as a leading cause of global disease burden. Our methodology re-conceptualizing and re-estimating the burden of mental illness was published in a top tier medical journal and spurred a fruitful exchange with the creators of the GBD framework.(67–69) It has subsequently been referenced in a growing number of peer-reviewed papers and editorials -including in Nature and Lancet (70,71)-, IHME publications,(72) reports -including by the WB & WHO, PAHO, and the Center for Global Development-,(73–75) social media -with an Altmetric score of 353(76)-. Finally, four major projects were commissioned using this framework by: the Centre for Applied Mental Health and Addictions and the Ministry of Health, British Columbia; Partners In Health; the Pan-American Health Organization; and the Lancet Commission on NCDs and Injuries in the context of Poverty. These four projects resulted in this Thesis, and are presented hereafter.

Results Statement

Chapter 2. The burden on countries

We have provided a critique of traditional burden estimation for mental disorders, a rationale and framework for improving them, and we have applied it at the global level. However, though this high-level view is useful for prioritizing interventions focused on mental health by multilateral health and development organizations -a process on which we will focus in the Epilogue-, it fails to provide a useful blueprint for local decision makers. In order to achieve this, the analysis of burden has to be tailored to the system under consideration, and grounded in local data when available. The estimation of burden is a form of needs-assessment that should provide, in addition to traditional prevalence and mortality measures, a metric to compare across disorders, prioritize areas of need, and design services accordingly. The ultimate goal is to inform health systems planning, for which it needs to consider the relevant local factors with enough nuance to understand how an effective and cost effective response should be developed. We have mentioned, however, that data is produced with dissimilar methodologies, and that local data is not always available. Indeed, one of the merits of the GBD framework is to provide estimates even in the absence of coherent or local data, by forcing consistency among inputs and by adjusting available data using covariates. In order to achieve this, the model includes a set of hierarchical geographic random effects models and study-level or country-level fixed effects models to adjust predicted values.

In this section, we will apply our framework to understanding the disease burden of mental illness in two contexts:

- As part of a needs-based system planning project in British Columbia, Canada

- As part of a needs-assessment project by Partners In Health (PIH) focusing on the 10 countries/regions where it has a mental health program: Chiapas (Mexico), Peru, Haiti, Liberia, Sierra Leone, Rwanda, Lesotho, Malawi, Russia, and Navajo Nation

This section will cover an important aspect of assessing the disease burden in real-world conditions, namely how to adapt the model to different problems: in British Columbia, Canada, available local data allowed for improvements over existing estimates; in the PIH project, local epidemiological data was scant and timeframe did not allow for additional data collection, so estimates needed to rely on country-level available data.

Estimating Prevalence and disability resulting from mental disorders in British Columbia[iii]

The goal of this section is to apply the burden of disease framework to estimating disability of mental disorders in British Columbia. The ultimate objective is to provide the best possible estimates of prevalence and disability by age-group and sex for all disorders upon which to base health system planning and service delivery. It is an ongoing project that will cover the full spectrum of mental illness, but here I will detail the process of producing such estimates for depressive disorders from the ground-up. In order to do so, it was necessary to develop a framework to combine multiple data sources to provide local estimates of age-sex specific prevalence and disability. The aim is building a framework than can then be adopted as a template to generate locally grounded estimates. For the following sections I will refer to the case of major

[iii] This study was a team effort led by Prof. Elliot Goldner, and including the author in a co-leading role as Senior Research Associate for overall decision-making and model development, as well as fully undertaking specific tasks such as integrating the burden of disease model to obtain severity distributions and disease burden estimations.(77)

depressive disorder as an exemplar, but the process was repeated for all disorder groupings referred to in the preliminary report.(77)

Methods and results

Generating locally grounded prevalence and disability estimates requires synthesizing multiple data sources in order to supplement each other. This study draws data from:

- Systematic review and meta-analysis of published epidemiological studies
- Health utilization data from administrative databases
- National representative population-level data from the Canadian community health survey (CCHS)

Figure 5 provides a process flowchart. An initial systematic review[iv] provided a set of published prevalence estimates a priori applicable to British Columbia. Inclusion criteria consisted in published papers from Canada, the US, Western Europe, and Australia; analyzing primary data obtained through population level surveys using probabilistic sampling and structured diagnostic interviews yielding DSMIII, IV, 5, or ICD 9, 10 psychiatric diagnoses. A detailed quality assessment of each systematic review was undertaken in order to restrict or expand the initial search as per diagnostic-group specific considerations, such as availability of studies, alternative methods of equal diagnostic validity (such as structured scales for ADHD). A set of published overall prevalence estimates was thus obtained, and meta-analyzed. Sub-group analyses were performed by region and disorder sub-group when enough data was available. Canadian sources were preferred when

[iv] The Depression systematic review was conducted by Research Assistant Te Su, and the author conducted a quality assessment and supervised the process.

significant difference compatible with prior knowledge of disease process existed. For example, in the case of major depressive disorder Canadian rates were significantly lower than overall and US rates. Considering the importance of social determinants of health in common mental illness phenotypes, and Canada's specific social arrangements (such as broad redistributive policies including education, health, and community services), this difference was judged to reflect a true difference. This process yielded an overall prevalence estimate per disorder for adults in BC. Applying this percentage to BC People 2016 data we obtained a set of age-sex specific expected numbers for BC. A parallel process of reviewing alternative sources of data for age-sex specific distribution of mental disorders applicable to BC yielded a set of disorder age-sex specific distributions corresponding to published papers, administrative data, and survey data obtained through the CCHS.[v] Using disorder specific prior knowledge these curves were integrated into a single curve. In the case of major depression, survey data and published data were judged to properly reflect most age-groupings, but administrative data, which captures individuals in nursing homes and other inpatient or chronic care facilities was considered to better reflect major depression prevalence for the older age groupings, but not earlier age-groups, where administrative data most likely reflects treatment-seeking rather than age of onset. Hence, for individuals older than 65 the three sources (CCHS survey data, epidemiologic studies, and administrative) were integrated through a summary statistical measure (median), whereas before that age only CCHS and epidemiological data were integrated. This provided an integrated prevalence curve, which was smoothed using the LOESS method,(78) and then iteratively adjusted through a multiplicative factor until it was within 0.1% of the expected overall BC population

[v] Administrative and CCHS data integration was led by Data Analyst Wayne Jones

estimate produced by the meta-analysis. This process produced an adjusted set of age-sex specific prevalence estimates for BC.[vi] The GBD framework was applied to these estimates, including the severity distributions as modeled by Burstein et al. (13) and the disability weights as empirically determined by Salomon et al. (11,12) Thus, a set of age-sex- specific estimates for total YLDs and YLD rates were obtained for each disorder (see Table 3 for estimates obtained for major depressive disorder and Figure 6 for a s et of six disorders and their disability estimates). These estimates were further broken down by severity for the purpose of health service planning, with the understanding that service delivery will in general need to be severity specific, rather that diagnosis-specific (i.e. mild cases of anxiety disorders, and stable residual schizophrenia will be most likely be dealt with in general health or community services most of the time, whereas severe major depressive disorder, severe PTSD, or acute psychosis will require specialized services).[vii]

[vi] Data integration and LOESS smoothing was co-led by Data Analyst Wayne Jones and the author

[vii] Application of the burden of disease framework and estimation of severity distributions and disease burden was led by the author

Figure 5. Process flowchart

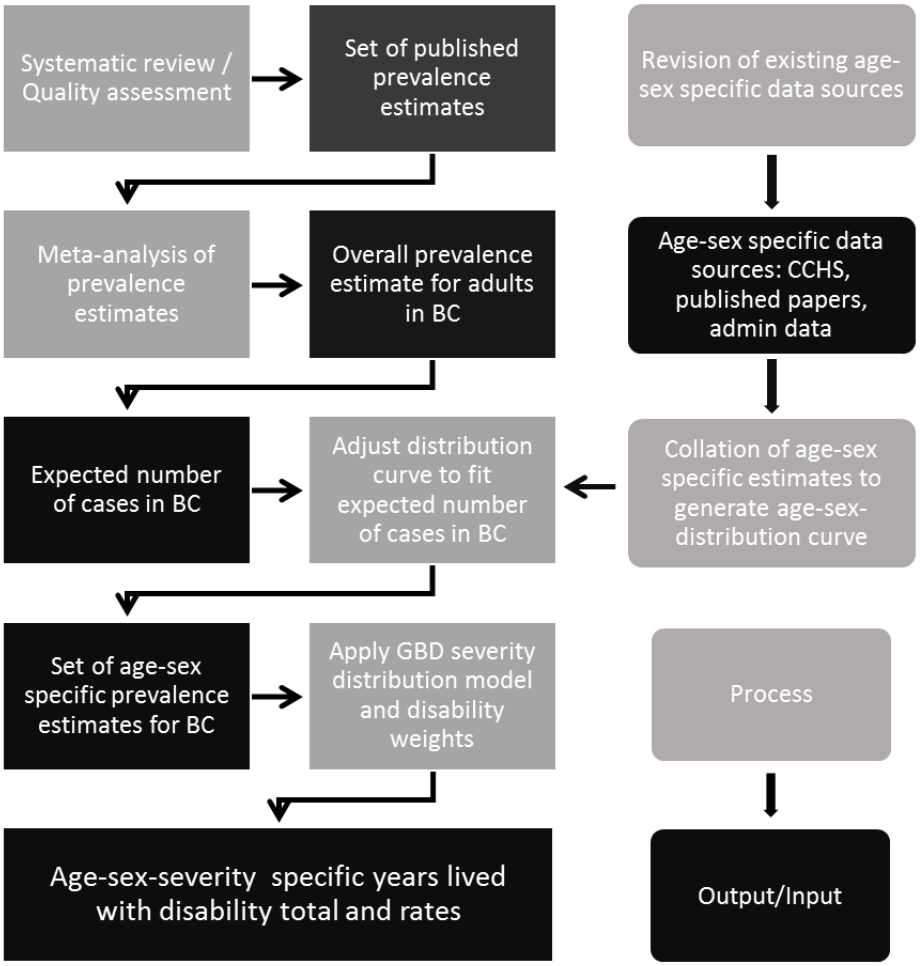


Table 3. Age-sex specific YLDs and YLD rate for MDD in BC

	Males			Females			Persons		
	Population	YLDs	YLDs per 1,000	Population	YLDs	YLDs per 1,000	Population	YLDs	YLDs per 1,000
Age									
15-19	131,457	917	7.0	122,932	1,622	13.2	254,389	2,540	10.0
20-24	166,176	1,144	6.9	152,798	1,935	12.7	318,974	3,079	9.7
25-29	164,698	1,111	6.7	163,838	1,987	12.1	328,536	3,098	9.4
30-34	162,206	1,060	6.5	166,794	1,927	11.6	329,000	2,987	9.1
35-39	155,864	969	6.2	157,413	1,728	11.0	313,277	2,697	8.6
40-44	150,716	878	5.8	154,497	1,599	10.4	305,213	2,477	8.1
45-49	163,303	881	5.4	166,960	1,603	9.6	330,263	2,484	7.5
50-54	173,945	850	4.9	179,258	1,566	8.7	353,203	2,416	6.8
55-59	172,722	686	4.0	179,117	1,336	7.5	351,839	2,022	5.7
60-64	156,560	482	3.1	159,393	1,003	6.3	315,953	1,485	4.7
65-69	138,827	361	2.6	141,158	811	5.7	279,985	1,173	4.2
70-74	99,134	231	2.3	102,721	557	5.4	201,855	788	3.9
75-79	68,753	158	2.3	76,531	404	5.3	145,284	563	3.9
80-84	48,515	120	2.5	57,047	305	5.3	105,562	425	4.0
85-89	30,451	86	2.8	41,756	233	5.6	72,207	319	4.4
90+	15,805	53	3.3	31,582	190	6.0	47,387	242	5.1
Total	1,999,132	9,988	5.0	2,053,795	18,805	9.2	4,052,927	28,793	7.1

Figure 6. Disability estimates for MDD, anxiety, alcohol use, opioid use, marihuana use disorders and ADHD.

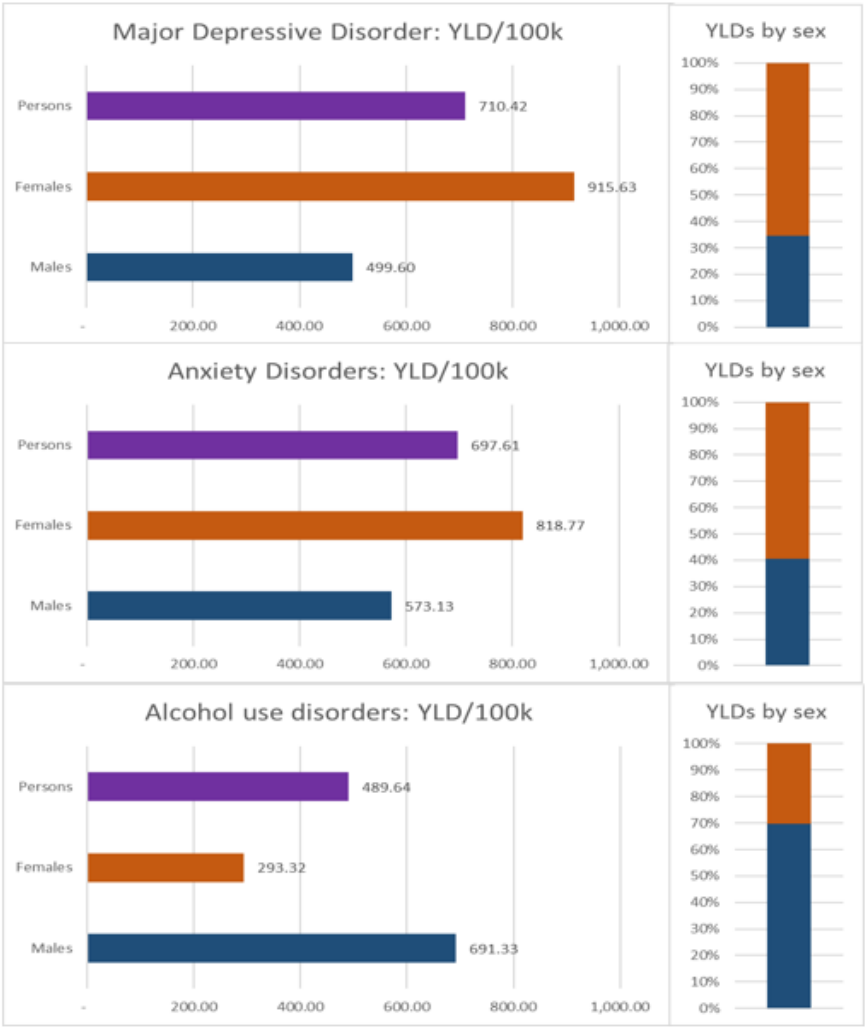
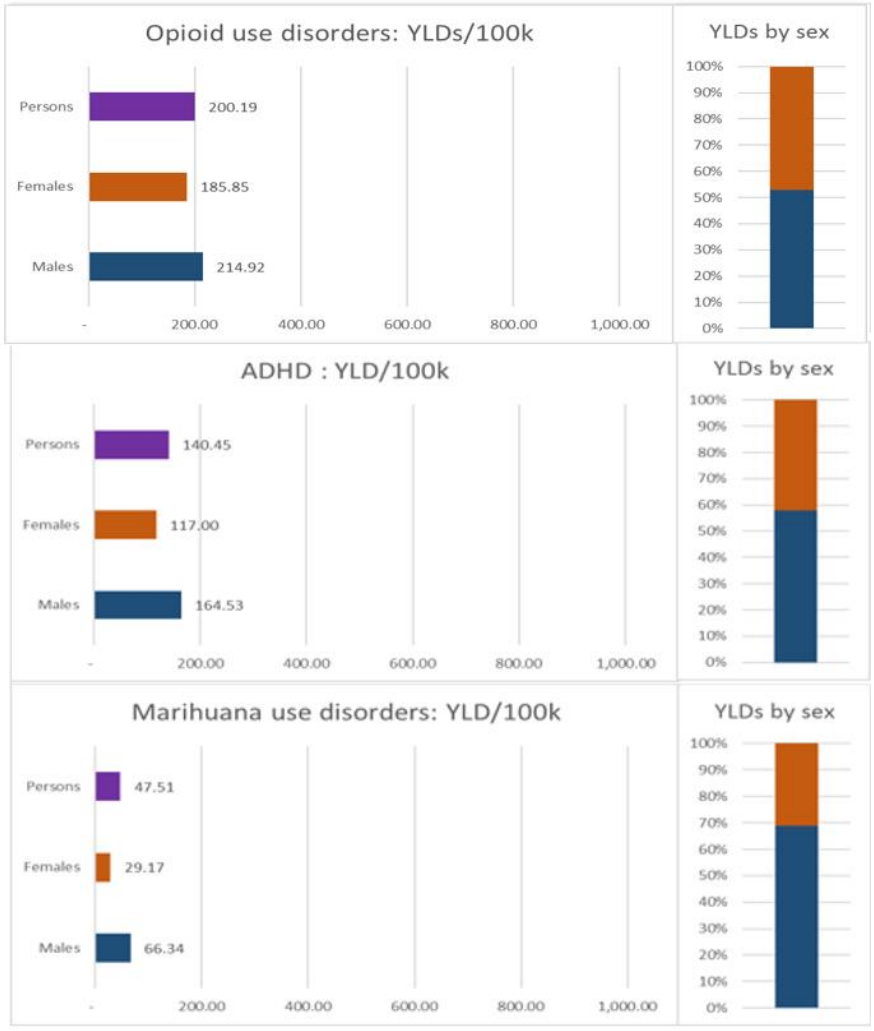


Figure 6 (Cont.)



Sub-section summary

In this sub-section, we saw how to build estimates for prevalence and disability from the ground up. This involved creating a method for improving on existing estimates by triangulating multiple data sources, combining metanalytic methods, statistical models, and using the GBD framework to obtain prevalence, severity distributions, and disability estimates for one of ten Canadian Provinces in a systematic manner that can be applied to any political-administrative unit, such as

a province or country. In the next section, we will work with existing country-level disability estimates in order to improve them, and we will also study disease distribution patterns and compare across countries in order to inform prioritization.

Multi-country needs assessment: informing priorities for Partners In Health's Mental Health Program

Partners In Health (PIH) is an NGO of global reach that provides health services in multiple low-income settings and underserved regions. It has developed an innovative and impactful health care model that seeks to work with local partners to provide high-quality cost-effective care that builds on local resources and favors integration with Government efforts.(79) Indeed, PIH is frequently convened by resource constrained but forward-thinking decision-makers who want a *start-up* partner to build health systems that can then be owned locally. This partnership strategy between local organizations, Governments, and PIH -and through PIH with academia- has yielded synergistic effects benefitting some of the poorest regions of the globe. By synergy I mean a surge in high quality clinical care, impactful applied research, systematic local capacity building, and health systems strengthening. Of note, this thesis is partly a reflection of PIHs local and global impact: this chapter studies the burden of mental illness in ten PIH sites, while chapter 5 is the mental health component of the Lancet Commission on NCDs and injuries in the context of poverty, a Commission that emerged from PIHs long-standing efforts to provide community care in the poorest settings, which highlighted the need to reframe NCDs for low-income settings.

PIH's Mental Health Program covers ten sites in the US (Navajo Nation), Mexico (Chiapas), Peru, Haiti, Liberia, Sierra Leone, Rwanda, Malawi, Lesotho and Russia (Siberia). In order to inform their priorities and service planning I developed a framework to assess the disease burden across their sites. Unlike the previous section -where the challenge was how to integrate a wealth of survey and administrative data to improve estimates-, here the task was to provide central planners and

local providers with a high-level assessment that could function as a starting point, to be refined later in collaboration with the latter. The starting point in this case would be the DALY and YLD estimates for the ten countries, reanalyzed with the method described in the General Methodological Approach section.

Methods and goals

Firstly, disaggregated age-specific country data was extracted from http://ghdx.healthdata.org/ and http://www.healthdata.org/gbd-data-tool. Secondly, the mental illness burden was re-estimated with corrections to include self-harm, neuropsychiatric disorders, and a fraction of psychiatric pain disorders. (69)

The goal was to obtain a detailed descriptive epidemiology by-country to inform differences across sites and contribute to prioritization and planning. The selected tools to present this data are 100% stacked area charts, which provide a visualization of age-specific burden divided by the groupings of interest. For each country, we will present:

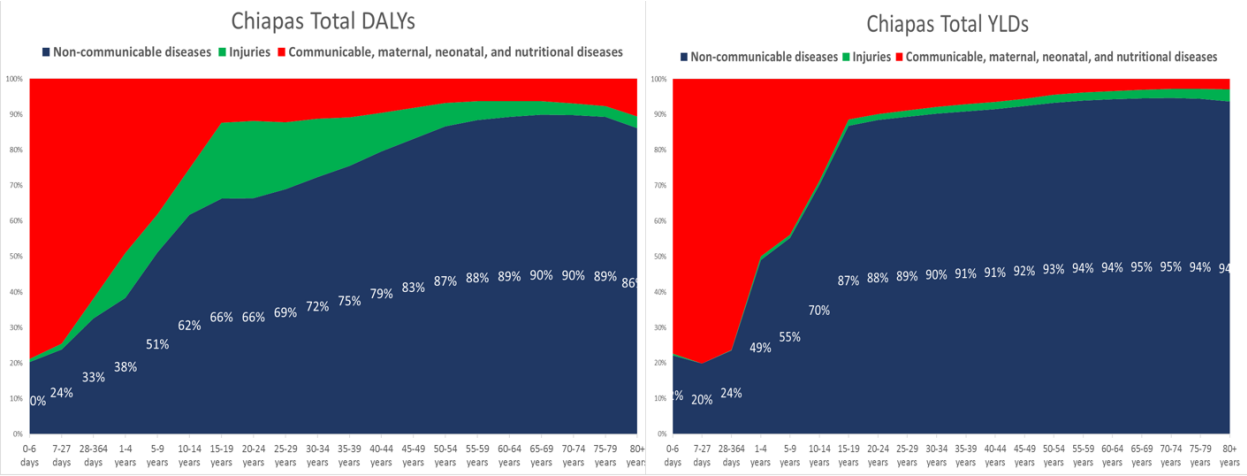
- Level 1 disease distribution: NCDs vs. communicable, maternal, child and nutritional vs. injuries
- Level 2 disease distribution: NCDs by sub-groups vs. communicable, maternal, child and nutritional vs. injuries
- Level 3 disease distribution: total mental burden by disorder

Results

Chiapas

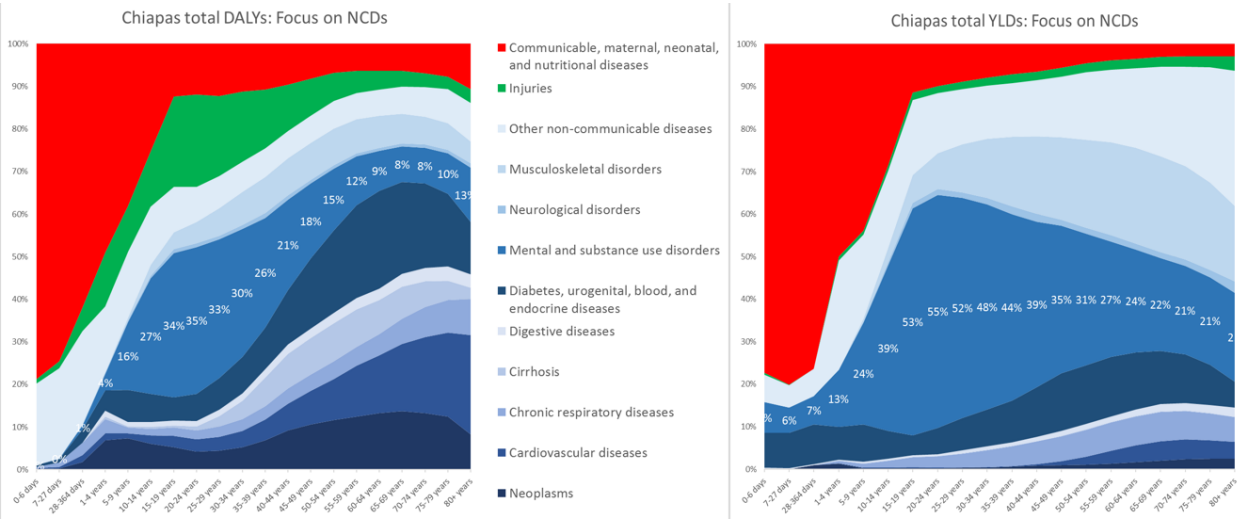
The distribution pattern we observe in Chiapas is fairly typical of middle-income countries in Latin America: the bulk of the burden is due to non-communicable diseases, which reach 50% of total combined disability and mortality burden in the 5 to 9-year-old group, 70% in the 30 to 34-year-old group, and 90% in the 65 to 69-year-old group. If we consider disability alone, NCDs peak faster, accruing 70% of the burden in the 10 to 14-year-old group, and 90% in the 30 to 34-year-old group (see Figure 7).

Figure 7. Overall distribution of disease burden in Chiapas



If we now delve deeper into the NCD group, we see that mental disorders are by far the largest sub-group of combined burden for children and adults up to around 50 years old, when the rather arbitrary grouping DUBE gains prominence, along with cardiovascular and neoplasms slightly later. If we focus on the disability burden, mental disorders stay the largest cause until around 70 years old, when musculoskeletal and neurological disorders increase significantly (see Figure 8).

Figure 8. Focus on non-communicable diseases in Chiapas



If we now look exclusively at the burden of mental, substance abuse, and neuropsychiatric disorders -ignoring all other disorders (Figure 9 highlights the fraction that will be expanded to 100% in Figure 10)- we see that common mental illness (in shades of blue) accrue 50% of total combined mental burden around 15 years old, and stay above 50% until after 65 years old. We can also see that depressive disorders are the largest cause -with around 25% throughout adulthood-, and that our estimation for psychiatric pain disorders accrues an increasing portion of disability. Severe mental illnesses -schizophrenia and bipolar disorders- accrue around 10% of mental burden in young adulthood throughout the working age, as do alcohol use disorders slightly later in life. Substance use disorders produce a comparatively smaller fraction of the burden during adult life, but a major fraction in neonates. As expected, epilepsy captures the largest remaining fraction of burden in the first years of life, autism and intellectual disability during childhood and conduct disorders during childhood and adolescence. Of note, migraine and

tension type headache accrue around 10% of mental burden throughout adulthood, and the older age-groups are dominated by the catastrophic burden of the dementias (see Figure 10).

Figure 9. Burden of mental disorders in Chiapas

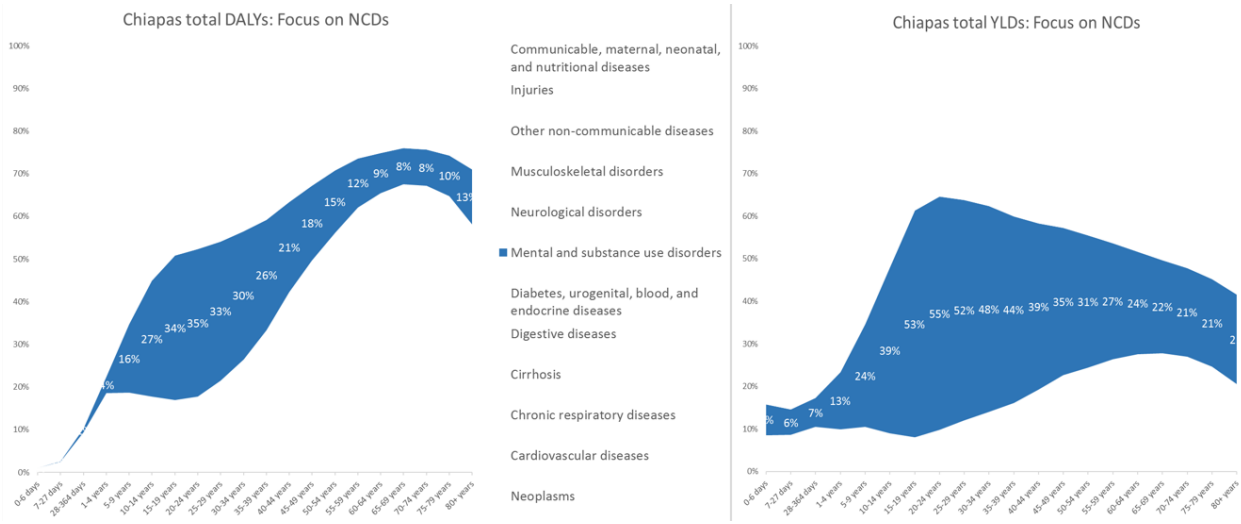
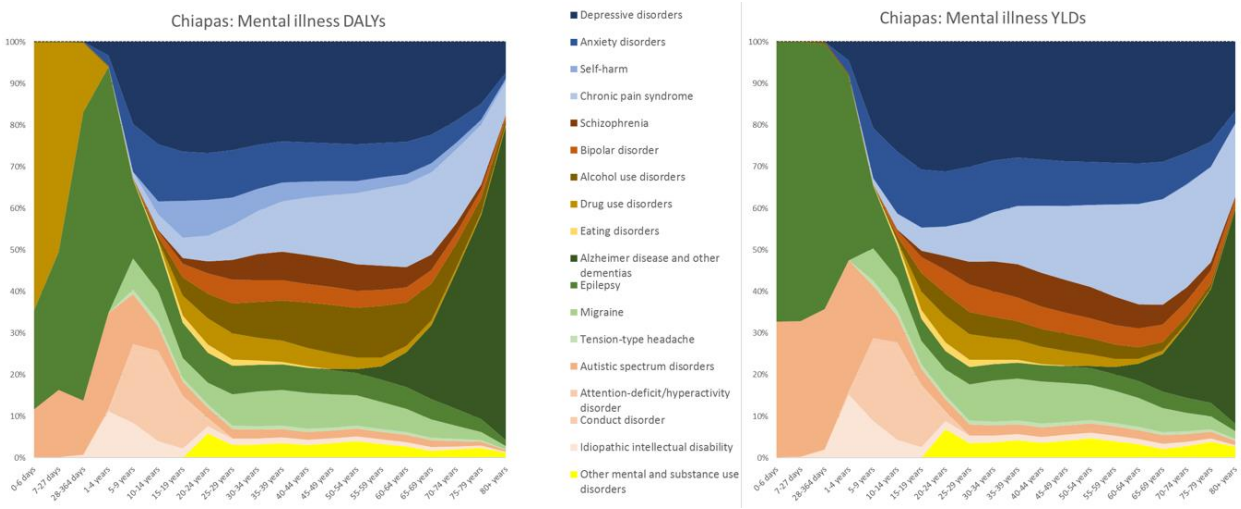


Figure 10. DALYs and YLDs attributable to mental illness in Chiapas.



Peru

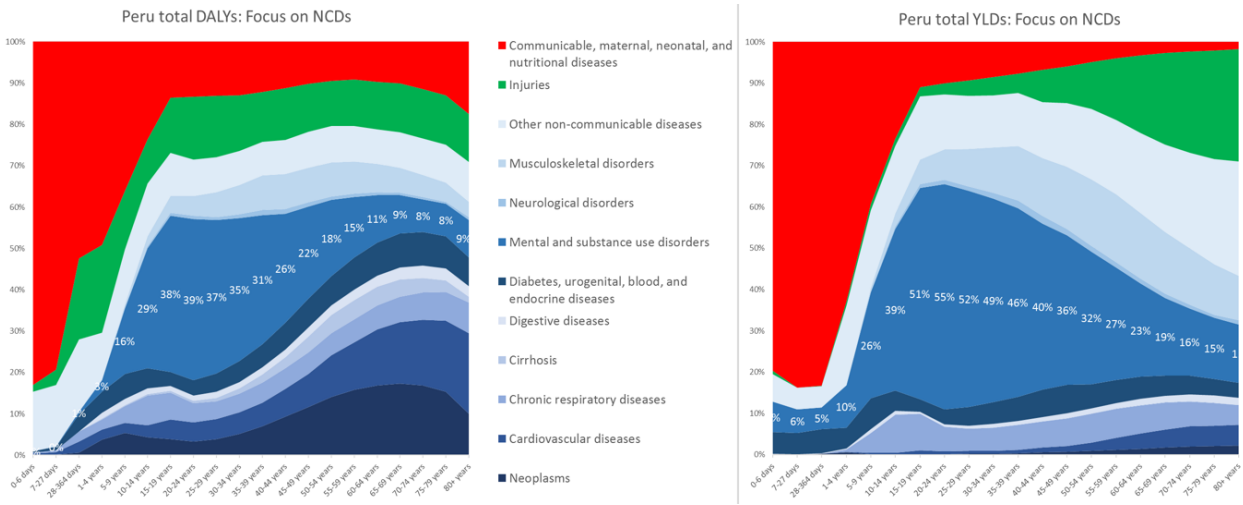
For simplicity, from now on we omit:

- The level 1 charts (see Figure 7), which are included in the level 2 chart (see Figure 8)
- The level 2 chart showing exclusively the mental disorder burden (see Figure 9), which was only included for clarity, but which is included in the general level 2 chart (see Figure 8)

The level 3 mental illness YLD chart (we keep only the level 3 DALY chart, see Figure 10)

The level 1 burden distribution in Peru follows a similar pattern, with the exception of a larger portion of burden attributable to injuries -excluding suicide, under the heading of mental disorder burden in our model-, which rapidly reaches 20% of combined burden -mostly at the expense of increased mortality-, and stays above 10% throughout all age groups. NCDs reach 70% around 15 years old, and stay above that threshold throughout the life-cycle (see Figure 11).

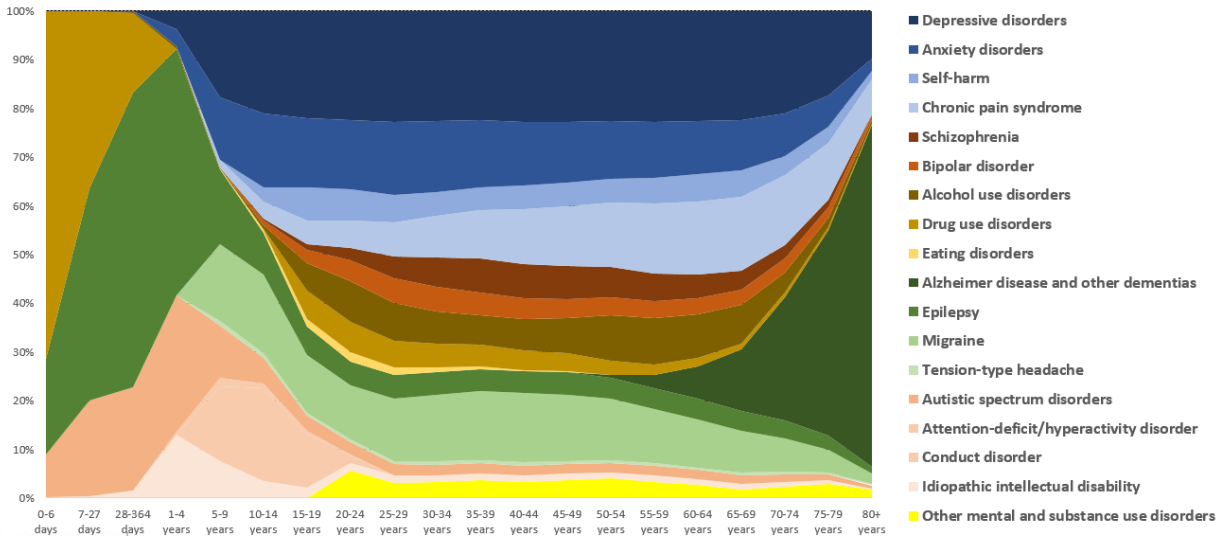
Figure 11. Focus on non -communicable diseases in Peru



Mental disorders reach a third of total combined burden around 10 years old, and stay the largest sub-group cause until around 60 years old, when cardiovascular and malignant causes take the lead. Common mental illnesses are the largest cause of mental burden, with depression reaching

20% of combined burden between late adolescence and after 70 years old. In all other respects the pattern is similar, with a larger fraction of burden attributable to migraine (see Figure 12).

Figure 12. DALYS attributable to mental illness in Peru



The pattern we have seen in Mexico (Chiapas) and Peru -and which to some extent we will re-encounter in Russia- can be considered a typical disease distribution pattern for upper-middle income countries: non-communicable diseases reach around 50% of total combined disability and mortality burden before 10 years of age, 70% in mid-adulthood, and 90% around retirement age. If we consider disability alone, NCDs peak faster, accruing 70% of the burden before adolescence, and 90% in mid-adulthood. Mental disorders reach a third of total combined burden around 10, and stay at the top until around retirement age, when cardiovascular disease and cancer take the lead.

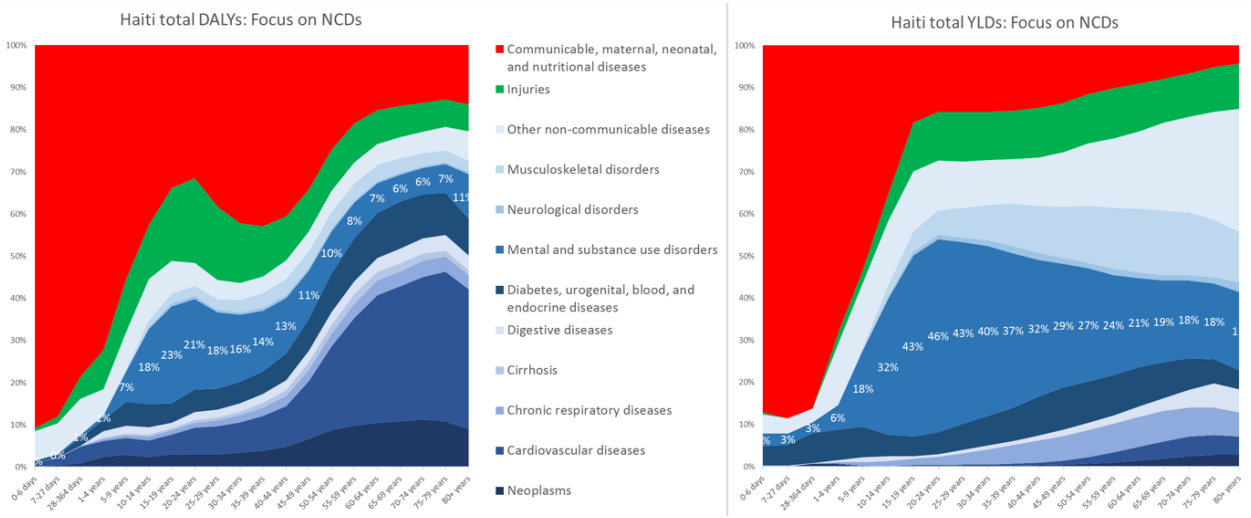
Within the mental disorder grouping, common mental illnesses are the largest cause of mental burden -around 50%-, with depression hovering around 20% of combined burden after

adolescence and throughout adult life. Schizophrenia and bipolar disorders produce around 10 % starting during early adulthood, a similar picture to substance use disorders, mostly due to alcohol. Epilepsy and drug use disorders -during pregnancy- capture the largest fractions of burden in the first years of life, autism and intellectual disability during childhood and conduct disorders during childhood and adolescence. Migraine and tension type headache accrue 10% or more of the burden throughout adulthood, while older age-groups are dominated by the burden of neurocognitive disorders.

Haiti

In Haiti, we start to see a very different disease distribution pattern, quite similar to the one we will see in African countries: communicable, maternal, neonatal and nutritional disorders accrue a much larger proportion of total burden than in middle-income countries, with an increase in mortality during early adulthood that was previously absent and takes combines burden back above 40% of total burden. This determines a comparatively lower proportion of burden attributable to non-communicable diseases, which don't surpass 50% until after 40 years old (see Figure 13).

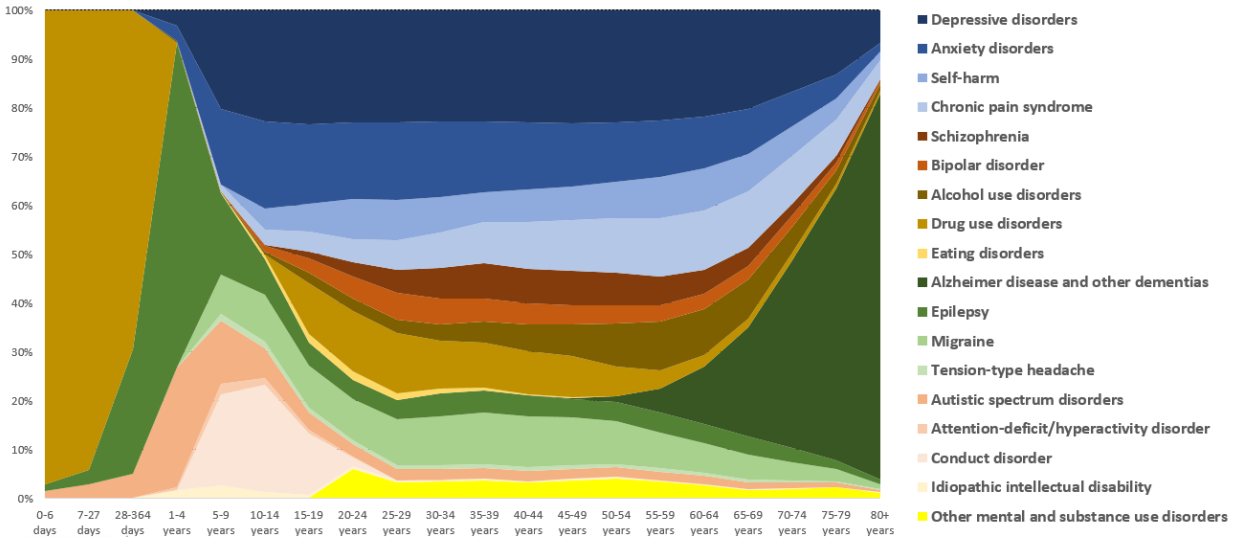
Figure 13. Focus on non-communicable diseases in Haiti



Similarly, the burden of mental disorders accrues a smaller percentage of total burden, though it must be remembered that this responds to being crowded-out by other disease causes, rather than by lower per-capita DALYs. We will study this phenomenon in more detail in the next chapter. Of note, it is not only infectious diseases that capture a comparatively large fraction of burden: cardiovascular disease in Haiti becomes the largest cause of combined burden -due to death, not to disability, as we can appreciate comparing both sides of Figure 13- around 50 years old and remains there throughout.

The pattern of the mental, substance use, and neuropsychiatric disorder burden is similar to the one described before with two notable exceptions: self-harm accrues a more relevant fraction of burden, as do substance use disorders, which reach 10% of mental burden in adolescence and stay above it during youth and early adulthood, only to be surpassed by alcohol disorders around 50 years old (see Figure 14).

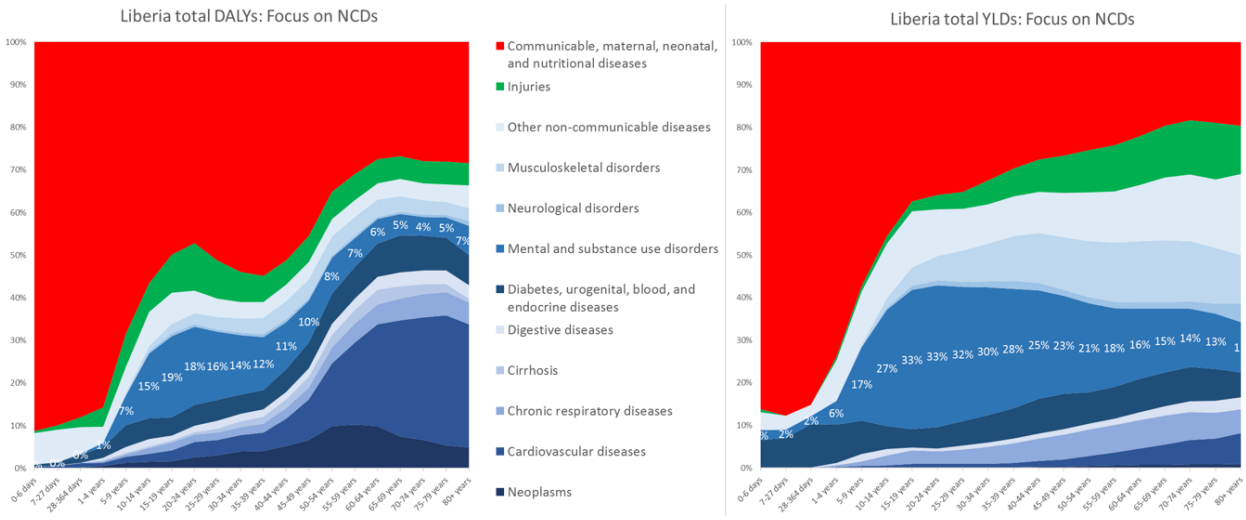
Figure 14. DALYS attributable to mental illness in Haiti



Liberia

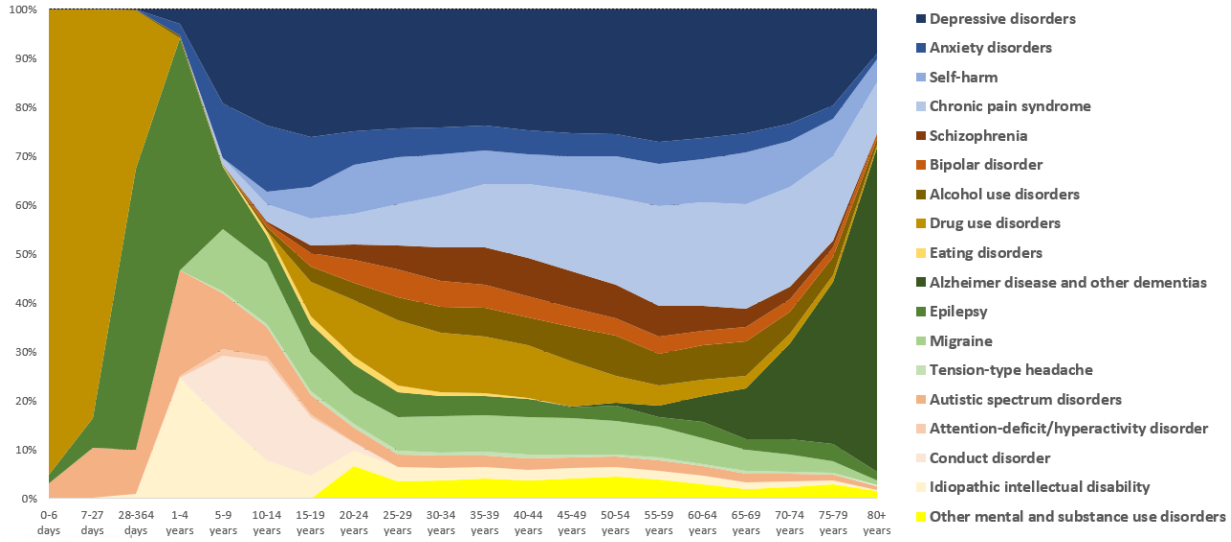
Here the pattern we saw emerge in Haiti is accentuated: communicable, maternal, child and nutritional disorders are by and large the bulk of combined burden, with a second bulge that takes it back to over 55% of combined burden at 35 years of age. Also of note, they never fall below 30% of combined burden. Conversely, NCDs never cross the 70% of burden threshold, hitting a peak around 67% at 70 years old, and mental disorders stay below 20% combined burden and 35% disability burden throughout the life-cycle (see Figure 15).

Figure 15. Focus on non-communicable diseases in Liberia



The picture of the burden attributable to mental, substance use, and neuropsychiatric disorders is similar to Haiti, with some differences: in the early years, intellectual disability surpasses 20% of mental burden, anxiety disorders peak during adolescence and then recede; and our estimation for psychiatric pain syndromes increase significantly with aging, reaching more than 20% of the mental burden around 50 years old (see Figure 16).

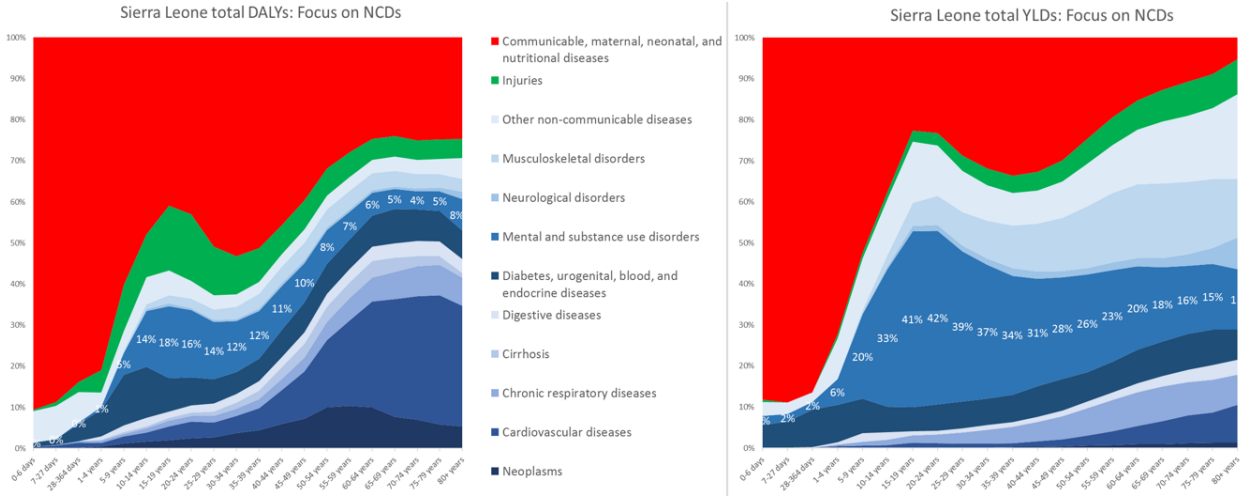
Figure 16. DALYS attributable to mental illness in Liberia



Sierra Leone

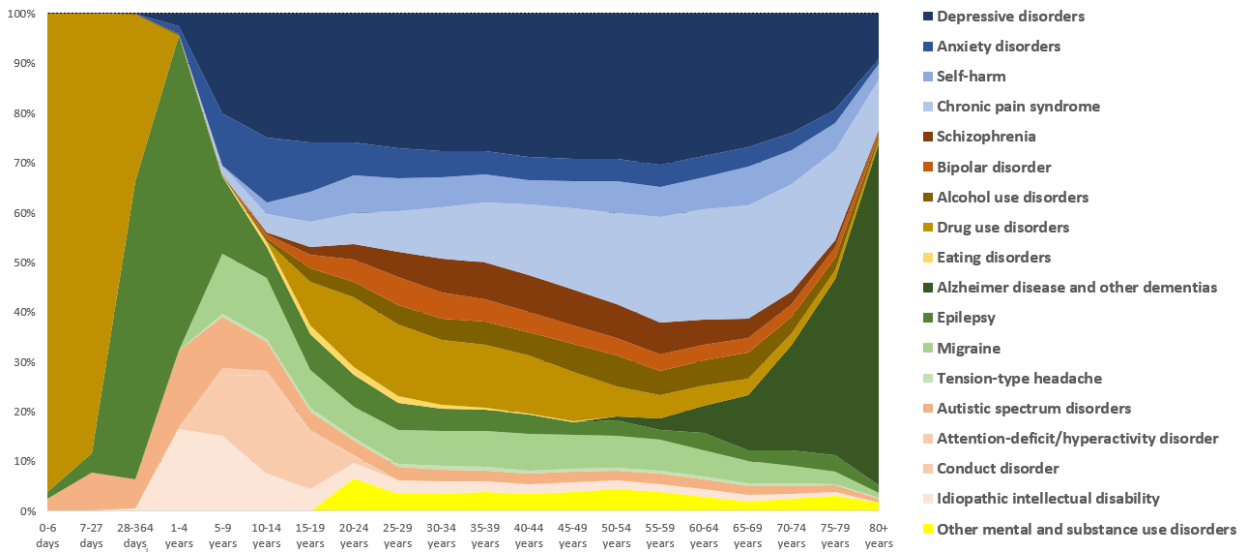
The combined burden profile in Sierra Leone is similar to Liberia's, but with a lower specific disability burden attributable to communicable, maternal, child, and nutritional disorders, as well as to injuries. Disability resulting from NCDs is higher in the older age groups, mainly due to sharp increases in the other NCDs category, which captures disability resulting from sensory impairments and skin disorders (see Figure 17).

Figure 17. Focus on non-communicable diseases in Sierra Leone



Mental disorders are the largest cause of disability from adolescence onwards, with the exception of disability resulting from the second peak of communicable, maternal, child and nutritional burden during young adulthood, and of the other NCDs category in the elderly. The pattern within mental disorders is similar to Liberia's, but with an even larger fraction attributable to depression, substance use disorders, and our estimation for psychiatric pain syndromes (see Figure 18).

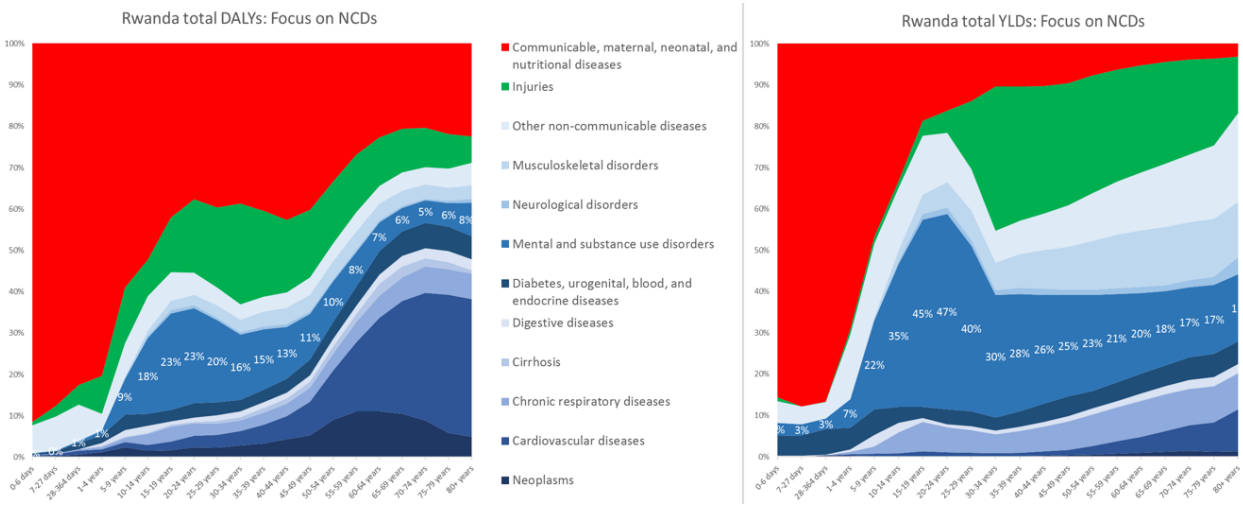
Figure 18. DALYS attributable to mental illness in Sierra Leone



Rwanda

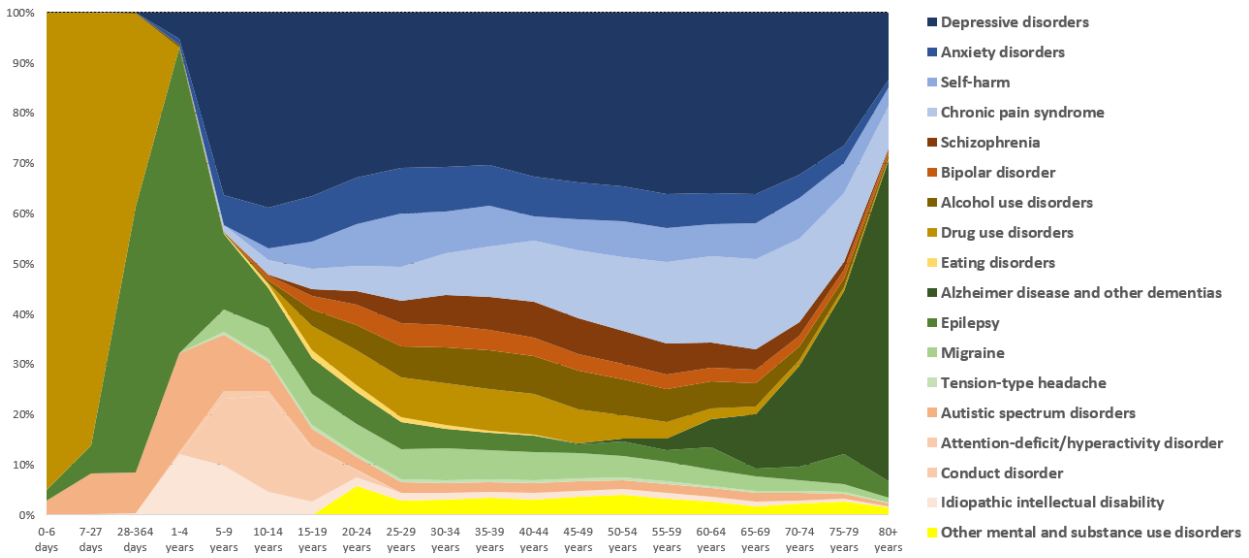
The overall disease burden profile in Rwanda is also dominated by communicable, maternal, child and nutritional causes, but most notably by the mortality and disability resulting from injuries -excluding self-harm- affecting age-groups of 25-year-old and older, a grim reminder of the Rwandan genocide that took place in 1994 (see Figure 19). Disability resulting from mental disorders is comparably higher than in previous African countries, reaching by itself 47% of total disability in young adulthood, and second only to injury-related disability throughout the rest of the life-cycle.

Figure 19. Focus on non-communicable diseases in Rwanda



Within the mental burden, depression plus anxiety capture more than 40% of combined disability throughout adulthood -versus around 30% in previous African countries-, and nearly 50% if we add self-harm. We can hypothesize that increased depression and anxiety disability accompany the physical sequelae of genocide, along with an increased alcoholism-related burden.

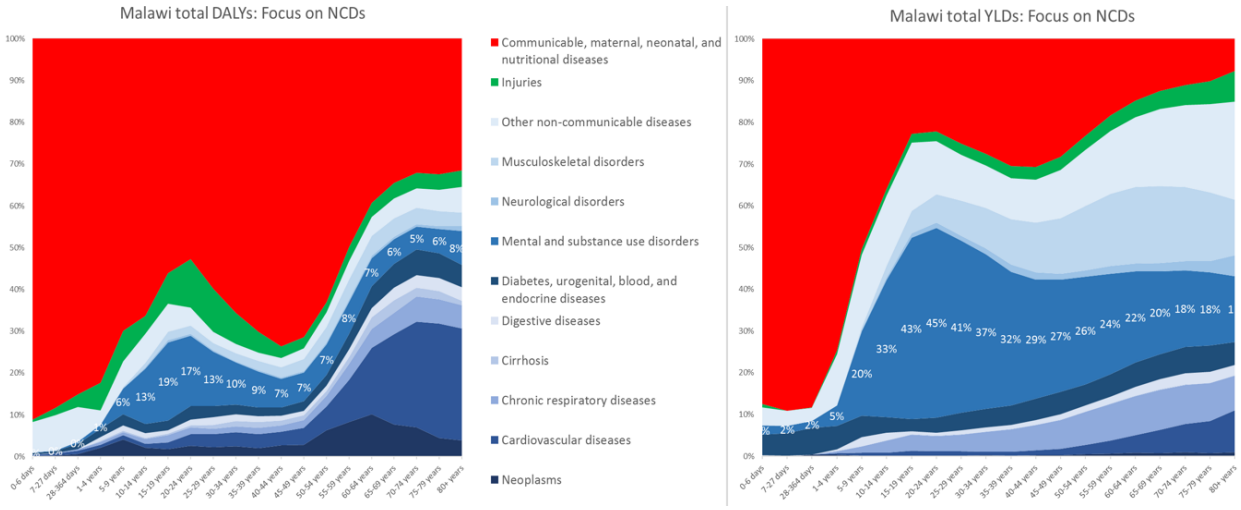
Figure 20. DALYS attributable to mental illness in Rwanda



Malawi

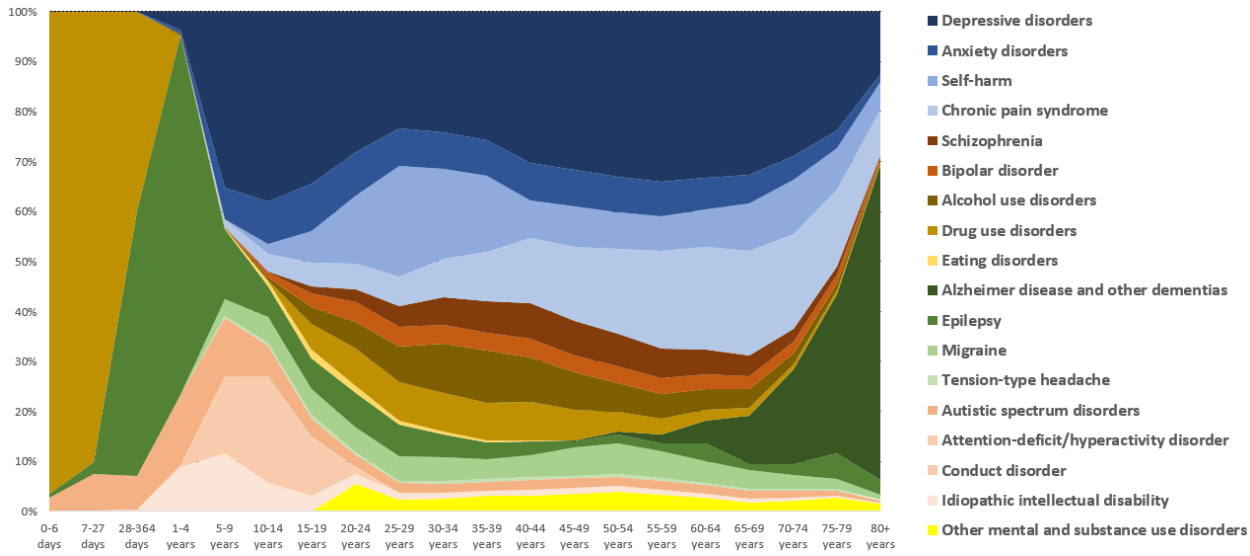
The overwhelming majority of the combined burden in Malawi is caused by communicable, maternal, child, and nutritional disorders, mostly at the expense of HIV and common infections, responsible for 17 and 20% of total all-age DALYs respectively. Of note, the second peak of HIV related mortality pushes the combined burden of communicable diseases to nearly 75% of total burden around 40 years of age. NCDs remain a comparatively smaller cause of burden, only surpassing the 40% mark after the second HIV mortality peak has passed, and stabilizing around 60% only after 60 years old. If we focus on disability, we see that mental disorders become the largest cause around 15 years of age and stay at the top until other NCDs -sensory and skin disorders- take the lead in the elderly.

Figure 21. Focus on non-communicable diseases in Malawi



Within mental illness we see a dramatic increase in suicides between 15 and 40 years old. Together with depression and anxiety these three disorders explain up to 50% of the mental burden until the burden of Alzheimer starts to capture a large fraction of disability (see Figure 22).

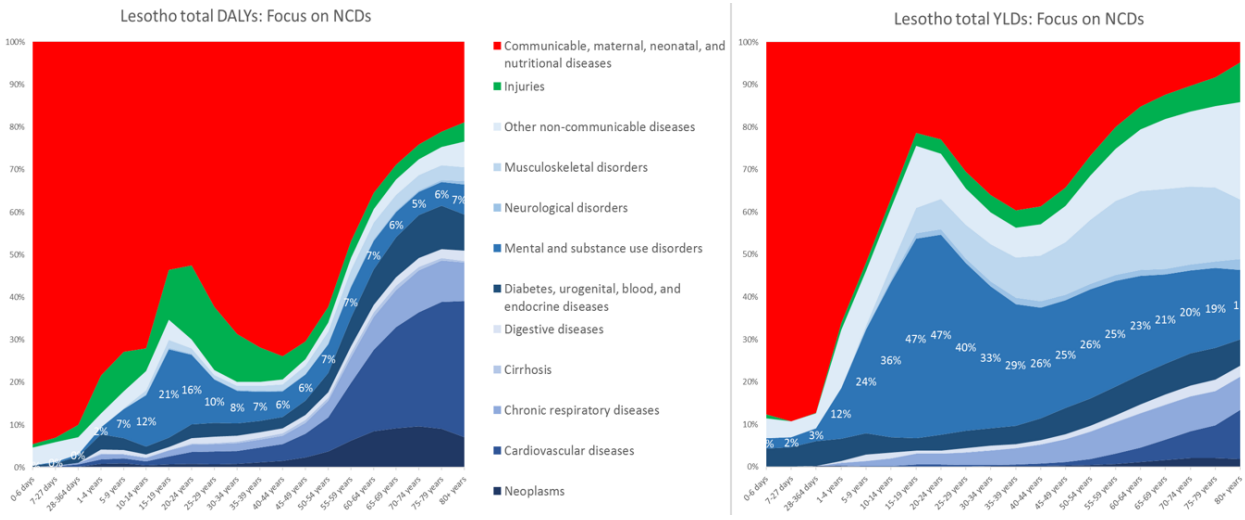
Figure 22. DALYS attributable to mental illness in Malawi



Lesotho

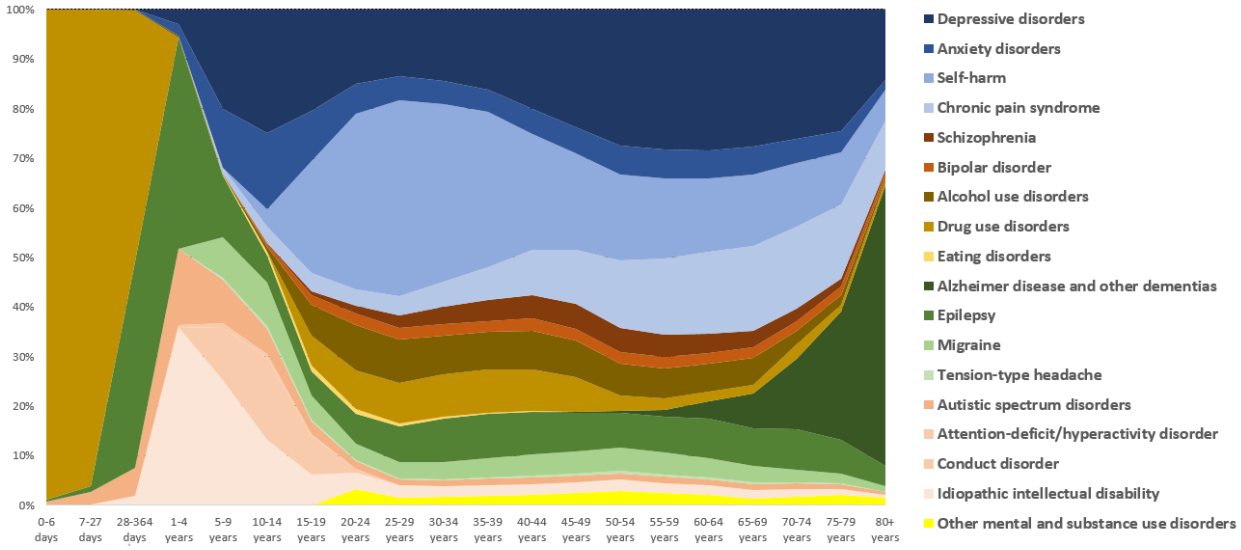
The communicable, maternal, child, and nutritional category in Lesotho has a similar shape than in Malawi. Indeed, the burden of HIV in Lesotho captures by itself 37% of total combined all-age burden. The NCD combined burden captures around 70% of combined burden after 70 years old, and mental disorders are a very relevant cause of disability, reaching 47% of total disability between 15 and 25 years old, and staying above a fourth of total disability throughout the life-cycle.

Figure 23. Focus on non-communicable diseases in Lesotho



The most dramatic change we see in the mental disorder disease burden is the increases of suicides starting around 10 years old, reaching almost 40% of combined mental burden between 25 and 30-year-old, taking the combined burden of depression, anxiety and self-harm to 60% of burden in that age group. Also of note, intellectual disability surpasses 30% of combined mental burden between 1 and 5 years of age.

Figure 24. DALYS attributable to mental illness in Lesotho



The pattern we have seen in Haiti, Liberia, Sierra Leone, Rwanda, Lesotho and Malawi can be considered a typical disease distribution pattern for low income countries: communicable, maternal, child and nutritional disorders are by and large the bulk of combined burden during childhood and adolescence, with a second bulge that takes them back over the 50% mark of combined burden at the peak of adult life. Also of note, they tend to remain a significant % of combined burden until death. NCDs tend to hit a much lower peak around retirement age, and mental disorders usually stay around 20% of combined burden and 30% disability burden throughout the life-cycle.

Within mental illness, common mental disorders exceed 50% early and remain high -comparatively higher than in middle-income countries-, with depression apparently capturing a lower share, and suicide being a larger cause of burden in a number of our low-income countries. Severe mental illness captures a lower fraction of burden, under 10%, while substance use disorders capture a

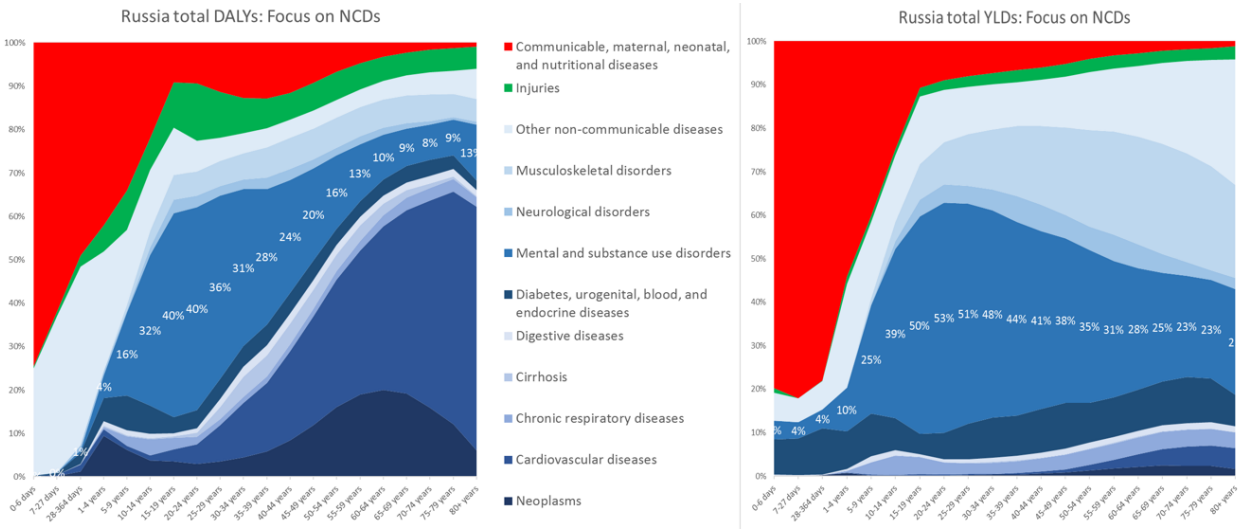
larger fraction, around 15% during most adulthood. Intellectual disability and conduct disorders seem to capture a more significant fraction of burden than autism in the early years in our limited sample.

Russia

The distribution of burden in Russia is consistent with middle-income countries, more similar to the one we saw in the Americas: NCDs capture an even larger fraction of combined burden, reaching 80% as soon as the 20-year-old group, and settling around 90% at 65.

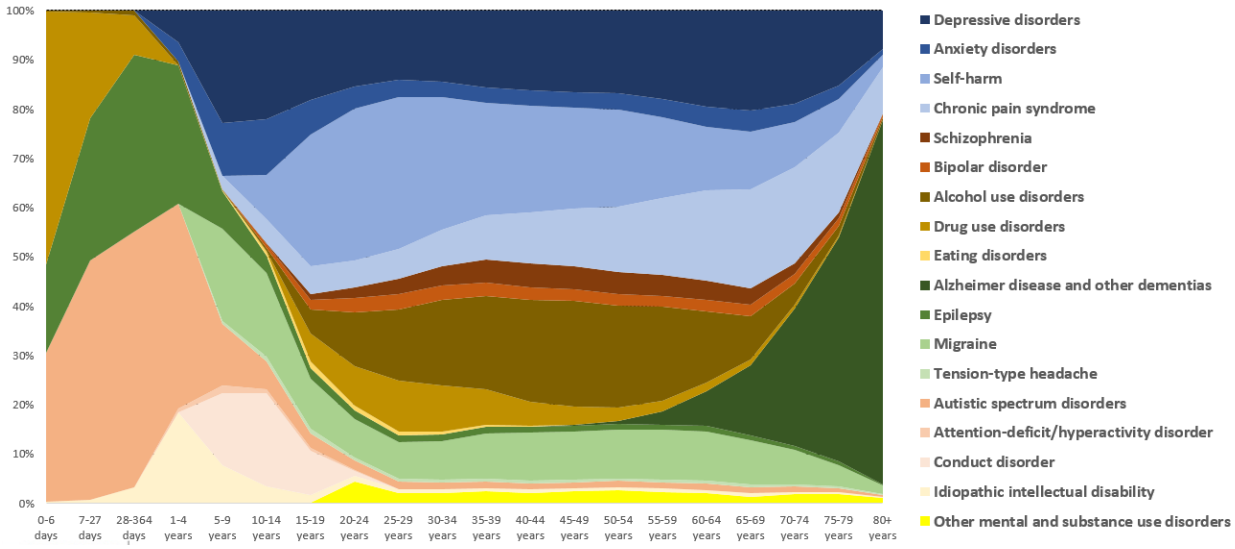
Disability burden alone is 90% due to NCDs as soon as the 20-year-old group, and mental health is by far the largest contributor, surpassing 50% of total disability in the same age group (see Figure 25).

Figure 25. Focus on non-communicable diseases in Russia



The mental, substance use, and neuropsychiatric burden show some distinctive patterns, such as: the enormous burden of autism in the early years -reaching 40% of mental burden in the 1 to 4 age group; the increased burden of suicide, which reaches 30% of the mental burden during youth and stays among the top 5 causes until retirement age; the comparatively smaller fraction attributable to depression and anxiety after adolescence; and the dominating burden of alcoholism, which reaches 20% of mental burden during adulthood.

Figure 26 DALYS attributable to mental illness in Russia



Navajo Nation

Estimating the disease burden of the Navajo Nation using available data presents a singular challenge: there are no comprehensive mental health epidemiology studies covering these two populations, and there are no burden estimates available through IHME, WHO, or any other organization. So, a specific method was designed and implemented to present the best possible estimates in a limited timeframe. As a starting point, a rapid review of evidence yielded a study of

acceptable methodological quality by Beals and others.(80) This study presented, however, a notable limitation: the authors believed that cultural considerations made measurement of psychotic disorders difficult or culturally inappropriate in a context in which psychotic experiences had non-pathological implications, such as is the case with Native Americans. As a result of this methodological decision, the universe of measured disorders was restricted to depression, anxiety, and substance use, which allowed for very restricted disability burden estimations (see

Table 4 and Table, and Figure 27).

Table 4. Prevalence of mental disorders in tribal territories

	N	Any disorder	Depressive disorders	MDD	Dysthymia	Anxiety disorders	Alcohol use	Drug use
Southwest tribes	1446	21.0%	7.3%	6.5%	2.1%	7.5%	9.6%	3.5%
Northern plains tribes	1638	24.3%	4.6%	4.3%	0.9%	7.0%	20.9%	5.9%

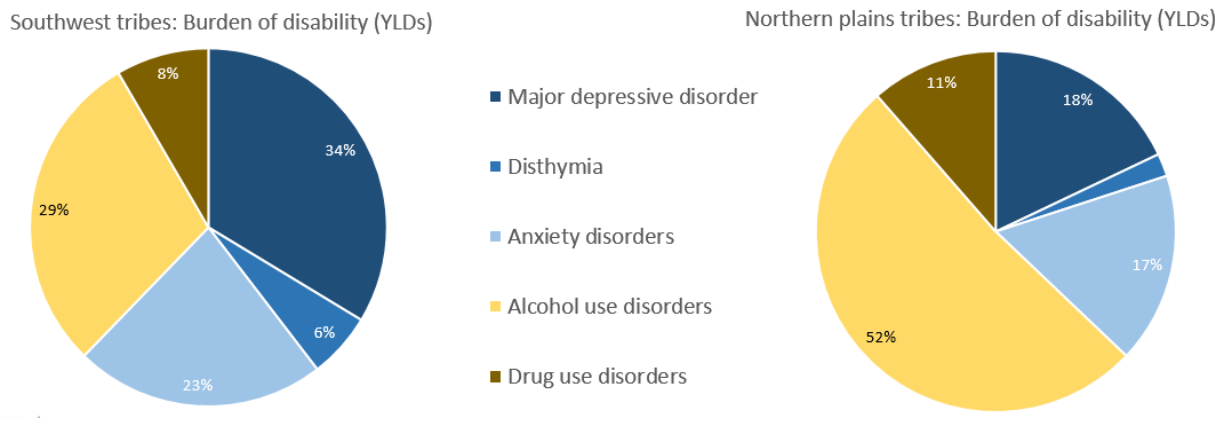
Extracted from: Beals et al 2005(80)

Table 5. Burden of disease in Navajo Nation and Rosebud: YLDs attributable to mental disorders

		MDD	Dysthymia	Anxiety disorders	Alcohol use	Drug use (*opioid-like*)	Drug use (*thc-like*)
Southwest tribes	YLDs	16	3	11	14	3	1
	YLDs /100000	1125	198	759	980	211	70
Northern plains tribes	YLDs	12	1	12	35	6	2
	YLDs /100000	744	85	708	2134	356	118

Author's estimations based on (80)

Figure 27. Burden of disease in Navajo Nation and Rosebud: % of YLDs attributable to available mental disorders

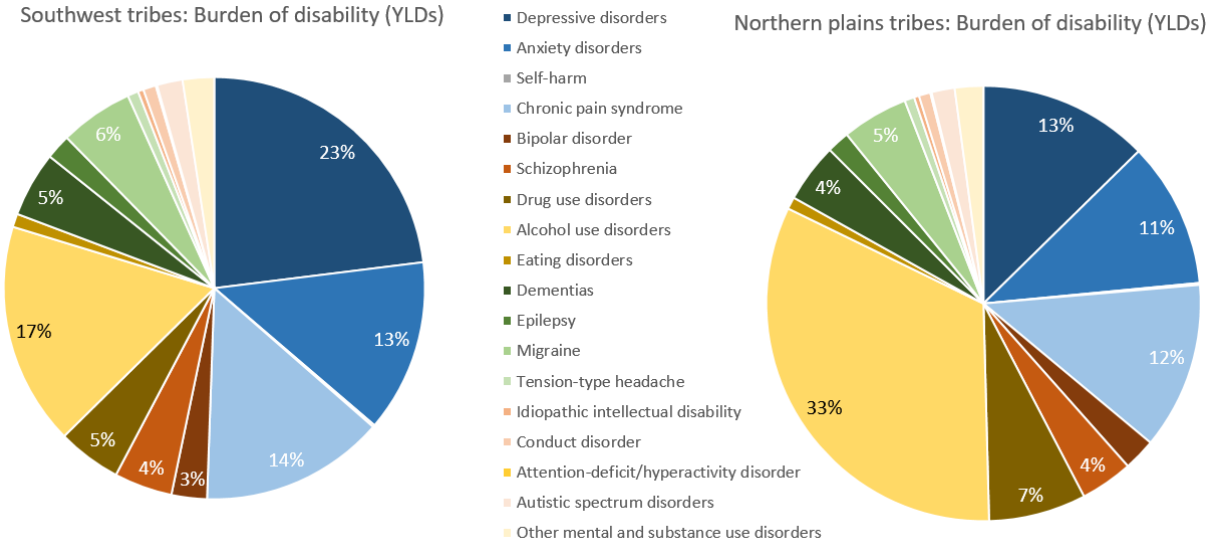


In order to provide a more realistic and actionable estimation, I developed a simple model with the following assumption: besides the disorders that were effectively measured by Beals et al, there are a number of other disorders than should not be simply written off due to cultural considerations: schizophrenia, bipolar disorders, and autism, to name a few, have been found to be multi-determined disorders, including large effects of multiple genes. Though it is true that cultural traits may indeed increase the prevalence of psychotic phenomena, it does not follow that schizophrenia would be thus be fully normalized by culture. So, in order to provide a tentative full picture in the absence of local data, United States disaggregated country-level data was obtained from the global health data exchange,(81) corrections as per our model were applied, and imputed in lieu of the missing data for Northern Plains and South West Tribes (see Figure 28).

Our estimations provide a picture of disability burden dominated by alcoholism and depression, with the former more relevant in the Northern Plains and the latter in the South West Tribes. Anxiety is high and comparable in both sites (at 11 and 13%), and we estimate that important

fractions of burden can be expected from psychiatric pain syndromes, drug use disorders, migraine, Alzheimer, and schizophrenia (see Figure 28).

Figure 28. Burden of disease in Navajo Nation and Rosebud: % of YLDs attributable to mental, substance use, and neuropsychiatric disorders



Author's estimations based on(80,82,83), with data imputed from the US population when missing

Section Summary

This chapter provides a blueprint for estimating locally grounded prevalence and disability, and a method for comparing country-level disease burden distribution across the life-cycle. Indeed, we have identified within our limited set of countries two distinct patterns of disease burden distribution that seem to characterize how the epidemiologic transition plays out in low income vs. middle income countries, including for mental illness. Given the limited number of countries, these findings should be interpreted carefully, but the identification of distinct life-cycle pattern

for how the epidemiologic transition shapes disease burden across income levels could represent an innovative contribution to the understanding of broad global epidemiological patterns.

Chapter 3. The burden on a continent: mental illness in the Americas

In the previous chapters I described the methodology used to improve the estimation of disease burden attributable to mental disorders, and I applied that methodology from the ground-up to provide an adequate and comprehensive description of disease burden at the country level. We will now apply the same methodology at the continent-level and we will later go beyond descriptive epidemiology by studying the associations of disease burden with expenditures, allocative efficiency, and country level income.

This section aims at improving the assessment of mental health needs in the Americas[viii] by providing an updated and nuanced picture of the disease burden in terms of the disability resulting from mental disorders, alone and in combination with premature mortality. The goal is to present:

1. A regional population-level view of mental disorders in the context of an overall-health perspective, understanding how the disease burden varies between sub-regions and from country to country, particularly in relation to the other NCDs; to the communicable, maternal, nutritional, and neonatal conditions; and to injuries.

2. A detailed analysis of the mental, substance use, and neuropsychiatric disorder burden at the continental level and by country, specifying the percentage of the total disease burden that is due to the different mental disorders in terms of disability and combined with premature mortality.

[viii] Throughout this work we use *the Americas* or *America* indistinctly to refer to the American continent, comprising North, Central, South America and the Caribbean region

3. A mapping of how the most relevant mental disorders are distributed across the continent, considering how the different countries and sub-regions are affected.

Methods

Estimating the local, national, and regional disease burden allows for rational disease prioritization, resource allocation, and health system planning -in conjunction with other criteria such as the broader social and economic burden, ethical considerations, and local resources or preferences-. As we have mentioned before, the GBD framework provides global estimates of disease burden, but in the case of mental illness it may lead to inaccurate conclusions, with the most egregious example being the zero deaths and YLLs that have been attributed globally to affective disorders -which include major depressive disorder and bipolar disorders- in almost three decades of burden assessments. In order to partially address these limitations, we extracted 2015 disaggregated data (country-age-sex-specific absolute numbers, rates, and percentages) from the Global Health Data Exchange for all disease causes and countries in the Americas, and re-estimated the disease burden for mental, substance use, and neuropsychiatric disorders following the framework described in chapter 1, which partially rectifies current underestimation by including: (a) self-harm related disability and mortality; (b) neurologic conditions with prominent mental and behavioral syndromes that present frequently at the primary care level; and (c) a fraction of painful syndromes, which frequently constitute either a comorbidity with or a presentation of mood, anxiety, and personality disorders, particularly in contexts of high stigma towards common mental illness. (69,81,84,85)

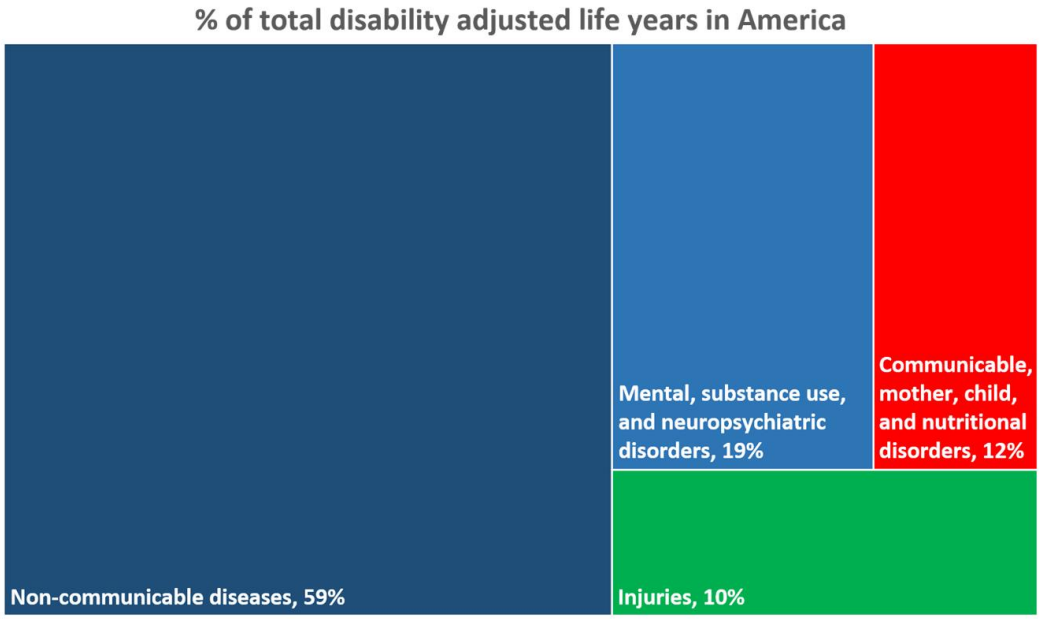
Results

Regional disability and mortality: disability adjusted life-years (DALYs)

Globally, NCDs accrued 60% of total DALYs in 2015, of which 12% corresponded to mental, substance use, and neuropsychiatric disorders. In America, NCDs accrued a much larger 78% of total DALYs, with mental, substance use, and neuropsychiatric disorders taking up a 60% larger fraction of DALYs: 19%. The remaining 59% of NCD DALYs are distributed among cardiovascular disease, cancer, musculoskeletal disorders, diabetes, neurologic, respiratory, digestive, urinary, gynecologic disorders, and others. Therefore, mental disorder DALY burden is equivalent to a third of the burden of all other NCD sub-groups combined, even though our analysis still misses a fraction of the excess death attributable to mental illness, estimated by some authors in up to 8% of the global deaths.(55) Indeed, people with severe mental illness die between 10 and 30 years ahead of their peers in high and low-income countries respectively, even earlier than heavy smokers.(52,53) Finally, communicable, maternal, child, and nutritional disorders are responsible for 12%, and injuries for 10% of total DALYs. This distribution highlights the fact that mental, substance use, and neuropsychiatric disorders -a sub-group of NCDs-, with nearly a fifth of total DALYs, are the largest sub-group cause of disease burden in terms of disability and mortality combined, even larger than the other two higher level groupings - injuries and communicable, maternal, etc. -. Figure 29 shows the three groups of disorders -NCDs; communicable, maternal, child, and nutritional; and injuries-, with mental disorders as a sub-group of NCDs. The largest mental cause of DALYs are depressive disorders, which account for 3.4% of total DALYs, followed

by anxiety disorders with 2.1%. A regional ranking of specific mental disorder DALYs is available in Figure 33.

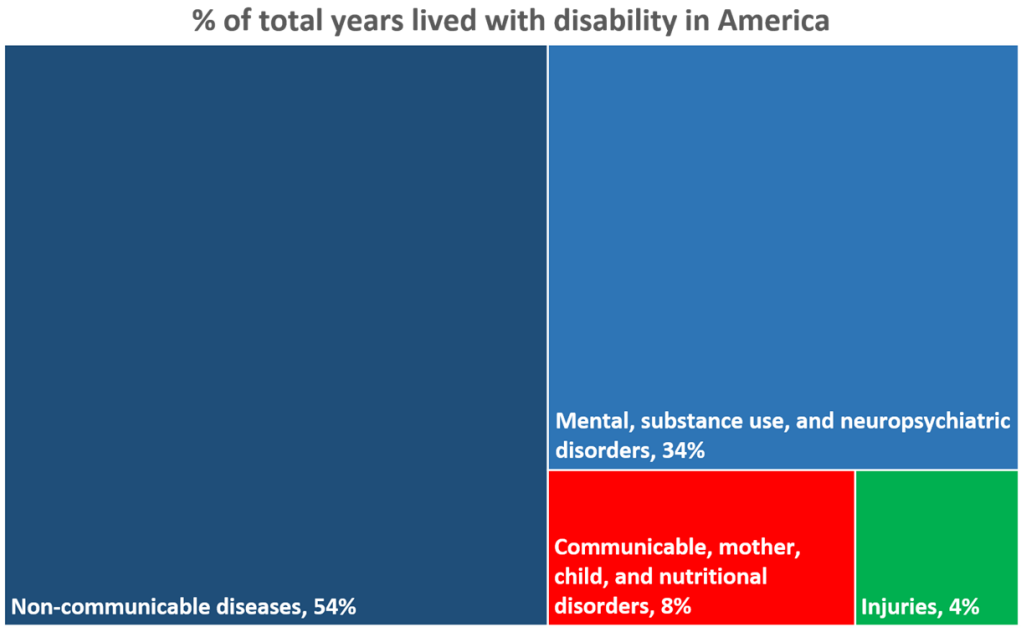
Figure 29: Regional DALY distribution treemap



Regional disability: years lived with disability (YLDs)

As was mentioned before, mortality data does not adequately capture the deaths caused by mental illness; therefore, it is useful to compare disability separately, as measured by YLDs. This metric is not affected by the exclusion of mental illness deaths and provides a valid comparison across disease groupings. Our analysis shows that mental illness is by far the largest source of disability in the region, accounting by itself for more than a third of total disability in the Americas: 34% of total YLDs. All the other NCD sub-groups combined account for an additional 54% of YLDs; communicable, maternal, child and nutritional for 8% of disability; and injuries for 4%, making mental, substance use and neuropsychiatric disorders by far the largest sub-group (Figure 30).

Figure 30: Regional YLD distribution



Country-level analysis

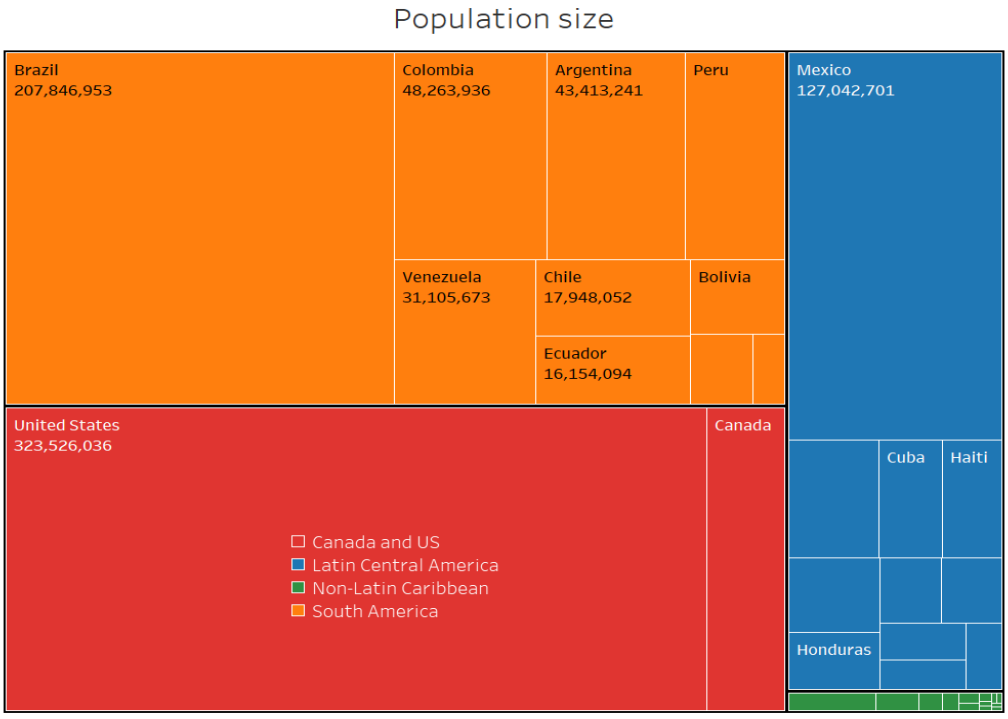
In order to complement the regional analysis, we performed a by-country study of the disease burden of mental disorders. This detailed country-level focus is important because of two main reasons:

(a) America comprises a vast number of countries and territories -36 of which have been included in this report- of very dissimilar population numbers. Figure 31 shows a treemap of all countries grouped by sub-regions, with the size of each square reflecting the population size. It can be easily grasped that three countries -the United States, Brazil, and Mexico- comprise two thirds of the billion-people living in America, so the aggregated regional disease burden will be highly determined by the disease-profile of these three countries. Furthermore, an exclusively regional

perspective would obscure the disease burden of the Non-Latin Caribbean, given their comparatively small populations (the green fraction of Figure 31). Besides the country-specific percentages, we will provide average country-level percentages when meaningfully different from the regional aggregate.

(b) The ultimate goal of a needs-assessment exercise is to provide an actionable tool that can inform mental health system planning and service delivery organization at the national level. National Governments are the appropriate political and administrative entities that can set country-level health priorities and system planning, so it is the national level data that can best illuminate country level decision-making.

Figure 31: Population distribution



Country-level disability and mortality (DALYs)

There is significant heterogeneity in the distribution of the main causes of disability combined with mortality in America. DALYs caused by NCDs -including mental illness- are the largest fraction of total burden in every American country, ranging from 50% in Haiti to 89% of total burden in Canada. The second regional cause-group of DALYs, comprising communicable, maternal, child, and nutritional disorders, ranges between 5.5% in Canada and the United States and 39% in Haiti. The third regional cause of DALYs is the group of injuries, which range from 6% in Canada, Cuba, Barbados and Bermuda, to 20% in El Salvador. Figure 32 highlights that NCDs remains the largest cause of disability and mortality combined across countries despite large individual variations, whereas the group of communicable, maternal, child and nutritional disorders and the group of injuries alternate in the second and third rank-order, with a primacy of the former, especially in lower-income countries. The sub-group of mental, substance use, and neuropsychiatric disorders also shows large between-country variation, ranging from 9% of total DALYs in Haiti to 23% in Canada (see Figure 32, Figure 33, Figure 34).

Figure 32: DALYs by country

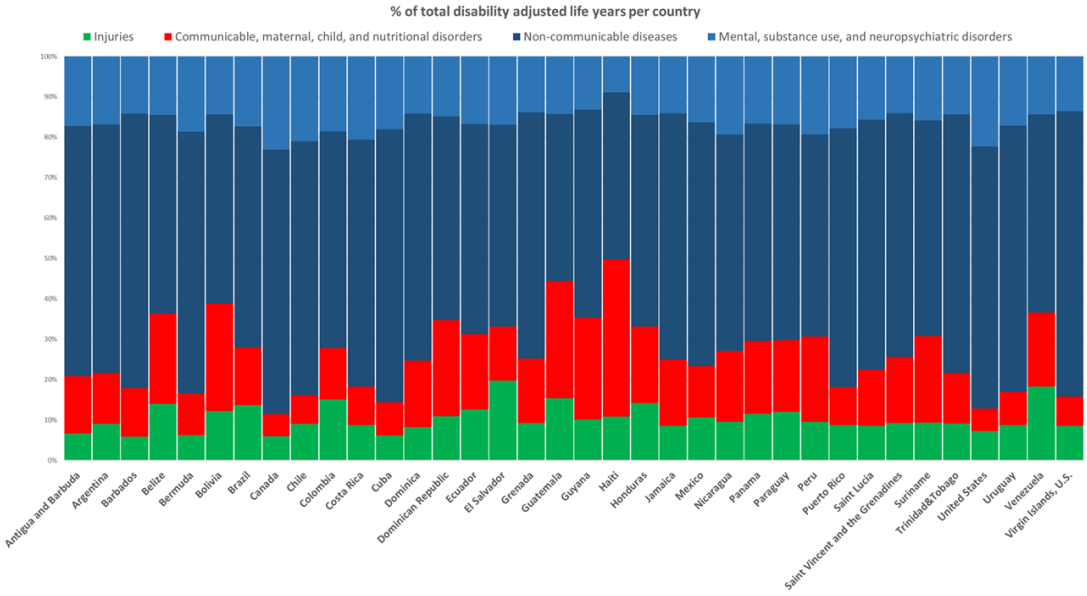


Figure 33: DALY map

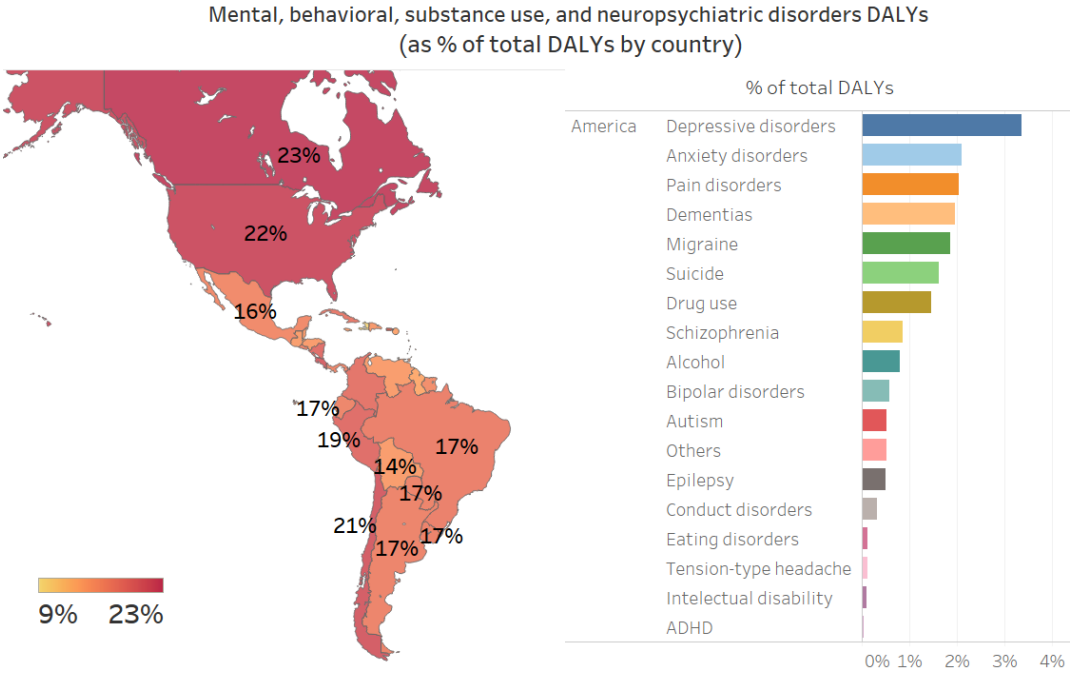
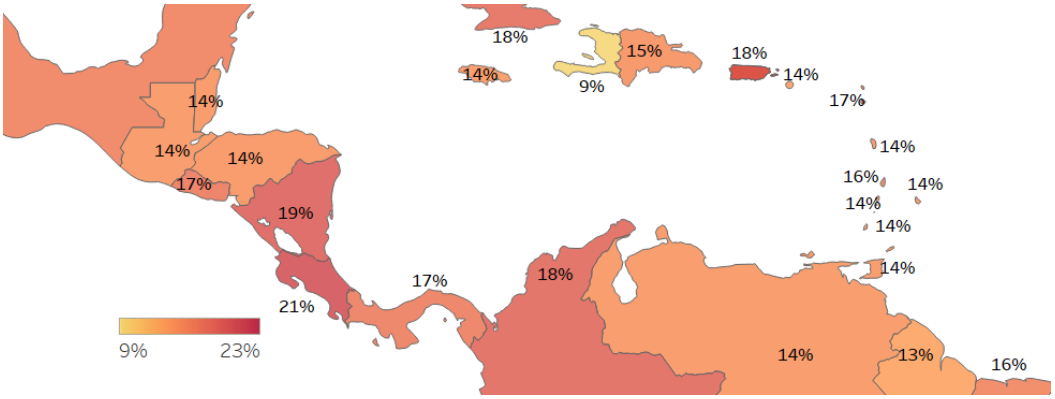
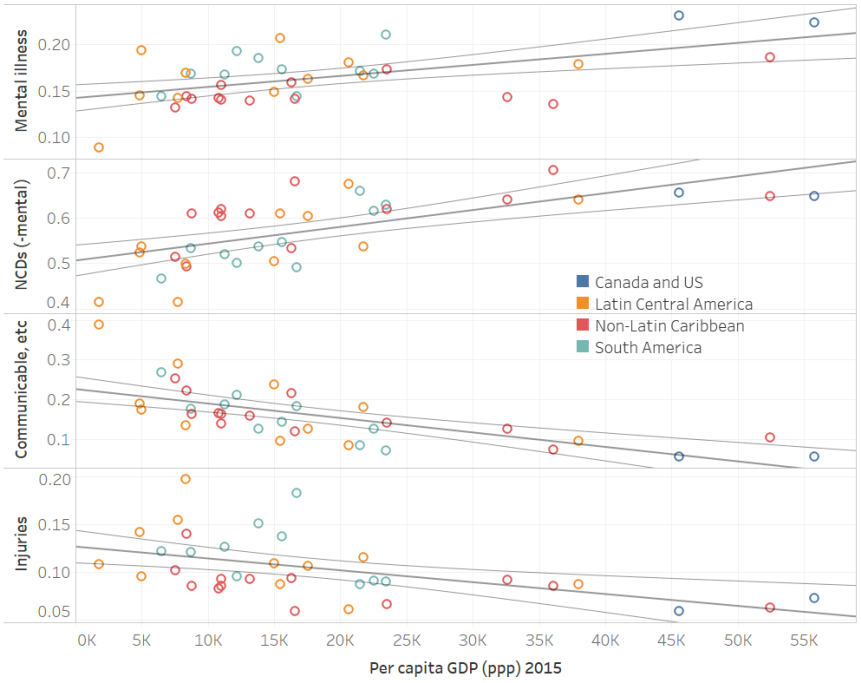


Figure 34: DALY map (Caribbean region)



There is a significant inverse correlation between country income-level and the fraction of total DALYs that are caused by communicable, maternal, child and nutritional disorders. A model including 2015 GDP (ppp) as independent and communicable, maternal, child and nutritional disorders DALYs as dependent variable appears highly significant ($p<0.0001$), and explains 45% of the variation. This simple correlation is not helpful to establish causation, since confounding factors remain unaccounted for, but highlights the very different health landscapes faced by decision-makers in different countries. When looking at proportions of the disease burden, the decrease in one cause-group results in the relative increase of the other groups, which is the case of non-communicable diseases in general, and mental disorders in particular, both of which seem to increase linearly as country- level income increases (Figure 35).

Figure 35: Illness and *income*



Linear models: Mental, substance use, and neuropsychiatric DALY% given 2015 GDP. R-Squared: 0.298445. Standard error: 0.0241254. p-value: 0.0005671; NCD DALY% given GDP2015. R-Squared: 0.420993. Standard error: 0.0579261. p-value:< 0.0001; Communicable… DALY % given GDP2015. R-Squared: 0.453384. Standard error: 0.0533626. p-value: < 0.0001; Injuries DALY% given GDP2015. R-Squared: 0.244789. Standard error: 0.0290336. p-value: 0.0021584[ix]

We will review later one of the consequences of this changing disease burden landscape in the next chapter: as income level falls, countries seem to invest a dwindling proportion of their -also decreasing- health budget in services for the mentally ill. A superficial analysis might posit that a decreasing burden is met by decision makers with a decreasing portion of the budget. It should be noted however that a nuanced analysis of the burden of mental disorders points in a different direction: as we will see in a later section, this apparent decrease is largely a methodological artifact. Aggregate disability resulting from mental illness does not decrease with poverty, and in

[ix] Graphics and statistics in this and later sections produced with Tableau 10.1 and Stata MP14

fact increases for certain sub-groups, in particular the disability resulting from common mental illness (see Figure 42, and Figure 43).

Country level disability (YLDs)

As we mentioned earlier, death registry for the overwhelming majority of mental illnesses is immaterial due to methodological constraints, so in fact DALYs for mental illness comprise almost exclusively YLDs. Our analysis partially rectifies this pitfall -by including suicide-, but a separate comparison of disability alone provides a picture that (a) complements the DALY burden analysis, and (b) is not biased by the differential exclusion of excess mortality resulting from mental illness. The between-country variation of YLDs as a percentage of total disability is much lower than the DALY variation we studied above, with the exception of the injuries cause-group, for which disaster-related disability in Haiti drives injury disability up to 10% of total YLDs. The overall variation of NCD disability ranges from 70% of total YLDs in Haiti to 91% in Mexico. Focusing on mental illness, the variation is between 28% in Haiti and 36% in Brazil, Chile and Paraguay. Communicable, maternal, child and nutritional disorders range from 5% of YLDs in the US and Chile, and 20% of YLDs in Venezuela and Haiti (see Figure 36, Figure 37, Figure 38).

Figure 36: YLDs by country

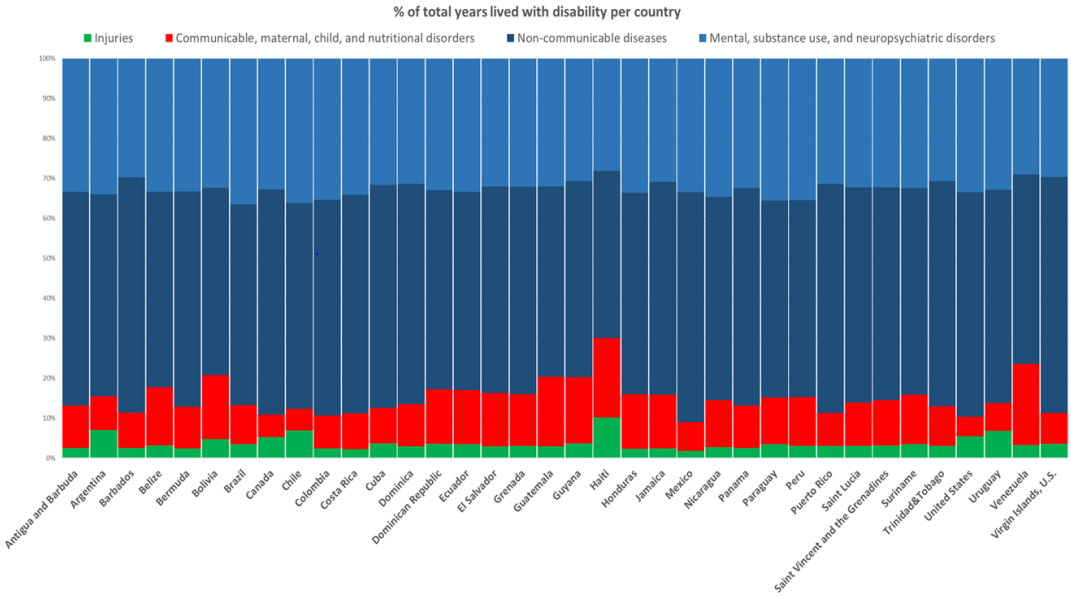


Figure 37: YLD map

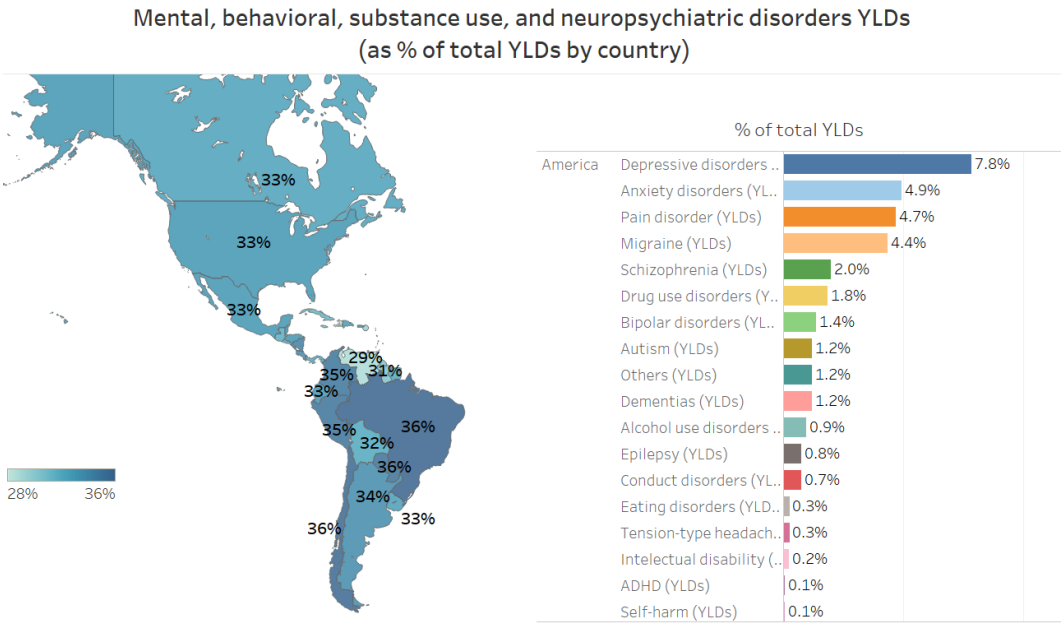


Figure 38: YLD map (Caribbean region)

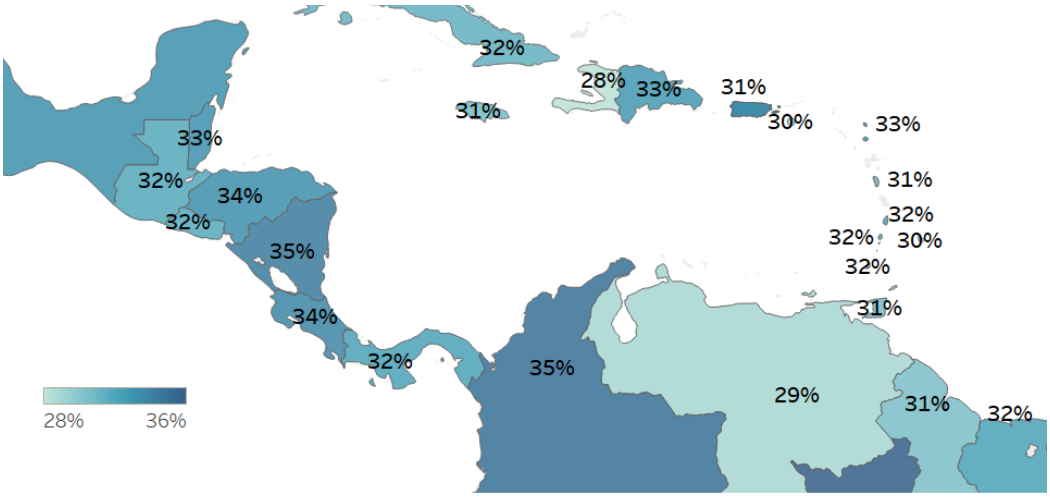
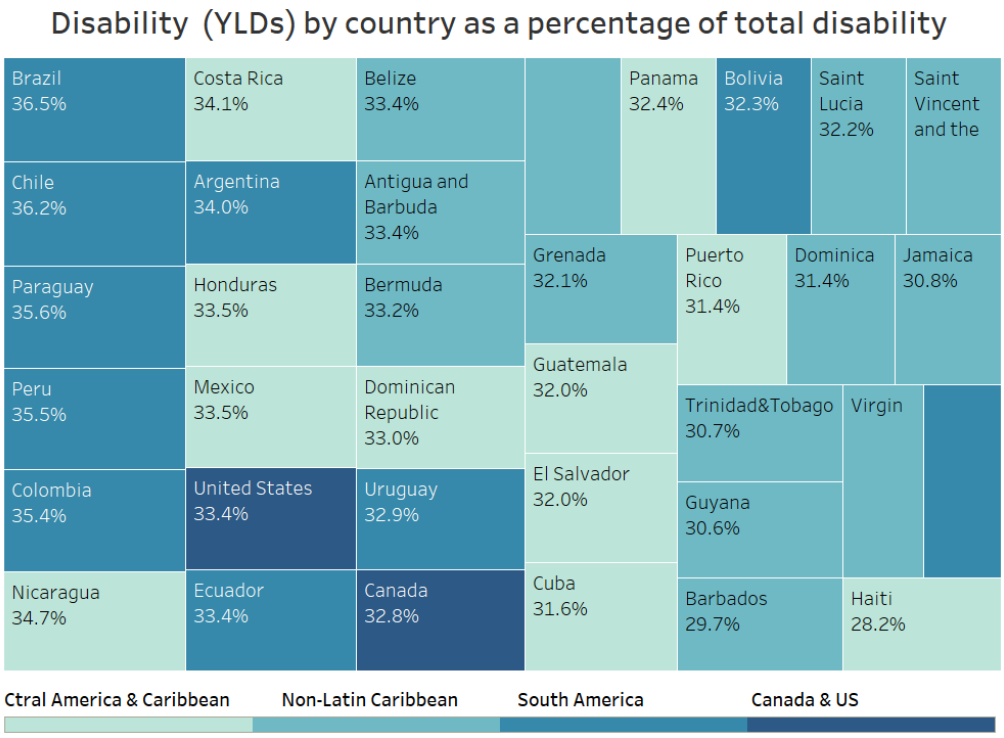


Figure 36, Figure 37, Figure 38, and Figure 39 show that disability resulting from mental, substance use, and neuropsychiatric disorders is remarkably similar -and high- throughout the region. It constitutes indisputably -and by a wide margin- the largest sub-group cause of disability in every country, regardless of income level or sub-region. There appears to be a sub-regional gradient in the disability resulting from aggregated mental, substance use, and neuropsychiatric disorders (see Figure 39), with South American countries occupying the top five positions in terms of YLDs, and a majority of them showing both above regional average (33%), and above regional aggregate (34%) disability. As we will see in the disorder-specific sections, there is a wide variation across countries in terms of the specific mental disorders that cause the largest burden. It is important for decision-makers to focus on the specific disease profile that affects their country to adequately prioritize specific conditions, allocate investments, and plan service delivery.

Figure 39: Mental, substance use, and neuropsychiatric disorders disability treemap



Treemaps visually display variation in three ways: the size, position, and color of each rectangle. Larger numeric values are represented by larger rectangles, with the largest values appearing in the top-left corner, moving down and right as numeric values decrease, with the lowest values appearing in the bottom-right corner. In all treemaps from now we use shades of different colors -blue in this graph- to represent the four sub-regions, from lighter to darkest: Latin Central America and the Caribbean; Non-Latin Caribbean; South America; and US and Canada

Disability resulting from specific disorders

Common mental illness

Common mental illness generally comprises depressive and anxiety disorders. As was previously mentioned, a number of other very common mental and behavioral syndromes are not considered in usual burden of disease calculations and analyses, despite their significant prevalence, disability, and mortality.(34,69) Of note, personality disorders and somatic symptom disorders are excluded due to lack of consistent cross-country data, and self-harm and suicide are considered under the heading of injuries, despite the well-established fact that mental illness and related syndromes are

largely responsible for intentional self-harm.(68,69) Following the method described in detail earlier, we include an estimation for pain disorders and also self-harm, thus indirectly capturing a fraction of the disability resulting from personality disorders and the excess death from depression and other mental illnesses due to suicide. Given the high prevalence of these mental and behavioral syndromes, we consider them in this section of common mental illness.

Depressive disorders

At the regional level, our analysis puts depression at the top of disability causes, with 7.8% of total disability, and a range from 5.9% in Canada to 9.4% in Paraguay. We find a sub-regional pattern of increased disability in South America, as indicated by: (a) Paraguay, Brazil, Peru, Ecuador, and Colombia constituting the top-five of the depression disability ranking; and (b) a clear majority of South American countries at or above the regional average (7.7%) and aggregate (7.8%) (see Figure 40). Another important aspect of depression is that it affects mainly the young: nearly 10 million of the 14.5 million depression YLDs in America fall upon the 15 to 50-year-old age-group (see Figure 41).

Figure 40: Depression disability treemap

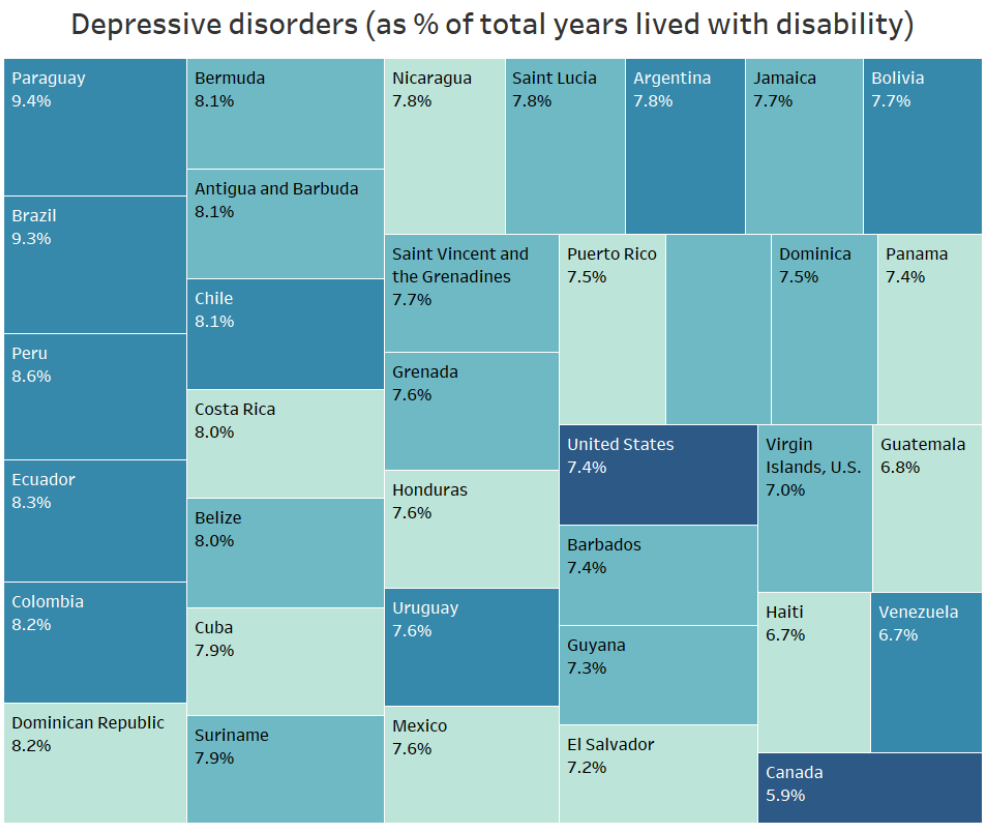
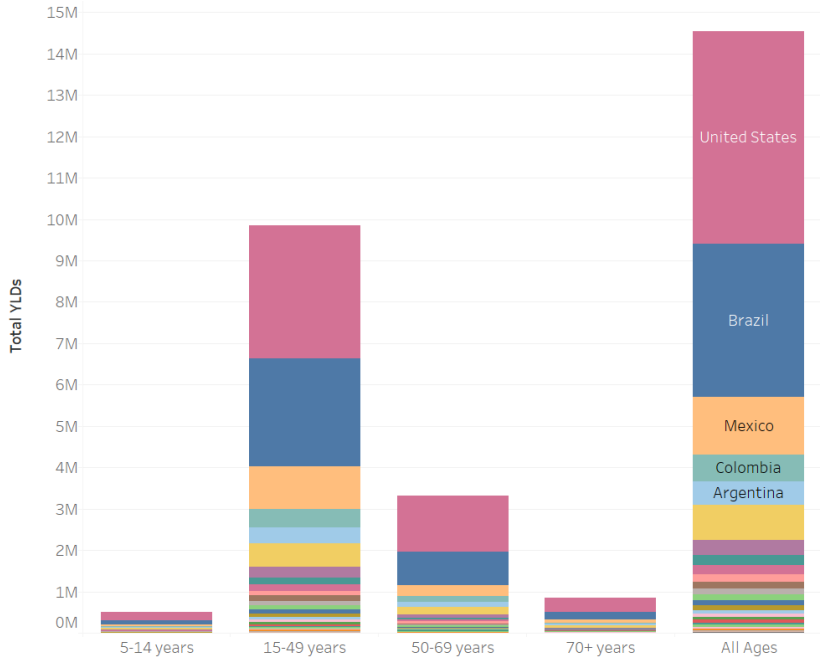


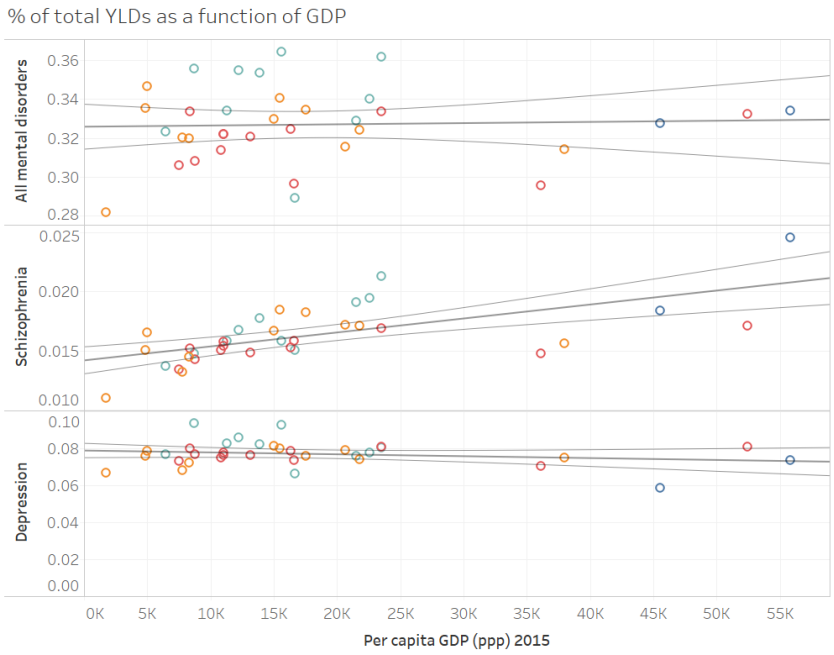
Figure 41: Depression YLDs by age



As we discussed above, disease distribution is correlated with income at the country level. Indeed, it is a well-established fact that communicable, maternal, child, and nutritional disorders are more prevalent and lethal in low-income countries, and that non-communicable diseases tend to cause a larger proportion of disability as income increases, mainly due to decreased mortality leading to increased survival with disability.(27,84,85) The epidemiologic transition embodies these sweeping global changes in disease landscape. Less transparent is how mental illness varies in different income settings. Individual level evidence points towards a direct correlation between poverty and common mental illness, in keeping with the evidence-based role of social determinants of health, which result in a socioeconomic gradient of illness.(86,87) However, we have seen that the overall mental illness burden as measured by percentage of total DALYs seems to be directly correlated with gross domestic product, that is, inversely correlated with country

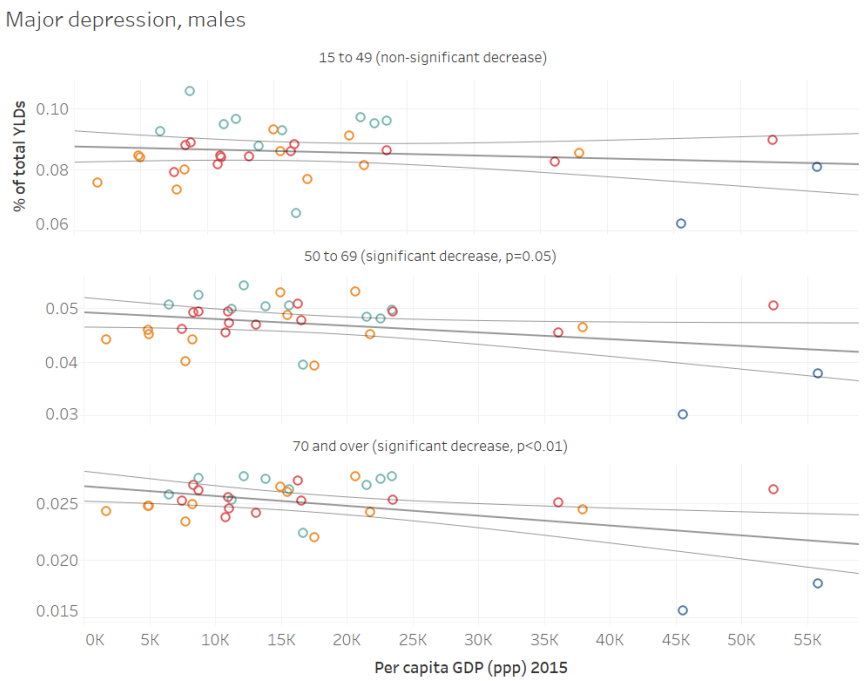
level *poverty*. As was noted earlier, deaths resulting from mental illnesses are under-registered, so YLDs would be a more appropriate metric to compare across groups of illnesses. Furthermore, it is quite likely that specific disorders vary differently in relation to income settings. Figure 42 illustrates this differential variation: in aggregate, mental disability is not correlated with GDP, as expressed by the flat non-significant trend-line. Focusing on specific disorders separately, however, we see that while schizophrenia shows a significant increase in relation to country-level income, depression shows a non-significant decrease (see Figure 42 for model details). It is important to bear in mind that this analysis is based upon aggregate country-level data for both sexes and all ages. Studying specific age-sex groups we see that this non-significant decrease in depression disability turns however highly significant for males, specifically for older age-groups (see Figure 43). This model does not allow for causal inference, but it does illustrate the need to look beyond high-level aggregate results to inform health systems planning. We find that the disability burden of depression tends to be higher in South America, affects mostly the young, and can be expected to increase in lower-income settings, as indicated by abundant individual-level evidence and supported by our country-level analysis, particularly for men. For women, the disability burden resulting from depression is uniformly higher than for men, and does not seem to vary with country-level income.

Figure 42: Mental illness and income



Aggregate mental illness disability and major depression disability do not decrease with national income. Schizophrenia disability significantly decreases with national income. Linear models: Mental illness YLD% given GDP2015. R-Squared: 0.0017092. Standard error: 0.0196943. p-value: 0.813584 (non-significant); Schizophrenia YLD% given GDP2015. R-Squared: 0.393935. Standard error: 0.0019416. p-value: < 0.0001; Depressive disorders YLD% given GDP2015. R-Squared: 0.0402674. Standard error: 0.006634. p-value: 0.247741 (non-significant)

Figure 43: Major depression disability in males

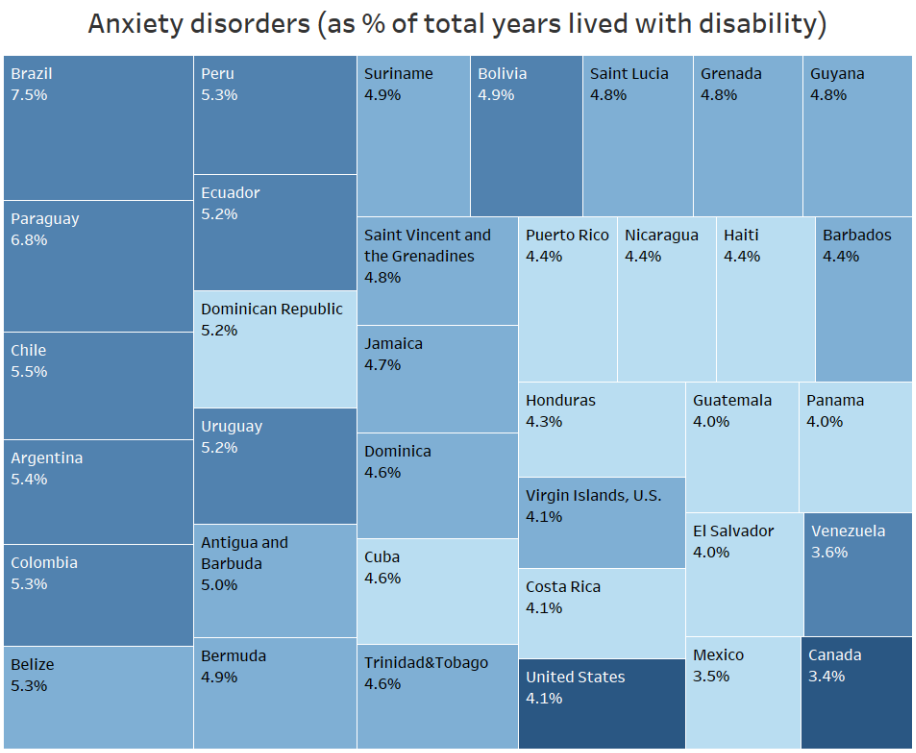


Linear models for Major Depressive Disorder YLD rates: Males, 15-49, given GDP2015. R-Squared: 0.0216939. Standard error: 0.0087242. p-value: 0.398477; Males, 50-69, given GDP2015. R-Squared: 0.111394. Standard error: 0.0047355.p-value: 0.05; Males, >70, given GDP2015. R-Squared: 0.207482. Standard error: 0.0022542. p-value: 0.0059655.

Anxiety disorders

Anxiety characterizes the second most disabling group of mental disorders in most American countries -in 24 of 36 countries-. A sub-regional pattern is even more discernible than for depression, with: Brazil at the top (7.5%); all but one South American countries showing above average (4.7%) and aggregate (4.9%) disability; and eight of the top-ten countries in terms of disability corresponding to this sub-region (see Figure 44). North America falls at the other end of the spectrum, with Canada showing the least disability (3.4%), followed by Mexico (3.6%) and with the US (4.1%) also well below regional average and aggregate.

Figure 44: Anxiety disability treemap



Self-harm and suicide

Given the well-established relationship of common mental illnesses -such as depression and personality disorders- with suicide and self-harm, we consider them in this section. As was mentioned before, the burden of disease framework does not include personality disorders -a well-established cause of non-lethal self-harm(49,88)-, and YLDs resulting from self-harm are not captured in the burden of disease framework, so for this section we will focus on suicide DALYs, which are largely due to years of life lost due to premature death.

Suicide is the 5th cause of DALYs in America with an almost nine-fold range, from 0.4% in Antigua and Barbuda to 3.6% in Suriname. There is a remarkable sub-regional pattern affecting Suriname

(3.6%), Guyana (3.5%), and -to a lesser extent- nearby Trinidad & Tobago (2.1%). Uruguay (2.6%), Chile (2.5%), and Argentina (2%) in South America, and the United States (2.2%) plus Canada (2.1) also configure sub-regional clusters affected by suicide well in excess of the regional average (1.5%) and aggregate (1.6%) percentages (see Figure 45). Such sub-regional clustering calls for trans-country initiatives to study the cultural and socioeconomic determinants that might lead to these adverse outcomes, and present an opportunity for coordinated sub-regional interventions. The toll that suicide takes on America is daunting, and it falls mainly on the younger working-age population: there were 97,034 estimated suicide deaths in 2015, of which 60% occurred between 15 and 50 years of age. 4,129,576 years of life were lost, of which around 75% were lost by this same age-group (see Figure 46). Total deaths reflect population size, with the exception of Colombia that despite having a larger population trails Argentina and Canada in total deaths and in total years of life lost. In terms of rates, the picture changes substantially: Mexico and Brazil are not in the top ten countries in terms of suicide and YLL rates, and the largest rates can be seen in the three clusters mentioned earlier, with some noteworthy additions: El Salvador, Cuba, and Bolivia, which have high suicide and YLL rates for quite different reasons. El Salvador has the fifth largest regional YLL rate for the 15 to 50 age-group, and the eighth largest overall rate. Cuba has the fourth largest suicide rate in the region, driven by a notably high rate in the elderly, the highest in America. Similarly, Bolivia has the tenth largest overall death rate, also driven by a higher elderly suicide rate, the fourth in America (see Figure 47)

Figure 45: Suicide burden treemap

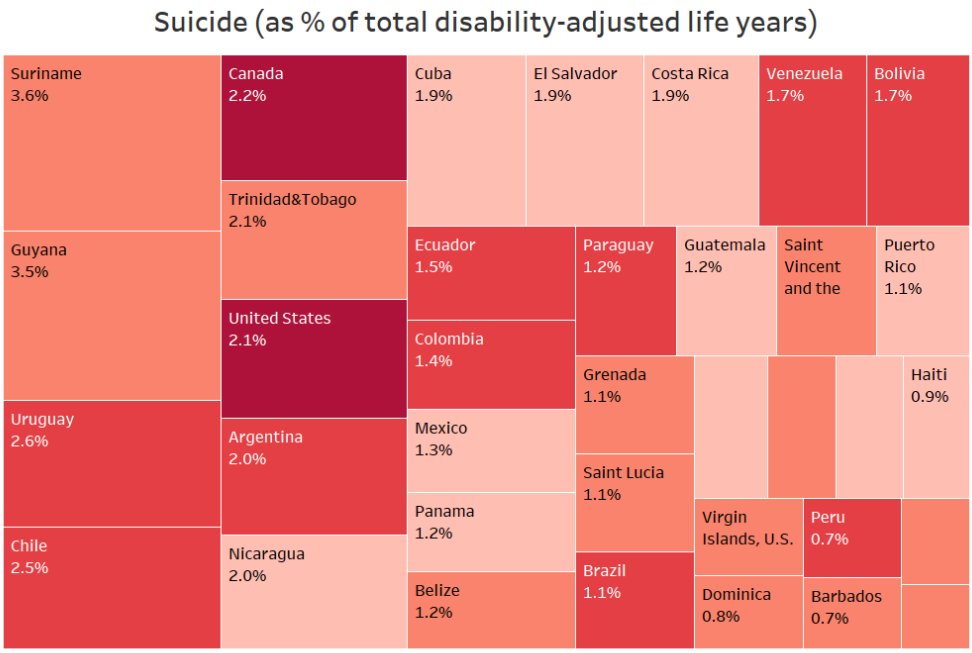
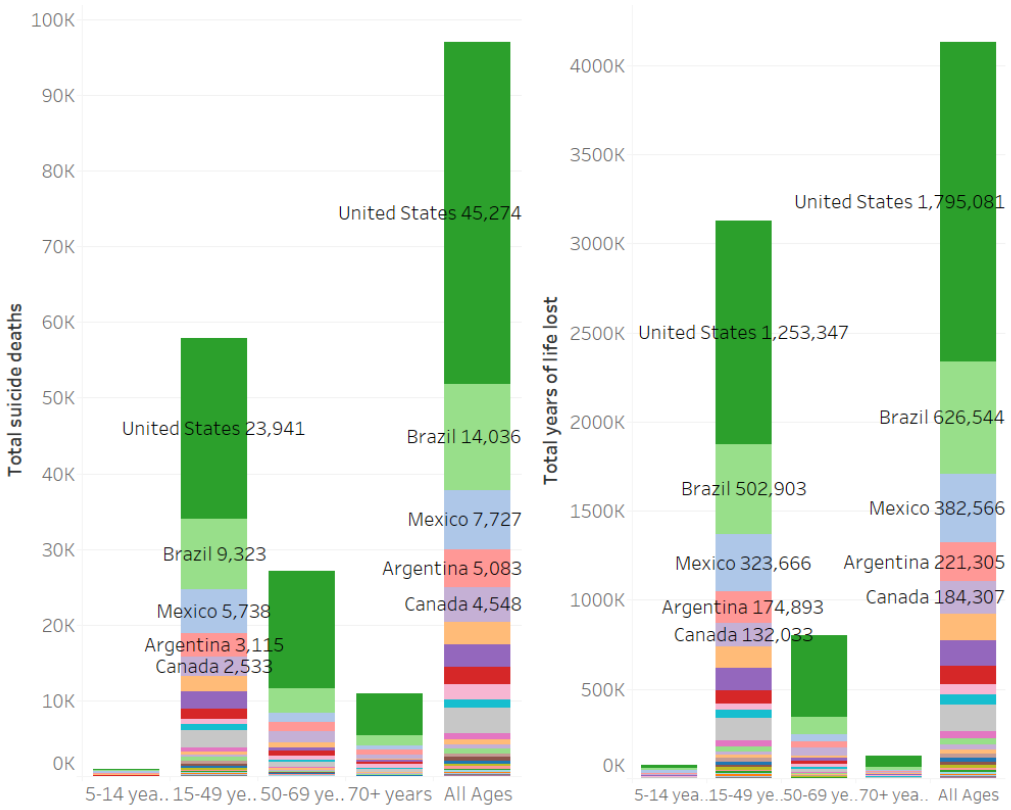
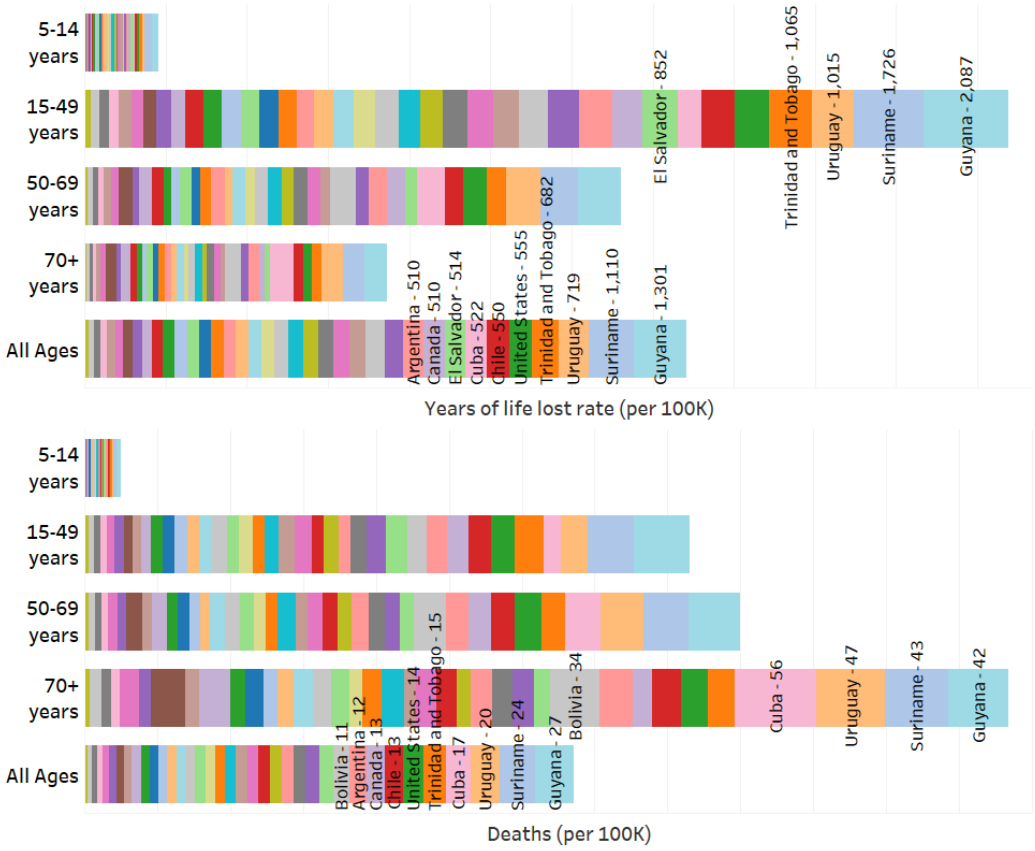


Figure 46: Total suicides and total years of life lost by age-group



Columns represent total deaths and YLLs in America for 4 separate age groups, and a fifth column for all ages. Each color represents a country, including details for the 5 largest contributors to suicide deaths and YLLs in the All Ages and in the 15-49 columns.

Figure 47: Suicide and YLL rates by age group



Bars represent YLL (upper graph) and death (lower graph) rates in America for 4 different age groups, and a fifth bar for all ages. Each color represents a country, ordered left to right from lower to higher all-age rate, including country name and rate for the top 10 countries in the all-ages column, and for the top 5 countries in the age group with the largest rates (15-49 years for YLL rate and 70+ years for death rate). Note that the age-specific bars follow the country order indicated by the all-age bar ranking.

Somatoform pain disorders / somatic symptom disorder with predominant pain

Pain disorders are poorly understood syndromes, frequently ignored as such by clinicians, psychiatrists, and epidemiologists.(42,43) When properly studied, however, they are highly prevalent, especially in women: the 12-month prevalence of DSMIV pain disorder has been

established by one study in 11% for females and 4% for males, with an overall rate of 8%, the largest for any mental disorder.(44) 56% of pain disorder patients meet criteria for another psychiatric disorder, most frequently depression or anxiety. Prevalence of painful syndromes in patients diagnosed with depression or anxiety have been found to be in excess of 30%, and up to 80% in specific PTSD populations.(89) Routine burden of disease assessments assign 0% of the burden of painful syndromes to mental disorders, an assumption lacking minimal face validity. We estimate that 4.7% of total YLDs in America are due to pain disorders better considered to be neuropsychiatric rather than musculoskeletal in nature and clinical presentation.(69) The estimated range is between 6.2% in Canada and 3.2% in Haiti, and higher-income countries seem to be more affected than those of lower-income. These estimates should be considered indicative until primary data on somatoform disorder disability becomes available.

Severe mental illness

Schizophrenia and bipolar disorders are usually referred to as severe mental illnesses. Indeed, they exact some of the largest tolls conceivable on human beings: acute psychotic episodes in the context of schizophrenia are considered the most disabling health state in the burden of disease framework;(12) manic episodes are highly disabling medical emergencies, frequently leading to socioeconomic ruin, injury, or death if untreated; and depressive episodes in the context of bipolar illness can be as severe as those of major depressive disorder. Severe mental illness is particularly lethal in low-income settings, which tend to also be contexts of high stigma. The lack of effective, accessible -or even available- services, coupled with the catastrophic economic and emotional burden on families frequently lead to systematic human right abuses in-lieu of treatment, resulting

in what has been memorably labeled a “failure of humanity”.(90) Indeed, we will see here and in the chapter devoted to the health system response that lower country-income predictably results in: decreased availability of services; worse services when available; and earlier death for severe mental illness.

Schizophrenia-spectrum disorders

In the burden of disease framework, the schizophrenias are considered the most disabling human disorders, particularly during acute episodes. But even *residual* schizophrenia -a health state of decreased symptomatology but persistent dysfunction- is considered equally disabling as for example the severe long term consequences of stroke with cognitive impairment. In the long term, people with schizophrenia die between 10 and 30 years younger than their peers, with the worst outcomes seen in low-income countries.(53,54)

The regional variation of schizophrenia disability as a percentage of total disability is between 1.1% in Haiti and 2.5% in the United States. Sub-regional patterns are less clear, but the US, Canada, and most South American countries are above the regional average (1.6%) (see Figure 48). There seems to be, however, a clear correlation with GDP. As we showed previously, the % of disability resulting from schizophrenia seems to be directly correlated with income at the country-level. Indeed, looking at YLD rates in relation to income yields an even more significant linear correlation, which appears to account for more than 60% of the variation between countries (see Figure 49 for model details). Reasons for this correlation are not transparent, and causal interpretations would be particularly inadequate. Several factors could explain this increasing share of the disability as income level grows, most notably increased premature mortality and/or decreased

case-detection capacity in poor settings. As we have noted in the beginning of this section, patients with schizophrenia die significantly earlier in lower-income settings, which by itself would explain a decreasing share of the resulting survival with disability. We will explore this issue further in chapter 5.

Figure 48: Schizophrenia disability treemap

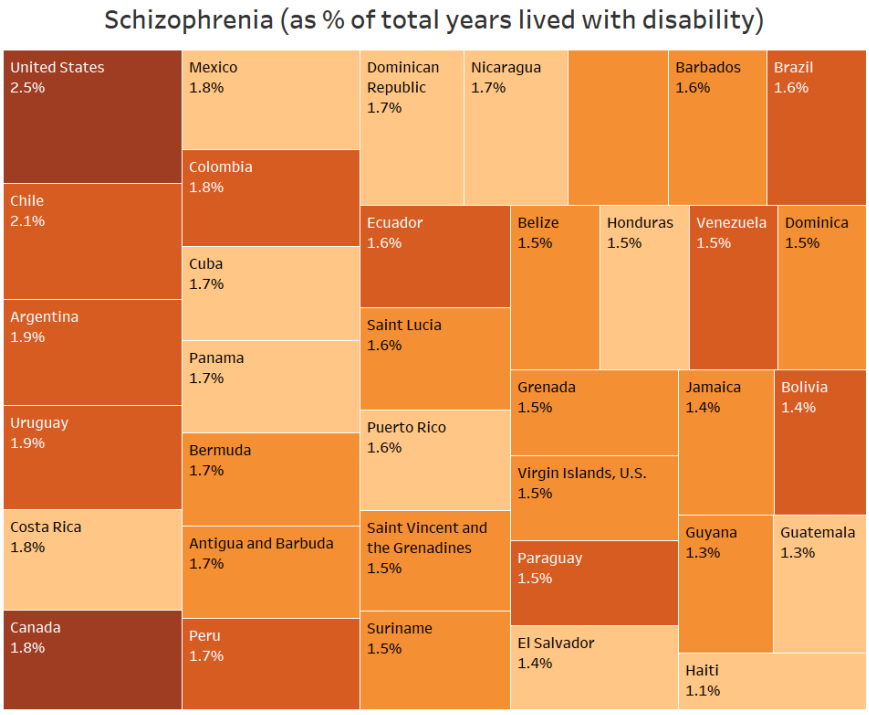
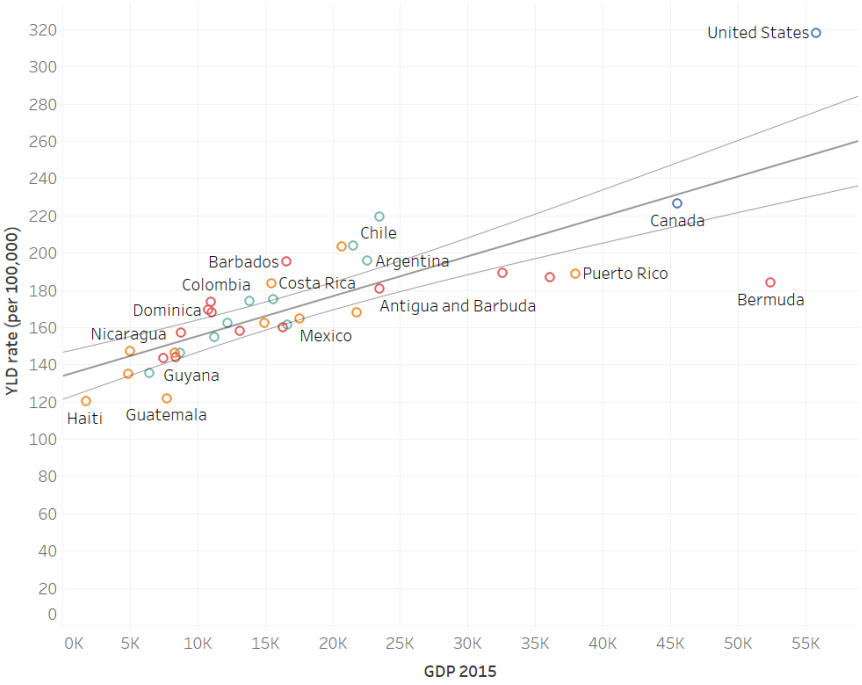


Figure 49: Schizophrenia and income



Linear model: Schizophrenia YLD rate given 2015 GDP. R-Squared: 0.636038. Standard error: 21.5881. $p < 0.0001$

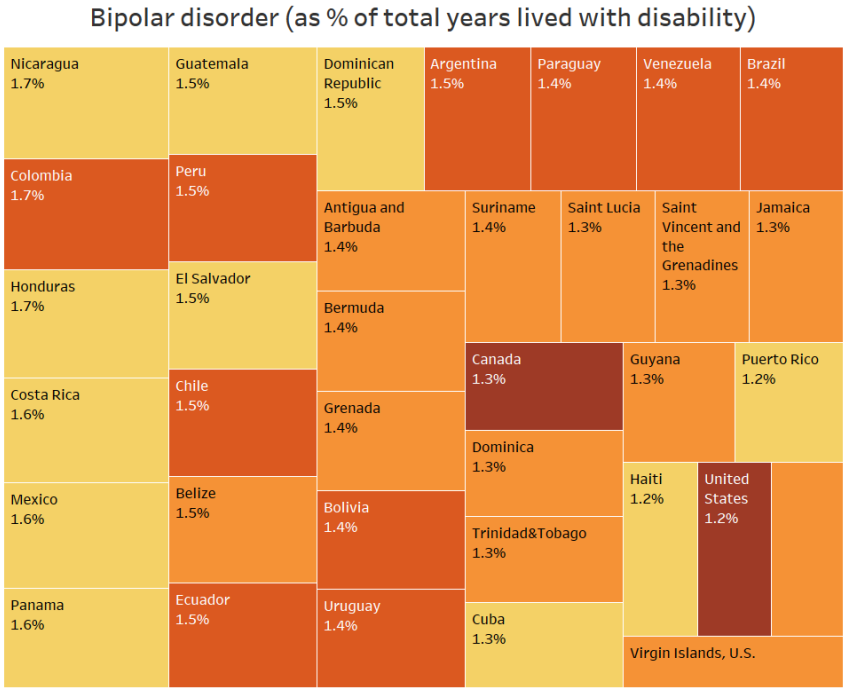
Bipolar disorders

Unlike the uniformly high disability resulting from schizophrenia, disability resulting from bipolar disorders can range from mild dysfunction during *residual* states to almost complete impairment during severe manic and depressive episodes. For the purposes of our analysis bipolar disorders comprise types I and II, characterized respectively by -alternating with depression- manic and hypomanic episodes, the latter constituting a milder and briefer behavioral and psychological activation syndrome than the former.

A sub-regional pattern seems to emerge for bipolar disorder disability: every country in continental Central America is above the regional average -and aggregate- of 1.4% (see Figure 50),

while both Canada and the US are below (1.3% and 1.2% respectively). The range is between 1.1% of total YLDs in the Virgin Islands to 1.7% in Nicaragua.

Figure 50: Bipolar disorder disability treemap



Substance use and eating disorders

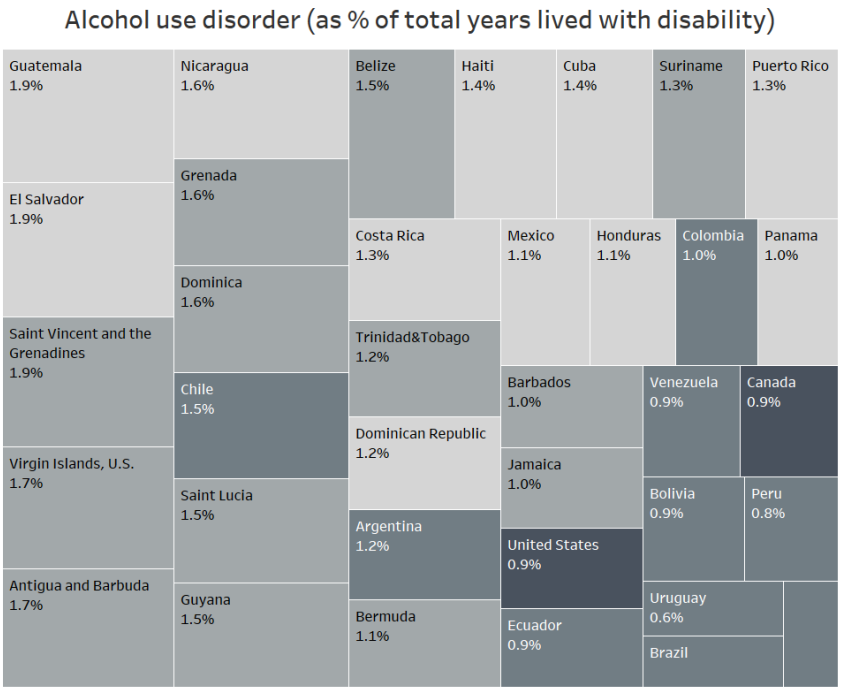
Disorders stemming from the use of alcohol, drugs, and food are frequently considered together due to a similar clinical pattern, mostly related to their compulsive nature and the direct behavioral dysfunction they entail -which makes them different from smoking, which entails mostly indirect disability through its physical consequences-. For the purpose of our analysis we will focus on alcohol use disorder, drug use disorders, and eating disorders. They include varying severities that according to the burden of disease framework range from the low impairment of mild cannabis use disorder -comparable to partially-controlled asthma- to the complete disability resulting from

severe heroin dependence, and including the moderate disability resulting from anorexia and bulimia, comparable in the burden of disease framework to moderate chronic respiratory disease.

Alcohol use disorders

The disability resulting from alcoholism ranges from 0.5% in Paraguay to 1.9% in Guatemala and El Salvador. It presents a sub-regional pattern with the US, Canada, and most South American countries well-below the regional average of 1.2% -only Chile exceeds it at 1.5%-, and at or below the regional aggregate (0.9%). At the same time, every country in Central America and the Caribbean is above the regional aggregate percentage, and most are above the regional average (see Figure 51).

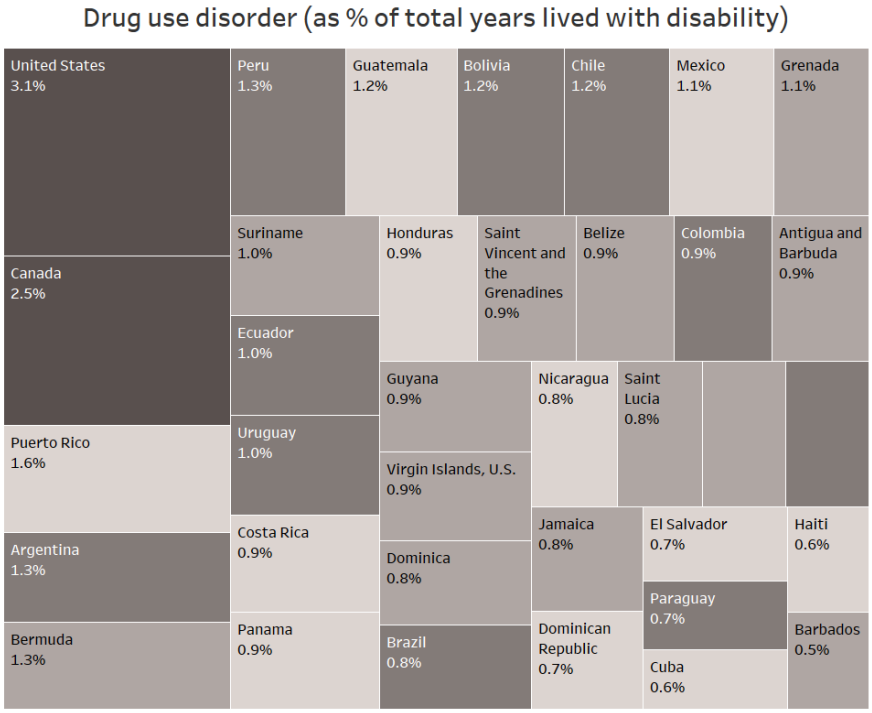
Figure 51: Alcohol use disorder disability treemap



Drug use disorders

We consider here together cannabis, cocaine, amphetamine, and opioid use disorders. The variation in disability burden resulting from drug use ranges from 0.5% in Barbados and 0.6 in Haiti and Cuba, to 3.1% in the United States (see Figure 52). This six-fold variation reflects the raging epidemic of opioid use disorders affecting the US (3.1%) and Canada (2.5%), in both of which the specific burden of opioid use disorders constitutes around 70% of all drug use disability.

Figure 52: Drug use disorder disability treemap



Eating disorders

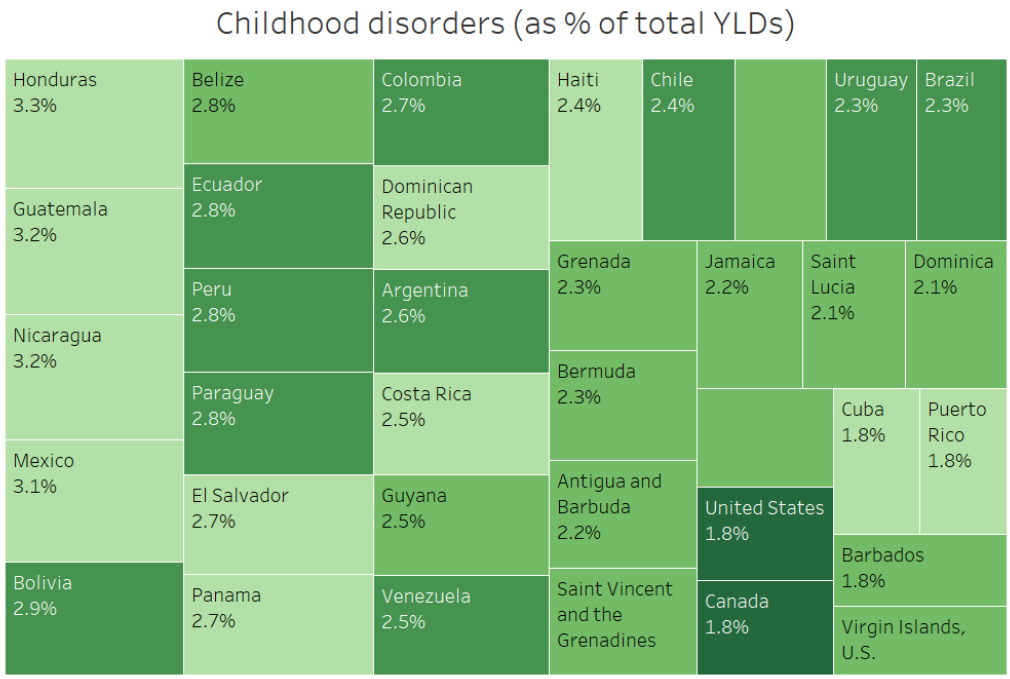
Anorexia and bulimia together account for a comparably much smaller fraction of total burden: between 0.07% in Haiti and 0.42% in the United States. Indeed, only the US and Canada are above

the regional aggregate percentage of 0.3%, signaling that the burden of eating disorders falls more heavily on well-off countries. Indeed, eating disorder disability increases linearly with income, with GDP explaining 66% of the variation (Eating disorder YLD%= 3.71685e-08*Gdp2015 + 0.00119611. R^2=0,66. Standard error: 0.0003545. p<0.0001).

Childhood onset disorders

Collectively, disorders that affect mainly children and adolescents account for 2.2% of total YLDs in America. They include, in order of importance: autism (1.2%), conduct disorders (0.7%), intellectual disability (0.2%), and attention-deficit and hyperactivity disorder (0.1%). They show a clear sub-regional pattern, with all continental Central American countries and all South American countries above the regional aggregate percentage. Conversely, most of the English-speaking Caribbean islands, the United States, and Canada (1.8% in both) show the lowest burden (see Figure 53).

Figure 53: Childhood disorder disability treemap



Neuropsychiatric disorders

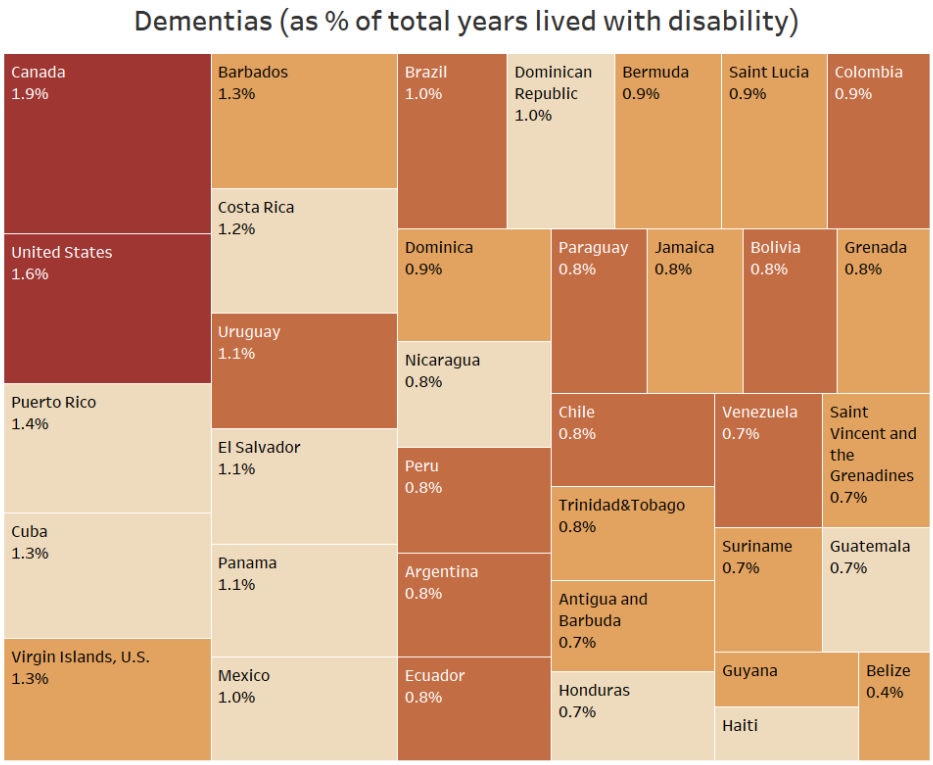
We include here the disability resulting from Alzheimer's disease and other dementias, epilepsy, migraine, and tension-type headache, all of them disorders with prominent mental and behavioral syndromes.

Dementias

Alzheimer and other dementias account for 1.2% of total disability, ranging from 0.4% in Haiti to 1.9% in Canada, reflecting a highly significant trend correlating higher GDP with a higher percentage of total disability attributable to the dementias (Dementia YLD%= 1.5842e-07*Gdp2015 + 0.00625382. R^2: 0.453987. Standard error: 0.0023147. p-value: < 0.0001). This is an expression of the demographic change in age- structure, where increased survival -and

disability resulting from the disorders of older adults- accompanies economic development (see Figure 54).

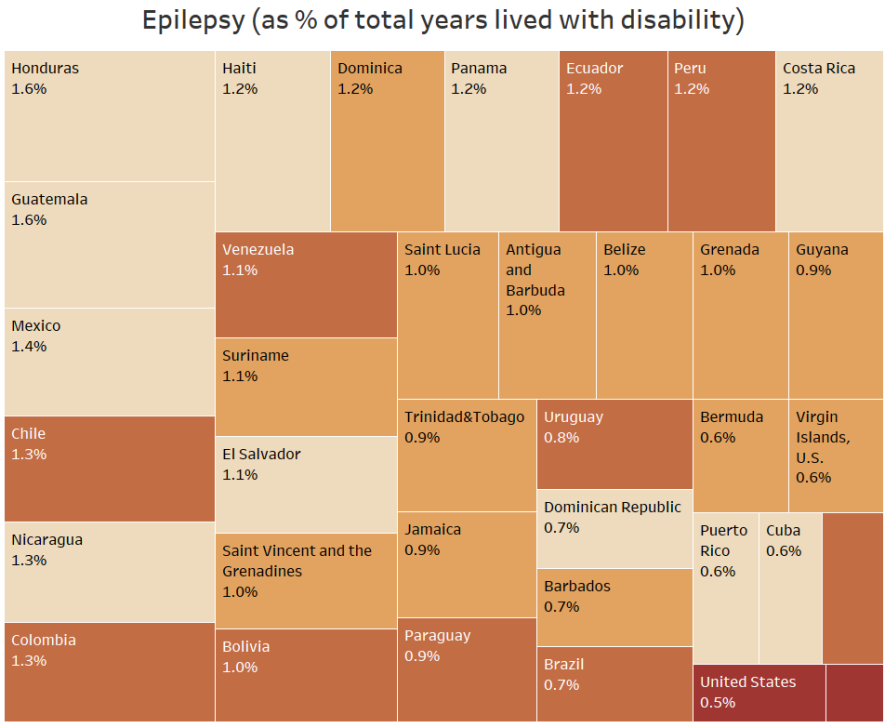
Figure 54: Dementia disability treemap



Epilepsy

Epilepsy causes 0.8% of total disability in the region, with a range of between 0.2 in Canada and 1.6 in Honduras. Sub-regionally, epilepsy produces a lower percentage of disability in Canada and the United States, and a larger proportion in Honduras, Guatemala, and Mexico. In fact, most countries in Central, South America and the Caribbean are above the regional aggregate percentage, which reflects the lowest percentage of burden in a few countries with large population, such as the US, Brazil, Argentina, and Canada (see Figure 55).

Figure 55: Epilepsy disability treemap



Migraine and tension-type headaches

Migraine produces 4.4% of regional disability burden, with a minimum in the US (3.6%) and a maximum in Peru (5.4%). Tension-type headache produces a comparatively much lower regional burden (0.3%), and there doesn't appear to be a sub-regional pattern for either.

Section summary

Mental, substance use, and neuropsychiatric disorders are the largest sub-group cause of disease burden in America, both when considering disability alone and combined with mortality: they comprise a third of total years lived with disability and a fifth of total disability adjusted life-years. Of the different mental disorders, depression is the largest cause of disability alone and

combined with mortality, accruing 3.4% of total DALYs and 7.8% of total YLDs. Second are anxiety disorders, with 2.1% and 4.9% respectively. Self-harm and somatization disorders should also be considered common mental disorders, accountable respectively for 1.6% of DALYs and an estimated 4.7% of YLDs. Severe mental illness leads to increased mortality, particularly in low-income settings.(53) High-income settings thus cope with an increased share of the disability burden due to schizophrenia. Several sub-regional patterns emerge in the distribution of specific mental disorders, and this report provides decision-makers with a nuanced picture of mental disorders in most American countries or territories. South America has in general higher proportions of disability due to common mental illness; suicide imposes a disproportionately high burden on three sub-regional clusters: Suriname, Guyana, and Trinidad & Tobago; Uruguay, Chile, and Argentina; and Canada and the US. Of note, specific sub-populations are also affected in excess of local trends: the elderly in Cuba and Bolivia, and the young in El Salvador. Depression takes its largest toll on young working-age populations, and seems to be increasingly disabling in lower income settings -for males in particular-. Continental Central America has a larger proportion of disability due to bipolar and childhood onset disorders than other sub-regions, as well as from epilepsy; and the US and Canada suffer a high disability toll from schizophrenia and dementia, as well as devastating rates of drug –mainly opioid- use disorder disability.

Chapter 4. The burden on health systems: Imbalance between disease burden and government spending on mental health in the Americas

In this section, we will focus on how our societies respond to the challenge presented by the largest cause of disability in the region. We will study how investment in mental health services and allocation of spending varies as a function of national income, providing simple intuitive metrics that allow for assessment of the gap between disease burden and effective government spending, cross-country comparison, and rank ordering of countries.

As we have mentioned in previous chapters, an epidemiologic transition is transforming the global burden of disease from one characterized by mortality due to communicable, maternal, childhood, and nutritional disorders, to one dominated by non-communicable diseases (NCDs), multi-morbidity, and survival with disability.(27,85) In this transition, mental illnesses represents a particularly complex challenge, carrying by far the highest disability burden among NCDs.(69,84) Despite higher recent visibility among global health and development communities, pervasive stigma and discrimination, outdated institutional practices, and organizational fragmentation means health systems are still unprepared to adequately assess, prioritize, resource, and respond to mental illness.(73,91)

This study analyses how nations in the Americas have responded to the challenge of mental illness. Based on the disease burden estimates produced in last chapter, our goal is to assess the ratio between burden and expenditures, and analyze how allocation of spending varies in relation to national income, as measured by Gross Domestic Product (GDP) per capita (purchasing power parity, PPP).

Methods

In addition to our disease burden estimates, we obtained estimates of health spending and allocation by collating data reported to Pan-American Health Organization by governments of the Americas and published in the World Health Organization Assessment Instrument for Mental Health Systems (WHO-AIMS).(92) This was supplemented with other published data when missing, or when more recent WHO-AIMS country-level data were available.(61,92–97) For countries or territories with unavailable data for mental health spending or for fraction spent on neuropsychiatric hospitals, we imputed the median regional value. We excluded countries missing both data points. We also obtained country income data for 2015 from the International Monetary Fund's World Economic Outlook Database.(98) For a small number of island territories with 2015 GDP (ppp) data missing (n=4), and disease burden data missing (n=5), we imputed their specific sub-regional median (i.e.: the median for non-Latin Caribbean countries). Based on these data we obtained the following percentages and ratios:

a. Percentage of total disability adjusted life years (DALYs) attributable to mental, substance use, and neuropsychiatric disorders
b. Percentage of total DALYs attributable to schizophrenia
c. Percentage of DALYs attributable to schizophrenia that correspond to an acute psychotic state in the burden of disease framework severity distribution(13)
d. Percentage of government health spending allocated to mental health
e. Percentage of government mental health spending allocated to neuropsychiatric hospitals

f. a/d = Percentage of total disability adjusted life years (DALYs) attributable to mental, substance use, and neuropsychiatric disorders / Percentage of government health spending allocated to mental health

g. (a-b*c)/(d-e*d) = (mental, substance use, and neuropsychiatric DALYs as a % of total DALYs - schizophrenia DALYs * % acutely psychotic patients in severity distribution for schizophrenia) / % of total spending allocated to MH - % of MH spending * % spent on mental hospitals)

With respect to point (c), which is calculated in order to be used as a component of (g), the goal is to capture the fraction of the burden that can arguably not be dealt with directly through community-based resources. We propose two metrics of imbalance: the first one -(f)- is simply a ratio of % of health burden to % of health spending; the second metric –(g)- factors in allocative efficiency by including in the denominator a proxy for effective spending, which is the fraction of spending that is available for community-based resources after deducting the fraction allocated to mental hospitals. For this metric to be consistent, the fraction of the burden that can't be directly and fully treated in the community should be deducted from the numerator. One option would entail capturing the burden that emerges from the patients that are currently being treated in mental hospitals, who are to a large extent -mostly in LAMICS, where mental hospitals are still the mainstay of treatment- patients with schizophrenia spectrum disorders, plus very small fractions of patients with the most severe forms of affective disorders, frequently comorbid with substance use or personality disorders. This option would however produce an unacceptable overestimate of the burden not amenable to community interventions, since most of these patients could and should be treated in the community. The burden of disease framework has

modeled a distribution of health states by severity for most disorders.[21] For schizophrenia it provides the following distribution: 63% of prevalent cases correspond to *acute schizophrenia*, which carries a disability weight of 0·778; and 37% of prevalent cases correspond to a still highly disabling state termed *residual schizophrenia*, carrying a disability weight of 0·588 (disability weights range from 0 -perfect health- to 1 -equivalent to death-). For our purpose - since YLLs are negligible and YLDs are calculated by multiplying prevalent cases in each health state by the disability weight-, this means that 69% of the disease burden of schizophrenia is attributable to the acute state and 31% to the residual state. To be conservative, we have chosen to extrapolate the full percentage of disability burden attributable to acute schizophrenia and subtract it from the numerator, though most of this burden also could and should be treated in distributed services, such as general hospitals or mobile crisis teams. So, our final metric of imbalance, which factors in allocative efficiency, is in fact a conservative estimate, since the numerator excludes the full 69% of schizophrenia burden, and considers that the remaining 31% should be treated outside mental hospitals, along with the rest of the MNSS.

With these data points, we produced three linear regression models:

1) A regression of the percentage of total Government health spending allocated to mental health on 2015 gross domestic product ($ purchasing power parity):

$$\ln(\%\ of\ government\ health\ spending\ allocated\ to\ mental\ health\ services_c) = \beta_0 + \beta_1 GDP\ 2015\ (ppp)_c + \epsilon$$

(subscript *c = country*)

2) A regression of the percentage of mental health spending allocated to mental hospitals on 2015 gross domestic product ($ purchasing power parity):

$$\ln(\%\ of\ mental\ health\ spending\ allocated\ to\ mental\ hospitals_c) = \beta_0 + \beta_1 GDP\ 2015\ (ppp)_c + \epsilon$$

3) A regression of our metric of imbalance in efficiently allocated spending on 2015 gross domestic product ($ purchasing power parity):

$$\ln((\%MNSS\ DALYs - 0.63 * schizophrenia\ DALYs)/(\%MH\ spending - \%MH\ spending * \%\ mental\ hospital\ spending))_c = \beta_0 + \beta_1 GDP\ 2015\ (ppp)_c + \epsilon$$

We also produced ranked bar-charts for both imbalance ratios:

1) % of MNSS burden/% spent on mental health services

2) % of MNSS burden to be treated in the community/% of resources available for community services.

Graphs and models were computed with Tableau 10.1

Results

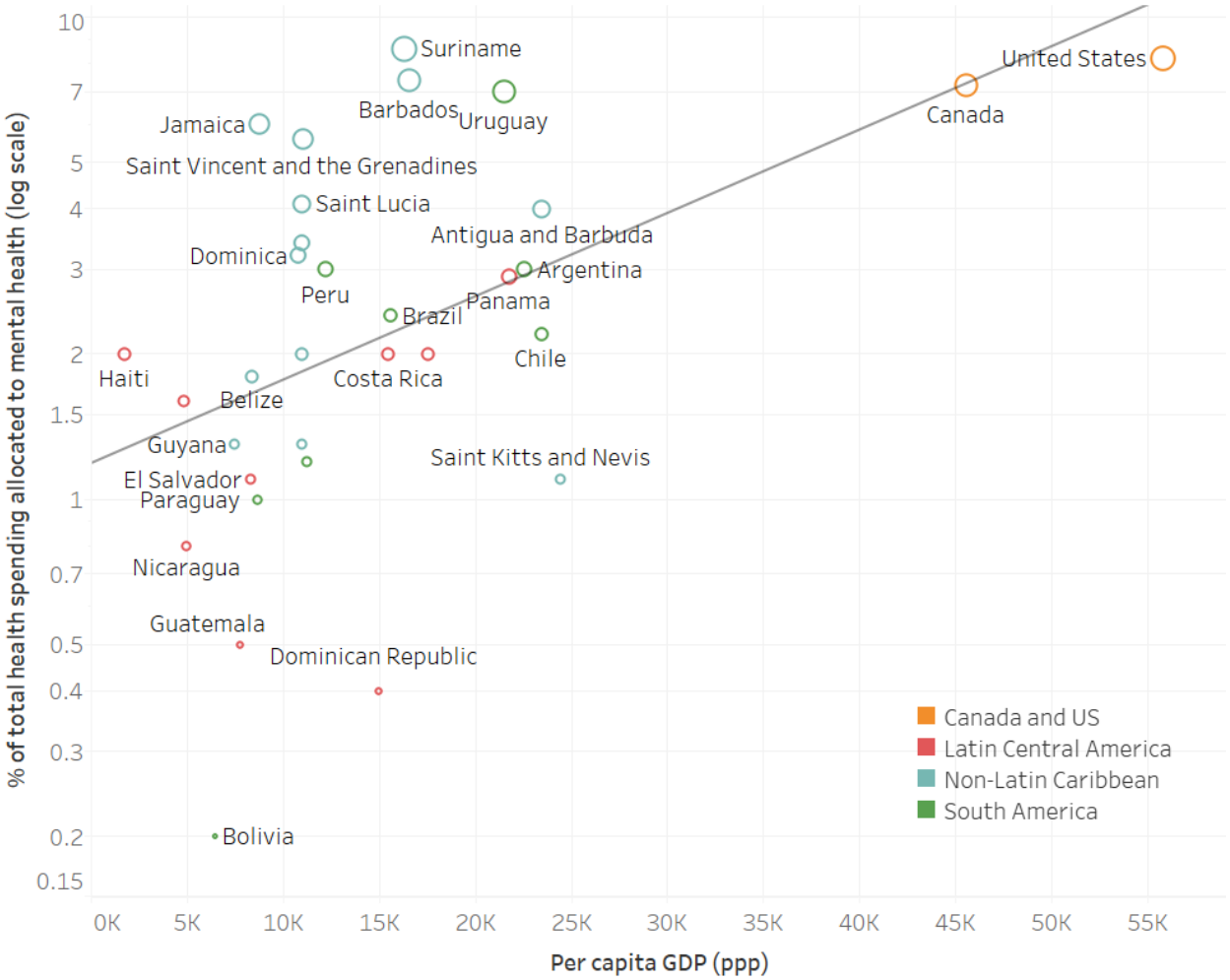
Mental health spending as a percentage of government health spending

Globally, median spending on mental health stands at 2.8% of total government health spending, while mental disorders account for 12% of total DALYs and 35% of total YLDs as per our estimations updated to 2015.(69,84,85) Low-income countries spend around 0.5% of their health budget in mental health services, lower-middle-income countries around 1.9%, upper-middle-income

countries 2.4%, and high-income countries 5.1%.(61) The median in the Americas is 2.4% and the range is between 0.2% in Bolivia and 8.6% in Suriname, while the regional disease burden attributable to mental, substance use, and neuropsychiatric disorders comprises 19% of total DALYs and 34% of total YLDs. There is a significant direct correlation between national income and government spending for mental health as a proportion of the government health expenditures (see Figure 56).

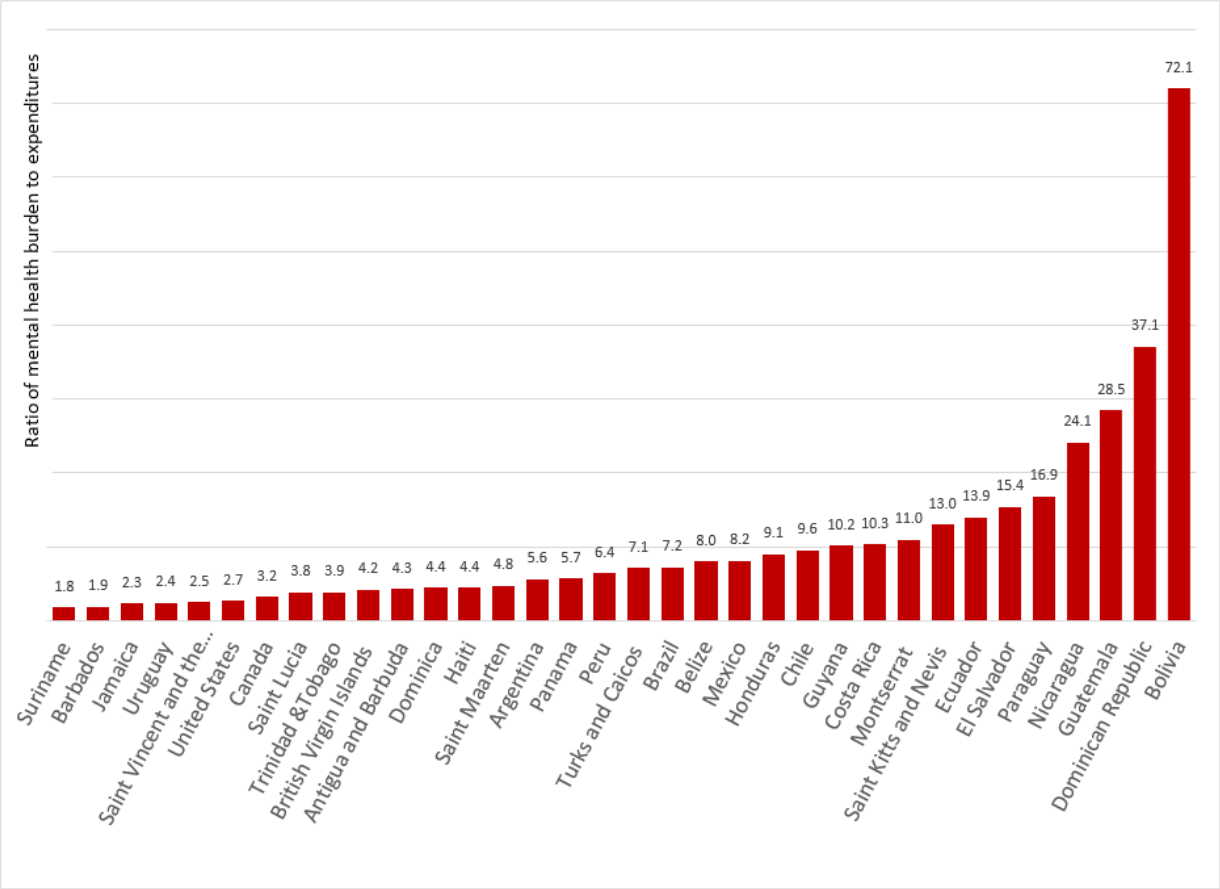
Figure 57 shows all countries with available data ordered by how disproportionate the burden of mental illness (DALYs) is in relation to their reported spending in mental health. There is a wide regional variation, ranging from a burden that is 1.8 times the spending in Suriname, to 72 times in Bolivia. The median imbalance for American countries is 6.4: the percentage of total disease burden attributable to mental disorders is six times the percentage of health funds allocated to mental health.

Figure 56: Mental health spending vs. GDP per capita



Linear model: Ln (% of health expenditures spent on MNSS) = 3·98074e-05*GDP2015 + 0·172161. R-Squared:0·24. p<0·005

Figure 57: Ratio of % of *total DALYs attributable to mental, substance use, and neuropsychiatric disorders* to *% of health spending allocated to mental health*, ordered from smallest to largest



Allocation of mental health spending

We next considered allocative efficiency of spending. International guidelines and evidence indicate that services for mental disorders should largely aim to care for people in the community, providing integrated services in primary care and general hospitals for common mental illness, and community treatment and social support for severely affected individuals.(60) The fraction of spending that is *not* allocated to psychiatric hospitals can be considered a suitable proxy for mental

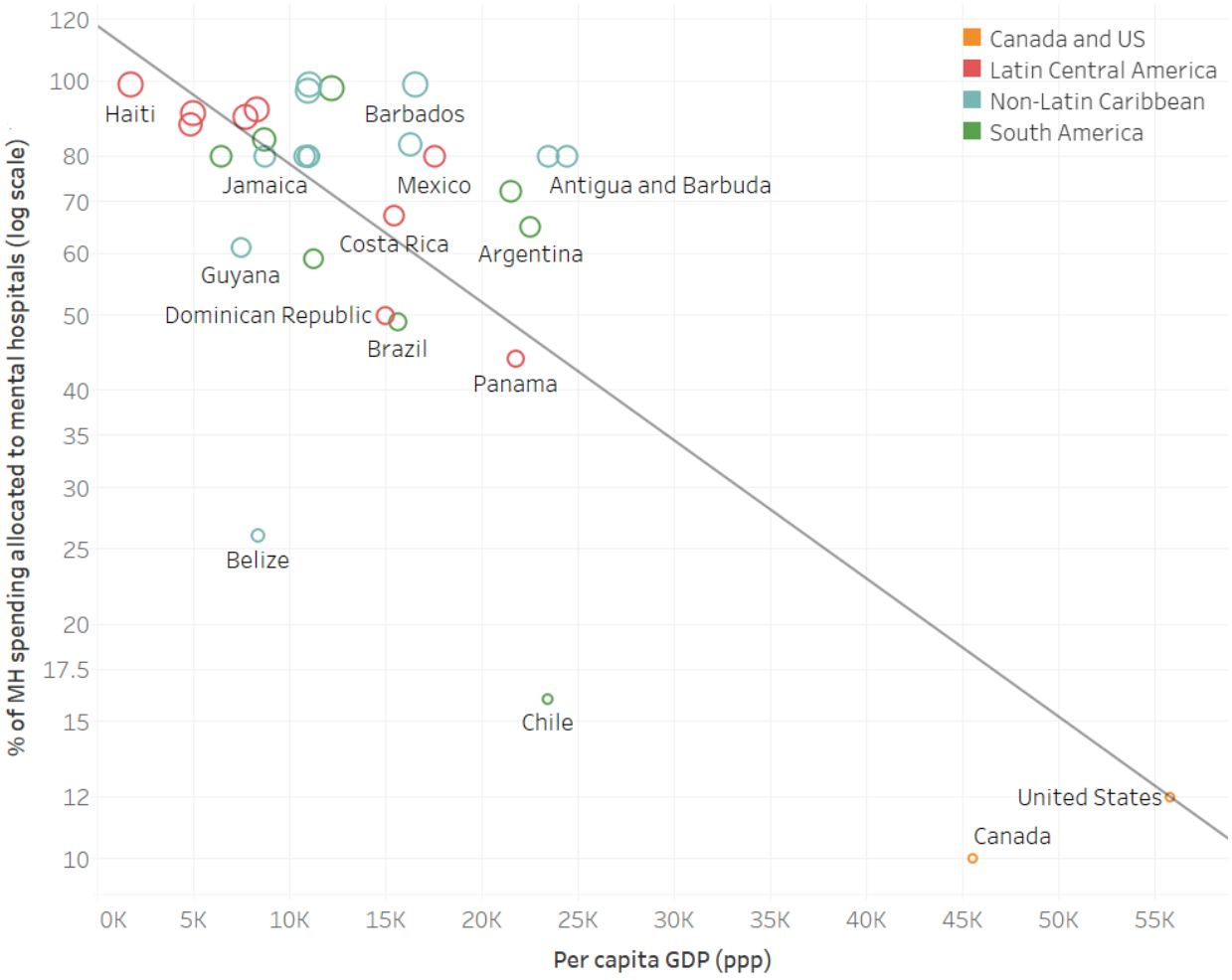
health allocative efficiency, since there is lack of evidence on the effectiveness of psychiatric hospitals in managing mental illness, they are inefficient, can lead to iatrogenic practices, and are consistently rejected by users and advocates over concerns for human rights violations. A linear model correlating the natural logarithm of the percentage of mental health spending allocated to neuropsychiatric hospitals and GDP is highly significant ($p < 0.0001$) (see Figure 58 for model details).

Higher income countries not only spend a larger proportion of their health budget on mental health services, but also allocate that increasing proportion better, i.e. to mental health services that are evidence-based and follow international guidelines, providing integrated treatment in general health services and community support. Whereas, in lower income countries a low percentage of spending on mental health is compounded both by a low health budget, and by inefficient allocation within mental health services, with psychiatric hospitals capturing the majority of funds. The median allocation to mental hospitals in the Americas is 80%.

Considering now the fraction of mental burden that should be cared for in the community - i.e.: all the burden with the exception of a fraction of highly acute, most severely affected individuals - divided by the spending not absorbed by neuropsychiatric hospitals we obtain a very different ordering than when we consider only the percentage of the health expenditures spent on mental health, without taking into account the misallocation (compare Figure 57 and Figure 59). In order to estimate the magnitude of the compounded imbalance in spending, Figure 59 orders countries from the lowest ratio of % of burden over % of spending efficiently allocated. The imbalance varies two orders of magnitude: from the burden being three times the spending in the US and Canada, to 352 and 435 times the spending in Bolivia and Haiti respectively. Indeed, a model correlating

imbalance in effective spending as previously defined with GDP is highly significant (p< 0.0001) and explains nearly half the regional variation in the effective spending gap (see Figure 60 for model details).

Figure 58: Allocation of spending on mental health vs. income



Linear model: Ln (% MNSS expenditures spent on mental hospitals) = -4·09228e-05*GDP2015 + 4·76939. R-Squared: 0·57. p < 0·0001

Figure 59: Imbalance in effective spending

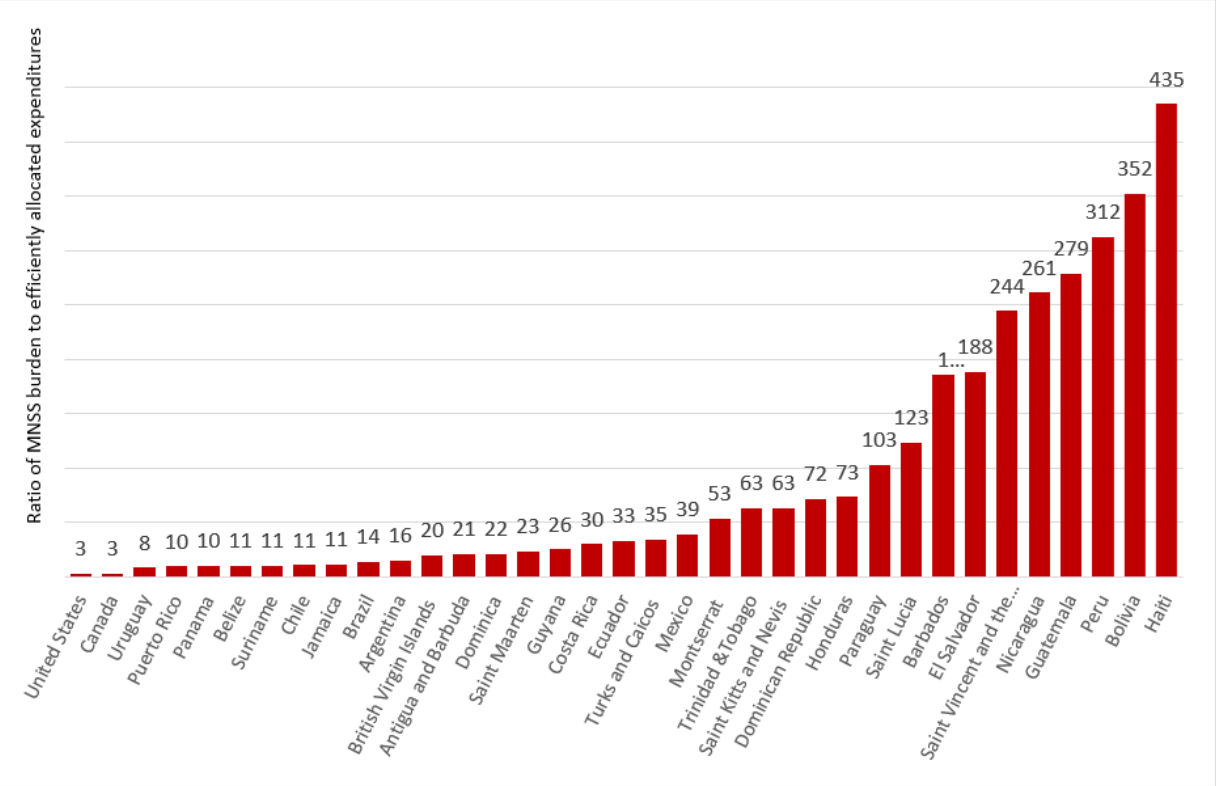
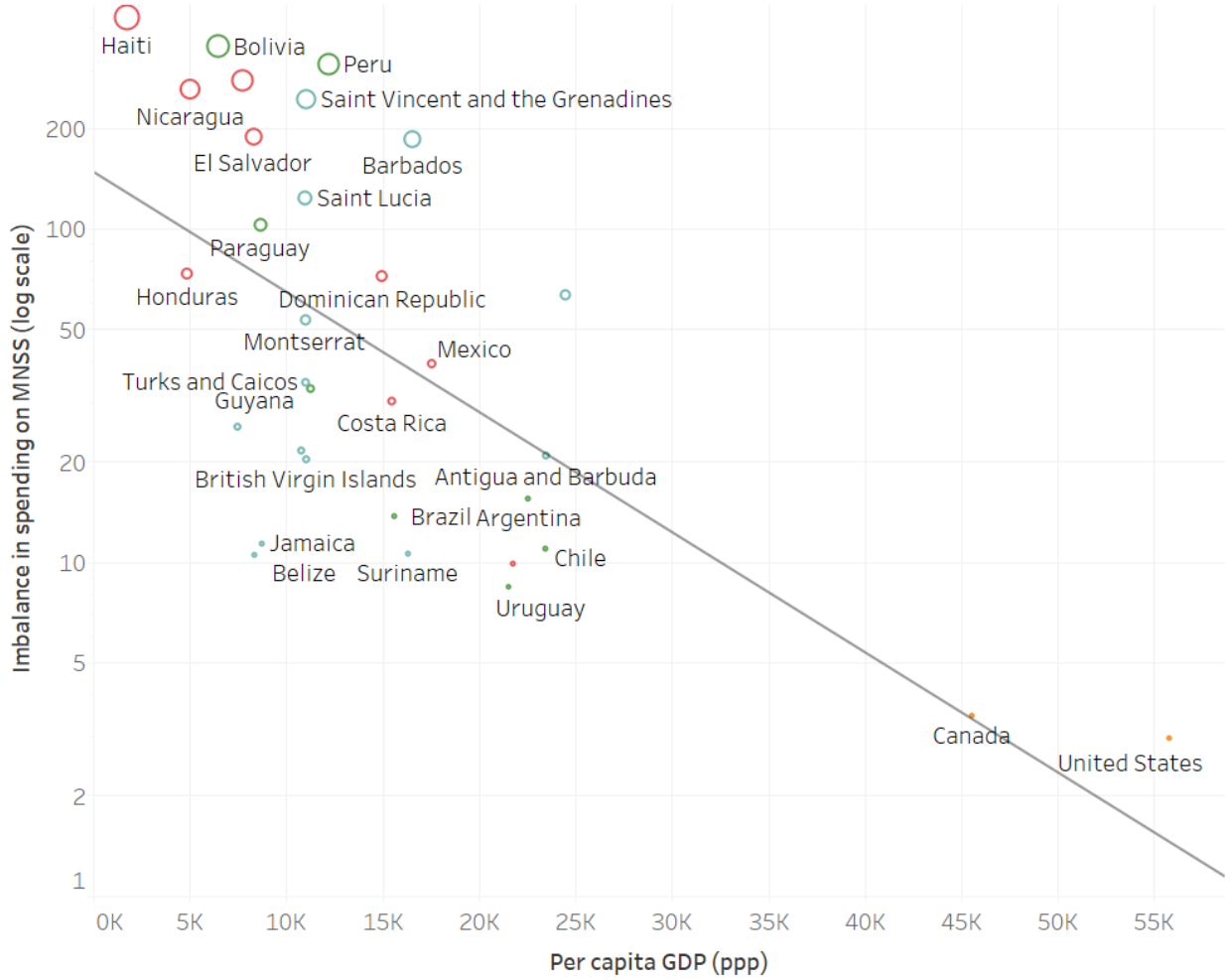


Figure 60. Imbalance in effective spending vs. GDP



Linear model: Ln (%MNSS DALYs-63%*schizophrenia DALYs)/%MH spending-%MH spending*% mental hospital spending= -8·2905e-05*GDP2015 + 5·00065. R-Squared: 0·434769. p < 0·0001

Discussion and limitations

The WHO recommends that health spending allocation should be in proportion to burden, and that there should be parity between physical and mental aspects of health care.(60,62) In practical terms, this means that physical and mental health services should be provided in an integrated manner, and that the percentage of spending allocated to mental health should be proportionate to the percentage of its attributable burden. There are several challenges to operationalizing these

concepts: (a) As we noted earlier, the DALY burden for mental disorders is usually underestimated due to immaterial registration of deaths attributable to most mental illnesses. YLDs provide a more even comparator for disability across diseases, but since they exclude mortality they wouldn't be appropriate as a single measure of overall burden. Hence, for our metric we use DALYs as corrected per our model.(69) (b) Reporting of mental health expenditures as a percentage of total government health spending is inconsistent across countries due to lack of a unified reporting strategy (e.g.: which types of interventions are included or excluded; how to estimate services delivered through other sectors, etc.); also, it does not account for private spending, which in many countries is the main source of mental health funding. (c) Strict proportionality of expenditures to burden would require an assumption of similar cost-effectiveness across health interventions.

A limitation to our conclusions emerges from the nature of the data pertaining to expenditures and allocation to mental hospitals. As was mentioned before, these data are self-reported by Ministries of Health to the World Health Organization, and its quality is variable due to lack of a unified reporting strategy (e.g.: which types of interventions are included or excluded; how to estimate services delivered through other sectors, etc.); also, it does not account for private spending, which in many countries is the main source of mental health funding. There is, however, no comparable data source to the WHO repository, and until these quality issues are resolved, our only option as researchers is to utilize existing sources noting their limitations and supplementing them when possible, as is done here. Considering that the scatterplots show that Canada and the United States stand apart from the other countries, and in order to test the robustness of our results, we re-run the analyses excluding Canada and the US for our models, including both the

natural log transformed and the non-transformed outcome variables. The exclusion of Canada and the United States does not meaningfully change the results. It does increase the p values, which nevertheless remain at or below 0.05 for all models with the exception of the non-transformed % of health expenditures spent on mental health regressed on GDP (p=0.08). We therefore find our results to be robust, despite the limitations of the data source.

Despite these limitations, we provided an innovative approach to assessing the imbalance in effective spending in the Americas. The first step provides a measure of the mental health spending gap resulting from dividing the % of total DALYs attributable to mental, substance abuse, and neuropsychiatric disorders by the % of government health spending allocated to mental health. A ratio of one would require equality between the proportions of disease burden and spending. However, we must acknowledge that such equality would be largely aspirational, and we are not aware of any country having actually achieved it. Furthermore, even though accrued evidence points to the cost-effectiveness of a broad range of mental health interventions,(99) the assumption of homogenous cost-effectiveness across health sectors is not grounded on evidence, so strict proportionality is not a reasonable expectation.

In order to provide a reasonable benchmark, we can use the case of the United Kingdom's National Health Service as a realistic comparator of proportionate mental health spending. Despite recent decreases in funding and services,(100) since the early 2000s the UK has achieved notable outcomes in terms of provision of evidence-based interventions, effective universal coverage, mental health integration in primary care, and community rehabilitation, all leading to comparatively high user satisfaction.(101) Also, being a single payer system, the UK ratio actually reflects the imbalance, since there is no other relevant source of spending. The disease burden of

mental, substance, and neuropsychiatric disorders as estimated with our methodology for the UK yields 20% of total DALYs. A recent report estimates national mental health spending to be 13% of the Government health expenditures,(100) so our real world comparator of % of health burden/% of health spending would be 1.5 in the UK.

We have seen that this first metric yields an imbalance in the Americas ranging from 1.8 to 72 times. Our second proposed metric provides a more accurate picture of the imbalance in spending by factoring in allocative efficiency of mental health spending. One caveat is in order here: we have considered psychiatric institutions as the epitome of ineffective care and inefficient spending, with abundant evidence to support both claims. However, this generalization is unfair to many individual institutions since it fails to capture: (a) the diversity of tertiary psychiatric institutions, which include some highly innovative ones that transformed themselves from chronic inpatient centers into integrated community treatment centers -such as CAMH in Toronto- or regional excellence centers and research beacons -such as McLean Hospital in Belmont-; and (b) the heroic efforts that many psychiatric institutions and their workers undertake to provide at least some form of medical alternative to total abandonment or imprisonment, particularly in regions where there is no medical alternative. Despite these caveats, we believe that our rather blunt approach is justified -and even required- in the light of the overabundance of evidence and guidelines supporting the abandonment of mental health strategies that revolve around tertiary care in favor of community care and general health service integration.

Given the UK's long-standing transformative process from segregated to integrated mental health services -consistent with evidence, guidelines, and leading to high user satisfaction-(101) we also consider the NHS to be a suitable real-world control for allocative efficiency. So, considering how

misallocation affects the imbalance of spending in the Americas, our results show that the regional median imbalance between mental health burden and spending is 33 to one, with a range of between three and 435. Our model indicates is that there is a gap in spending significantly -and inversely- associated with country-level income, disproportionately affecting lower income countries (see Figure 59 and Figure 60).

This observed imbalance cannot but result in: (a) an increasing treatment gap for poorer countries; and (b) increased private spending in mental health services, out-of-pocket spending in particular. For example, the three to one imbalance we find affecting Canada and the United states is consistent with recent findings establishing the treatment gap for major depressive disorder in high-income countries to be five to one: only 22.4% received minimally adequate treatment in high-income countries -26%, or four to one, specifically in the United States-.(102) In low or lower-middle income countries the gap was estimated in 27 to one: only 4.7% of people in need received minimally adequate services.

Specifically in Peru, Thornicroft et al. found that less than one person received minimally adequate treatment every 100 persons with a valid diagnosis of major depressive disorder.(102) These numbers are in line with our findings, which: (a) also indicate that the US and Canada show the lowest imbalance, three to one; (b) also find Peru to show one of the largest gaps in the continent, with a 313-fold imbalance in burden relative to efficiently allocated government spending; and (c) the 27 to one gap they find in low and lower middle income countries is also consistent with our American median of 33 to one. It merits further study whether the larger spending gap we found in some instances is partially closed by private spending -leading to the 100 to 0.9 undertreatment found by Thornicroft et al in Peru or the 27 to one in low and lower middle income. Private

spending on mental health means mostly out-of-pocket spending, piling potentially catastrophic economic burden upon the disease burden.

Section summary and conclusion

The priority accorded to mental disorders is rapidly increasing since the turn of the century thanks to the focused collaborative efforts of multilateral organizations, academic partners, patient and user advocates, and mental health workers. As we will study in detail in the Epilogue, this joint enterprise yielded milestones such as the World Mental Health Report, the WHO mhGAP, the Lancet Global Mental Health series, the Movement for Global Mental Health, and other initiatives that led to a better understanding of the disease burden of mental illness and of what the evidence-based response to it should be.(29,103–105) Mental health is increasingly acknowledged as a global health priority, and given its economic burden it is also beginning to be considered a global development priority.(20,73)

Ultimately, this emergent prioritization led to its inclusion in the Sustainable Development Goals and to a global consensus that the drive for universal health coverage should be inclusive of mental health and wellbeing. (106) Despite this emerging global consensus, the proportion of funds spent on mental health tends to be low and their allocation irrational, with the least effective and cost-effective interventions receiving the largest share, particularly in lower and middle income countries. In the Americas, mental, substance use, and neuropsychiatric disorders are the largest sub-group cause of disease burden, both when considering disability alone and combined with mortality: they comprise a third of total years lived with disability and a fifth of total disability adjusted life-years.

The health system's response to the challenge of mental illness in the Americas shows regional variations, most notably a correlation with national income. More developed countries spend a larger share of their health budgets on mental health services, and allocate their spending more efficiently, away from neuropsychiatric hospitals, towards integration of mental health into primary care and community resources. Conversely, lower income settings compound their lack of resources by allocating them to ineffective specialized hospitals instead of funding community and primary mental health services, a strategy that would target not only the increasing disability resulting from depression and common mental illness, but also the increased mortality resulting from severe mental illness, largely due to treatable causes that remain uncared for due to stigma, lack of community support, and inadequately integrated health services.(53,54) The imbalance between the burden and the effectively allocated mental health services is striking, ranging from three times in the United States and Canada to 352 times in Bolivia and 435 times in Haiti, with a regional median of 33. This government spending gap, which disproportionately affects lower-income countries, can be expected to result in (a) undertreatment and increased amenable disability and mortality; and (b) increased household-level spending, increased economic burden, and potentially catastrophic health spending.

Chapter 5. The burden of poverty: The toll from mental illness on the world's poorest people

Association of the percentage of the population in poverty with group level mental illness disease burden

We have argued in previous chapters that our modified GBD framework provides a more precise descriptive epidemiology of mental illness; we have also detected regional and potential income-level patterns in disease distribution, as well as an income gradient in overall mental health spending and in efficiently allocated spending. We will now delve deeper in the relationship between income and mental illness, through a detailed study of how the disability burden varies as a function of poverty at the group-level.

Mental illness has a bi-directional relationship with income and wealth: poverty is a social determinant that increases the risk of common mental illness, and mental illness itself increases the risk of poverty.(107,108) It affects not only the individual, but also the family and the community, and is estimated to be the first non-communicable disease (NCD)-related cause of lost global output.(109) These facts advance the argument for making mental health not only a health priority, but also an economic development priority. In order to achieve this, we need a nuanced understanding of what the specific mental disorder burden profile affecting people in poverty is. However, as with many other NCDs, most conceptualizations, research, and framing emerge from high income countries,(110) so the goal of this section is to understand the differential distribution of the mental illness burden in the context of poverty. Our approach to circumscribing the poorest billion is based on the multidimensional poverty index (MPI), a widely-used metric that integrates poverty measures from three major dimensions: education, health, and living standards (see

details in the methods section). We will focus our analysis on 102 countries of extremely diverse geographic and cultural contexts, and our independent variable will be the percentage of the population with 5 or more deprivations. We expect the wide variations in poverty fractions to inform our analysis: this work will study national disease burden data focusing on how mental illness distribution varies in relation to the different proportions of national population in poverty.

Firstly, in the methods section, we'll describe the poverty measure selected for this study, our approach to disease burden analysis, and the model used to explore the association. Secondly, we will describe the overall impact of mental illnesses in the context of poverty, and how they compare collectively to other groups of illnesses, such as infectious diseases, maternal and child conditions, and injuries. Thirdly, we will focus on how individual disorders are distributed in our sample of countries, with a focus on how an increased percentage of population in poverty might determine a differential risk for the burden of specific mental disorders. Fourthly, we'll focus on exploring an issue of interest in low-income settings: maternal depression and its potential impact on infant and child health and wellbeing, with the rationale that, from a life-course and trans-generational perspective, understanding this hypothetical link can provide an actionable target to improve current and future health outcomes, as well as economic growth.

Methods

Poverty

Social determinants are significant factors for understanding the distribution of illness at the individual and at the population level. Economic factors in particular significantly influence illness

distribution to the extent that some authors propose the existence of an economic gradient of illness, with the poorest suffering a disproportionately large share of disease burden.(86,111,112) Poverty and several related determinants, such as education, housing, socioeconomic status, and unemployment appear to increase the risk for common mental disorders –such as depression and anxiety-, an association that holds across age groups and gender. This correlation has been mostly studied in high income countries, but a review focused on low and middle income countries found consistent results.(107,111) Though determinants such as *unemployment* are fairly straightforward indicators -*employed-unemployed* at the individual level, and *% of unemployment* at the population level-, poverty is not, and its measurement in the context of psychiatric epidemiology is controversial.(113) The *money-metric* conceptualization of poverty -focused on the measurement of income or consumption- has been rightly criticized as reductionist, given the fact that poverty is a complex determinant that can include multiple other dimensions, from education and access to public services, to more complex assessments of living standards, social capital, etc. Also, contextual and subjective considerations are relevant: what's considered poverty in a high-income country might be different from a developing country, and each person might view her economic situation in a different light. So, the choice of metric needs to be grounded on the study's population and goals, and given our scope -studying the effect of poverty on national level disease distribution- we have assessed poverty through the Multidimensional Poverty Index, and focused our analysis on the 102 countries for which there is MPI data, disaggregated by age and sex. The MPI integrates indicators from health (nutrition and child mortality), education (years of schooling and children enrolled), and living standards (cooking fuel, toilet, water, electricity, floor, and assets). For our analysis, we will study the percentage of the population of each country

that is deprived in at least 5 of 10 poverty indicators.(114,115) Following the well-established literature on social determinants of health, particularly the evidence of association between poverty and disease distribution, we hypothesize that the presence of large pockets of poverty will impact national level disease distribution, and that the impact will be correlated with the size of the poor population. Furthermore, we hypothesize that the impact of poverty will be to some extent disorder-specific, as well as sex and age specific.

Disease burden

For this analysis we will follow the methodology proposed in detailed in chapter 1. (68,69) Our analysis is based on disaggregate disease burden data per country, cause, and risk factor available from the Global Health Data Exchange.(81) We will analyze both overall and age-sex specific disease burden to study the correlation of mental disorder disability and poverty. An important caveat relates to how the GBD methodology produces its estimates output: in order to provide a comprehensive set of country level estimates for all disorders, the existing data is collated and adjusted through an integrative meta-regression framework to predict missing values.(14) This complex and rigorous methodology has the unique merit of providing best-available estimates for countries lacking local data, grounded in existing data from the closest countries, regions, or globally. The downside is that we will be drawing conclusions of the correlation of poverty and mental illness based on country level disorder-specific estimates, and the validity of such conclusions is closely related to whether those estimates are at least partially grounded on local data, or on data from comparable countries. To consider an extreme example: if we study the correlation of disease x and poverty, and find an association, what would be the confidence we

would have in the validity of such conclusion if no actual studies of disease x from low and lower-income countries were included in the generation of the estimates? We would most likely be capturing the effects of the model rather than a real difference. In order to account for this methodological caveat, we extracted all GBD inputs and provide a full list of disease-specific studies that come from low and lower-middle income countries (see Appendix 1). This allows the reader to qualify the validity of the conclusion reached for each disorder.

Model

The general model used in the disorder-specific analysis is:

$$Log\ (Disorder\ YLD\ rate\ _{c,a,s}) = \beta_0 + \beta_1 \%\ of\ population\ with > 5\ deprivations_{c,a,s} + \beta_i Region_i + \epsilon$$

c=country; a=age-group; s=sex

In the instances where this model was modified to produce specific analyses, the changes are specified in the text and figures. In the results section, we present in detail the associations with a p value lower than 0.05, and only mention summarily those with p values equal or larger than 0.05, which are interpreted as without evidence of an association.

Results

Distribution of mental illness in the poorest billion

As a first step, we will describe the disease burden distribution for the three major groupings -NCDs; communicable, maternal, neonatal and nutritional disorders; and injuries-. In the case of NCDs, we'll analyze separately *mental disorders* and *all other NCDs*. There are several limitations to high-level analyses based on aggregate data:(116) regional and country level variations are

obscured by global results, and outcomes at the disorder-group level mask the true disorder-level outcomes, which can move in opposite directions. For example, to say that the disability resulting from the group of mental disorders is not correlated with poverty can mean that (a) all individual disorders are similar across income levels, or (b) that they are all correlated with poverty, but in different directions (some inversely, some directly correlated). Furthermore, even within specific disorders, looking at the aggregate all-ages disability can be misleading due to what's known as Simpson's reversal, where for example a consistent increase in adult age-specific burden can be wiped out in aggregate by comparatively larger population numbers in younger age groups. Given the age-structure of low income countries, this issue can be expected to affect analyses based on aggregate outcomes. In order to provide a comprehensive picture of disease distribution at the population level for the poorest billion, it is useful to start at the aggregate level, including all disorders -not restricting the initial analysis to NCDs- and then gradually home in on specific disorders, focusing on the age and sex distribution of disease, as well as on specific issues of poverty that might be obscured by how disease burden is estimated.

Our sample of countries with MPI data indicate that those who are deprived in at least 5 of 10 poverty indicators sum 1.25 billion people, who belong to South Asia (54%), Sub-Saharan Africa (40%), East Asia & the Pacific (4%), North Africa and Middle-East (1%), and Latin America and the Caribbean (1%).(114,115) To provide an aggregate picture of the disability burden in this population, Figure 62 presents the years lived with disability (YLDs) for our sample weighted by the percentage of the population with 5 or more deprivations. It shows that mental disorders account for a quarter of total disability, trailing closely the disability resulting from all communicable, maternal, neonatal, and nutritional diseases.

Figure 61. Disability distribution by country

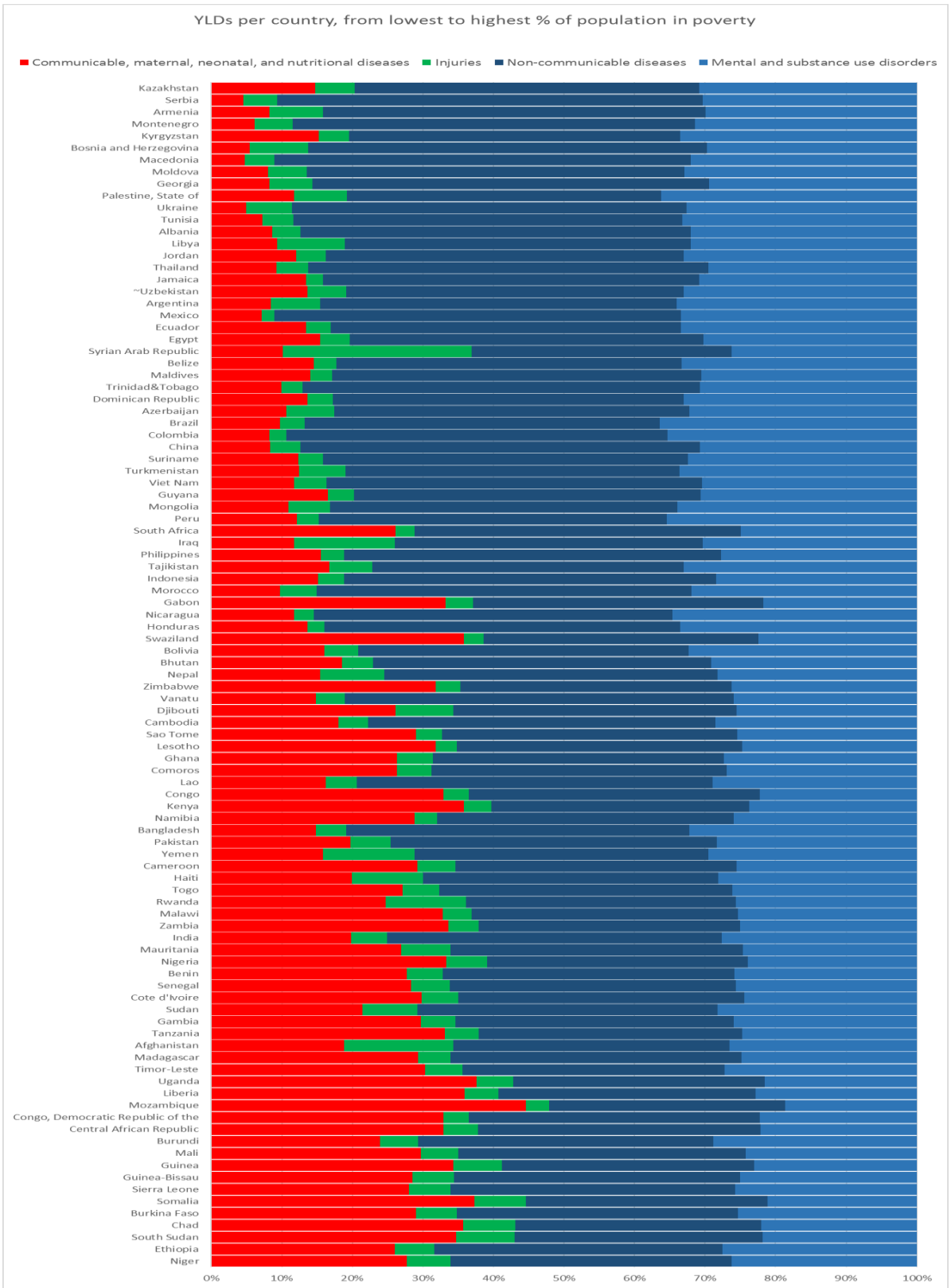


Figure 62. Disability burden in the poorest billion

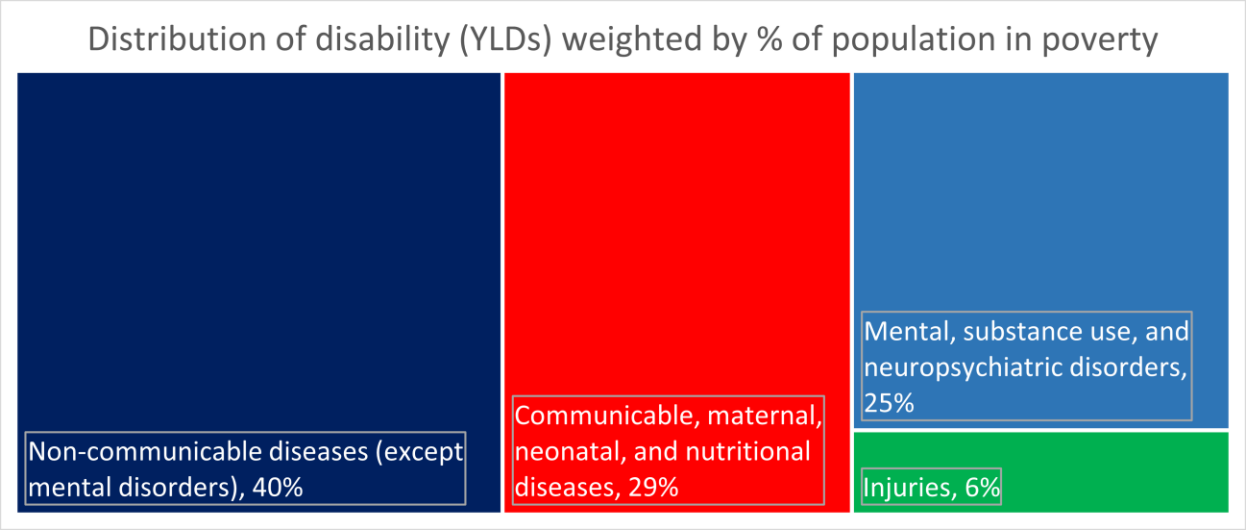


Figure 61 presents the disability burden by country, ordered from the lowest percentage (Kazakhstan) to the highest percentage of the population with at least 5 deprivations (Niger). We can see that while the burden of communicable, maternal, neonatal and nutritional diseases increases sharply as we move down the list (the red portion of the bars), the mental illness burden does not diminish so markedly (light blue bars). The increase in communicable, maternal, neonatal and nutritional disorders is a well-established fact: lower-income countries have less resources available to modify up-stream structural determinants of health, such as education, nutrition, sanitation, and preventive interventions, all the way down to health service availability, accessibility, and quality.(5,85,117,118) The immediate result of this inequity is that the poorest billion is disproportionately exposed to malnutrition and infections, with particularly deleterious effects on the most vulnerable populations, such as pregnant women and neonates. But despite these facts, in terms of disability, aggregate NCDs more than double the disability burden of communicable, maternal, neonate, and nutritional disorders. Several issues determine this

picture: on the one hand, poverty increases the population risk of NCDs through undersupply of nutrients and relative over-supply of low-quality nutrients -a more recent challenge-. Whereas high-income countries and high-income sectors in poor countries have access to healthier -much more expensive- food products, the vast majority of low-income households only have the option of either insufficient or inadequate nutrition. Also, the poorest billion is overwhelmingly rural: 88 to 96% of them, depending on the region, live outside of cities. A direct consequence of this is that modern sources of energy are not available for heating, hygiene, and cooking, which leads to in-house combustion of biomass for these purposes, resulting in a high burden of chronic respiratory disease, the cause of which is unheard of in higher income settings. And finally, a large fraction of the chronic disability in lower-income settings results from (a) preventable sequelae of infections, such as rheumatic heart disease and cardiomyopathies, or (b) failing health systems, such as hypertensive heart disease as an avoidable consequence of untreated hypertension-.(119)

Any approach to understanding mental disorders in low-income settings should expect to find similarly convoluted and multidetermined pathways to disease. Indeed, lower-income countries have a high prevalence of the neuropsychiatric sequelae of infections, most notably HIV and malaria, but also tuberculosis, cysticercosis and syphilis. And, we can expect to find more disabling outcomes for mental disorders in general due to the lack of services, as well as under-detection or atypical presentations due to stigma. As was mentioned earlier, the traditional burden of disease approach has limitations when it comes to capturing these nuances, since it is based on relatively scarce local data from low-income countries, and relies mostly on models for extrapolating available data -largely belonging to higher-income settings-. It provides however by far the most comprehensive and best-available picture, so we will base our analysis on it while

highlighting the potential limitations where present and attempting to provide supplementary perspectives when possible.

Common mental illness

Common mental illnesses, such as depression and anxiety disorders, are the largest cause of disability globally, and poverty has a well-established positive correlation with common mental illness at the individual level.(107,108) Similarly frequent are personality and somatoform disorders, which include a number of related but less well-defined syndromes involving personality traits, relational patterns, somatic or painful complaints and self-harmful behavior that frequently overlap with depression and anxiety but are seldom analyzed due to the methodological difficulties mentioned in previous sections. Painful somatic complaints can mask mood and anxiety disorders in the context of high stigma, such as can be found in most developing countries. Also, self-harm -which shows a well-established correlation with personality and depressive disorders(40,88)- presents a nuanced correlation with poverty, with most -but not all- studies finding a positive correlation between poverty and suicide.(120)

Depression

In aggregate, disability rates attributable to depressive disorders -major depressive disorder and dysthymia- appear to have a negative correlation with the percentage of the population living in poverty, a correlation that holds when controlling for sex and region (see Figure 63 and Table 6). However, an analysis of the age, sex, and disorder specific rates leads to a different conclusion: disability attributable to major depressive disorder is positively correlated ($p<0.05$) with the

percentage of the population in poverty for all 17 five-year age groups in all groups with the exception of under 10, over 80, and between 55 and 59 years old. This direct correlation is driven by men, for whom an increase can be seen in all age-groups ($p<0.05$), with the exception of the under 5 group. The largest effect can be seen in men between 20 and 30 years old ($p=0.001$; see Figure 64 and Table 7). Also of note, Sub-Saharan Africa tends to be more severely affected, with most other regions showing decreased disability. We find no correlation of dysthymia burden and poverty.

These results are highly meaningful for several reasons: Firstly, they are consistent with the body of evidence supporting a hypothetic causal link from poverty to depression, while also specifically tracking the brunt of this effect to working-age males. Given the fact that the poorest billion live mostly in rural settings, several mechanisms can be hypothesized: it may be that young men are typically the wage-earners, while women perform unpaid home labor. This might lead to young men's mood being more responsive to income heterogeneity, whereas women suffer a uniformly higher -more homogeneous- depression burden. Secondly, our findings would also be consistent with the reverse causal link: a more disabled working-age population would be less able to work and provide an income, perpetuating the cycle pf poverty and mental illness. This cross-sectional country-level study is not able to adjudicate which of these two processes produces the largest effect, nor extract conclusions of individual level associations, but existing literature highlights the importance of both.(108)

With respect to the validity of these findings, Appendix 1 shows a relatively abundant body of evidence: 45 data sources covering 24 low or lower-middle income countries or states (including 7 Indian States), so our confidence on the validity of our conclusion is high.

Figure 63. Depressive disorders YLD rate vs. % of the population with 5 or more deprivations

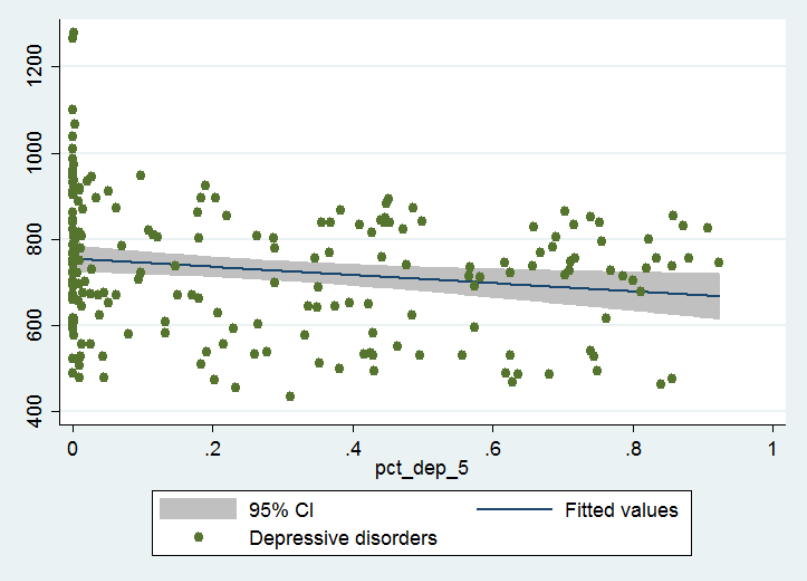


Table 3. Depressive disorders YLD rate vs. % of the population with 5 or more deprivations, controlling for sex and region

	Depressive disorders
% of population in poverty	-81.844
	(1.99)*
Sex	-194.492
	(14.12)**
Arab states	-153.137
	(5.24)**
East Asia	41.790
	(1.37)
Europe & Central Asia	49.129
	(1.74)
Latin America & Caribbean	-22.642
	(0.71)
South Asia	-85.677
	(2.77)**
_cons	1,051.525
	(32.18)**
R^2	0.60
N	202

Omitted: Sub-Saharan Africa * $p<0.05$; ** $p<0.01$

Figure 64. Log (MDD YLD rate) vs. % of the population with 5 or more deprivations, males, 20-24 & 25-29

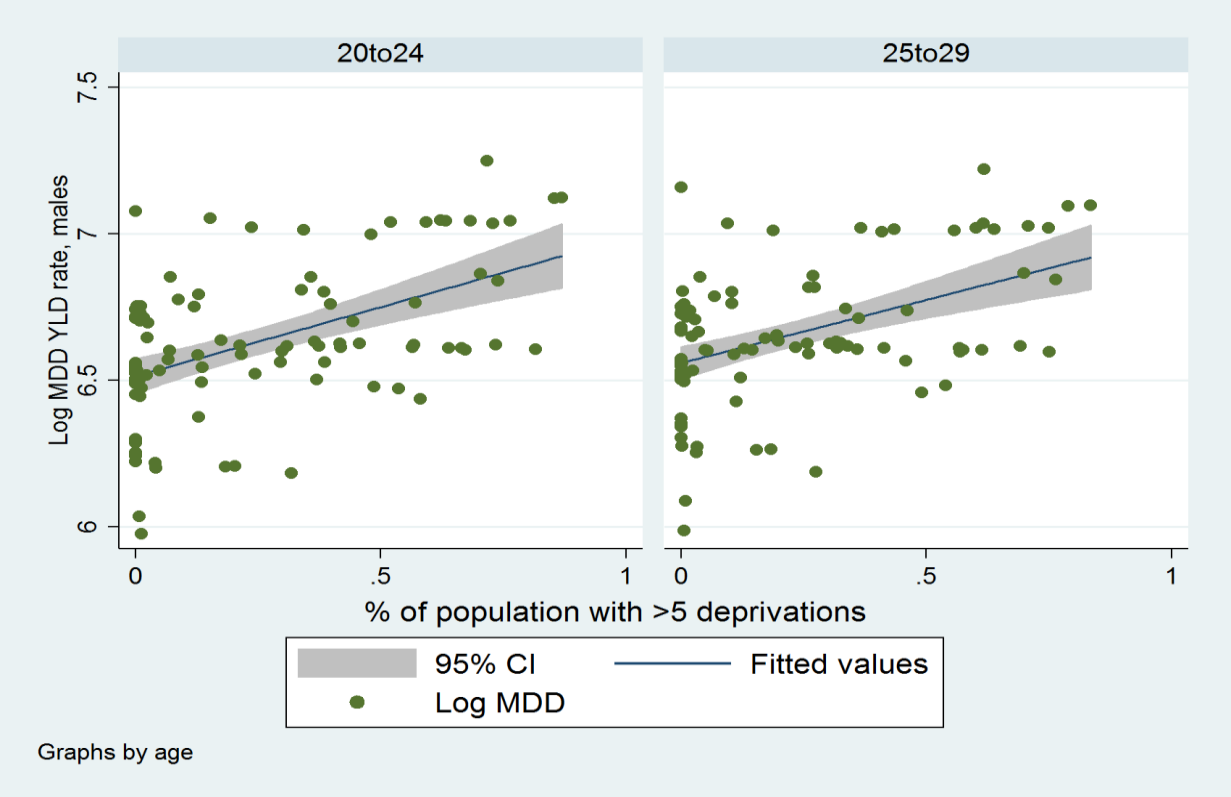


Table 4. Log (MDD YLD rate) vs. % of the population with 5 or more deprivations, males, 20-24 & 25-29, controlling for region

	Log (MDD YLD rate)	
	males, 20-24	males, 25-29
% of population in poverty	0.348 (exponentiated: 1.42)	0.349 (exponentiated: 1.42)
	(3.34)**	(3.45)**
East Asia	-0.454	-0.421
	(6.62)**	(6.61)**
Europe & Central Asia	-0.134	-0.120
	(1.88)	(1.85)
Latin America & Caribbean	0.055	0.057
	(0.82)	(0.94)
Middle East and North Africa	-0.032	0.063
	(0.42)	(0.91)
South Asia	-0.214	-0.147
	(2.90)**	(2.13)*
_cons	6.620	6.632
	(113.83)**	(129.02)**
R^2	0.59	0.57
N	101	101

Omitted: Sub-Saharan Africa * $p<0.05$; ** $p<0.01$

Anxiety disorders

The disability resulting from anxiety disorders doesn't appear to be correlated with poverty.

This is an unexpected result, given the face-validity of the link of poverty -and the higher exposure of the poor to everyday plights, deprivations, and violence- with stress and anxiety, and the suggestive evidence supporting this link.(87) With respect to the inclusion in the GBD estimates of data stemming from low and lower-middle income countries, 14 countries or states are covered by 18 sources, which represents a relevant source of locally grounded data. However, close inspection of the use of sources as inputs into the model shows that two important studies, covering precisely trauma and stress related disorders in Rwanda, and anxiety disorders in Ugandan children and adolescents (see Pham et al, and Abbo et al, in Appendix 1), were

considered outliers and excluded precisely due to the high prevalence found (between 20 and 30%). So, our confidence in the validity of these negative findings is comparatively low.

Self-harm and suicide

We have mentioned the importance of focusing on disability to study mental disorders, given the fact that mortality registry for most mental illnesses is immaterial. Self-harm and suicide present the exact opposite challenge: self-harm is mostly captured in the GBD framework through its lethal outcome -suicide- but not in terms of its disabling effects -which are highly relevant in the context of personality disorders and other self-harmful syndromes-. Therefore, the outcomes of interest for us are the disability-adjusted life years attributable to self-harm, which also include the years of life lost due to suicide.

Adult and older age-groups don't show meaningful correlations, but both sexes under 15-year-old show remarkable direct correlations between poverty and self-harm ($p<0.001$), with the largest effect visible in boys 10 to 15 years old (see Table 8 and Figure 65).

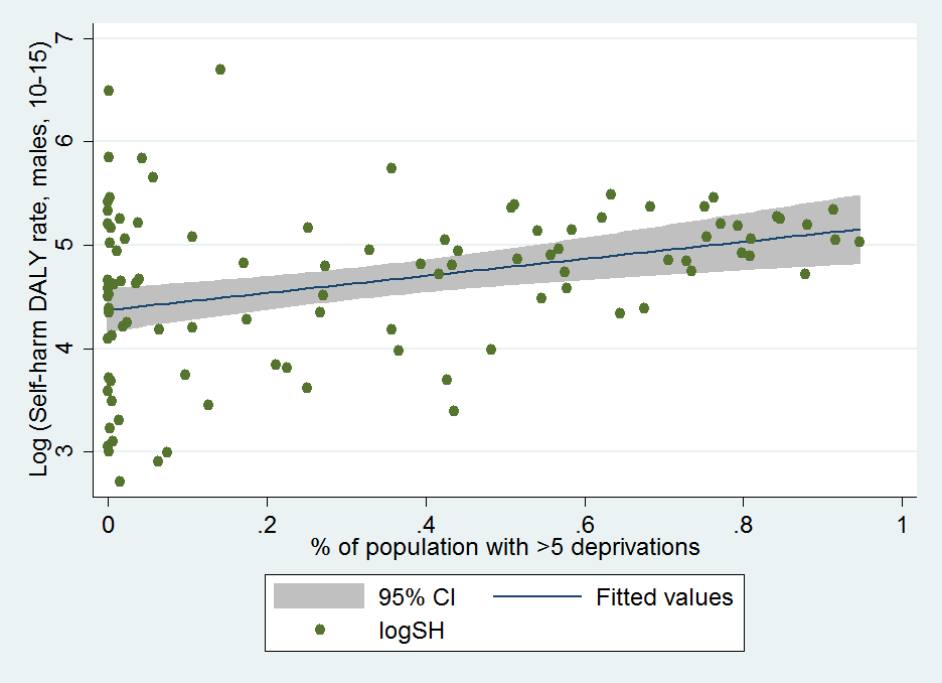
These findings are surprising and intriguing, both because of the effect size -the largest of all effects found for mental disorders -, and because of the early age-groups affected. Exploring the availability of local studies, we see that there are only 5 studies covering 1 low-income country and 3 lower-middle income countries. Also, the findings are relatively isolated -only two age-groups-, so we consider this finding only preliminary and worthy of further exploration.

Table 5. Log (Self-harm DALY rate, males, 10 to 15-year-old)

	Log (Self-harm DALY rate, males, 10-15)
% of population in poverty	1.515 (exponentiated: 4.55)
	(4.17)**
East Asia	0.221
	(0.81)
Europe & Central Asia	1.061
	(3.66)**
Latin America & Caribbean	0.590
	(2.23)*
Middle East and North Africa	-0.405
	(1.36)
South Asia	0.069
	(0.24)
_cons	3.903
	(16.02)**
R2	0.36
N	102

Omitted: Sub-Saharan Africa * $p<0.05$; ** $p<0.01$

Figure 65. Log (Self-harm DALY rate, males, 10 to 15-year-old)



Somatoform pain disorders (somatic symptom disorders with prominent pain)

As we mentioned before, there is no disability burden data specific to ICD-10 somatoform pain disorders (somatic symptom disorders with prominent pain in DSM5). In fact, there is very little epidemiologic evidence in general for these syndromes, but the existent evidence points to extremely high prevalence, at least in high income countries.(42,44) Our estimation for somatoform pain disorders shows negative correlations in some specific age-sex groups. Women show negative correlations in most age-groups after 39 years old ($p<0.05$), with the exception of the 60-64 and 80+ groups. Men show a similar but earlier pattern of negative correlation between 35 and 60 ($p<0.05$). Given the total lack of specific data in the GBD estimations, we consider this finding merely indicative of the need of further study.

Severe mental illness

Severe mental illnesses are among the most disabling human conditions, with schizophrenia having the highest disability weight of all illnesses in the GBD framework.(12) In the context of extreme poverty, where health services tend to be lacking and stigma tends to be higher, this translates in families and communities left to their own devices, frequently resorting to extreme measures that involve forced seclusion and other human right abuses, which raise the issue of improving care as one of basic social justice. Indeed, recent findings establish a significant inverse correlation of country-level income and efficiently allocated mental health resources, which translates in an increased treatment gap for severe mental illness in the lower income tiers.(121) In this respect, the dramatic sequelae of medically untreated schizophrenia in the context of extreme poverty -including withheld general health services, direct harmful practices, and

premature mortality- should be compared to hypertensive heart disease as a consequence of untreated hypertension or general paresis as the natural endpoint of syphilis, and thus be considered specific indicators of health system failure, and more broadly of humanity's failure.(90,116)

Schizophrenia

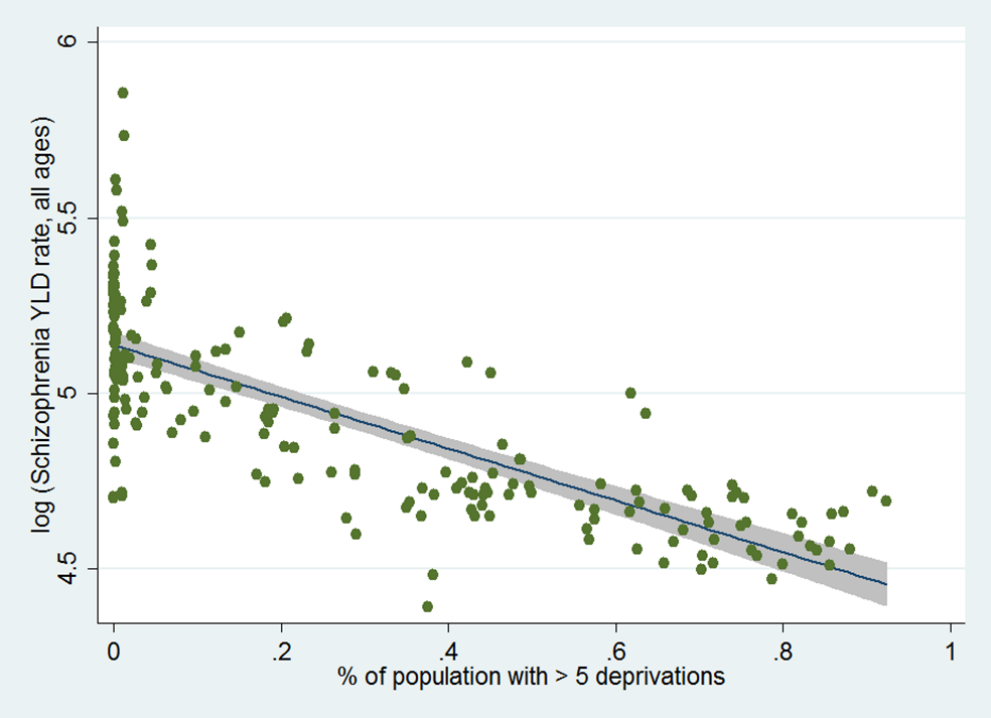
Schizophrenia disability is negatively correlated with the percentage of population in poverty for both men and women in all age-groups except under 15 -before age of onset-. There are two peaks in the negative effect of poverty on disability in both sexes: an early one around 25 years old, and a second in the oldest age groups. Of note, all these associations have a p<0.001, and the second peak involves a more than twofold increase of the negative effect (see Table 9 and Figure 66).

Table 9. Log (Schizophrenia YLD rate) vs. % of the population with 5 or more deprivations, controlling for sex and region

	Log (Schizophrenia YLD rate)	
	Both sexes, 25-30	Both sexes, >80
% of population in poverty	-0.25 (exponentiated=0.78)	-0.51 (exponentiated=0.6)
	(7.09)**	(9.11)**
Sex	0.030	0.030
	(2.71)**	(1.62)
East Asia	0.357	0.255
	(16.26)**	(6.78)**
Europe & Central Asia	0.030	-0.026
	(1.57)	(0.79)
Latin America & Caribbean	-0.022	-0.017
	(1.04)	(0.43)
Middle East and North Africa	-0.108	-0.104
	(4.96)**	(2.80)**
South Asia	0.028	0.194
	(1.13)	(4.53)**
_cons	5.373	3.374
	(256.37)**	(93.44)**
R2	0.78	0.70
N	203	202

Omitted: Sub-Saharan Africa * $p<0.05$; ** $p<0.01$

Figure 66. Log (Schizophrenia YLD rate) vs. % of the population with 5 or more deprivations

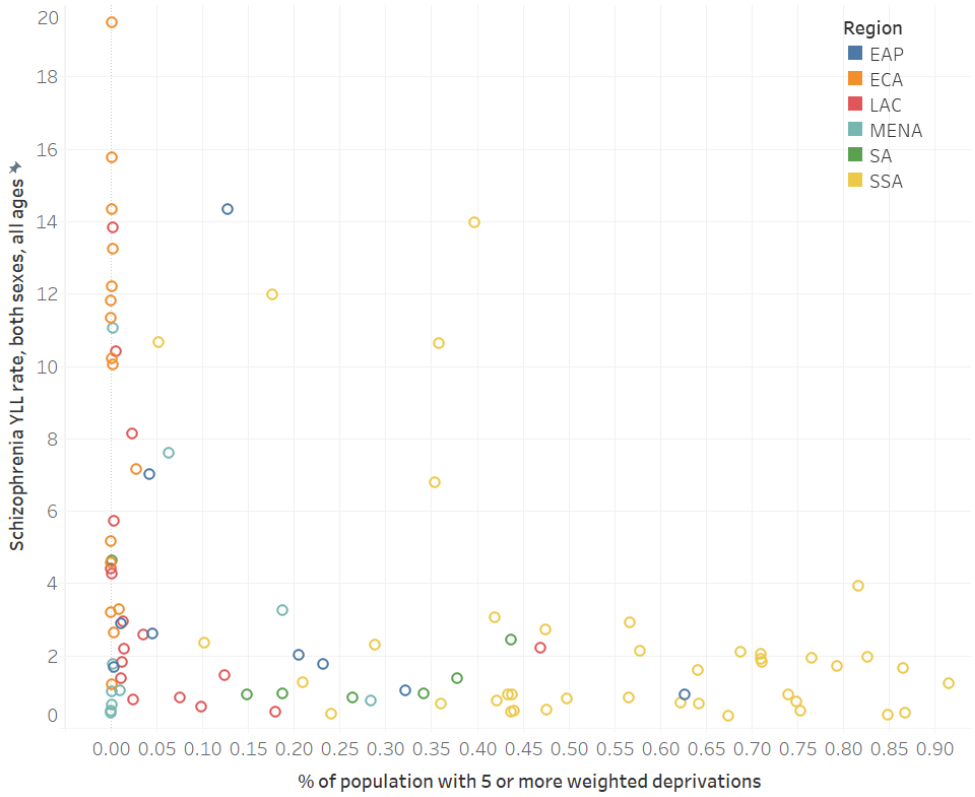


With respect to the availability of local studies, there are 11 prevalence studies covering 10 low or lower-middle income countries or states (including 5 Indian States). However, these presumably valid findings should be carefully interpreted, since in the case of schizophrenia decreased disability -particularly notable among the elderly- could point to an increased premature mortality rate: instead of a signal of a burden that decreases with poverty, a signal of a burden that becomes more lethal with poverty. Indeed, schizophrenia is correlated with premature death across income settings, but lowest-income settings are correlated with the largest prematurity of death, with patients dying 30 years before their peers.(53)

We have highlighted earlier that mortality due to mental illness is poorly captured by the GBD framework. Schizophrenia is, however, one of the few mental disorders that have deaths -and

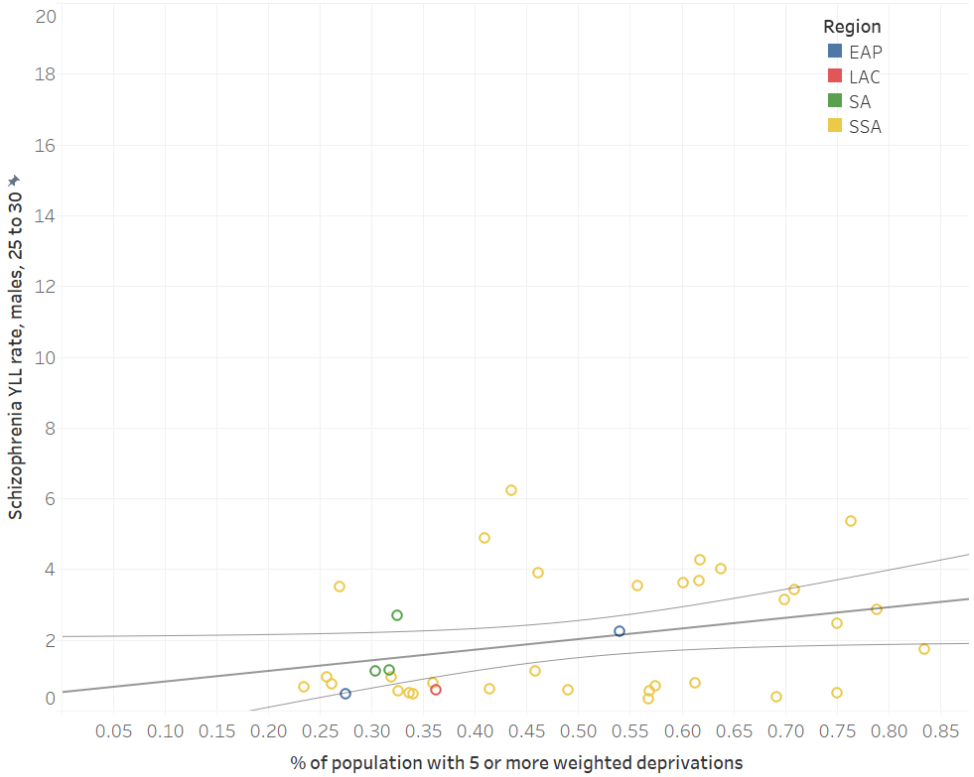
therefore YLLs- attributed to them. Attribution is however very low, most notably in low-income countries: globally, in 2015, a total of 16909 deaths were attributed to schizophrenia, of which only 235 (1.4%) were registered in low sociodemographic index (SDI, an index used by the GBD framework) countries which roughly coincide with countries with more than 60% with the population in multi-dimensional poverty as per our index. If we add the low-middle SDI countries as per GBD -roughly equivalent to countries with more than 20% of the population in poverty (with important exceptions such as India, which has >40% of the population in multidimensional poverty but is in the middle SDI range)-, deaths due to schizophrenia amount to 1615 (10% of global deaths attributed to schizophrenia). Despite these caveats, we will explore how the age-sex specific YLL rate varies as a function of the fraction of the population in multidimensional poverty. Unfortunately, our interest is precisely on countries with large fractions of the population in poverty, where the available data is not only scant (i.e.: 235 deaths in all low SDI countries), but also where the YLL rate varies widely from country to country. Including all the countries in our dataset, the scatter plot shows that two different distributions seem to overlap: an almost vertical distribution for countries with nearly zero % of the population in poverty, and a horizontal -potentially positive one- for poorer countries, plus some outliers (see Figure 67).

Figure 67. Full set of countries, years of life lost due to schizophrenia vs. % of population in poverty



If we restrict our observations to countries with 20% or more of poor population in order to capture the horizontal part of the distribution, and exclude 3 outliers (with YLL rates further than two standard deviations from the median) the sign of the correlation becomes positive for overall and age-sex specific rates, but with large p values ($p>0.1$) with the exception of the YLL rate for males between 25 and 30 which is positively correlated with the % of the population in poverty, with a $p<0.05$ (see Figure 68).

Figure 68. Countries with 20% or more of the population in poverty



Schizophrenia YLD rate, males, 25-29 = 2.99698*% of population with >5 deprivations + 0.521997. $p<0.05$

Given the caveats mentioned earlier and the existing literature, our interpretation of these findings is that the county-level burden of schizophrenia is lower in terms of disability as poverty increases, but with this decrease potentially due to an increase of the lethality of the burden, mainly due to decrease of available adequate care.(53,121)

Bipolar disorders

Bipolar disorder disability does not show overall or age-sex specific correlations with poverty, with the exception of a negative correlation for women older than 60 ($p<0.05$).

There are only four sources of data for bipolar disorders covering two low-income countries and two Indian States.

Substance abuse and eating disorders

Alcohol use disorder

Alcohol use disorder disability does not show overall nor age-sex specific correlations with poverty.

Drug use disorder

We find a large negative correlation in both sexes for all age-groups ($p<0.05$), with the exception of women under 15 years old. The largest effect can be seen in males under 40 and over 70 ($p<0.003$).

There are 24 data sources covering 23 low and lower-middle income countries or states (including 4 Indian States), so our confidence in this finding is high.

Table 6. Log (Drug use disorder YLD rate) vs. % of the population with 5 or more deprivations, controlling for sex and region

	Log (Drug use disorder YLD rate, males, 25-30)
% of population in poverty	-1.400 (exponentiated: 0.25)
	(4.95)**
East Asia	0.141
	(0.79)
Europe & Central Asia	0.276
	(1.53)
Latin America & Caribbean	-0.109
	(0.64)
Middle East and North Africa	0.583
	(3.01)**
South Asia	0.127
	(0.65)
_cons	5.775
	(40.14)**
R2	0.54
N	101

Omitted: Sub-Saharan Africa * $p<0.05$; ** $p<0.01$

Eating disorders

We found large negative correlations ($p<0.001$) in both sexes in all age-groups, with the largest effect in young and middle-aged females.

There is, however, only one study covering prevalence in low or lower-middle income countries, so we deem these findings preliminary and worthy of further investigation.

Table 7. Log (Eating disorder YLD rate) vs. % of the population with 5 or more deprivations, controlling for sex and region

	Log (Eating disorder YLD rate, females, 40-45)
% of population in poverty	-1.881 (exponentiated: 0.15)
	(9.99)**
East Asia	-0.132
	(0.96)
Europe & Central Asia	-0.242
	(1.71)
Latin America & Caribbean	0.097
	(0.73)
Middle East and North Africa	-0.324
	(2.18)*
South Asia	-0.319
	(2.18)*
_cons	3.316
	(28.66)**
R2	0.73
N	102

Omitted: Sub-Saharan Africa * $p<0.05$; ** $p<0.01$

Disorders with onset during childhood

Attention deficit and hyperactivity disorder and autism disability do not show overall nor age-sex specific correlations with poverty. Conduct disorder disability does show a negative correlation for boys between 5 and 15 ($p<0.05$). Intellectual disability shows an overall negative correlation in men older than 45 ($p<0.05$).

There are 10 studies covering conduct disorders in 10 low or lower middle income countries and territories (including 7 Indian States), so our confidence in these findings is moderately high.

Neuropsychiatric disorders

Of the neuropsychiatric disorders that we include in the mental disorder burden, only epilepsy shows a correlation with poverty. Alzheimer, migraine and tension-type headache do not.

Epilepsy

Epilepsy disability shows a positive correlation in most age-groups when controlling for sex and region ($p<0.05$), with the exception of the 45 to 64 age groups ($0.08>p>0.059$), and 10-15 ($p>0.1$). There are 101 studies covering 47 low or lower-middle income countries or territories (including 13 Indian States), so our confidence in these finding is quite high.

Maternal depression and child health

Maternal depression, frequently undetected and untreated in low-income settings, can have catastrophic consequences both for the woman and the child, constituting a potential risk factor for increased severity of infant and child sequelae produced by neonatal disorders, nutritional deficiencies and infections.(122) In order to explore this issue with our dataset, we studied the correlation of the combined burden rate for children under 5 years old with the YLD rate for women between 10 and 44 years old, overall and by 5-year groupings with the following model:

$$Communicable, neonatal, nutritional, under\ 5\ year\ old\ DALY\ rate\ _c = \beta_0 + \beta_1 Depressive\ disorders\ female\ YLD\ rate\ _{c,a} + \beta_2 \%\ of\ population\ with > 5\ deprivations_c + \epsilon$$

Interestingly, we found a small positive correlation between major depressive disorder disability burden in women of child-bearing age and under-five disability and mortality resulting from neonatal, nutritional, and common infectious disorders, even when controlling for % of population

in poverty ($p<0.01$). Of note, we also find that this positive correlation has a U shape, with larger effects in the youngest and oldest potentially fertile age-groups, and the lowest during peak-fertility (20-24), lending additional plausibility to the association (see Table 12).

With respect to the local grounding of these findings, we've already mentioned that there are 45 data sources covering depression in 24 low or lower-middle income countries or states (including 7 Indian States); also, data sources for group 1 disorders prevalence in low and lower-income countries are quite abundant (in the hundreds) so from that perspective we believe the findings are adequately grounded. A limitation is that we are looking at associations of a proxy variable (depression disability in women of child-bearing age for maternal depression) with the variable of interest (under 5 combined burden due to communicable, neonatal and nutritional disorders); however, the low p value (<0.01) plus the U-shaped association and its implications -that an increase in depression disability is particularly harmful for age-groups that already carry a biologically-determined higher risk for pregnancy outcomes- seems to support the face-validity of our proxy variable and the association.

Figure 69. Log (Communicable, child & nutritional disorders DALY rate, both sexes, <5 years old) vs. depression YLD rate, women, all groups 15 to 39 years of age

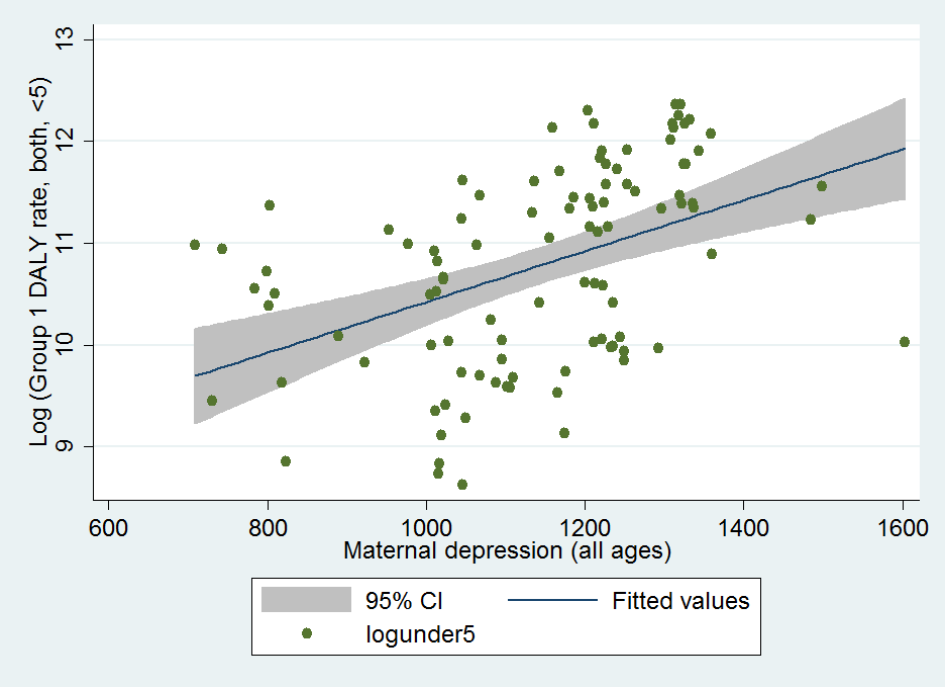


Table 8. Communicable, child & nutritional disorders DALY rate, both sexes, <5 years old) vs. depression YLD rate, women, all ages 15 to 39 and by 5-year group

YLD rate			Communicable, neonatal, nutritional, under-5-year-old DALY rate					
Maternal depression (overall)	48.746 (2.73)**							
Maternal depression (10-14)		141.719 (2.58)*						
Maternal depression (15-19)			53.689 (2.48)*					
Maternal depression (20-24)				37.232 (2.28)*				
Maternal depression (25-29)					43.124 (2.56)*			
Maternal depression (30-34)						49.600 (2.89)**		
Maternal depression (35-39)							53.996 (3.20)**	
Maternal depression (40-44)								54.007 (3.16)**
% >5 deprivations	172,466.644 (15.97)**	168,837.9 (15.22)**	172,395.994 (15.60)**	175,230.299 (16.28)**	174,523.581 (16.40)**	172,649.291 (16.22)**	168,811.307 (15.49)**	165,540.7 (15.04)**
R^2	0.78	0.79	0.78	0.78	0.78	0.78	0.79	0.79
N	102	102	102	102	102	102	102	102

* $p<0.05$; ** $p<0.01$

Discussion and limitations

We provide an exploratory picture of the potentially significant correlations between group-level poverty and disease burden for specific illnesses including major depressive disorder, schizophrenia, drug use disorders, eating disorders, suicide, epilepsy, and intellectual disability.

Most notably, we find that rates of major depressive disorder increase with poverty due to increased burden in men at the group level. Also, we find an increase in under-five combined disease burden resulting from communicable, nutritional and neonatal disorders, directly correlated with rates of depression in women of child-bearing age as a proxy for maternal depression. We also find that schizophrenia related disability shows an inverse correlation with poverty. We interpret this as the result of increased mortality for schizophrenia in low-income settings, which can be understood in the light of a growing body of evidence showing that in lower income settings resources for mental health are comparatively scarcer and less-well allocated, leading to premature mortality.(53,121) These results strengthen the evidence linking poverty with an increased risk for common mental illness, most notably for depression. At the same time, they are consistent with the notion of a vicious cycle mutually reinforcing depression and poverty, with depression itself a cause of decreased individual and societal economic output, and of increased expenditures. Our approach has two main limitations: (a) since our findings refer to group-level associations, they should be carefully interpreted in the light of existing and future knowledge regarding the impact of social determinants on people's mental health at the individual level, and the mechanisms through which this impact translates to the population level; and (b) we have produced multiple tests stratified by age-group, which increases the risk of false positives. We have therefore not assigned arbitrary significance cutoffs, but provided the p values for the reader to judge each specific conclusion. A substantive body of scholarship highlights the need to interpret exploratory findings and their p values in the light of prior knowledge and plausibility of the correlation, rather than by dichotomous significant/non-significant classifications.(123–125) Indeed, the pertinence of correcting for multiple tests by adjusting down α has been questioned

due to its tendency to obscure real differences, and our approach -acknowledging the multiple tests performed and providing the individual p values- has been recommended instead.(126) Considering previous knowledge, the locally grounded nature of the relevant evidence, and the non-isolated nature of the findings, our results provide a meaningful picture for a number of highly relevant disorders. Also, they are potentially significant given the extremely low p values. Of note, the p value of the association of percentage of the population in poverty with: depression disability in 15 to 35-year-olds, adjusting for sex and region, is 0.001 or lower; with schizophrenia in all age-groupings -above age of onset- is <0.001; and of the overall association between depression disability in females of child-bearing age and under five combined burden is 0.006.

Conclusion and section summary

Significant efforts have been made over the last decades to detect, treat, and prevent infectious diseases, which were at the time -and still are in some countries- the largest cause of disability. Health systems in poor countries were selectively strengthened to detect and treat for example HIV, but no comparable effort has been made with regards to NCDs. In the case of mental illnesses, health services in low income countries are still poorly prepared, and in many cases non-existent. We show that country-level depression disability seems to be particularly burdensome during the working years in low-income countries, placing a dramatic constraint on productivity and therefore on development and economic growth. Furthermore, we find a direct correlation between poverty and overall major depressive disorder ($p<0.005$), with the largest effect for the group of young men ($p<0.001$). The demographic dividend -the ability of developing countries to reap the benefits of a bulging young population due to decreased child mortality(127)- is

conditional on a population able to work and raise healthy children, so large causes of disability for working and child-bearing age-groups are particularly relevant in the context of poverty.

In summary, these findings offer a potentially high-value target for health systems strengthening in low-income countries: depression rates in young people as a group increase with poverty; this increased disability further prevents economic growth both directly -through reduced output- and trans-generationally -through increased death and disability of infants and children in areas of higher depression rates in women of child bearing age-. The ecological nature of our study precludes individual level conclusions, but we provide a picture that includes data from a substantial subset of countries (n=102) and a large number of age-sex-specific group-level unique observations (n=3447). With a focus on the poorest billion people, we test the hypothesis that group-level disease distribution will be a function of the relative size of the pockets of poverty. Our findings, most notably for major depression and schizophrenia, are supportive of existing individual level findings. Programs aimed at prevention, detection and treatment of major depressive disorder in young men and women seem to present the highest value target from an economic development perspective. Our results also highlight another high value target, this one from an ethical perspective: severe mental illness includes one of the most disabling of all human conditions, schizophrenia. Neglect of these patients in low-income settings leads to increased premature mortality, artificially decreasing subsequent county-level disability. Programs aimed at the detection and treatment of schizophrenia in the community offer a direct path to reversing this indicator of health systems -and humanity's- failure.

Epilogue. The burden of change: The global governance and health systems challenge of meeting the disease burden of mental illness

In previous chapters I've reviewed current methods to estimate the disease burden of mental illness; provided a detailed critique of the GBD methodology, inasmuch as it leads to underestimates; provided a framework to partially correct that underestimation; applied that framework to building locally grounded burden estimations through modeling that allows for improving them when additional data is available; studied how country-level burden varies across regions and sub-regions; analyzed how burden distribution varies with country-level income data, and also with age-sex specific multidimensional poverty; and how country income level largely determines how well-resourced mental health services are, and how well-allocated spending is. The data presented so far highlights the enormous fraction of total combined and disability burden that can be attributed globally to mental illness: mental disorders accrued 12.4% of global DALYs, and 35.9% of global YLDs in 2015. The largest fraction of this burden can be attributed to major depressive disorder, which mainly affects working-age populations, placing a major constraint on economic development. In summary, our evidence sustains the notion that mental disorders should be not only a health but also a development priority.

So, in the context of transitioning from the Millennium Development Goals (MDGs) to the Sustainable Development Goals (SDGs), I will focus this final section on the challenge of improving the global response to mental illness. We have made the case that disability and multi-morbidity constitute the bulk of the disease burden globally.(27,128) Non-communicable diseases have received increased attention, mostly focused on cardiovascular disease, stroke, cancer, and some of their associated risks factors, such as obesity, metabolic syndrome, diabetes, and smoking. Still

relatively absent from global priorities is the group of mental illnesses, despite accounting for 11 times the disability associated with cardiovascular disease and stroke. Underestimation, along with pervasive stigma and other factors we will address below, leads to insufficient funds and inadequate services. As was highlighted earlier, national spending on mental health ranges from 0.5% of health budgets in low income countries to 5.1% in high income countries (as a group), with a global median of 2.8%. Similarly, of the $372 billion disbursed in the past 15 years as development assistance for health (DAH), only 0.4% went to mental illness.(69) Compounding the lack of funds is their misallocation: 60 to 90% of funds go to stand alone neuropsychiatric hospitals, against all existing recommendations and evidence.(69) We have also shown that this misallocation gets worse the lower the income level is, highlighting the importance of globally set guidelines and priorities intending to counter this pervasive trend. The result of this untreated burden goes well beyond mental health: outcomes of frequently co-occurring conditions such as pregnancy, cardiovascular disease, cancer, diabetes, and HIV are sub-par, and the direct and indirect costs to society, estimated at $2.5 trillion for 2010, top the rank in terms of economic losses due to decreased national output.(109)

The multi-determined social neglect of mental illness

The causes of this social neglect are manifold, including the following:

An outdated framework: Mental illness has historically been considered a manifestation of moral or spiritual failure, and though these views are scientifically discredited, there is a pervasive tendency to view mental illness as fundamentally different from other illnesses, with a separate

etiology and a segregated approach to treatment. This segregation, spanning the conceptual, clinical, and delivery levels, is arguably at the root of its neglect.

Stigma and discrimination: Stigma and discrimination persist at all levels, literally adding insult to injury for the mentally ill. Self-stigma leads to underutilization of services; practitioners provide sub-par medical care, leading to increased mortality from treatable physical conditions; communities put barriers to integration, and decision-makers consistently prioritize other health areas.(24,129)

Insufficient social mobilization: Unlike with maternal and child health or HIV, society hasn't identified the care for the mentally ill as a priority, so it fails to demand services in force through petitioning, advocacy, and mobilization.

Underestimated burden: Epidemiologic data is insufficient and, as we have shown in previous chapters, disease burden estimations traditionally downplay mortality and morbidity resulting from mental illness.(69) Furthermore, the welfare loss associated to mental illness, plus the resulting family and economic burden are seldom considered despite mounting evidence placing it above all other groups of illnesses.(109) This leads to downplaying the stakes involved in persistent inaction: catastrophic personal disease burden, broken families, decreased economic output, and increased social suffering, all partly amenable to evidence-based cost-effective interventions.

Unclear policy package: Despite the well-established effectiveness and cost-effectiveness of scalable mental health interventions,(73,130,131) there are inconsistent messages respect to which are the *best-buy* interventions and the best policy path to achieve universal coverage inclusive of mental health.

Inadequate inter-sectoral coordination/governance: There is insufficient dialogue with other health and non-health sectors, insufficient coordination between initiatives within the global mental health field, and even silo-functioning of global mental health initiatives within large academic organizations. As a result, mental health lacks the organization, visibility, and political support achieved by other areas such as HIV and maternal/child health.

Insufficient funds and resources: Funding is disproportionately scarce in relation to burden. In the zero-sum game of national budgets and DAH, fragmentation in the face of the better-organized advocacy and consistent messages from other sectors, results in sidelining of our field.

Inadequate services: As we have shown, neuropsychiatric hospitals still receive the lion's share of domestic budgets in most low and middle income countries. In fact, country-level income by itself predicts nearly half the variation in: (a) the share of health expenditures allocated to mental health; (b) the share of spending captured by neuropsychiatric hospitals; and (c) the disproportion in effective spending as reflected by our proposed metric of imbalance between burden and spending (see chapter 4). In higher income countries, lack of parity with general health, regional polarization, and other inequities also pervade mental health systems. Recent models of care, including psychoeducation, self-care, and integration in general health services for common mental illness, and a stepped model of community treatment for the more severely affected are insufficiently diffused despite an adequate evidence base regarding effectiveness, cost-effectiveness, and scalability.(131–133)

Effectively tackling this complex web of determinants will demand a concerted global effort, comparable in many aspects to the one that took place in the last decades of the 20th century to prioritize the fight against AIDS. In terms of actors, the prioritization of mental health needs to

involve, to some extent, the full range of stake-holders: people with mental illness; family members and advocates; mental and general health practitioners, as well as other specialists and their associations; academia, including students, researchers and professors; policy and decision-makers, including line bureaucrats and elected officials; private donors; national governments; and bi-lateral, multi-lateral and hybrid organizations, initiatives, or partnerships. This ever-growing cadre of global stake-holders reflects the fact that the status of *health* as an issue of public interest has shifted during this century. Accompanying the increasing pluralism of actors, there has been a massive influx of funds towards the health sector, both in the form of development assistance for health (DAH), and Government expenditures. DAH increased from US$5.7 billion in 1990 to $36 billion in 2014, and Government expenditures on health in low and middle income countries increased from around US$175 billion in 1995 to US$759.7 billion in 2010.(57) The unprecedented nature of the health transition, leading to what is known as the *triple burden* -consisting of the unfinished agenda of communicable, maternal, child, and nutritional disorders; plus the emerging NCDs; and the health challenges resulting from globalization-, necessitates a similarly complex health system response, including innovations in financing, system design, and delivery of health services. Indeed, health has lost its previous *low-politics* status given its newfound gravitas in matters of global and national security; its impact on economic development plus the funds it commands for services; and concerns related to the human rights of affected populations. Mental disorders embody several of these challenges: youth disaffection frequently occurs with the backdrop of common mental disorders, making adolescents and younger adults vulnerable to capture by extremist worldviews; globalization produces its own set of global mental health concerns, most notably around refugees, displaced, and violence-torn populations; mental

disorders cause the largest economic impact of all NCDs in terms of lost output; and generate significant human rights concerns, mostly around still pervasive and outdated treatments for severe mental illness. Given the breadth and complexity of the challenge, a global governance framework can help guide our analysis.

In order to better define the global challenge of prioritizing mental health, we will study (a) the field's recent history, as well as (b) the history of a comparable global health challenge, with the goal of illuminating how the social process of prioritization occurs -or fails to do so-.

Previous approaches in the global mental health field

There have been several initiatives in the past that pursued the goal of prioritizing mental illness. I will focus on some of the most impactful actions of the current century, which capture both the wide array of stake-holders that energized this renewed push, as well as the varied forms these initiatives can take. Table 9 highlights some key features that might explain both their impact and their constraints.

Table 9. Global mental health (GMH) initiatives during this century

Name, year	Type	Organizational characteristics	Stake-holders	Output	Target audience	Funding source	Epicenter
Mental health Report, 2001; Mental Health Atlas, 2001; mhGAP Action Programme, 2002 & 2008	WHO-led partnership	Telic, durative collaboration.	WHO, academia, NGOs	Mental Health Atlas; mhGAP manual; pilot and scale-up projects WHO-AIMS	Policy makers, practitioners	WHO and partners	Geneva, Switzerland

Table 13. Global mental health (GMH) initiatives during this century (Cont.)

Lancet Series on GMH, 2007 & 2011	Journal series	Telic, punctual collaboration of academics convened by 1st tier journal	Academics, advocates	Series of papers on GMH	Academia, practitioners	The Lancet	London, UK
Movement for GMH, 2008	Network of individuals and organizations	Open-ended, durative collaboration. No budget.	Academics, practitioners, advocates, people with MI	Newsletter; Biennial Summit	Policy-makers, advocates, people with MI	Self-funded	New Delhi, India (Rotating Secretariat)
Grand Challenges in GMH, 2010-2011	Partnership between NIMH, academia, and donors	Telic, punctual collaboration of academics convened by NIMH. Funded by partners.	NIMH, donors, academia	List of priorities for MH research based on expert opinion; published in Nature	Academia	NIMH, Wellcome Trust	Bethesda, US
Mental Health Action Plan, 2013-2020	WHO Assembly Declaration and Plan	Telic, durative WHO initiative	Policy-makers, academia, advocates	Diffusion of published plan, follow-up through Secretariat, periodic reports to following WHAs	Policy-makers, academia, advocates	WHO	Geneva, Switzerland
Mental Health Innovation Network, 2013	Partnership between academia and WHO	Telic, durative collaboration. Funded by external donor.	Practitioners, policy-makers, users, researchers, donors	Online repository of evidence on MH innovations aimed at improving quality and coverage	Practitioners, policy-makers, users, researchers, donors	Grand Challenges Canada, other donors	Geneva, Switzerland; London, UK
Mental Health Summit, 2016	Collaboration between WB, WHO, and academia	Telic, punctual collaboration. Funded by WB and donors.	WHO, WB, policy-makers, academia, advocates	Committing funding agencies and governments to prioritize MH	Decision-makers, policy makers	WB, individual donors	Washington, US

These 15 years of intense work seem to stem from the *Call for Action and Mental Health Report* that the WHO's 54 World Health Assembly formulated in 2001.(134) The WHO's *Mental Health Global Action Programme (mhGAP)* followed suite, with an ambitious 5-year plan to lead a partnership including other UN agencies, donors, academia, governments and the civil society,

focusing on advancing four broad strategies: gathering information, integrating policy and service development, advocating against stigma, and enhancing research capacity.(135) Some of these strategies were already in place and continued to evolve, such as the WHO Mental Health Atlas, which gathers and provides national level data, and some emerged anew, such as the WHO-AIMS, a tool for assessing mental health systems. 7 years later, the *mhGAP* was re-branded as the *Mental Health Gap Action Plan*, a manualized primary care approach to neuropsychiatric conditions in low income countries.(103) It was accompanied by demonstration projects resulting from collaborations between the WHO, NGOs, academics, and local governments. Also during this period, high-income countries such as the UK implemented comprehensive mental health policy and service transformations. Considering that the UK framework and guidelines were published between 1999 and 2001,(136) the most likely scenario is that these processes were both expressions of an evolving mental health field, rather than the effect of one on the other. Also unclear is the footprint of these WHO initiatives in the donor community: they are present in the initial call to action, but absent from later references. More defined is the impact on academia: in 2007 -with an iteration on 2011-, *The Lancet Series on Global Mental Health* provided increased visibility to the field, spurred widespread academic collaborations, the creation of specific university programs, and the prioritization of certain topics -such as stigma, delivery platforms, integration in general health, and others-.(29,91) It also resulted in the creation the following year of the *Movement for Global Mental Health*, a more organic, grassroots-type collaboration that includes academics, practitioners, advocates, and persons with mental illness.(137) Again, it is impossible to adjudicate causality: most likely all these initiatives built on and supported one another, creating an increasing momentum for change. The 2010 *Grand Challenges in Global*

Mental Health initiative was led by the largest research funding agency in the world: the US National Institutes of Health.(132) After previous *Grand Challenges* rounds addressing *global health* (2003), and *non-communicable diseases* (2007), the NIMH led this research collaboration specifically citing the impact of the Lancet series, and garnering support from donors such as the Wellcome Trust -but not the Gates Foundation, despite previous involvement in the launching of the 2003 *Grand Challenges in Global Health* initiative-. In 2013, the WHO picked up the gauntlet and launched a *Mental Health Action Plan 2013-2020*, which besides offering frameworks, priorities, and targets, entailed periodic reporting to the World Health Assembly.(60) Also in 2013 the *Mental Health Innovation Network* was created, a collaboration between WHO and academia that offers an accessible and user friendly online repository of innovations.(138) It was funded by Grand Challenges Canada, one of the few relevant national funders -along with the National Institutes of Mental Health, US- that prioritizes mental health. Lastly, the World Bank and WHO co-hosted a Mental Health Summit in April 2016, co-chaired by Harvard's Professor Arthur Kleinman, WB President Jim Kim, and WHO Director General Margaret Chan, and supported by a working group comprised of global experts. One of the innovative aspect of this initiative is the direct engagement of financial stake-holders, such as the WB Head, Finance Ministers, and donors. What can we conclude about these initiatives? First, that the progress has been incremental. Also, that some actors -such as WHO and academia- are an enduring source of innovation and advocacy: they provide the motivation and tools that have gradually increased awareness, coverage and quality of care. Other actors, however, seem harder to engage: Governments in LAMICS and donors -with exceptions- still ignore mental health. The result is enhanced inequality: in the absence of Government funding, DAH is essential; and in the absence of both, the last resort is

out-of-pocket payment, a non-starter for impoverished populations. Despite these pitfalls, it is clear that the global response to mental illness is improving. But given the everyday human toll of untreated mental illness, key questions come up: is it possible to increase the pace of change? Is there an actionable strategy that would put in place the global governance mechanisms needed to further improve awareness, quality, and coverage?

Learning from a successful experience: the global response to HIV

As mentioned before, key determinants of the current neglect of mental illness globally are outdated frameworks, stigma, lack of social mobilization, poor coordination and governance, insufficient funds, inadequate services, and lack of policy clarity on platforms to deliver effective treatment at scale. The more salient difference with HIV is that whereas the burden of mental illness is undercounted and remains out of the public eye, the dissemination of HIV and AIDS led to widespread panic. Other aspects are, however, comparable: as we have shown throughout this work, standard metrics currently underestimate the burden of mental illness; likewise, before the 90s there were no reliable metrics to gauge the impact of HIV and compare it across disorders and regions. All the other determinants we highlighted for mental illness were also present during the challenge of addressing the AIDS epidemic in the 90s: outdated and stigmatizing frameworks to understand the social and behavioral aspects of infectious diseases; initial lack of mobilization, coordination and governance; and inadequate funding, service delivery, and policy recommendations. There are of course countless differences both in the type of illness and the response needed, but given the paucity of models for understanding major global shifts in the social perception of health challenges leading to the creation of innovative governance

mechanisms, I will focus on the experience of how the AIDS challenge was addressed, looking for clues that can inform today's mental illness conundrum.

Box 10 provides a brief overview of the HIV case, and Table 11 highlights the similarities and differences of both responses.

Box 10. The Global Governance Challenge of HIV

Several factors converged in the late 1990s and early 2000s that led to a sea change in the global response to AIDS, among them:

- The establishment of a set of health metrics -the global burden of disease model- that pointed to infectious diseases as the top health priority;(19)
- The World Bank's 1993 World Development Report, which made the case for *Investing in Health* based on those health metrics;(141)
- The impact of this report on global donors, most notably Bill Gates, who credits it with his decision to focus his new philanthropy -the Gates Foundation- on global health;
- The consolidation, in 1996, of an effective combination treatment strategy;
- The Millennium Development Goals, launched in 2000 by the UN, including a commitment to fight HIV (Goal 6);
- The unique 2001 UN session on HIV/AIDS, where Presidents pledged $7 to $10 billion annually by 2005;
- The creation in 2002 of the Global Fund, an innovative hybrid organization created to fight HIV, TBC and malaria;
- The *3 by 5* commitment by WHO and UNAIDS in 2003, setting the global target of providing 3 million people in LAMICS with treatment by 2005;
- The 2003 US President's Emergency Plan for AIDS Relief, pledging 15 Billion dollars to treat HIV in Africa.

Though impossible to locate on a timeline, a key achievement was the reduction of social stigma and the consolidation of a moral discourse to support the need to care for the sick: from the early *pink plague* to today's chronic condition, countless advocacy and education campaigns, books, movies and other instances of popular culture are to be credited for changing the social perception of HIV. Of particular importance, the surge of a moral movement with epicenters in highly-educated and active gay communities in the US, Europe, and Australia, quickly galvanized diverse groups of activists into highly effective organizations such as the AIDS Coalition to Unleash Power (ACT UP). Key ingredients were the ability of early activists to understand and diffuse the science behind HIV and its treatment, as well as the political economy of health and illness, particularly the global vested interests of pharmaceutical and regulatory organizations. Of note, the broad ideological spectrum of the emerging moral discourse allowed both secular and religious worldviews to converge, and mobilize massive social support and funds. It can be hypothesized that the tipping-point -from a global prioritization perspective- was this convergence of disparate ideologies: (a) the academic and economic rationale underlying the WB report -based on HSPH-designed metrics-, which mobilized Bill Gates and his foundation, with (b) the religious conviction that unpredictably spurred George Bush into action with PEPFAR, which he characterized as "a work of mercy" to help the people of Africa, and which effectively signaled to the world that the *war chest* proposed by UN Secretary General Kofi Annan would be stocked for the long haul.(144)

Table 11. HIV vs MH

	UN-Global commitments	WHO	WB	Private Donors, Hybrids	Donor Countries	Disease burden (% of DALYs)	Public Health Field	Community
HIV, 2000	Main focus of MDG 6 (1 of 8); Funding pledges; Personal advocacy by UN SG Kofi Annan	Strong engagement in technical support and advocacy	Strong engagement in technical support, advocacy and financing	Strong engagement in advocacy and funding. Global Fund.	All major donors strongly engaged	Infectious diseases: 1st in 1990	Strong support for focus on HIV	Reduced barriers to integration
Mental Illness, 2017	Partial focus of SDG 3 (1 of 17); No funding pledges	Strong engagement in technical support and advocacy; World Health Day '17: Depression	Mild engagement in technical support, advocacy, potential financing	Mild engagement in advocacy, scarce funding. No hybrid organization.	Canada, GACD, others (0.4% Of all DAH)	2nd in 2015 (undercount-ted DALYs; clear 1st in YLDs)	Ambivalence on focus on mental illness	Persistent barriers to integration

The main difference is that AIDS presented an urgent challenge that could not be ignored, mainly due to its puzzling origins, its rapid spread, and its lethality. And on the response side, once an effective treatment became available, the question focused mostly on designing and financing appropriate delivery platforms. Conversely, mental illness has been around -literally- forever; its burden is mainly due to disability, not mortality; and treatment is multifaceted, including pharmacology, psychotherapy, and support for community integration. The perceived complexity of the interventions for mental illness coupled with the traditionally segregated approach to it lead to lack of engagement, even from public health officials and the medical profession. Focusing on the non-health actors, we notice that -until recently- there is a lack of interest on mental illness from economic decision makers, donors, and the World Bank. Whereas unprecedented funding was committed early on for HIV, funds for mental health have so far barely trickled. The compelling case for HIV presented in 2001 by Kofi Annan -the need to create a *global war chest* pooling

unprecedented funds- led to the creation of the Global Fund, which revolutionized the way DAH is pooled and disbursed. The case for a *war chest* for mental illness has not been made, and there is no organizational equivalent to the Global Fund. The comparison also indicates that with respect to advocacy and aspirational goals, mental illness does not command the urgency and monopoly of attention garnered by HIV: as was mentioned before, it has accompanied humanity since time immemorial, and has been ignored, stigmatized, or punished for most of that time. Though it was included in the SDG 3 dealing with health -addressed in 2 of 13 targets vs. 1 for infectious diseases-, the galvanizing power of the MDG 6 will hardly be repeated. Finally, most societies have embraced people with HIV. The stigma, discrimination, and outright segregation that met the initial outbreak has been, though not fully, superseded by social acceptance and support for integration of people with HIV into everyday life, such as in school, work, and housing. Stigma against people with mental illness is still pervasive, and surveys across the world show the general public still discriminates them.(22,23,139) Treatment remains largely segregated, and meaningful work or housing integration is the exception rather than the rule.(90,140)

Next steps to improve the global response to mental illness

The involvement of the World Bank (WB) in the early stages of the AIDS epidemic, through a report that provided the health metrics necessary to understand and gauge its impact cannot be overestimated (see

Box 10).(141) Though not directly comparable, in April 2016 a potentially meaningful step was taken toward prioritizing mental health in the global agenda: the WB co-hosted with WHO a Mental Health Summit during the WB-International Monetary Fund Spring Meeting, making the

case that mental health was a global development priority. The question is whether this will represent another incremental advance, or if it offers -in the sense of Kingdon(142)- a policy window for a qualitative leap in terms of decision-maker prioritization, impactful partnerships, societal awareness, increased funding, and service scale-up. Achieving meaningful advances on these fronts is by no means guaranteed, but the Summit presented the unique opportunity of making the economic case directly to financial stake-holders and donors, and a more compelling case for service integration to the public health and medicine fields, with the WB and WHO as underwriters.

The most conspicuous absence in the response to mental illness has been funding (see Table 11). Understandably so, since a compelling case for mitigating the economic cost of mental illness has not been made at this level: important steps have been taken, such as the joint HSPH-World Economic Forum 2010 report on the cost of non-communicable diseases.(109) But an overarching picture focused on mental illness, linking the costs of inaction with the most effective and cost effective interventions available, and tailored to the different income levels, is yet to be fully made. Also, though a consensus has emerged on the importance of mental health integration in primary care and community-based stepped care,(131) this message has not been successfully formatted as a blueprint to address the mental illness burden globally. The Mental Health Summit and a number of previous and accompanying papers presented these messages -the costs of inaction, the net benefits of the best interventions, and the platforms to deliver them at scale(69,73,130)- to relevant economic decision-makers. In parallel, it sought to advance the cause against stigma, by engaging the community -youth in particular- through the participation of youth organizations and public personalities willing to share their experience with mental illness. So, the Summit and

the resulting commitments can potentially add community, public health, and decision-makers support to the goal of increasing funds for scaling-up mental health services.

An element that remains missing is the organizational setting that would move this agenda forward at a different pace: we have seen that the loose flotilla composed of WHO, academia, and advocates has spearheaded a remarkable advance during the past 15 years, but an adequate organizational setting could increase that pace. Without such a setting, and based on previous experience, momentum would arguably be short lived: actors would revert to previous positions and dynamics, and the part-time attention they devote to this specific issue will again determine an incremental pace of progress. Conversely, if a setting is created with the specific goal of improving the global governance mechanisms in order to advance the Summit's recommendations, the pace of change could be significantly altered: a cadre of full-time staff with expertise in the fields of global governance, mental health, fund raising, research, and health economics, instead of the existing network of advocates, academics, mental health workers, and psychiatrists, struggling to include this issue on their packed schedule would work, at least, as an accelerant. The question is whether the cost of such an organization would be offset by potential results, and if so, what kind of organizational setting should be sought. One difference with the HIV response is the lack of a specific fund pooling and disbursing organization for mental illness. On the one hand, the paucity of DAH funds for mental illness does not seem to justify the creation of a Global Fund-like organization. On the other, the lack of *any* organization with expertise on global mental health, specifically geared at facilitating the global challenge of fund pooling and disbursing, arguably impinges on the intake of funds in the first place: willing donors would have to develop expertise themselves or tap potential partners, such as WHO. However, we have seen

that though WHO has done a remarkable job at convening actors to produce a growing evidence-base and a set of actionable frameworks, it has not been able to mobilize the kind of resources needed as per its own recommendations.

Providing a specific organizational setting to improve the governance mechanisms needed to prioritize mental health in the global agenda represents a previously unexplored and potentially impactful next step. Key goals of such an organization would be:

- Keeping the main stake-holders committed and engaging new participants
- Providing a clearing-house for knowledge and evidence related to the implementation challenges involved in scale-up and integration of mental health services
- Raising, pooling, and funneling funds for global mental health
- Making expertise and capacity building available globally for public health authorities

There are several organizational models that could carry out these goals. In Table 12, I present three potentially useful templates and their main pros and cons: A University-based partnership; a WB consultative group; and a hybrid organization.

Table 12. Options for improved governance

Organizational model	Main characteristics, advantages and disadvantages
University-based partnership with donors	Harvard could provide an appropriate base for a core group to work on the points set out in the text. This model would provide an expert, nimble, and versatile group with the Harvard brand. Disadvantages would stem from Harvard's institutional implications, both in terms of bureaucracy and perceived hegemony. A useful template for this model might be the Governor's Climate and Forests Task-Force, whose Secretariat is housed by the University of Colorado's Law School (see http://www.gcftaskforce.org/about).
WB-based Group	Current WB Head has shown a personal vision aligned with the prioritization of mental health, and this could be leveraged to house a working group within its structure. Working under the aegis of the WB would have some advantages: it would provide legitimacy as per the donor community and national authorities, particularly from a global implementation perspective.

	Potential disadvantages would be the political implications of working for the WB, particularly vis-à-vis the WHO and political elites in some developing countries. A useful blueprint for this setting would be the Consultative Group to Assist the Poor (CGAP), and other similar ventures (seehttp://www.cgap.org/about).
Hybrid Organization	Formalizing a partnership of states, donors, civil society, and the private sector. The advantages of a Global Fund-style framework would be: a shared governance structure including key public and private stake-holders, which provides relative autonomy from each specific actor; a minimum of initial bureaucratic constraints and path dependence; a favorable setting for innovative funding, development, implementation, and evaluation practices. Potential disadvantages are the large up-front costs of creating and maintaining such organization, as well as rivalry with existing hybrid organizations focused on other health priorities, particularly in a time of plateauing or decreasing development assistance for health (see http://www.theglobalfund.org/en/overview/).

Section summary

Mental illness presents a governance challenge that is global in scope: the knowledge base -from basic to implementation research- to make possible universal coverage inclusive of mental health is a public good that, given its positive externalities, will remain undersupplied without government intervention. However, there are no meaningful incentives nor sufficient resources at the national level -most dramatically, as we have seen in previous chapters, in developing countries- to resolve this market failure; hence, a global governance effort is needed to fill this gap, which can be summarized as funding the knowledge base and implementation capacity for providing universal mental health coverage. The *multilateral health* approach -through WHO-led collaborations- results in incremental change, and involves the persistence of significant amenable human costs and economic losses. One reason is that it fails to engage key non-health and non-state actors, such as finance ministers and global donors respectively, as well as the private sector in general and even physicians from other specialties. So, a main criterion to assess if a new organizational setting meets good global governance standards would be having the potential to meaningfully engage these reluctant but essential actors. To different degrees, the three options

presented have such potential (see Table 12 for details): a partnership between a University and donors is feasible, though arguably limited in scope and impact; a WB-based consultative group has the potential to engage a larger cadre of donors and compel governments, but might alienate other partners; a specific hybrid organization is by nature a partnership between multilateral organizations, governments, donors, and the community, so it has the largest potential.(143) It also carries the largest risks of failure, since it would demand higher stakes for all involved. Any of these three models should be implemented in a way that upholds procedural and outcome legitimacy: the decision-making process should include all partners (the ideal being a board that comprises all sectors), and the results should clearly outweigh the costs. This last caveat argues against a full-blown but premature hybrid organization, that might hold-up in terms of procedural legitimacy, but falter and lose outcome legitimacy if proportional funds or successful implementation experiences fail to materialize rapidly. A hybrid appears however to be the best end-point scenario, providing that adequate funds and large scale implementation successes materialize in the process. So, a rational template for action would be building an intermediate organizational setting, which could start as a steering committee including stake-holders from the WB, WHO, donors, the mental health field, the general health field, and the community, building an inclusive partnership following the University-based or the WB-based model, with the goal of pooling an initial round of seed capital to fund large scale implementation projects. Building on these (eventually) successful outcomes, a second round of funding should allow for the creation of an autonomous sustainable hybrid organization focused on mental health.

Conclusion

This thesis puts the burden of mental disorders at the top of the disability ranking -and second in the combined ranking of disability and mortality- globally and in the Americas. It also provides a systematic framework to produce actionable needs-assessments for governments, multilateral organizations, and non-profits. It provides a life-course perspective on how the epidemiologic transition shapes disease distribution across country-income levels, finds a direct correlation of the percentage of the population in poverty with group-level depression disability, an inverse correlation with schizophrenia disability -which I posit can be ascribed to increased lethality in low-income settings-, and a direct effect -controlling for group-level poverty- of depression disability in women of child-bearing age, on under-five combined burden due to communicable, perinatal, and nutritional disorders. Also, this study found that the imbalance between burden and spending on mental health -factoring in allocative efficiency- is inversely correlated with country income-level in the Americas: poorer countries spend a lower fraction of their health expenditures on mental health and allocate it less efficiently. And finally, I argue that in order to make mental health a global health and development priority, a governance and advocacy effort is required, including the creation of a specific organizational setting of global reach capable of engaging key partners that have so far been elusive, such as Governments, global donors, and economic actors.

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Bibliography:

1. Riley JC. Estimates of Regional and Global Life Expectancy. Riley Source Popul Dev Rev. 2005;31(3):537–43.
2. WHO. World Health Statistics 2016: Monitoring health for the SDGs. 2016.
3. United Nations Department of Economic and Social Affairs Population Division. World Population Prospects: The 2015 Revision. [Internet]. 2015. Available from: https://esa.un.org/unpd/wpp/DataQuery/
4. Bloom DE, Canning D. Commentary: The Preston curve 30 years on: Still sparking fires. Int J Epidemiol. 2007;36(3):498–9.
5. David E. Bloom, David Canning, Jaypee Sevilla. ECONOMIC GROWTH AND THE DEMOGRAPHIC TRANSITION. 2001.
6. Jamison DT, Sandbu M, Wang J. Cross-Country Variation in Mortality Decline, 1962-87: The Role of Country-Specific Technical Progress. 2001.
7. Cutler DM, Deaton AS, Lleras-muney A. The determinants of mortality. NBER Working Paper Series. 2006.
8. Gold MR, Stevenson D, Fryback DG. HALYS and QALYS and DALYS, Oh My: similarities and differences in summary measures of population Health. Annu Rev Public Health. 2002;23:115–34.
9. Kahneman D, Tversky A. Prospect Theory: An Analysis of Decision under Risk E C O N OMETRICA I C I VOLUME 47 MARCH, 1979 NUMBER 2 PROSPECT THEORY: AN ANALYSIS OF DECISION UNDER RISK. Source Econom. 1979;47(2):263–92.
10. Murray CJL, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C, et al. Comprehensive

Systematic Analysis of Global Epidemiology: Definitions, Methods, Simplification of DALYs, and Comparative Results from the Global Burden of Disease Study 2010. Lancet. 2012. p. Supplementary Appendix.

11. Salomon J a., Vos T, Hogan DR, Gagnon M, Naghavi M, Mokdad A, et al. Common values in assessing health outcomes from disease and injury: Disability weights measurement study for the Global Burden of Disease Study 2010. Lancet. 2012;380:2129–43.

12. Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Heal. 2015 Nov;3(11):e712-23.

13. Burstein R, Fleming T, Haagsma J, Salomon JA, Vos T, Murray CJ. Estimating distributions of health state severity for the global burden of disease study. Popul Health Metr. Population Health Metrics; 2015;13:31.

14. Flaxman AD, Murray CJL, Vos T. An integrative metaregression framework for descriptive epidemiology. Seattle: University of Washington Press,; 2015.

15. Kleinman A, Das V, Lock MM. Social suffering. University of California Press; 1997. 404 p.

16. World Health Organization. What is Mental Health? [Internet]. 2007. Available from: http://www.who.int/features/qa/62/en/

17. Ginn S, Horder J. “One in four” with a mental health problem: the anatomy of a statistic. BMJ. 2012 Jan;344:e1302.

18. Steel Z, Marnane C, Iranpour C, Chey T, Jackson JW, Patel V, et al. The global prevalence of common mental disorders: a systematic review and meta-analysis 1980-2013. Int J Epidemiol. Oxford University Press; 2014 Apr 1;43(2):476–93.

19. Lopez AD, Murray CC. The global burden of disease, 1990-2020. Nat Med. 1998 Nov;4(11):1241–3.

20. Bloom DE, Cafiero ET, Jané-Llopis E, Abrahams-Gessel S, Bloom LR, Fathima S, et al. The Global Economic Burden of Noncommunicable Diseases. Geneva; 2011.

21. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. Lancet. 2007 Sep 8;370(9590):878–89.

22. Thornicroft G, Brohan E, Rose D, Sartorius N, Leese M. Global pattern of experienced and anticipated discrimination against people with schizophrenia: a cross-sectional survey. Lancet. 2009 Jan 31;373(9661):408–15.

23. Lasalvia A, Zoppei S, Van Bortel T, Bonetto C, Cristofalo D, Wahlbeck K, et al. Global pattern of experienced and anticipated discrimination reported by people with major depressive disorder: a cross-sectional survey. Lancet (London, England). 2013 Jan 5;381(9860):55–62.

24. Henderson C, Noblett J, Parke H, Clement S, Caffrey A, Gale-Grant O, et al. Mental health-related stigma in health care and mental health-care settings. The Lancet Psychiatry. 2014 Nov;1(6):467–82.

25. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012 Dec 15;380(9859):2095–128.

26. Vos T et al., Collaborators. GB of DS 2013. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries

in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. Elsevier Ltd; 2015;6736(15):1990–2013.

27. Atun R. Transitioning health systems for multimorbidity. Lancet. Elsevier Ltd; 2015;6736(14):8–9.

28. Bloom DE. 7 billion and counting. Science. 2011 Jul 29;333(6042):562–9.

29. Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, et al. No health without mental health. Lancet. Elsevier; 2007 Sep 8;370(9590):859–77.

30. Alonso J, Chatterji S, He Y. The Burdens of Mental Disorders: Global Perspectives from the WHO World Mental Health Surveys. Cambridge University Press; 2013. 319 p.

31. International Advisory Group for the Revision of ICD-10 Mental and Behavioural Disorders. A conceptual framework for the revision of the ICD-10 classification of mental and behavioural disorders. World Psychiatry. 2011 Jun;10(2):86–92.

32. IHME (Institute for Health Metrics and Evaluation). Global Burden of Disease 2010 [Internet]. Data Visualizations. 2013 [cited 2015 Jul 15]. Available from: http://vizhub.healthdata.org/gbd-cause-patterns/

33. Murray CJL, Barber RM, Foreman KJ, Ozgoren AA, Abd-Allah F, Abera SF, et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. Lancet. 2015;1990–2013.

34. Whiteford HA, Degenhardt L, Rehm J, Baxter AJ, Ferrari AJ, Erskine HE, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. The Lancet . 2013 Nov 9;382(9904):1575–86.

35. Ferrari A, Norman R, Freedman G, Baxter A, Pirkis J. The Burden Attributable to Mental and Substance Use Disorders as Risk Factors forn Suicide: Findings from the Global Burden of Disease Study 2010. PLoS ONE 9(4) e91936. 2014;

36. Jiang C, Li X, Phillips MR, Xu Y. Matched case-control study of medically serious attempted suicides in rural China. Shanghai Arch psychiatry. 2013 Feb;25(1):22–31.

37. Phillips MR, Shen Q, Liu X, Pritzker S, Streiner D, Conner K, et al. Assessing depressive symptoms in persons who die of suicide in mainland China. J Affect Disord. 2007 Feb;98(1–2):73–82.

38. Yang G-H, Phillips MR, Zhou M-G, Wang L-J, Zhang Y-P, Xu D. Understanding the unique characteristics of suicide in China: national psychological autopsy study. Biomed Environ Sci. 2005 Dec;18(6):379–89.

39. Phillips MR. Rethinking the role of mental illness in suicide. Am J Psychiatry. 2010 Jul;167(7):731–3.

40. Arsenault-Lapierre G, Kim C, Turecki G. Psychiatric diagnoses in 3275 suicides: a meta-analysis. BMC Psychiatry. 2004 Nov 4;4(1):37.

41. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380:2197–223.

42. Vigo D V, Selle V, Baldessarini R. [Enduring pain I. Nosology and epidemiology]. Vertex. 2013 Sep;24(111):345–50.

43. Baldessarini R, Selle V, Vigo D V. [Enduring pain II. Treatment]. Vertex. 2013 Sep;24(111):351–8.

44. Fröhlich C, Jacobi F, Wittchen H-U. DSM-IV pain disorder in the general population. An exploration of the structure and threshold of medically unexplained pain symptoms. Eur Arch Psychiatry Clin Neurosci. 2006 Apr;256(3):187–96.

45. Demyttenaere K, Bruffaerts R, Lee S, Posada-Villa J, Kovess V, Angermeyer MC, et al. Mental disorders among persons with chronic back or neck pain: results from the World Mental Health Surveys. Pain. 2007 Jun;129(3):332–42.

46. Diatchenko L, Nackley AG, Slade GD, Fillingim RB, Maixner W, Edwards RR, et al. Idiopathic pain disorders - Pathways of vulnerability. Pain. 2011 Apr 9;123(3):226–30.

47. Phillips K, Clauw DJ. Central pain mechanisms in chronic pain states--maybe it is all in their head. Best Pract Res Clin Rheumatol. 2011 Apr;25(2):141–54.

48. Giesecke T, Gracely RH, Grant MAB, Nachemson A, Petzke F, Williams DA, et al. Evidence of augmented central pain processing in idiopathic chronic low back pain. Arthritis Rheum. 2004 Feb;50(2):613–23.

49. Tyrer P, Reed GM, Crawford MJ. Classification, assessment, prevalence, and effect of personality disorder. Lancet. 2015 Feb 21;385(9969):717–26.

50. Sansone RA, Sansone LA. Chronic pain syndromes and borderline personality. Innov Clin Neurosci. 2012 Jan;9(1):10–4.

51. World Health Organization (WHO). Mental health action plan 2013-2020. Geneva, Switzerland; 2013.

52. Lawrence D, Hancock KJ, Kisely S. The gap in life expectancy from preventable physical illness in psychiatric patients in Western Australia: retrospective analysis of population based registers. BMJ. 2013 Jan;346:f2539.

53. Fekadu A, Medhin G, Kebede D, Alem A, Cleare AJ, Prince M, et al. Excess mortality in severe mental illness: 10-year population-based cohort study in rural Ethiopia. Br J Psychiatry. 2015 Apr;206(4):289–96.

54. Walker ER, McGee RE, Druss BG. Mortality in Mental Disorders and Global Disease Burden Implications: A Systematic Review and Meta-analysis. JAMA psychiatry. 2015 Feb 11;72(4):334–41.

55. Charlson FJ, Baxter AJ, Dua T, Degenhardt L, Whiteford HA, Vos T. Excess mortality from mental, neurological and substance use disorders in the Global Burden of Disease Study 2010. Epidemiol Psychiatr Sci. 2015 Apr;24(2):121–40.

56. United Nations. The Millennium Development Goals Report. 2015.

57. Institute for Health Metrics and Evaluation. Financing Global Health 2014: Shifts in Funding as the MDG Era Closes. Seattle, WA; 2015.

58. Atun R. Decisive action to end apathy and achieve 25×25 NCD targets. Lancet (London, England). 2014 Aug 2;384(9941):384–5.

59. Eaton J, McCay L, Semrau M, Chatterjee S, Baingana F, Araya R, et al. Scale up of services for mental health in low-income and middle-income countries. Lancet. 2011 Oct 29;378(9802):1592–603.

60. World Health Organization (WHO). Mental Health Action Plan 2013-2020. Geneva, Switzerland; 2013.

61. World Health Organization (WHO). Mental Health Atlas. 2011.

62. World Health Organization (WHO). THE MENTAL HEALTH CONTEXT - Mental Health Policy and Service Guidance Package. 2003.

63. World Health Organization. WHO mental health atlas. Geneva, Switzerland; 2011.

64. PAHO. Strategy and plan of action on mental health. 49th DIRECTING COUNCIL - 61st SESSION OF THE REGIONAL COMMITTEE; 2009, Washington DC

65. United Nations. Resolution adopted by the General Assembly on 27 July 2012. 2012.

66. WHO Department of Health Statistics and Information Systems (HSI). 2015 Global Reference List of 100 Core Health Indicators. 2015; Geneva, Switzerland

67. Whiteford H, Ferrari A, Degenhardt L. Global Burden Of Disease Studies: Implications For Mental And Substance Use Disorders. Health Aff. 2016;35(6):1114–20.

68. Atun R, Vigo D, Thornicroft G. Challenges to estimating the true global burden of mental disorders - Authors' reply. The lancet Psychiatry. Elsevier; 2016 May 1;3(5):403–4.

69. Vigo D, Thornicroft G, Atun R. Estimating the True Global Burden of Mental Illness. Lancet Psychiatry. 2016;3: 171-78.

70. Collins PY, Saxena S. Action on mental health needs global cooperation. Nature. 2016 Apr 7;532(7597):25–7.

71. The Lancet. The health crisis of mental health stigma. Lancet. Elsevier Ltd; 2016;387(10023):1027.

72. Charara R, Forouzanfar M, Naghavi M, Moradi-Lakeh M, Afshin A, Vos T, et al. The Burden of Mental Disorders in the Eastern Mediterranean Region, 1990-2013. PLoS One. Public Library of Science; 2017;12(1):e0169575.

73. Mnookin S, Kleinman A, Evans T, Marquez P, Saxena S, Chisholm D, et al. OUT OF THE SHADOWS: Making mental health a grlobal development priority. Washington DC; 2016.

74. Menil V De, Glassman A. Making Room for Mental Health : Recommendations for

Improving Mental Health Care in Low- and Middle-Income Countries. Center for Global Development. 2016.

75. Pan-American Health Organization. Health Situation in the Americas.

76. Altmetric. Overview of attention for Estimating the true global burden of mental illness article published in The Lancet Psychiatry, February 2016 [Internet]. Available from: https://www.altmetric.com/details/5089133/news

77. Goldner E, Jones W, Vigo D, Dove N, Samji H, Su T, et al. Estimated Prevalence and Distribution of Selected Mental Health and Substance Use Disorders in British Columbia - Preliminary Report. Vancouver; 2017.

78. Cleveland WS. Robust locally weighted regression and smoothing scatterplots. J Am Stat Assoc. 1979;74:829–36.

79. Bukhman G, Kidder A. The PIH Guide to Chronic Care Integration for Endemic Non-Communicable Diseases: Rwanda Edition. Health PI, editor. Boston, MA:; 2011.

80. Beals J, Novins DK, Whitesell NR, Spicer P, Mitchell CM, Manson SM. Prevalence of mental disorders and utilization of mental health services in two American Indian reservation populations: mental health disparities in a national context. Am J Psychiatry. 2005 Sep;162(9):1723–32.

81. Institute for Health Metrics and Evaluation (IHME). Global Burden of Disease Study 2015 (GBD 2015) Results. [Internet]. Seattle, United States. Available from: http://ghdx.healthdata.org/gbd-results-tool.

82. Murray CJL, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C, et al. GBD 2010: a multi-investigator collaboration for global comparative descriptive epidemiology. Lancet. 2012

Dec 15;380(9859):2055–8.

83. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012 Dec 15;380(9859):2163–96.

84. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016 Oct 8;388(10053):1545–602.

85. GBD 2015 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016 Oct 8;388(10053):1603–58.

86. Marmot M. Social determinants of health inequalities. Lancet. 2005;365(9464):1099–104.

87. Lund C, Breen A, Flisher AJ, Kakuma R, Corrigall J, Joska JA, et al. Poverty and common mental disorders in low and middle income countries: A systematic review . Soc Sci Med. Elsevier Ltd; 2010;71(3):517–28.

88. Black DW, Blum N, Pfohl B, Hale N. Suicidal Behavior in Borderline Personality Disorder: Prevalence, Risk Factors, Prediction, and Prevention. J Pers Disord. 2004 Jun;18(3):226–39.

89. Asmundson GJG, Katz J. Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. Depress Anxiety. 2009 Jan;26(10):888–901.

90. Kleinman A. Global mental health: a failure of humanity. Lancet. 2009 Aug 22;374(9690):603–4.

91. Chisholm D, Flisher A, Lund C, Patel V, Saxena S, Thornicroft G, et al. Scale up services for mental disorders: a call for action. Lancet. 2007;370:1241–52.

92. OPS. WHO-AIMS:INFORME REGIONAL SOBRE LOS SISTEMAS DE SALUD MENTAL EN AMÉRICA LATINA y EL CARIBE. Washington; 2013.

93. WHO-AIMS. SISTEMA DE SALUD MENTAL DE CHILE. Santiago de Chile; 2014.

94. Institute of Health Economics. The Cost of Mental Health Services in Canada. 1. Institute of Health Economics. Cost of Mental Health Services in Canada Report June 2010. 2010;(June):50. Available from: http://www.ihe.ca/documents/Cost of Mental Health Services in Canada Report June 2010.pdf. Edmonton, Canada; 2010.

95. Substance Abuse and Mental Health Services Administration. Projections of National Expenditures for Treatment of Mental and Substance Use Disorders, 2010-2020. Rockville; 2014.

96. Murray CJ, Frenk J. A framework for assessing the performance of health systems. Bull World Health Organ. 2000 Jan;78(6):717–31.

97. World Health Organisation. Mental health systems in selected low- and middle-income countries: a WHO-AIMS cross-national analysis. 2009.

98. International Monetary Fund. World Economic Outlook Database [Internet]. 2016 [cited 2017 Jan 1]. Available from: https://www.imf.org/external/pubs/ft/weo/2016/01/weodata/index.aspx

99. Levin C, Chisholm D. Cost-Effectiveness and Affordability of Interventions, Policies, and

Platforms for the Prevention and Treatment of Mental, Neurological, and Substance Use Disorders. Mental, Neurological, and Substance Use Disorders: Disease Control Priorities, Third Edition (Volume 4). 2016.

100. Centre for Economic Performance's Mental Health Policy Group. How Mental Illness Loses Out in the NHS. London; 2012.

101. Department of Health UK. Statistical bulletin : Overall patient experience scores 2012 adult inpatient survey update. London; 2016.

102. Thornicroft G, Chatterji S, Evans-Lacko S, Gruber M, Sampson N, Aguilar-Gaxiola S, et al. Undertreatment of people with major depressive disorder in 21 countries. Br J Psychiatry. 2016 Dec 1;

103. World Health Organization. Mental Health Action Gap. Scaling up care for mental, neurological, and substance use disorders. Geneva, Switzerland; 2008.

104. WHO. The world health report 2001 -Mental Health: New Understanding, New Hope. Geneva, Switzerland; 2001.

105. Patel V, Chisholm D, Dua T, Laxminarayan R, Medina-Mora ME. Mental, Neurological, and Substance Use Disorders. Disease Control Priorities, third edition, volume 4. Washington, DC; 2015.

106. United Nations, Statistical Commission. United Nations Fundamental Principles of Official Statistics Implementation guidelines. 2015.

107. Lund C, Breen A, Flisher AJ, Kakuma R, Corrigall J, Joska JA, et al. Poverty and common mental disorders in low and middle income countries: A systematic review. Soc Sci Med. 2010 Aug;71(3):517–28.

108. Patel V, Kleinman A. Poverty and common mental disorders in developing countries. Bull World Heal Organ. 2003;81:6.

109. Bloom, D.E., Cafiero, E.T., Jané-Llopis, E., Abrahams-Gessel, S., Bloom, L.R., Fathima, S., Feigl, A.B., Gaziano, T., Mowafi, M., Pandya, A., Prettner, K., Rosenberg, L., Seligman, B., Stein, A.Z., & Weinstein C. The Global Economic Burden of Noncommunicable Diseases. Glob Demogr Ageing. 2011;(87).

110. Bukhman G, Mocumbi AO, Horton R. Reframing NCDs and injuries for the poorest billion: A Lancet Commission. Lancet. Elsevier Ltd; 2015;386(10000):1221–2.

111. Allen J, Balfour R, Bell R, Marmot M. Social determinants of mental health. Int Rev Psychiatry. 2014;26(4):392–407.

112. Marmot M, Friel S, Bell R, Houweling TA, Taylor S. Closing the gap in a generation: health equity through action on the social determinants of health. Lancet. 2008;372(9650):1661–9.

113. Cooper S, Lund C, Kakuma R. The measurement of poverty in psychiatric epidemiology in LMICs: Critical review and recommendations. Soc Psychiatry Psychiatr Epidemiol. 2012;47(9):1499–516.

114. Alkire S, Robles G. Multidimensional Poverty Index -2015: Brief Methodological Note and Results. Oxford; 2015.

115. Oxford Poverty & Human Development Initiative. MPI database [Internet]. Available from: http://www.ophi.org.uk/multidimensional-poverty-index/mpi-2015/mpi-data/

116. Nulu S. Neglected chronic disease: The WHO framework on non-communicable diseases and implications for the global poor. Glob Public Health. 2016;1692(March):1–20.

117. Preston SH. The changing relation between mortality and level of economic development. Popul Stud (NY). 1975 Jul;29:231–48.

118. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet. 1997 May 3;349(9061):1269–76.

119. Kwan GF, Mayosi BM, Mocumbi AO, Miranda JJ, Ezzati M, Jain Y, et al. Endemic Cardiovascular Diseases of the Poorest Billion. Circulation. 2016;133:2561-2.

120. Rehkopf DH, Buka SL. The association between suicide and the socio-economic characteristics of geographical areas: a systematic review. Psychol Med. 2005;36(2):145.

121. Vigo D V, Kestel D, Thornicroft G, Atun R. Imbalance between disease burden and government spending on mental health: health system response in the Americas. Prep. 2017;1–15.

122. Patel V, Rahman A, Jacob KS, Hughes M. Effect of maternal mental health on infant growth in low income countries: new evidence from South Asia. BMJ. BMJ Group; 2004 Apr 3;328(7443):820–3.

123. Gelman A, Stern H. The Difference Between “Significant” and “Not Significant” is not Itself Statistically Significant. Am Stat. 2006;60(4):328–31.

124. Gelman A, Hill J, Yajima M. Why We (Usually) Don’t Have to Worry About Multiple Comparisons. J Res Educ Eff. 2012;5(2):189–211.

125. Saville DJ. Multiple Comparison Procedures: The Practical Solution. J Sav Source Am Stat. 1990;44(2):174–80.

126. Rothman KJ, Epidemiology S, Jan N, Rothman K. No Adjustments Are Needed for Multiple Comparisons No Adjustments Are Needed for Multiple Comparisons. 2017;1(1):43–6.

127. Bloom D, Canning D. Realizing the demographic dividend: Is Africa any different. PROGRAM ON THE GLOBAL DEMOGRAPHY OF AGING. 2007.

128. Murray CJE Al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. Lancet. 2015;1990–2013.

129. Thornicroft G. Shunned: Discrimination against People with Mental Illness. Oxford: Oxford University Press; 2006.

130. Chisholm D, Sweeny K, Sheehan P, Rasmussen B, Smit F, Cuijpers P, et al. Scaling-up treatment of depression and anxiety: a global return on investment analysis. The Lancet Psychiatry. 2016 Apr 12;3(5):415–24.

131. Thornicroft G, Tansella M. Components of a modern mental health service: a pragmatic balance of community and hospital care: overview of systematic evidence. Br J Psychiatry. 2004 Oct;185:283–90.

132. Collins PY, Patel V, Joestl SS, March D, Insel TR, Daar AS, et al. Grand challenges in global mental health. Nature. 2011 Jul 6;475(7354):27–30.

133. Becker AE, Kleinman A. Mental health and the global agenda. N Engl J Med. 2013 Jul 4;369(1):66–73.

134. Who. Mental Health a call for action by World Health Ministers. 54th World Health Assembly. Geneva, Switzerland; 2001.

135. World Health Organisation. GAP mental health Global Action Programme. Geneva, Switzerland; 2002.

136. Department of Health. The Mental Health Policy Implementation Guide. London; 2001.

137. Patel V, Collins PY, Copeland J, Kakuma R, Katontoka S, Lamichhane J, et al. The movement for global mental health. Br J Psychiatry. 2011 Feb;198(2):88–90.

138. LSHTM, WHO. Mental Health Inovation Network [Internet]. [cited 2016 Aug 3]. Available from: http://mhinnovation.net/

139. Lauber C, Rössler W. Stigma towards people with mental illness in developing countries in Asia. Int Rev Psychiatry. 2007;19(April):157–78.

140. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. Lancet. 2007;370(9590):878–89.

141. World Bank. Investing in health. Washington; 1993.

142. Kingdon J. Agendas, Alternatives, and Public Policies. Boston: Longman; 2011.

143. Gómez EJ, Atun R. Emergence of multilateral proto-institutions in global health and new approaches to governance: analysis using path dependency and institutional theory. Global Health. 2013;9:18.

144. Farmer P, Kim JY, Kleinman A, Basilico M. Reimagining global health : an introduction. University of California Press; 2013. 478 p.

Appendix 1. Studies from low and lower-middle income countries used as GBD data sources

Major depressive disorder

Country	Study
Africa	
Central African Republic	Vinck P, Pham PN. Association of exposure to violence and potential traumatic events with self-reported physical and mental health status in the Central African Republic. JAMA. 2010; 304(5): 544-52.
South Sudan	Ayazi T, Lien L, Eide AH, Ruom MM, Hauff E. What are the risk factors for the comorbidity of posttraumatic stress disorder and depression in a war-affected population? A cross-sectional community study in South Sudan. BMC Psychiatry. 2012; 12: 175.
	Roberts B, Damundu EY, Lomoro O, Sondorp E. Post-conflict mental health needs: a cross-sectional survey of trauma, depression and associated factors in Juba, Southern Sudan. BMC Psychiatry. 2009; 7.
Sudan	Shaaban KMA, Baashar TA. A community study of depression in adolescent girls: prevalence and its relation to age. Med Princ Pract. 2003; 12(4): 256-9.
The Gambia	Coleman R, Morison L, Paine K, Powell RA, Walraven G. Women's reproductive health and depression: a community survey in the Gambia, West Africa. Soc Psychiatry Psychiatr Epidemiol. 2006; 41(9): 720-7.
Uganda	Kinyanda E, Kizza R, Abbo C, Ndyanabangi S, Levin J. Prevalence and risk factors of depression in childhood and adolescence as seen in four districts of North-Eastern Uganda. BMC Int Health Hum Rights. 2013; 13: 19.
	Bolton P, Wilk CM, Ndogoni L. Assessment of depression prevalence in rural Uganda using symptom and function criteria. Soc Psychiatry Psychiatr Epidemiol. 2004; 39(6): 442-7.
	Ovuga E, Boardman J, Wasserman D. The prevalence of depression in two districts of Uganda. Soc Psychiatry Psychiatr Epidemiol. 2005; 40(6): 439-45.
	Vinck P, Pham PN, Stover E, Weinstein HM. Exposure to war crimes and implications for peace building in northern Uganda. JAMA. 2007; 298(5): 543-54.
	Mugisha J, Muyinda H, Malamba S, Kinyanda E. Major depressive disorder seven years after the conflict in northern Uganda: burden, risk factors and impact on outcomes (The Wayo-Nero Study). BMC Psychiatry. 2015; 15: 48.
Rwanda	Bolton P, Neugebauer R, Ndogoni L. Prevalence of depression in rural Rwanda based on symptom and functional criteria. J Nerv Ment Dis. 2002; 190(9): 631-7.
Ethiopia	Kebede D, Alem A. Major mental disorders in Addis Ababa, Ethiopia. II. Affective disorders. Acta Psychiatr Scand Suppl. 1999; 397: 18-23.
	Hailemariam S, Tessema F, Asefa M, Tadesse H, Tenkolu G. The prevalence of depression and associated factors in Ethiopia: findings from the National Health Survey. Int J Ment Health Syst. 2012; 6(1): 23.
	Ashenafi Y, Kebede D, Desta M, Alem A. Prevalence of mental and behavioural disorders in Ethiopian children. East Afr Med J. 2001; 78(6): 308-11.
	Mogga S, Prince M, Alem A, Kebede D, Stewart R, Glozier N, Hotopf M. Outcome of major depression in Ethiopia: population-based study. Br J Psychiatry. 2006; 189: 241-6.
Nigeria	Amoran O, Lawoyin T, Lasebikan V. Prevalence of depression among adults in Oyo State, Nigeria: a comparative study of rural and urban communities. Aust J Rural Health. 2007; 15(3): 211-5.
	Gureje O, Kola L, Afolabi E. Epidemiology of major depressive disorder in elderly Nigerians in the Ibadan Study of Ageing: a community-based survey. Lancet. 2007; 370(9591): 957-64.
	Uwakwe R. The pattern of psychiatric disorders among the aged in a selected community in Nigeria. Int J Geriatr Psychiatry. 2000; 15(4): 355-62.

	Gureje O, Lasebikan VO, Kola L, Makanjuola VA. Lifetime and 12-month prevalence of mental disorders in the Nigerian Survey of Mental Health and Well-Being. Br J Psychiatry. 2006; 188(5): 465-71.
	Adewuya AO, Ola BA, Aloba OO, Mapayi BM, Oginni OO. Depression amongst Nigerian university students. Prevalence and sociodemographic correlates. Soc Psychiatry Psychiatr Epidemiol. 2006; 41(8): 674-8.
Lesotho	Hollifield M, Katon W, Spain D, Pule L. Anxiety and depression in a village in Lesotho, Africa: a comparison with the United States. Br J Psychiatry. 1990; 156: 343-50.
Liberia	Vinck P, Pham PN. Association of exposure to intimate-partner physical violence and potentially traumatic war-related events with mental health in Liberia. Soc Sci Med. 2013; 77: 41-9.
Americas	
Honduras	Kohn R, Levav I, Garcia ID, Machuca ME, Tamashiro R. Prevalence, risk factors and aging vulnerability for psychopathology following a natural disaster in a developing country. Int J Geriatr Psychiatry. 2005; 20(9): 835-41.
Asia	
Nepal	Subedi S, Tausig M, Subedi J, Broughton CL, Williams-Blangero S. Mental illness and disability among elders in developing countries: the case of Nepal. J Aging Health. 2004; 16(1): 71-87.
	Luitel NP, Jordans MJD, Sapkota RP, Tol WA, Kohrt BA, Thapa SB, Komproe IH, Sharma B. Conflict and mental health: a cross-sectional epidemiological study in Nepal. Soc Psychiatry Psychiatr Epidemiol. 2013; 48(2): 183-93.
	Kohrt BA, Hruschka DJ, Worthman CM, Kunz RD, Baldwin JL, Upadhaya N, Acharya NR, Koirala S, Thapa SB, Tol WA, Jordans MJD, Robkin N, Sharma VD, Nepal MK. Political violence and mental health in Nepal: prospective study. Br J Psychiatry. 2012; 201(4): 268-75.
Afghanistan	Scholte WF, Olff M, Ventevogel P, de Vries G-J, Jansveld E, Cardozo BL, Crawford CAG. Mental health symptoms following war and repression in eastern Afghanistan. JAMA. 2004; 292(5): 585-93.
	Cardozo BL, Bilukha OO, Gotway CA, Wolfe MI, Gerber ML, Anderson M. Report from the CDC: mental health of women in postwar Afghanistan. J Womens Health (Larchmt). 2005; 14(4): 285-93.
Pakistan	Mumford DB, Minhas FA, Akhtar I, Akhter S, Mubbashar MH. Stress and psychiatric disorder in urban Rawalpindi. Community survey. Br J Psychiatry. 2000; 557-62.
	Mumford DB, Nazir M, Jilani FU, Baig IY. Stress and psychiatric disorder in the Hindu Kush: a community survey of mountain villages in Chitral, Pakistan. Br J Psychiatry. 1996; 168(3): 299-307.
	Mumford DB, Saeed K, Ahmad I, Latif S, Mubbashar MH. Stress and psychiatric disorder in rural Punjab. A community survey. Br J Psychiatry. 1997; 473-8.
	Nisar N, Billoo N, Gadit AA. Prevalence of depression and the associated risks factors among adult women in a fishing community. J Pak Med Assoc. 2004; 54(10): 519-25.
Palestine	Madianos MG, Sarhan AL, Koukia E. Major depression across West Bank: a cross-sectional general population study. Int J Soc Psychiatry. 2012; 58(3): 315-22.
Vietnam	Hanoi School of Public Health, Ministry of Health (Vietnam), School of Population Health, University of Queensland (Australia). Vietnam Burden of Disease and Injury Study 2008.
Timor-Leste	Silove D, Bateman CR, Brooks RT, Fonseca CAZ, Steel Z, Rodger J, Soosay I, Fox G, Patel V, Bauman A. Estimating clinically relevant mental disorders in a rural and an urban setting in postconflict Timor Leste. Arch Gen Psychiatry. 2008; 65(10): 1205-12.
Indian states	
Jharkhand, Urban	Sarkar S, Sinha VK, Praharaj SK. Depressive disorders in school children of suburban India: an epidemiological study. Soc Psychiatry Psychiatr Epidemiol. 2012; 47(5): 783-8.
Karnataka, Urban	Srinath S, Girimaji SC, Gururaj G, Seshadri S, Subbakrishna DK, Bhola P, Kumar N. Epidemiological study of child and adolescent psychiatric disorders in urban and rural areas of Bangalore, India. Indian J Med Res. 2005; 122(1): 67-79.

Maharashtra, Urban	Patil RN, Nagaonkar SN, Shah NB, Bhat TS. A Cross-sectional Study of Common Psychiatric Morbidity in Children Aged 5 to 14 Years in an Urban Slum. J Family Med Prim Care. 2013; 2(2): 164-8.
	Silvanus V, Subramanian P. Epidemiological study of mental morbidity in an urban slum community in India for the development of a community mental health programme. Nepal Med Coll J. 2012; 14(1): 13-7.
Punjab, Urban	Bansal PD, Barman R. Psychopathology of school going children in the age group of 10-15 years. Int J Appl Basic Med Res. 2011; 1(1): 43-7.
Tamil Nadu, Urban	Poongothai S, Pradeepa R, Ganesan A, Mohan V. Prevalence of depression in a large urban South Indian population - the Chennai Urban Rural Epidemiology Study (CURES-70). PLoS One. 2009; 4(9): e7185.
	Rajkumar AP, Thangadurai P, Senthilkumar P, Gayathri K, Prince M, Jacob KS. Nature, prevalence and factors associated with depression among the elderly in a rural south Indian community. Int Psychogeriatr. 2009; 21(2): 372-8.
	Kessler RC, Birnbaum HG, Shahly V, Bromet E, Hwang I, McLaughlin KA, Sampson N, Andrade LH, de Girolamo G, Demyttenaere K, Haro JM, Karam AN, Kostyuchenko S, Kovess V, Lara C, Levinson D, Matschinger H, Nakane Y, Browne MO, Ormel J, Posada-Villa J, Sagar R, Stein DJ. Age differences in the prevalence and co-morbidity of DSM-IV major depressive episodes: results from the WHO World Mental Health Survey Initiative. Depress Anxiety. 2010; 27(4): 351-64.
Uttar Pradesh, Urban	Ahmad A, Khalique N, Khan Z, Amir A. Prevalence of psychosocial problems among school going male adolescents. Indian J Community Med. 2007; 32(3): 219-21.
Karnataka, Rural	Sathyanarayana Rao TS, Darshan MS, Tandon A, Raman R, Karthik KN, Saraswathi N, Das K, Harsha GT, Krishna VST, Ashok NC. Suttur study: An epidemiological study of psychiatric disorders in south Indian rural population. Indian J Psychiatry. 2014; 56(3): 238-45.

Dysthymia

Country	Study
Africa	
Ethiopia	Kebede D, Alem A. Major mental disorders in Addis Ababa, Ethiopia. II. Affective disorders. Acta Psychiatr Scand Suppl. 1999; 397: 18-23.
	Ashenafi Y, Kebede D, Desta M, Alem A. Prevalence of mental and behavioural disorders in Ethiopian children. East Afr Med J. 2001; 78(6): 308-11.
Nigeria	Gureje O, Lasebikan VO, Kola L, Makanjuola VA. Lifetime and 12-month prevalence of mental disorders in the Nigerian Survey of Mental Health and Well-Being. Br J Psychiatry. 2006; 188(5): 465-71.
Indian States	
Jharkhand, Urban	Sarkar S, Sinha VK, Praharaj SK. Depressive disorders in school children of suburban India: an epidemiological study. Soc Psychiatry Psychiatr Epidemiol. 2012; 47(5): 783-8.
Maharashtra, Urban	Silvanus V, Subramanian P. Epidemiological study of mental morbidity in an urban slum community in India for the development of a community mental health programme. Nepal Med Coll J. 2012; 14(1): 13-7.
Karnataka, Rural	Sathyanarayana Rao TS, Darshan MS, Tandon A, Raman R, Karthik KN, Saraswathi N, Das K, Harsha GT, Krishna VST, Ashok NC. Suttur study: An epidemiological study of psychiatric disorders in south Indian rural population. Indian J Psychiatry. 2014; 56(3): 238-45.

Self-harm and suicide

Country	Study
Africa	
Mozambique	Macro International, Inc, National Institute of Statistics (INE) (Mozambique). Mozambique Demographic and Health Survey 2003. Calverton, United States: Macro International, Inc.
Sudan	Central Bureau of Statistics (Sudan), Federal Ministry of Health (Sudan), Government of Sudan, Ministry of Health (South Sudan), Southern Sudan Centre for Census, Statistics and Evaluation. Sudan - South Multiple Indicator Cluster Survey 2010. New York, United States: United Nations Children's Fund (UNICEF), 2015.
Asia	
Vietnam	Hanoi School of Public Health, The Alliance for Safe Children (TASC), United Nations Children's Fund (UNICEF). Vietnam Multi-Center Injury Survey 2001.
Vietnam	Nguyen TV, Dalman C, Le TC, Nguyen TV, Tran NV, Allebeck P. Suicide attempt in a rural area of Vietnam: Incidence, methods used and access to mental health care. Int J Ment Health Syst. 2010; 4(1): 3.
India	International Institute for Population Sciences (India), World Health Organization (WHO). India WHO Study on Global Ageing and Adult Health 2007. Geneva, Switzerland: World Health Organization (WHO), 2007.

Anxiety disorders

Country	Study
Africa	
Ethiopia	Awas M KD, Alem A. Major mental disorders in Butajira, southern Ethiopia. Acta Psychiatr Scand Suppl. 1999; 56-64.
	Ashenafi Y, Kebede D, Desta M, Alem A. Prevalence of mental and behavioural disorders in Ethiopian children. East Afr Med J. 2001; 78(6): 308-11.
Lesotho	Hollifield M, Katon W, Spain D, Pule L. Anxiety and depression in a village in Lesotho, Africa: a comparison with the United States. Br J Psychiatry. 1990; 156: 343-50.
Kenya (Nairobi)	Seedat S, Nyamai C, Njenga F, Vythilingum B, Stein DJ. Trauma exposure and post-traumatic stress symptoms in urban African schools Survey in CapeTown and Nairobi. Br J Psychiatry. 2004; 184(2): 169-75.
Nigeria	Adewuya AO, Ola BA, Adewumi TA. The 12-month prevalence of DSM-IV anxiety disorders among Nigerian secondary school adolescents aged 13-18 years. J Adolesc. 2007; 30(6): 1071-6.
	World Health Organization (WHO). WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders. Cambridge, United Kingdom: Cambridge University Press, 2008.
Rwanda	Pham PN, Weinstein HM, Longman T. Trauma and PTSD symptoms in Rwanda: implications for attitudes toward justice and reconciliation. JAMA. 2004; 292(5): 602-12.
Uganda	Orley J, Wing JK. Psychiatric disorders in two african villages. Arch Gen Psychiatry. 1979; 36(5): 513-20.
	Abbo C, Kinyanda E, Kizza RB, Levin J, Ndyanabangi S, Stein DJ. Prevalence, comorbidity and predictors of anxiety disorders in children and adolescents in rural north-eastern Uganda. Child Adolesc Psychiatry Ment Health. 2013; 21.
Zimbabwe	Abas MA BJ. Depression and anxiety among women in an urban setting in Zimbabwe. Psychol Med. 1997; 27(1): 59-71.
Asia	
Vietnam	Hanoi School of Public Health, Ministry of Health (Vietnam), School of Population Health, University of Queensland (Australia). Vietnam Burden of Disease and Injury Study 2008.
Afghanistan	Ventevogel P, Vries GD, Scholte WF, Shinwari NR, Faiz H, Nassery R, Brink W van den, Olff M. Properties of the Hopkins Symptom Checklist-25 (HSCL-25) and the Self-Reporting Questionnaire (SRQ-20) as screening instruments used in primary care in Afghanistan. Soc Psychiatry Psychiatr Epidemiol. 2007; 42(4): 328-35.
Bangladesh	Monawar Hosain GM, Chatterjee N, Ara N, Islam T. Prevalence, pattern and determinants of mental disorders in rural Bangladesh. Public Health. 2007; 121(1): 18-24.
	Mullick MSI, Goodman R. The prevalence of psychiatric disorders among 5-10 year olds in rural, urban and slum areas in Bangladesh: an exploratory study. Soc Psychiatry Psychiatr Epidemiol. 2005; 40(8): 663-71.
	Islam MM, Ali M, Ferroni P, Underwood P, Alam MF. Prevalence of psychiatric disorders in an urban community in Bangladesh. Gen Hosp Psychiatry. 2003; 25(5): 353-7.
Indian States	
Goa, Urban	Pillai A, Patel V, Cardozo P, Goodman R, Weiss HA, Andrew G. Non-traditional lifestyles and prevalence of mental disorders in adolescents in Goa, India. Br J Psychiatry. 2008; 192(1): 45-51.
Haryana, Urban	Joshi K, Kumar R, Avasthi A. Morbidity profile and its relationship with disability and psychological distress among elderly people in Northern India. Int J Epidemiol. 2003; 32(6): 978-87.
Tamil Nadu, Urban	Premarajan KC, Danabalan M, Chandrasekar R, Srinivasa DK. Prevalence of psychiatry morbidity in an urban community of Pondicherry. Indian J Psychiatry. 1993; 35(2): 99-102.

Tamil Nadu, Urban	World Health Organization (WHO). WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders. Cambridge, United Kingdom: Cambridge University Press, 2008.
Goa, Rural	Pillai A, Patel V, Cardozo P, Goodman R, Weiss HA, Andrew G. Non-traditional lifestyles and prevalence of mental disorders in adolescents in Goa, India. Br J Psychiatry. 2008; 192(1): 45-51.

Schizophrenia

Africa	
Botswana	Ben-Tovim DI, Cushnie JM. The prevalence of schizophrenia in a remote area of Botswana. Br J Psychiatry. 1986; 576-80.
Tanzania	Bondestam S, Garssen J, Abdulwakil AI. Prevalence and treatment of mental disorders and epilepsy in Zanzibar. Acta Psychiatr Scand. 1990; 81(4): 327-31.
Ethiopia	Awas M KD, Alem A. Major mental disorders in Butajira, southern Ethiopia. Acta Psychiatr Scand Suppl. 1999; 56-64.
	Kebede D, Alem A. Major mental disorders in Addis Ababa, Ethiopia. I. Schizophrenia, schizoaffective and cognitive disorders. Acta Psychiatr Scand Suppl. 1999; 11-7.
Asia	
Timor-Leste	Silove D, Bateman CR, Brooks RT, Fonseca CAZ, Steel Z, Rodger J, Soosay I, Fox G, Patel V, Bauman A. Estimating clinically relevant mental disorders in a rural and an urban setting in postconflict Timor Leste. Arch Gen Psychiatry. 2008; 65(10): 1205-12.
India	Premarajan KC, Danabalan M, Chandrasekar R, Srinivasa DK. Prevalence of psychiatry morbidity in an urban community of Pondicherry. Indian J Psychiatry. 1993; 35(2): 99-102.
Maharashtra, Urban	Seby K, Chaudhury S, Chakraborty R. Prevalence of psychiatric and physical morbidity in an urban geriatric population. Indian J Psychiatry. 2011; 53(2): 121-7.
Punjab, Urban	Sachdeva JS, Singh S, Sidhu BS, Goyal RK, Singh J. An epidemiological study of psychiatric disorders in rural Faridkot (Punjab). Indian J Psychiatry. 1986; 28(4): 317-23.
Tamil Nadu, Urban	Padmavathi R, Rajkumar S, Kumar N, Manoharan A, Kamath S. Prevalence of schizophrenia in an urban community in madras. Indian J Psychiatry. 1988; 30(3): 233-9.
Kerala, Rural	Shaji S, Verghese A, Promodu K, George B, Shibu VP. Prevalence of priority psychiatric disorders in a rural area in kerala. Indian J Psychiatry. 1995; 37(2): 91-6.
Tamil Nadu, Rural	Mehta P, Joseph A, Verghese A. An epidemiologic study of psychiatric disorders in a rural area in Tamilnadu. Indian J Psychiatry. 1985; 27(2): 153-8.

Bipolar disorder

Africa	
Ethiopia	Kebede D, Alem A. Major mental disorders in Addis Ababa, Ethiopia. II. Affective disorders. Acta Psychiatr Scand Suppl. 1999; 397: 18-23.
Asia	
Timor-Leste	Silove D, Bateman CR, Brooks RT, Fonseca CAZ, Steel Z, Rodger J, Soosay I, Fox G, Patel V, Bauman A. Estimating clinically relevant mental disorders in a rural and an urban setting in postconflict Timor Leste. Arch Gen Psychiatry. 2008; 65(10): 1205-12.
Indian States	
Tamil Nadu, Urban	Merikangas KR, Jin R, He J-P, Kessler RC, Lee S, Sampson NA, Viana MC, Andrade LH, Hu C, Karam EG, Ladea M, Medina-Mora ME, Ono Y, Posada-Villa J, Sagar R, Wells JE, Zarkov Z. Prevalence and correlates of bipolar spectrum disorder in the World Mental Health Survey Initiative. Arch Gen Psychiatry. 2011; 68(3): 241-51.
Karnataka, Rural	Sathyanarayana Rao TS, Darshan MS, Tandon A, Raman R, Karthik KN, Saraswathi N, Das K, Harsha GT, Krishna VST, Ashok NC. Suttur study: An epidemiological study of psychiatric disorders in south Indian rural population. Indian J Psychiatry. 2014; 56(3): 238-45.

Substance, alcohol use, and eating disorders

Alcohol use disorders

Country	Study
Africa	
Nigeria	World Health Organization (WHO). Mental Illness in General Health Care: An International Study. Geneva, Switzerland: World Health Organization (WHO), 1995.
Asia	
Vietnam	Giang KB, Spak F, Dzung TV, Allebeck P. The use of audit to assess level of alcohol problems in rural Vietnam. Alcohol Alcohol. 2005; 40(6): 578-83.
Indian States	
Chhattisgarh, Urban	Ghulam R, Rahman I, Naqvi S, Gupta SR. An epidemiological study of drug abuse in urban population of madhya pradesh. Indian J Psychiatry. 1996; 38(3): 160-5.
Goa, Urban	Alcohol Research Group, Public Health Institute, Sangath. India - Goa Alcohol Use Study 2004-2008.
Goa, Urban	Sharma S, Singh MM. Prevalence of mental disorders: An epidemiological study in Goa. Indian J Psychiatry. 2001; 43(2): 118-26.
Karnataka, Urban	World Health Organization (WHO). Mental Illness in General Health Care: An International Study. Geneva, Switzerland: World Health Organization (WHO), 1995.
Maharashtra, Urban	Seby K, Chaudhury S, Chakraborty R. Prevalence of psychiatric and physical morbidity in an urban geriatric population. Indian J Psychiatry. 2011; 53(2): 121-7.
Punjab, Urban	Chavan BS, Arun P, Bhargava R, Singh GP. Prevalence of alcohol and drug dependence in rural and slum population of Chandigarh: A community survey. Indian J Psychiatry. 2007; 49(1): 44-8.
West Bengal, Urban	Ghosh S, Samanta A, Mukherjee S. Patterns of alcohol consumption among male adults at a slum in Kolkata, India. J Health Popul Nutr. 2012; 30(1): 73-81.
Tamil Nadu, Rural	Kumar SG, Premarajan KC, Subitha L, Suguna E, Vinayagamoorthy, Kumar V. Prevalence and Pattern of Alcohol Consumption using Alcohol Use Disorders Identification Test (AUDIT) in Rural Tamil Nadu, India. J Clin Diagn Res. 2013; 7(8): 1637-9.

Substance use disorders

Country	Study
Africa	
Zimbabwe	Acuda SW, Eide AH. Epidemiological study of drug use in urban and rural secondary schools in Zimbabwe. Cent Afr J Med. 1994; 40(8): 207-12.
Tanzania	World Health Organization (WHO). WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders. Cambridge, United Kingdom: Cambridge University Press, 2008.
Zambia	World Health Organization (WHO). WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders. Cambridge, United Kingdom: Cambridge University Press, 2008.
Burkina Faso	National Center for Scientific and Technological Research (Burkina Faso). Burkina Faso School Health Survey 2006.
Nigeria	World Health Organization (WHO). WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders. Cambridge, United Kingdom: Cambridge University Press, 2008.

	Oshodi OY, Aina OF, Onajole AT. Substance use among secondary school students in an urban setting in Nigeria: prevalence and associated factors. Afr J Psychiatry (Johannesbg). 2010; 13(1): 52-7.
Togo	United Nations Office on Drugs and Crime (UNODC). Togo - LomE Consumption of Drugs in Secondary Schools Study 2007.
Kisumu (Kenya)	Some ES. Misuse of drugs: perceptions of household heads in Kisumu district, Kenya. East Afr Med J. 1994; 71(2): 93-7.
Asia	
Laos	National Drug and Alcohol Research Centre, University of New South Wales, United Nations Office on Drugs and Crime (UNODC). Laos Analysis of, and Proposed Methodology for, Measuring the Socioeconomic Impact of Drugs, Crime, and Corruption 2008.
Indonesia	National Narcotics Board (Indonesia), University of Indonesia. Indonesia National Survey on Drug Abuse and Illicit Drugs 2005.
Vietnam	United Nations Office on Drugs and Crime (UNODC). World Drug Report 2008. Vienna, Austria: United Nations Office on Drugs and Crime (UNODC), 2008.
Afghanistan	Cottler L, Ruktanonchai C, Ghani MA, Gold M, Martin D. The Prevalence of Drug and Alcohol Use in Urban Afghanistan: Data from the Afghanistan National Urban Drug Use Study (ANUDUS). Lancet Glob Health. 2014; 2(10): e592-600.
Pakistan	Mufti KA, Said S, Farooq S, Haroon A, Nazeer A, Naeem S, Hussain I. Five year follow up of 100 heroin addicts in Peshawar. J Ayub Med Coll Abbottabad. 2004; 16(3): 5-9.
	Ministry of Narcotics Control (Pakistan), United Nations Office on Drugs and Crime (UNODC). Pakistan National Drug Abuse Assessment Study 2006-2007.
	Government of Pakistan, Pakistan Bureau of Statistics, United Nations Office on Drugs and Crime (UNODC). Drug Use in Pakistan 2013. Vienna, Austria: United Nations Office on Drugs and Crime (UNODC).
Indian States	
Chhattisgarh, Urban	Ghulam R, Rahman I, Naqvi S, Gupta SR. An epidemiological study of drug abuse in urban population of Madhya Pradesh. Indian J Psychiatry. 1996; 38(3): 160-5.
Delhi, Urban	Mohan D, Chopra A, Sethi H. Incidence estimates of substance use disorders in a cohort from Delhi, India. Indian J Med Res. 2002; 128-35.
Manipur	Ningombam S, Hutin Y, Murhekar MV. Prevalence and pattern of substance use among the higher secondary school students of Imphal, Manipur, India. Natl Med J India. 2011; 24(1): 11-5.
Punjab, Urban	Chavan BS, Arun P, Bhargava R, Singh GP. Prevalence of alcohol and drug dependence in rural and slum population of Chandigarh: A community survey. Indian J Psychiatry. 2007; 49(1): 44-8.
Americas	
Haiti	Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Haiti Evaluation of Progress in Drug Control 2005-2006. Washington, D.C., United States: Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS), 2008.
Bolivia	Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Bolivia Evaluation of Progress in Drug Control 2005-2006. Washington, D.C., United States: Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS), 2008.
Guatemala	Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Guatemala Evaluation of Progress in Drug Control 2005-2006. Washington, D.C., United States: Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS), 2008.

Nicaragua	Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Nicaragua Evaluation of Progress in Drug Control 2005-2006. Washington, D.C., United States: Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS), 2008.
Honduras	Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Honduras Evaluation of Progress in Drug Control 2005-2006. Washington, D.C., United States: Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS), 2008.
El Salvador	Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). El Salvador Evaluation of Progress in Drug Control 2005-2006. Washington, D.C., United States: Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS), 2008.
Oceania	
Samoa	Odden HL. Alcohol, tobacco, marijuana and hallucinogen use in Samoan adolescents. Drug Alcohol Rev. 2012; 31(1): 47-55.

Eating Disorders

Country	Study
Tanzania	Eddy KT, Hennessey M, Thompson-Brenner H. Eating pathology in East African women: the role of media exposure and globalization. J Nerv Ment Dis. 2007; 195(3): 196-202.

Childhood onset disorders

Conduct disorders

Country	Study
Africa	
Ethiopia	Ashenafi Y, Kebede D, Desta M, Alem A. Prevalence of mental and behavioural disorders in Ethiopian children. East Afr Med J. 2001; 78(6): 308-11.
Nigeria	Abiodun OA. Emotional illness in a paediatric population in Nigeria. East Afr Med J. 1992; 69(10): 557-9.
Asia	
Bangladesh	Mullick MSI, Goodman R. The prevalence of psychiatric disorders among 5-10 year olds in rural, urban and slum areas in Bangladesh: an exploratory study. Soc Psychiatry Psychiatr Epidemiol. 2005; 40(8): 663-71.
Indian States	
Goa	Pillai A, Patel V, Cardozo P, Goodman R, Weiss HA, Andrew G. Non-traditional lifestyles and prevalence of mental disorders in adolescents in Goa, India. Br J Psychiatry. 2008; 192(1): 45-51.
Uttar Pradesh	Ahmad A, Khalique N, Khan Z, Amir A. Prevalence of psychosocial problems among school going male adolescents. Indian J Community Med. 2007; 32(3): 219-21.
Karnataka, Urban	Srinath S, Girimaji SC, Gururaj G, Seshadri S, Subbakrishna DK, Bhola P, Kumar N. Epidemiological study of child and adolescent psychiatric disorders in urban and rural areas of Bangalore, India. Indian J Med Res. 2005; 122(1): 67-79.
Maharashtra, Urban	Patil RN, Nagaonkar SN, Shah NB, Bhat TS. A Cross-sectional Study of Common Psychiatric Morbidity in Children Aged 5 to 14 Years in an Urban Slum. J Family Med Prim Care. 2013; 2(2): 164-8.
Jharkhand, Rural	Sarkhel S, Sinha VK, Arora M, Desarkar P. Prevalence of conduct disorder in schoolchildren of Kanke. Indian J Psychiatry. 2006; 48(3): 159-64.
Karnataka, Rural	Sathyanarayana Rao TS, Darshan MS, Tandon A, Raman R, Karthik KN, Saraswathi N, Das K, Harsha GT, Krishna VST, Ashok NC. Suttur study: An epidemiological study of psychiatric disorders in south Indian rural population. Indian J Psychiatry. 2014; 56(3): 238-45.
Kerala, Rural	Hackett R, Hackett, Latha, Bhakta, Preeta, Gowers, Simon. The Prevalence and Associations of Psychiatric Disorder in Children in Kerala, South India. J Child Psychol Psychiatry. 1999; 40(5): 801-7.

Attention Deficit Hyperactivity Disorder

Country	Study
Africa	
Ethiopia	Ashenafi Y, Kebede D, Desta M, Alem A. Prevalence of mental and behavioural disorders in Ethiopian children. East Afr Med J. 2001; 78(6): 308-11.
Asia	

Bangladesh	Mullick MSI, Goodman R. The prevalence of psychiatric disorders among 5-10 year olds in rural, urban and slum areas in Bangladesh: an exploratory study. Soc Psychiatry Psychiatr Epidemiol. 2005; 40(8): 663-71.
Goa, Urban	Pillai A, Patel V, Cardozo P, Goodman R, Weiss HA, Andrew G. Non-traditional lifestyles and prevalence of mental disorders in adolescents in Goa, India. Br J Psychiatry. 2008; 192(1): 45-51.
Karnataka, Urban	Srinath S, Girimaji SC, Gururaj G, Seshadri S, Subbakrishna DK, Bhola P, Kumar N. Epidemiological study of child and adolescent psychiatric disorders in urban and rural areas of Bangalore, India. Indian J Med Res. 2005; 122(1): 67-79.
Maharashtra, Urban	Patil RN, Nagaonkar SN, Shah NB, Bhat TS. A Cross-sectional Study of Common Psychiatric Morbidity in Children Aged 5 to 14 Years in an Urban Slum. J Family Med Prim Care. 2013; 2(2): 164-8.
Maharashtra, Urban	Suvarna BS, Kamath A. Prevalence of attention deficit disorder among preschool age children. Nepal Med Coll J. 2009; 11(1): 1-4.
Tamil Nadu, Urban	Deivasigamani TR. Psychiatric morbidity in primary school children - an epidemiological study. Indian J Psychiatry. 1990; 32(3): 235-40.
Karnataka, Rural	Sathyanarayana Rao TS, Darshan MS, Tandon A, Raman R, Karthik KN, Saraswathi N, Das K, Harsha GT, Krishna VST, Ashok NC. Suttur study: An epidemiological study of psychiatric disorders in south Indian rural population. Indian J Psychiatry. 2014; 56(3): 238-45.
Kerala, Rural	Hackett R, Hackett, Latha, Bhakta, Preeta, Gowers, Simon. The Prevalence and Associations of Psychiatric Disorder in Children in Kerala, South India. J Child Psychol Psychiatry. 1999; 40(5): 801-7.
The Six Minor Territories, Urban	Malhotra S, Kohli A, Arun P. Prevalence of psychiatric disorders in school children in Chandigarh, India. Indian J Med Res. 2002; 116: 21-8.

Autism

Country	Study
Indonesia	Wignyosumarto S, Mukhlas M, Shirataki S. Epidemiological and clinical study of autistic children in Yogyakarta, Indonesia. Kobe J Med Sci. 1992; 38(1): 1-19.

Intellectual disability

Country	Study
Africa	
Kenya	Mung'ala-Odera V, Meehan R, Njuguna P, Mturi N, Alcock KJ, Newton CRJC. Prevalence and risk factors of neurological disability and impairment in children living in rural Kenya. Int J Epidemiol. 2006; 35(3): 683-8.
Zambia	Stein Z, Belmont L, Durkin M. Mild mental retardation and severe mental retardation compared: experiences in eight less developed countries. Ups J Med Sci Suppl. 1987; 44: 89-96.

Asia	
India	Anita, Gaur DR, Vohra AK, Subhash S, Khurana H. Prevalence Of Psychiatric Morbidity Among 6 To 14 Years Old Children. Indian J Community Med. 2003; 28: 133-7.
	Stein Z, Belmont L, Durkin M. Mild mental retardation and severe mental retardation compared: experiences in eight less developed countries. Ups J Med Sci Suppl. 1987; 44: 89-96.
	Srinath S, Girimaji SC, Gururaj G, Seshadri S, Subbakrishna DK, Bhola P, Kumar N. Epidemiological study of child and adolescent psychiatric disorders in urban and rural areas of Bangalore, India. Indian J Med Res. 2005; 122(1): 67-79.
	Dave U, Shetty N, Mehta L. A community genetics approach to population screening in India for mental retardation - a model for developing countries. Ann Hum Biol. 2005; 32(2): 195-203.
Pakistan	Durkin MS, Hasan ZM, Hasan KZ. Prevalence and correlates of mental retardation among children in Karachi, Pakistan. Am J Epidemiol. 1998; 147(3): 281-8.
	Hasan Z, Aziz H. Report on a population survey of mental retardation in Pakistan. Int J Ment Health. 1981; 10(1): 23-7.
	Stein Z, Belmont L, Durkin M. Mild mental retardation and severe mental retardation compared: experiences in eight less developed countries. Ups J Med Sci Suppl. 1987; 44: 89-96.
	Gustavson K-H. Prevalence and aetiology of congenital birth defects, infant mortality and mental retardation in Lahore, Pakistan: a prospective cohort study. Acta Paediatr. 2005; 94(6): 769-74.
Sri Lanka	Stein Z, Belmont L, Durkin M. Mild mental retardation and severe mental retardation compared: experiences in eight less developed countries. Ups J Med Sci Suppl. 1987; 44: 89-96.
Philippines	Stein Z, Belmont L, Durkin M. Mild mental retardation and severe mental retardation compared: experiences in eight less developed countries. Ups J Med Sci Suppl. 1987; 44: 89-96.

Neuropsychiatric disorders

Alzheimer

Country	Study
Africa	
Central African Republic	Guerchet M, M'belesso P, Mouanga AM, Bandzouzi B, Tabo A, Houinato DS, ParaÃ¯so MN, Cowppli-Bony P, Nubukpo P, Aboyans V, ClEment J-P, Dartigues J-F, Preux P-M. Prevalence of dementia in elderly living in two cities of Central Africa: the EDAC survey. Dement Geriatr Cogn Disord. 2010; 30(3): 261-8.
Central African Republic	Mbelesso P, Tabo A, Guerchet M, Mouanga AM, Bandzouzi B, Houinato D, Paraiso MN, Cowppli-Bony P, Aboyans V, Nubukpo P, Preux PM, Dartigues JF, ClEment JP. Epidemiology of dementia in elderly living in the 3rd borough of Bangui (Central African Republic). Bull Soc Pathol Exot. 2012; 105(5): 388-95.
Congo	Guerchet M, M'belesso P, Mouanga AM, Bandzouzi B, Tabo A, Houinato DS, ParaÃ¯so MN, Cowppli-Bony P, Nubukpo P, Aboyans V, ClEment J-P, Dartigues J-F, Preux P-M. Prevalence of dementia in elderly living in two cities of Central Africa: the EDAC survey. Dement Geriatr Cogn Disord. 2010; 30(3): 261-8.
Nigeria	Ogunniyi A, Baiyewu O, Gureje O, Hall KS, Unverzagt F, Siu SH, Gao S, Farlow M, Oluwole OSA, Komolafe O, Hendrie HC. Epidemiology of dementia in Nigeria: results from the Indianapolis-Ibadan study. Eur J Neurol. 2000; 7(5): 485-90.
Tanzania	Paddick S-M, Longdon AR, Kisoli A, Dotchin C, Gray WK, Dewhurst F, Chaote P, Kalaria R, Jusabani AM, Walker R. Dementia prevalence estimates in sub-Saharan Africa: comparison of two diagnostic criteria. Glob Health Action. 2013; 6: 19646.
Asia	
Sri Lanka	De Silva HA, Gunatilake SB, Smith AD. Prevalence of dementia in a semi-urban population in Sri Lanka: report from a regional survey. Int J Geriatr Psychiatry. 2003; 18(8): 711-5.
Bangladesh	Palmer K, Kabir ZN, Ahmed T, Hamadani JD, Cornelius C, Kivipelto M, Wahlin Ã…. Prevalence of dementia and factors associated with dementia in rural Bangladesh: data from a cross-sectional, population-based study. Int Psychogeriatr. 2014; 26(11): 1905-15.
Indian States	
Delhi, Urban	Chandra V, Ganguli M, Pandav R, Johnston J, Belle S, DeKosky ST. Prevalence of Alzheimer's disease and other dementias in rural India: the Indo-US study. Neurology. 1998; 51(4): 1000-8.
Kerala, Urban	Mathuranath PS, Cherian PJ, Mathew R, Kumar S, George A, Alexander A, Ranjith N, Sarma PS. Dementia in Kerala, South India: prevalence and influence of age, education and gender. Int J Geriatr Psychiatry. 2010; 25(3): 290-7.
Kerala, Urban	Shaji S, Bose S, Verghese A. Prevalence of dementia in an urban population in Kerala, India. Br J Psychiatry. 2005; 186: 136-40.
Maharashtra, Urban	Vas CJ, Pinto C, Panikker D, Noronha S, Deshpande N, Kulkarni L, Sachdeva S. Prevalence of Dementia in an Urban Indian Population. Int Psychogeriatr. 2001; 13(04): 439-50.
Tamil Nadu, Urban	Llibre Rodriguez JJ, Ferri CP, Acosta D, Guerra M, Huang Y, Jacob KS, Krishnamoorthy ES, Salas A, Sosa AL, Acosta I, Dewey ME, Gaona C, Jotheeswaran AT, Li S, Rodriguez D, Rodriguez G, Kumar PS, Valhuerdi A, Prince M, 10/66 Dementia Research Group. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. Lancet. 2008; 372(9637): 464-74.
Tamil Nadu, Urban	Rajkumar S, Kumar S, Thara R. Prevalence of dementia in a rural setting: A report from India. Int J Geriatr Psychiatry. 1997; 12(7): 702-7.

Tamil Nadu, Urban	Llibre Rodriguez JJ, Ferri CP, Acosta D, Guerra M, Huang Y, Jacob KS, Krishnamoorthy ES, Salas A, Sosa AL, Acosta I, Dewey ME, Gaona C, Jotheeswaran AT, Li S, Rodriguez D, Rodriguez G, Kumar PS, Valhuerdi A, Prince M, 10/66 Dementia Research Group. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. Lancet. 2008; 372(9637): 464-74.
West Bengal, Urban	Banerjee TK, Mukherjee CS, Dutt A, Shekhar A, Hazra A. Cognitive dysfunction in an urban Indian population - some observations. Neuroepidemiology. 2008; 31(2): 109-14.
Kerala, Rural	Shaji S, Promodu K, Abraham T, Roy KJ, Verghese A. An epidemiological study of dementia in a rural community in Kerala, India. Br J Psychiatry. 1996; 168(6): 745-9.
Tamil Nadu, Rural	Llibre Rodriguez JJ, Ferri CP, Acosta D, Guerra M, Huang Y, Jacob KS, Krishnamoorthy ES, Salas A, Sosa AL, Acosta I, Dewey ME, Gaona C, Jotheeswaran AT, Li S, Rodriguez D, Rodriguez G, Kumar PS, Valhuerdi A, Prince M, 10/66 Dementia Research Group. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. Lancet. 2008; 372(9637): 464-74.

Epilepsy

Countries	Study
Africa	
Benin	Gbenou H. Contribution to the Study of Onchocerciasis-Epilepsy Association [MD thesis]. Cotonou, Benin: National University of Benin; 1995.
	Debrock C, Preux PM, Houinato D, Druet-Cabanac M, Kassa F, Adjien C, Avode G, Denis F, Boutros-Toni F, Dumas M. Estimation of the prevalence of epilepsy in the Benin region of Zinvie using the capture-recapture method. Int J Epidemiol. 2000; 29(2): 330-5.
	Dossou GA, Houinato D, Tevoedjre M, Adjien C, Adoukonou T, Guedou F. Epilepsy in Schools in Cotonou (Benin). Afr J Neurol Sci. 2004; 22(2).
	Houinato D, Yemadje L-P, Glitho G, Adjien C, Avode G, Druet-Cabanac M, Preux P-M. Epidemiology of epilepsy in rural Benin: prevalence, incidence, mortality, and follow-up. Epilepsia. 2013; 54(4): 757-63.
	Yemadje L-P, Houinato D, Boumediene F, Ngoungou EB, Preux P-M, Druet-Cabanac M. Prevalence of epilepsy in the 15 years and older in Benin: a door-to-door nationwide survey. Epilepsy Res. 2012; 99(3): 318-26.
	Avode DG, Capo-Chichi OB, Gandaho P, Bouteille B, Dumas M. [Epilepsy caused by cysticercosis. Apropos of a sociological and cultural investigation conducted at Savalou in Benin]. Bull Soc Pathol Exot. 1996; 89(1): 45-7.
Burkina Faso	Kabore J, Preux P, Kabre D. PrEvalence de l'Epilepsie dans le bassin de la Bougouriba. Bull Soc Pathol Exot. 2000; 93: 267-8.
	NitiEma P, Carabin H, Hounton S, Praet N, Cowan LD, Ganaba R, KompaorE C, Tarnagda Z, Dorny P, Millogo A, EfEcab. Prevalence case-control study of epilepsy in three Burkina Faso villages. Acta Neurol Scand. 2012; 126(4): 270-8.
	Debouverie M, Kabore J, Dumas M, Weber M, Duboz P, Vaugelade J. Epidemiology of Epilepsy in Burkina Faso. In: Dumas M, Giordano C, Gentilini M, Chieze F, editors. Neurologie Tropicale. Paris, France: John Libbey Eurotext, 1993. 57-61.
	Kabore JK, Cabore JW, Melaku Z, Druet-Cabanac M, Preux PM. Epilepsy in a focus of onchocerciasis in Burkina Faso. Lancet. 1996; 347(9004): 836.
Burundi	Newell E, Vyungimana F, Geerts S, Van Kerckhoven I, Tsang VCW, Engels D. Prevalence of cysticercosis in epileptics and members of their families in Burundi. Trans R Soc Trop Med Hyg. 1997; 91(4): 389-91.
Cambodia	Preux P-M, Chea K, Chamroeun H, Bhalla D, Vannareth M, Huc P, Samleng C, Cayreyre M, GErard D, Dumas M, Oum S. First-ever, door-to-door cross-sectional representative study in Prey Veng province (Cambodia). Epilepsia. 2011; 52(8): 1382-7.
Cameroon	Dongmo L, Druet-Cabanac M, Moyou SR, Zebaze DRM, Njamnshi AK, Sini V, Mapoure N, Echouffo TJB, Djeumen WC, Ndumbe PM. [Cysticercosis and epilepsy: a case-control study in Mbam Valley, Cameroon]. Bull Soc Pathol Exot. 2004; 97(2): 105-8.
	Nkwi PN, Ndonko FT. The epileptic among the Bamileke of Maham in the Nde Division, West Province of Cameroon. Cult Med Psychiatry. 1989; 13(4): 437-48.
	Njamnshi A, Dongmo L, Sini V, Echouffo B, Kamdem P, Pepouomi M, Atchou A. Epilepsy in rural Cameroon: the alarming prevalence rates in the Mbam valley. J Neurol Sci. 2005; 238(Suppl 1): S136.
	Boussinesq M, Pion SDS, Demanga-Ngangue, Kamgno J. Relationship between onchocerciasis and epilepsy: a matched case-control study in the Mbam Valley, Republic of Cameroon. Trans R Soc Trop Med Hyg. 2002; 96(5): 537-41.

Central African Republic	Druet-Cabanac M, Preux PM, Bouteille B, Bernet-Bernady P, Dunand J, Hopkins A, Yaya G, Tabo A, Sartoris C, Macharia W, Dumas M. Onchocerciasis and epilepsy: a matched case-control study in the Central African Republic. Am J Epidemiol. 1999; 149(6): 565-70.
Congo	Petitjeans F, Gandin C, Sturtz F. Epilepsie dans les pays en voie de dEveloppement: recensement et description de cas dans deux villages congolais. Epilepsies. 1995; 7: 167-78.
Cote d'Ivoire	Kouadjo Y. GEnEtique et Epilepsie: Ã€ propos dâ€™un foyer dâ€™Epilepsie observE dans un village ivoirien [medical thesis]. Abidjan, CÃ´te dâ€™Ivoire; 1990.
	Kouassi B, Koffi J, Diarra J, Delorme H, Akani A, Yapi P, Sonant, Boa Y, Piquemal M, Fadiga D, Guessennd G, Giordano C. PrEvalence de l'Epilepsie en milieu rural ivoirien Etude pilote. Publ Med Africaines. 1988; 89: 25-30.
Ethiopia	Tekle-Haimanot R, Abebe M, Gebre-Mariam A, Forsgren L, Heijbel J, Holmgren G, Ekstedt J. Community-based study of neurological disorders in rural central Ethiopia. Neuroepidemiology. 1990; 9(5): 263-77.
	Almu S, Tadesse Z, Cooper P, Hackett R. The prevalence of epilepsy in the Zay Society, Ethiopia - an area of high prevalence. Seizure. 2006; 15(3): 211-3.
	Haimanot RT, Abebe M, Mariam AG, Forsgren L, Holmgren G, Heijbel J, Ekstedt J. Community-based study of neurological disorders in Ethiopia: development of a screening instrument. Ethiop Med J. 1990; 28(3): 123-37.
Kenya	Snow RW, Williams RE, Rogers JE, Mung'ala VO, Peshu N. The prevalence of epilepsy among a rural Kenyan population. Its association with premature mortality. Trop Geogr Med. 1994; 46(3): 175-9.
Kilifi (Kenia)	Edwards T, Scott A, Munyoki G, Odera V, Chengo E, Bauni E, Kwasa T, Sander L, Neville B, Newton C. Active convulsive epilepsy in a rural district of Kenya: a study of prevalence and possible risk factors. Lancet Neurol. 2008; 7(1): 50-6.
	Mung'ala-Odera V, White S, Meehan R, Otieno GO, Njuguna P, Mturi N, Edwards T, Neville BG, Newton CRJC. Prevalence, incidence and risk factors of epilepsy in older children in rural Kenya. Seizure. 2008; 17(5): 396-404.
	Ngugi AK, Bottomley C, Scott JA, Mung'ala-Odera V, Bauni E, Sander JW, Kleinschmidt I, Newton CR. Incidence of convulsive epilepsy in a rural area in Kenya. Epilepsia. 2013; 54(8): 1352-9.
Liberia	Gerrits C. A West African epilepsy focus. Lancet. 1983; 1(8320): 358.
	Goudsmit J, Van Der Waals FW. Endemic epilepsy in an isolate region of Liberia. Lancet. 1983; 321(8323): 528-9.
	Van der Waals FW, Asher DM, Goudsmit J, Pomeroy KL, Karabatsos N, Gajdusek DC. Post-encephalitic epilepsy and arbovirus infections in an isolated rainforest area of central Liberia. Trop Geogr Med. 1986; 38(3): 203-8.
Madagascar	Andriantseheno LM, Ralaizandriny D. PrEvalence communautaire de l'Epilepsie chez les Malgaches. Epilepsies. 2004; 16(2): 83-6.
Malawi	Watts AE. The natural history of untreated epilepsy in a rural community in Africa. Epilepsia. 1992; 33(3): 464-8.
Mali	Farnarier G, Diop S, Coulibaly B, Arborio S, Dabo A, Diakite M, Traore S, Banou A, Nimaga K, Vaz T, Doumbo O. [Onchocerciasis and epilepsy. Epidemiological survey in Mali]. Med Trop (Mars). 2000; 60(2): 151-5.
	Beneduce R, Salamanta O, Fiore B. L'Epilepsie en pays Dogon. Une perspective anthropologique et mEdicale [Epilepsy in Dogon Country. An Anthropological and

	Medical Perspective]. In: Coppo P, Keita A, editors. MEdecine Traditionnelle. Acteurs, ItinEraires ThErapeutiques. Trieste, Italy: Erga Edizioni; 1990. 194-243.
	Coppo P. [Mental disorders and epilepsy in a traditional African community. Epidemiologic study]. Minerva Psichiatr. 1983; 24(1): 9-18.
	Traore M, Tahny R, Sacko M. PrEvalence de l'Epilepsie chez les enfants de 3 Ã 15 ans dans 2 communes du district de Bamako. Rev Neurol (Paris). 2000; 156(Suppl 1): S18.
Mauritania	Diagana M, Preux PM, Tuillas M, Ould Hamady A, Druet-Cabanac M. [DEpistage de l'Epilepsie en zones tropicales: validation d'un questionnaire en Mauritanie]. Bull Soc Pathol Exot. 2006; 99(2): 103-7.
Mozambique	Patel V, Simbine APF, Soares IC, Weiss HA, Wheeler E. Prevalence of severe mental and neurological disorders in Mozambique: a population-based survey. Lancet. 2007; 370(9592): 1055-60.
Nigeria	Longe AC, Osuntokun BO. Prevalence of neurological disorders in Udo, a rural community in southern Nigeria. Trop Geogr Med. 1989; 41(1): 36-40.
	Osuntokun BO, Adeuja AO, Schoenberg BS, Bademosi O, Nottidge VA, Olumide AO, Ige O, Yaria F, Bolis CL. Neurological disorders in Nigerian Africans: a community-based study. Acta Neurol Scand. 1987; 75(1): 13-21.
	Sykes RM. Epilepsy in children in Benin City, Nigeria. Ann Trop Paediatr. 2002; 22(3): 287-96.
	Obi JO, Sykes RM. Neurological diseases as seen at the outpatient Paediatric Neurology Clinic in Benin City. Ann Trop Paediatr. 1984; 4(4): 217-20.
	Nwani PO, Nwosu MC, Enwereji KO, Asomugha AL, Arinzechi EO, Ogunniyi AO. Epilepsy treatment gap: prevalence and associated factors in Southeast Nigeria. Acta Neurol Scand. 2013; 128(2): 83-90.
	Dozie INS, Onwuliri COE, Nwoke BEB, Chukwuocha UM, Chikwendu CI, Okoro I, Njemanze PC. Onchocerciasis and epilepsy in parts of the Imo river basin, Nigeria: a preliminary report. Public Health. 2006; 120(5): 448-50.
	Danesi MA. Epilepsy and the secondary schools in Nigeria. Trop Geogr Med. 1994; 46(3 Suppl): S25-27.
Rwanda	Simms V, Atijosan O, Kuper H, Nuhu A, Rischewski D, Lavy C. Prevalence of epilepsy in Rwanda: a national cross-sectional survey. Trop Med Int Health. 2008; 13(8): 1047-53.
Senegal	Agbohoui O, Sene-Diouf F, Ba M, Ndiaye M, Diagne M, Diop AG, Ndiaye IP. [Neuroepidemiology of epilepsy in Senegalese school milieu]. Dakar Med. 1999; 44(1): 99-104.
	Ndoye NF, Sow AD, Diop AG, Sessouma B, SEne-Diouf F, Boissy L, Wone I, TourE K, Ndiaye M, Ndiaye P, de Boer H, Engel J, Mandlhate C, Meinardi H, Prilipko L, Sander JWAS. Prevalence of epilepsy its treatment gap and knowledge, attitude and practice of its population in sub-urban Senegal an ILAE/IBE/WHO study. Seizure. 2005; 14(2): 106-11.
	N'Diaye IP, Mauferon JB, Diagne M. Ã‰pidEmiologie de lâ€™Epilepsie au SEnEgal [Epidemiology of Epilepsy in Senegal]. Presented at: 7th Congress of the Pan-African Association of Neurological Sciences; 1986 Apr 23-30; Abidjan, Cote dâ€™Ivoire.
Tanzania	Bondestam S, Garssen J, Abdulwakil AI. Prevalence and treatment of mental disorders and epilepsy in Zanzibar. Acta Psychiatr Scand. 1990; 81(4): 327-31.
	Hunter E, Rogathi J, Chigudu S, Jusabani A, Jackson M, McNally R, Gray W, Whittaker RG, Iqbal A, Birchall D, Aris E, Walker R. Prevalence of active epilepsy in rural Tanzania: a large community-based survey in an adult population. Seizure. 2012; 21(9): 691-8.

	Ngugi AK, Bottomley C, Kleinschmidt I, Wagner RG, Kakooza-Mwesige A, Ae-Ngibise K, Owusu-Agyei S, Masanja H, Kamuyu G, Odhiambo R, Chengo E, Sander JW, Newton CR, SEEDS group. Prevalence of active convulsive epilepsy in sub-Saharan Africa and associated risk factors: cross-sectional and case-control studies. Lancet Neurol. 2013; 12(3): 253-63.
	Winkler AS, Kerschbaumsteiner K, Stelzhammer B, Meindl M, Kaaya J, Schmutzhard E. Prevalence, incidence, and clinical characteristics of epilepsy--a community-based door-to-door study in northern Tanzania. Epilepsia. 2009; 50(10): 2310-3.
	Rwiza H, Kilonzo G, Haule J, Matuja W, Mteza I, Mbena P, Kilima P, Mwaluko G, Mwang'ombola R, Mwaijande F. Prevalence and incidence of epilepsy in Ulanga, a rural Tanzanian district: a community-based study. Epilepsia. 1992; 33(6).
	Dent W, Helbok R, Matuja WBP, Scheunemann S, Schmutzhard E. Prevalence of active epilepsy in a rural area in South Tanzania: a door-to-door survey. Epilepsia. 2005; 46(12): 1963-9.
	Burton KJ, Rogathe J, Whittaker R, Mankad K, Hunter E, Burton MJ, Todd J, Neville BGR, Walker R, Newton CRJC. Epilepsy in Tanzanian children: association with perinatal events and other risk factors. Epilepsia. 2012; 53(4): 752-60.
	Matuja WB, Kilonzo G, Mbena P, Mwango'mbola RL, Wong P, Goodfellow P, Jilek-Aall L. Risk factors for epilepsy in a rural area in Tanzania. A community-based case-control study. Neuroepidemiology. 2001; 20(4): 242-7.
	Mosser P, Schmutzhard E, Winkler AS. The pattern of epileptic seizures in rural Tanzania. J Neurol Sci. 2007; 258(1-2): 33-8.
The Gambia	Coleman R, Loppy L, Walraven G. The treatment gap and primary health care for people with epilepsy in rural Gambia. Bull World Health Organ. 2002; 80(5): 378-83.
Togo	Balogou AA, Doh A, Grunitzky KE, others. [Neurological disorders and endemic goiter: comparative analysis of 2 provinces in Togo]. Bull Soc Pathol Exot. 2001; 94(5): 406.
	Dumas M, Grunitzky E, Deniau M, Dabis F, Bouteille B, Belo M, Pestre-Alexandre M, Catanzano G, Darde ML, d' Almeida M. Epidemiological study of neuro-cysticercosis in northern Togo (West Africa). Acta Leiden. 1989; 57(2): 191.
Uganda	Kaiser C, Kipp W, Asaba G, Mugisa C, Kabagambe G, Rating D, Leichsenring M. The prevalence of epilepsy follows the distribution of onchocerciasis in a west Ugandan focus. Bull World Health Organ. 1996; 74(4): 361-7.
	Kaiser C, Asaba G, Kasoro S, Rubaale T, Kabagambe G, Mbabazi M. Mortality from epilepsy in an onchocerciasis-endemic area in West Uganda. Trans R Soc Trop Med Hyg. 2007; 101(1): 48-55.
	Kipp W, Kasoro S, Burnham G. Onchocerciasis and epilepsy in Uganda. Lancet. 1994; 343(8890): 183-4.
	Kaiser C, Asaba G, Leichsenring M, Kabagambe G. High incidence of epilepsy related to onchocerciasis in West Uganda. Epilepsy Res. 1998; 30(3): 247-51.
Asia	
Laos	Tran D-S, Odermatt P, Le T-O, Huc P, Druet-Cabanac M, Barennes H, Strobel M, Preux P-M. Prevalence of epilepsy in a rural district of central Lao PDR. Neuroepidemiology. 2006; 26(4): 199-206.
Vietnam	Tuan NA, Cuong LQ, Allebeck P, Chuc NTK, Persson HE, Tomson T. The prevalence of epilepsy in a rural district of Vietnam: a population-based study from the EPIBAVI project. Epilepsia. 2008; 49(9): 1634-7.

	Tuan NA, Cuong LQ, Allebeck P, Chuc NTK, Persson HE, Tomson T. The incidence of epilepsy in a rural district of Vietnam: a community-based epidemiologic study. Epilepsia. 2010; 51(12): 2377-83.
Indonesia	Wandra T, Subahar R, Simanjuntak GM, Margono SS, Suroso T, Okamoto M, Nakao M, Sako Y, Nakaya K, Schantz PM, Ito A. Resurgence of cases of epileptic seizures and burns associated with cysticercosis in Assologaima, Jayawijaya, Irian Jaya, Indonesia, 1991-95. Trans R Soc Trop Med Hyg. 2000; 94(1): 46-50.
Nepal	Rajbhandari KC. Epilepsy in Nepal. Can J Neurol Sci. 2004; 31(2): 257-60.
Sri Lanka	Senanayake N, RomÃ¡n GC. Epidemiology of epilepsy in developing countries. Bull World Health Organ. 1993; 71(2): 247.
Bangladesh	Murthy GV, Mactaggart I, Mohammad M, Islam J, Noe C, Khan AI, Foster A. Assessing the prevalence of sensory and motor impairments in childhood in Bangladesh using key informants. Arch Dis Child. 2014; 99(12): 1103-8.
Pakistan	Malik MA, Akram RM, Tarar MA, Sultan A. Childhood epilepsy. J Coll Physicians Surg Pak. 2011; 21(2): 74-8.
India	Sohi D, Walia I, Singh A. Prevalence and treatment of epilepsy in a Chandigarh slum. Bull PGI. 1993; 27: 175-8.
	Pandey S, Singhi P, Bharti B. Prevalence and treatment gap in childhood epilepsy in a north Indian city: a community-based study. J Trop Pediatr. 2014; 60(2): 118-23.
	Pal DK, Carpio A, Sander JWAS. Neurocysticercosis and epilepsy in developing countries. J Neurol Neurosurg Psychiatry. 2000; 68(2): 137-43.
	Kumar R, Bhave A, Bhargava R, Agarwal GG. Prevalence and risk factors for neurological disorders in children aged 6 months to 2 years in northern India. Dev Med Child Neurol. 2013; 55(4): 348-56.
Indian States	
Karnataka, Urban	Mani KS, Rangan G, Srinivas HV, Kalyanasundaram S, Narendran S, Reddy AK. The Yelandur study: a community-based approach to epilepsy in rural South India - epidemiological aspects. Seizure. 1998; 7(4): 281-8.
Kerala, Urban	Radhakrishnan K, Pandian JD, Santhoshkumar T, Thomas SV, Deetha TD, Sarma PS, Jayachandran D, Mohamed E. Prevalence, knowledge, attitude, and practice of epilepsy in Kerala, South India. Epilepsia. 2000; 41(8): 1027-35.
	Hackett RJ, Hackett L, Bhakta P. The prevalence and associated factors of epilepsy in children in Calicut District, Kerala, India. Acta Paediatr. 1997; 86(11): 1257-60.
Maharashtra, Urban	Bharucha NE, Bharucha EP, Bharucha AE, Bhise AV, Schoenberg BS. Prevalence of epilepsy in the Parsi community of Bombay. Epilepsia. 1988; 29(2): 111-5.
	Bharucha NE, Bharucha EP, Dastur HD, Schoenberg BS. Pilot survey of the prevalence of neurologic disorders in the Parsi community of Bombay. Am J Prev Med. 1987; 3(5): 293-9.
Tamil Nadu, Urban	Rajshekhar V, Raghava MV, Prabhakaran V, Oommen A, Muliyil J. Active epilepsy as an index of burden of neurocysticercosis in Vellore district, India. Neurology. 2006; 67(12): 2135-9.
Uttar Pradesh, Urban	Prasad KN, Prasad A, Gupta RK, Nath K, Pradhan S, Tripathi M, Pandey CM. Neurocysticercosis in patients with active epilepsy from the pig farming community of Lucknow district, north India. Trans R Soc Trop Med Hyg. 2009; 103(2): 144-50.
West Bengal, Urban	Banerjee TK, Ray BK, Das SK, Hazra A, Ghosal MK, Chaudhuri A, Roy T, Raut DK. A longitudinal study of epilepsy in Kolkata, India. Epilepsia. 2010; 51(12): 2384-91.

	Das SK, Biswas A, Roy T, Banerjee TK, Mukherjee CS, Raut DK, Chaudhuri A. A random sample survey for prevalence of major neurological disorders in Kolkata. Indian J Med Res. 2006; 124(2): 163-72.
	Saha SP, Bhattacharya S, Das SK, Maity B, Roy T, Raut DK. Epidemiological study of neurological disorders in a rural population of Eastern India. J Indian Med Assoc. 2003; 101(5): 299-304.
	Banerjee TK, Hazra A, Biswas A, Ray J, Roy T, Raut DK, Chaudhuri A, Das SK. Neurological disorders in children and adolescents. Indian J Pediatr. 2009; 76(2): 139-46.
Andhra Pradesh, Rural	Murthy J, Vijay S, Ravi Raju C, Thomas J. Acute symptomatic seizures associated with neurocysticercoses: A community based prevalence study and comprehensive rural epilepsy study in South India (CRESSI). Neurology Asia. 2004; 9(Suppl 1): 86.
Haryana, Rural	Singh A, Kaur A. Epilepsy in rural Haryana - prevalence and treatment seeking behaviour. J Indian Med Assoc. 1997; 95(2): 37-47.
	Kokkat AJ, Verma AK. Prevalence of seizures and paralysis in a rural community. J Indian Med Assoc. 1998; 96(2): 43-5.
Jammu and Kashmir, Rural	Koul R, Razdan S, Motta A. Prevalence and pattern of epilepsy (Lath/Mirgi/Laran) in rural Kashmir, India. Epilepsia. 1988; 29(2): 116-22.
Orissa, Rural	Premarajan KC, Danabalan M, Chandrasekar R, Srinivasa DK. Prevalence of psychiatry morbidity in an urban community of Pondicherry. Indian J Psychiatry. 1993; 35(2): 99-102.
Rajasthan, Rural	Sureka RK, Sureka R. Prevalence of epilepsy in rural Rajasthan--a door-to-door survey. J Assoc Physicians India. 2007; 55: 741-2.
Uttarakhand, Rural	Goel D, Dhanai JS, Agarwal A, Mehlotra V, Saxena V. Neurocysticercosis and its impact on crude prevalence rate of epilepsy in an Indian community. Neurol India. 2011; 59(1): 37-40.
West Bengal, Rural	Das S, S. Neuroepidemiology of major neurological disorders in rural Bengal. Neurol India. 1996; 44(2): 47-58.
	Saha, S. P., Bhattachrya, S., Roy, B. K., Basu, A., Roy, T., Maity, B., & Das, S. K. (2008). A prospective incidence study of epilepsy in a rural community of West-Bengal, India. Neurology Asia, 13, 41-48.
America	
Bolivia	Nicoletti A, Bartoloni A, Sofia V, Bartalesi F, Chavez JR, Osinaga R, Paradisi F, Dumas JL, Tsang VCW, Reggio A, others. Epilepsy and Neurocysticercosis in Rural Bolivia: A Population-based Survey. Epilepsia. 2005; 46(7): 1127-32.
	Marinkovic Uzqueda T, Sanchez M, Salinas M, Rojas W, Coimbra D, Carlos Pereira J, Delgado M. Estudio Neuroepidemiologico Piloto. Gac Med Bol. 1988; 12(2): 47-50.
Guatemala	Garcia-Noval J, Allan JC, Fletes C, Moreno E, de Mata F, Alvarez R-T, de Alfaro HS, Yurrita P, Higueros-Morales H, Mencos F, Craig PS. Epidemiology of Taenia solium taeniasis and cysticercosis in two rural Guatemalan communities. Am J Trop Med Hyg. 1996; 55(3): 282.
	Mendizabal JE, Salguero LF. Prevalence of epilepsy in a rural community of Guatemala. Epilepsia. 1996; 37(4): 373-6.