June 2016

Challenges and Options for Estimating the Prevalence of Schizophrenia, Psychotic Disorders, and Bipolar Disorders in Population Surveys

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This paper was commissioned by the National Academies of Sciences, Engineering, and Medicine Standing Committee on Integrating New Behavioral Health Measures into the Substance Abuse and Mental Health Services Administration's Data Collection Programs. Opinions and statements included in the paper are solely those of the individual author, and are not necessarily adopted, endorsed or verified as accurate by the National Academies of Sciences, Engineering, and Medicine. Support for the Standing Committee was provided by a contract between the National Academy of Sciences and the U.S. Department of Health and Human Services.

Acknowledgement: JJM is supported by grant APP1056929 from the John Cade Fellowship from the National Health and Medical Research Council.

Introduction

To understand the causes and consequences of mental disorders, it is essential to measure the frequency of these disorders in the general community. Mapping the epidemiological landscape is the basis upon which researchers can develop hypotheses related to causal mechanisms – for example why is schizophrenia more common in men than women (Aleman et al., 2003), in some migrant groups (McGrath et al., 2004, Cantor-Graae and Selten, 2005), and why does the incidence and prevalence vary between sites (McGrath, 2006, Saha et al., 2006)? However, from a policy and planning perspective, the research questions tend to more pragmatic and user-focused. Are those with serious mental disorders accessing services and are they receiving an optimal mix of services? Do people who use services have better outcomes? Are there unmet needs that can be better addressed? In order to address these issues, high quality epidemiologically-informed research is required.

In order to distribute the limited health dollar effectively, governments need to understand the causes and distribution of health loss, both in terms of premature mortality and disability. This has been brought into sharp focus in recent years with influential research initiatives, such as the Global Burden of Disease Studies, which synthesize epidemiological data from around the world to produce directly comparable estimates of health loss due to a large number of diseases and injuries using standardized metrics (Murray et al., 2012). The core standardized metric of burden of disease is the disability-adjusted life year (DALY) which is the sum of years of life lost (YLL) and years lived with disability (YLD). Estimates for each metric are age-, sex-, disease-, and country-specific. As a result of this work, there is now robust evidence to show how mental disorders contribute substantially to global burden of disease (Whiteford et al., 2015, Whiteford et al., 2013).

Despite the strengths of such research, it is important to recognize that accurate estimates rely on the availability of high-quality epidemiological data. Large research collaborations such as the World Mental Health Survey and Global Burden of Disease Studies have successfully increased awareness amongst Governments and research institutions around the world of the need for regular epidemiological data collection to chart the health of nations. With respect to the US, there is a rich tradition of regular surveys of substance use (National Survey on Drug Use and Health (Substance Abuse and Mental Health Services Administration (SAMHSA), 2016) and for several years an associated National Survey on Drug Use and Health-Mental Health Surveillance Study (Substance Abuse and Mental Health Services Administration (SAMHSA), 2014). International consortia have

been developed in order to combine outputs from studies for transnational analyses (Kessler and Ustun, 2008). Indeed, psychiatric epidemiology can be justly proud of its achievements over the last few decades.

In the most recent Global Burden of Disease Study (GBD 2013), over 300 studies met inclusion criteria and reported estimates for the prevalence of mental disorders (see Table 1). The inclusion criteria included the requirement that case definitions met DSM or ICD diagnostic criteria, and sampling was representative of the general population. GBD 2013 identified 30 studies from 20 different countries that provided data on the prevalence of bipolar disorder, and 48 studies from 21 different countries that provided data on the prevalence of schizophrenia and related disorders.

Table 1: Data sources from GBD 2013

Disorder	Parameter	No of studies	No of countries
Depressive disorders	Prevalence	125	51
	Incidence	5	3
	Remission	2	1
	Mortality	10	7
Anxiety disorders	Prevalence	79	45
	Incidence	-	-
	Remission	5	4
	Mortality	-	-
Schizophrenia	Prevalence	48	21
	Incidence	32	13
	Remission	18	17
	Mortality	34	21
Bipolar disorder	Prevalence	30	20
	Incidence	-	-
	Remission	-	-
	Mortality	5	5
Eating disorders	Prevalence	31	19
	Incidence	6	5
	Remission	9	6
	Mortality	8	5
Conduct disorder and ADHD	Prevalence	61	27
	Incidence	3	3
	Remission	13	4
	Mortality	-	-
Autism and Asperger's disorder	Prevalence	28	15
	Incidence	4	3
	Remission	4	3
	Mortality	3	3

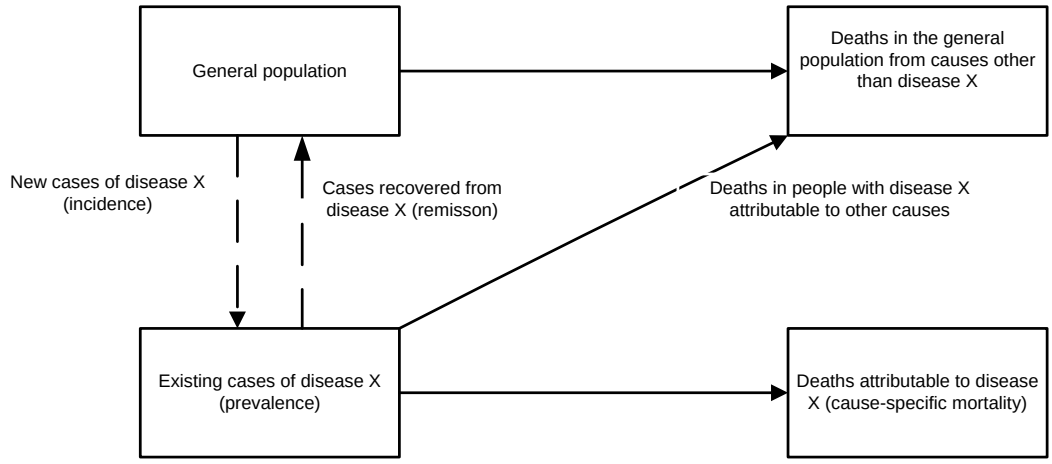
However, the availability and accuracy of data varies across the spectrum of mental disorders. A particular challenge for low prevalence psychotic disorders is sample size. For low prevalence disorders, many well individuals will need to be screened and assessed in order to identify a sufficient number of cases required for epidemiological purposes. Statistically, this creates inherent difficulties in generating reliable prevalence estimates within reasonable bounds of uncertainty. Yet, it is typically these low prevalence mental disorders which, as a group, are most disabling and most likely to use services. For example, whilst schizophrenia is a relatively low prevalence disorder (1-3% projected lifetime risk (Saha et al., 2006), it ranked 12th globally in terms of years lived with disability (YLDs) amongst the 291 diseases and injuries in GBD 2013 (Institute for Health Metrics and Evaluation., 2013). The ranking is largely a function of this disorder typically emerging in young adults, often having a persistent or recurrent course of illness and having a high disability. In fact the acute phase of schizophrenia has the highest disability of all 291 diseases and injuries in GBD 2013 (Salomon et al., 2015).

This report will address selected topics related to epidemiological data collection of psychotic disorders, with a focus on the advantages and challenges of different study designs and data collection methods. The report is based on narrative reviews and expert opinions; however the authors have been involved in extensive data collection including major systematic reviews and meta-analyses of the incidence, prevalence and outcomes (i.e. recovery and mortality) of psychotic disorders.

What to measure – frequency estimates

A range of frequency measures are available to help create a comprehensive epidemiological profile of disease. Measures such as prevalence, incidence, mortality and remission are inter-related and it is important to understand their relationship for any particular disease in a population. Saha and colleagues have applied this model to schizophrenia (Saha et al., 2008).

Figure 1: Generic disease model



Central to the generic disease model in Figure 1 is the pool of cases of a disease, referred to as prevalent cases, and usually expressed as a ratio or proportion of a given population (for example 5 cases in a population of 1000 would a prevalence of 0.5). It is common to have a time specifier attached to prevalence estimates to provide context and meaning. Prevalence in the model is the proportion of individuals who currently have the disorder, or have had it in the past month ('point' prevalence). Sometimes we may wish to know what proportion of the population has had the disorder at any time in their life ('lifetime' prevalence).

The number of prevalent cases at any time is influenced by the proportion of a given population that develops a disorder during a given period of time, measured as incidence. This metric has a numerator (count of new cases), a denominator (the count of the risk set or background population, which included the new cases), and a time reference (usually per annum). In order to better capture the impact of different population age structures on incidence metrics, incidence rates can also be expressed in person-time (e.g. 6 cases in a population of individuals with 100 person-years).

The number of prevalent cases at any time is also influenced by the cases which leave the pool of prevalent cases. This either happens as a result of recovery from a disease (remission) or death (either from the disease or another cause). Remitted cases may, of course, reenter the prevalent case pool at times of relapse and in reality there will be a proportion of cases which are in a state of flux between the two pools. Deriving prevalence estimates from those in contact with services, brings a potential bias of underestimating the true prevalence and assuming the characteristics of those with a disorder is the same as those accessing services (who may be a more severe or persistent subgroup). While risk factor epidemiology prefers estimates from representative samples (e.g. sites with comprehensive case registers can derive frequency metrics from population-based

birth cohorts), observational studies that focus on service access and unmet need may be able to accommodate more relaxed sampling strategies.

Mortality also depletes the number of prevalent cases in the model and premature mortality depletes the prevalent population more quickly. There is a particular focus on the increased risk of premature mortality in those with psychotic disorders (Suetani et al., 2015, Walker et al., 2015) which can be described by standardized mortality ratios (SMRs), calculated by dividing the observed mortality rates in a given population (e.g. the number of deaths in a group of individuals with schizophrenia) by the expected mortality rates in that same group as predicted by age- and sex-specific mortality rates for a standard population. Thus, an SMR of 2.0 would indicate that people with schizophrenia are twice as likely to die compared with the general population during a given time period. The SMRs can be calculated for overall mortality (all-cause) or for more specific, widely used categories (e.g. cancer, cardiovascular disease, endocrine disorders or suicide).

As shown in Table 1, the overwhelming majority of epidemiological studies have focused on reporting estimates of mental disorder prevalence. The likely reason is that it is generally more straight-forward and less resource intensive to conduct a cross-sectional population-based prevalence survey. Incidence studies of low prevalence disorder require very large catchment areas and/or prolonged recruitment windows in order to accumulate sufficient cases to derive reliable estimates. Studies related to recovery or mortality require record linkage or prospective longitudinal research design. Prevalence itself is a product of the interplay of incidence, remission and mortality and the strategies for reducing prevalence are those that reduce incidence and mortality, and/or increase remission.

What to measure - disability and functional impairment

Both psychosis and bipolar disorder are known to carry substantial disability and impairment. GBD disability weights rank acute schizophrenia as the most disabling disease state of all GBD causes (Salomon et al., 2015). In the NCS-R study in the US, bipolar disorder had the highest percentage of severe cases (82.9%) among mood disorders (Kessler et al., 2005). This fact, combined with the low remission rates seen in these disorders could perhaps rationalise a case for shifting our understanding of meaningful positive mental health outcomes away from untenable reductions in prevalence to reductions in disorder severity and associated functional impairment.

Both the Short Form-12 (SF-12) and Sheehan disability scale (SDS) are instruments which have been used to quantify mental disorder severity (or more accurately the functional impairment it causes). They are quick to conduct and can be used independently or as add-on modules to other surveys. Reducing disability is arguably the target that would result in the most impact on improving health outcomes for the most severe mental disorders such as psychosis and bipolar disorder given the limited capacity of current interventions to reduce incidence and increase remission rates.

Disability as measured by these instruments will persist for most individuals with psychosis and bipolar disorder, even with optimal clinical treatment. It is important therefore to collect information on engagement with services, usually provided through non-government agencies that promote social inclusion and enhance personal recovery and quality of life.

Epidemiological studies from the US

As mentioned previously, the Global Burden of Disease Study models health estimates by drawing upon available epidemiological data and Table 2 shows the US epidemiological studies for schizophrenia and bipolar disorder which met GBD inclusion criteria. Two nationally representative prevalence surveys have been conducted in the US adult population. These are large studies capturing prevalence estimates of a range of mental disorders. The first, the Epidemiological Catchment Area Survey (ECA), conducted in 1989, used DSM-III diagnostic criteria and reported age-, sex- and race-specific, one-month prevalence estimates for schizophrenic disorders (0.7%), schizophrenia (0.6%) and schizophreniform disorders (0.1%) (Regier et al., 1993, Leaf et al., 1991). The ECA also reported one-month prevalence estimates for bipolar disorder (0.8% (SE=0.2)) (Weissman et al., 1988).

The second was the National Comorbidity Survey Replication (NCS-R) conducted in 2001-2003 (Kessler et al., 2005, Gum et al., 2009), and was preceded by the original National Comorbidity Survey (NCS) conducted in 1990-1992 (Kessler et al., 1994). The NCS-R reports an age-standardised bipolar disorder (I and II) prevalence of 2.6% (SE=0.2). Schizophrenia and other non-affective psychoses were not included in the NCS-R due to challenges discussed later in this report.

In addition to these two large national surveys, Table 2 shows several other studies held in the GBD datasets. These studies are smaller and less representative studies and/or report epidemiological parameter estimates other than prevalence. From Table 1 we can see that data sources for

schizophrenia are dominated by prevalence studies to a lesser extent than for other disorders. In fact, the ECA is the only population-based survey meeting GBD inclusion criteria reporting the prevalence of schizophrenia in the US. Additionally, with the exception of the NCS-R, the studies found in Table 2 are relatively old with data collection generally taking place well over 20 years ago.

Table 2: GBD data sources for USA for schizophrenia and bipolar disorder

Study	Year	Representativeness	Measure	Study design
Schizophrenia				
Regier DA, Farmer ME, Rae DS, et al. One-month prevalence of mental disorders in the United States and sociodemographic characteristics: the Epidemiologic Catchment Area study. *Acta Psychiatrica Scandinavica* 1993; 88(1): 35-47.	1980	National (ECA Study)	Prevalence	Cross-sectional survey (general population)
Auslander LA, Jeste DV. Sustained remission of schizophrenia among community-dwelling older outpatients. Am J Psychiatry. 2004; 161(8): 1490-3.	1990	National	Remission	Longitudinal cohort study (clinical sample)
Bresnahan MA, Brown AS, Schaefer CA, Begg MD, Wyatt RJ, Susser ES. Incidence and cumulative risk of treated schizophrenia in the prenatal determinants of schizophrenia study. Schizophr Bull. 2000; 26(2): 297.	1959	California	Incidence	Longitudinal birth cohort study (general population)
Harrison G, Hopper K, Craig T, Laska E, Siegel C, Wanderling J, Dube KC, Ganev K, Giel R, an der Heiden W, Holmberg SK, Janca A, Lee PW, León CA, Malhotra S, Marsella AJ, Nakane Y, Sartorius N, Shen Y, Skoda C, Thara R, Tsirkin SJ, Varma VK, Walsh D, Wiersma D. Recovery from psychotic illness: a 15- and 25-year international follow-up study.Br J Psychiatry. 2001; 178: 506-17.	1978	Hawaii	Remission	Longitudinal cohort study (clinical sample)
Martin RL, Cloninger CR, Guze SB, Clayton PJ. Mortality in a follow-up of 500 psychiatric outpatients. I. Total mortality. Arch Gen Psychiatry. 1985; 42(1): 47-54.	1967	Missouri	Standardised mortality ratio	Longitudinal cohort study (clinical sample)
Bipolar disorder				
Weissman MM, Leaf PJ, Tischler GL, Blazer DG, Karno M, Bruce ML, Florio LP. Affective disorders in five United States communities. Psychol Med. 1988; 18(1): 141-53	1980	National (ECA Study	Prevalence	Cross-sectional survey (general population)
Kessler RC, Chiu W, Demler O, Walters EE. Prevalence, severity, and	2001	National (NCS-R	Prevalence	Cross-sectional survey

comorbidity of 12-month DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry* 2005; 62(6): 617-27.		Study)		(general population)
Gum AM, King-Kallimanis B, Kohn R. Prevalence of mood, anxiety, and substance-abuse disorders for older Americans in the national comorbidity survey-replication. Am J Geriatr Psychiatry. 2009; 17(9): 769-81.	2001	National (NCS-R Study)	Prevalence	Cross-sectional survey (general population, older adults)
Black DW, Winokur G, Nasrallah A. Mortality in patients with primary unipolar depression, secondary unipolar depression, and bipolar affective disorder: a comparison with general population mortality. Int J Psychiatry Med. 1987; 17(4): 351-60	1970	Iowa	Standardised mortality ratio	Longitudinal cohort study (clinical sample with record linkage)
Lewinsohn PM, Hops H, Roberts RE, Seeley JR, Andrews JA. Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. J Abnorm Psychol. 1993; 102(1): 133-44.	1987	West Central, Oregon	Prevalence and incidence	Longitudinal cohort study (general population)
Lewinsohn PM, Klein DN, Seeley JR. Bipolar disorders in a community sample of older adolescents: prevalence, phenomenology, comorbidity, and course. J Am Acad Child Adolesc Psychiatry. 1995; 34(4): 454-63.	1987	West Central, Oregon	Prevalence and incidence	Longitudinal cohort study (general population)
Costello EJ. Child psychiatric disorders and their correlates: a primary care pediatric sample. J Am Acad Child Adolesc Psychiatry. 1989; 28(6): 851-5.	1984	Pittsburgh, Pennsylvania	Prevalence	Cross-sectional survey (clinical sample)

How to measure

In the previous section we discussed the very limited national estimates of psychotic and bipolar disorder prevalence. In this section we will explore the advantages and disadvantages of a range of study designs and data sources which can be utilised in psychiatric epidemiology. We will begin with potential study designs and data sources for ascertaining prevalence.

Cross-sectional surveys

Cross-sectional surveys are the most commonly used study design in ascertaining prevalence, providing a snapshot in time of population mental health status. Although specific skills are required (e.g. sampling techniques for a representative sample), study design and data analysis are arguably more straightforward than most other study designs used in psychiatric epidemiology. For example, these study designs require no follow-up and thus are more efficient to conduct than longitudinal study designs.

Several well validated instruments are available for the assessment of a range of mental disorders. These include the Composite International Diagnostic Interview (Kessler and Ustun, 2004), the Structured Clinical Interview for DSM-IV (First et al., 2001), the Schedule for Clinical Assessment in Neuropsychiatry (Wing et al., 1990) , and the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998). A significant advantage of a number of instruments is that they are designed to be administered by trained lay-interviewers allowing for rapid surveying of large samples. However, these instruments are designed for the screening for a range of disorders (especially common mental disorders), and less suited for the confirmation of one particular group of disorders (such as psychotic disorders). In response to this issue, the Diagnostic Interview for Psychosis (DIP) was developed (Castle et al., 2006) . The DIP contains interview questions and probes, including items from the WHO Schedules for Clinical Assessment in Neuropsychiatry (Wing et al., 1990) mapped onto the 90 diagnostic items of the Operational Criteria Checklist for Psychotic and Affective Illness (OPCRIT) (McGuffin et al., 1991) A computer algorithm provides diagnostic classification in accordance with ICD-10 and DSM-IV criteria on the basis of the DIP ratings, thus reducing subjective bias in the interpretation of symptoms and signs.

There are some drawbacks to cross-sectional study designs (they often need to be large and can be expensive); however, two major challenges in using this study design are specifically inherent to the nature of psychosis and bipolar disorder. Some studies have elected to exclude non-affective psychoses because previous studies have shown lay-administered interviews over-estimate

prevalence (e.g. NCS-R) (Kessler, 2005). While originally thought of as an epidemiological nuisance, it is now widely appreciated that many otherwise well individuals in the community report experiencing isolated psychotic experiences (e.g. lifetime prevalence = 5.8%) (McGrath et al., 2015a). The second significant challenge for population-based surveys of low prevalence disorders, such as psychosis, is that very large sample sizes (in the thousands) are required to detect enough cases for results to be meaningful. Both of these issues are major barriers to traditional population-based cross-sectional survey designs and are likely the reason for the dearth of reliable and recent prevalence estimates shown in Table 2.

Administrative data

Another method to ascertain disorder prevalence is to draw upon administrative data. A popular source of administrative data is from health service/patient records – sometimes referred to as 'treated' prevalence as presumably all cases from such a dataset have undergone some form of treatment (optimal or otherwise). The advantage is that this data is routinely recorded and readily available at relatively low cost. A clear disadvantage of this method is that people who have not come into contact with a health service will not be captured, thereby underestimating the true population prevalence of a disorder. The argument may be made that this has less implications for severe disorders such as psychosis in high income countries where the likelihood of someone being in contact with a health service at some point in time is fairly high; however, much of this depends on other factors such as accessibility to publicly funded health services. Generally speaking, treated prevalence estimates are not considered representative of the general population are excluded from GBD mental disorder datasets. For service planning, it is especially important to assess unmet need, thus those who have not made contact with treatment setting will be missed.

Another type of administrative data relates to insurance databases. As with hospital datasets, these datasets underestimate prevalence in the general population; however, it is an accessible and rich data source which can be informative if its limitations are acknowledged and accounted for in epidemiological research. One way in which to do this is to create a crosswalk between administrative data and data obtained from the general population (data from both sources are required) which makes upwards corrections to data from 'suboptimal' sources. Inbuilt covariates within meta-regression methods are commonly used and this is the basic process employed in creating epidemiological models in GBD.

Another form of administrative data is from health registries (typically state or national level). These store detailed data on people with a specific disease or condition and known registries exist for

some mental disorders. Again, this data is readily available but is likely to be incomplete. The comprehensiveness of these registries varies enormously from country to country; however some countries (such as those in Scandinavia) are known to have registries for schizophrenia of sufficient quality that they provide data which can be considered reliable enough to approximate true population prevalence. However, the available data from US population surveys suggest that approximately 40% of individuals with schizophrenia are not in contact with services for extended periods even while experiencing significant symptoms (Mojtabai et al., 2009).

What other options are available?

Earlier we noted that disease prevalence is a function of the other epidemiological parameters (incidence, remission and mortality). Prevalence holds important information about the *status* of population mental health but, when viewed on its own, it provides little opportunity to *improve* mental health. However, key metrics related to mortality and remission can be used to explore and complement prevalence estimates (Saha et al., 2008).

Record linkage

While outside the scope of this report, the mortality associated with psychosis has received considerable attention in recent years (Saha et al., 2007, Olfson et al., 2015). Excess mortality in those with psychosis and bipolar disorder, largely due to comorbid conditions, is well-documented and of particular interest because it offers real opportunities for improving health outcomes (the issue of physical comorbidity is discussed later in the report). Record linkage studies (e.g. between treatment services and/or national death registers) are also regularly utilized to provide an index of mortality associated with mental disorders (Mortality and Causes of Death, 2015, Olfson et al., 2015, Walker et al., 2015). National registers of death can be linked to other administrative data, such as hospital records, in order to calculate the standardized mortality ratio (SMR), which compares mortality in people with schizophrenia vs the general population. Opportunities for data linkage often arise after data collection and study completion, thus seeking consent for future unspecified (but ethically approved) studies is prudent.

Longitudinal research

From Table 1 we can see that longitudinal cohort study designs are regularly employed in psychiatric epidemiology. Drawing a cohort from a population without the disorder permits the estimation of incidence (hence a general population sample); whilst drawing on a population with the disorder provides the opportunity to study remission (hence a clinical sample). Typically, these studies are

prospective in nature but, in the presence of high quality administrative data, retrospective designs are also feasible. Prospective studies are necessarily lengthy and can be costly. However, longitudinal research also provides opportunities for other relevant health outcomes to be assessed using repeated measures. For example, prevalent samples based on administrative settings can seek permission for follow-up assessment of the entire sample or a selected subsample (i.e. build a 'panel study'), and/or record linkage (e.g. with insurance agencies, national death registers etc). The focus on early psychosis services in many nations now allow for the opportunity to build incidence-like cohorts for follow up.

Access to patients via smart phones and other internet related devices is an area of enormous growth currently and this disruptive technology will influence the design of future epidemiological studies (Aanensen et al., 2014, Palmier-Claus et al., 2012, Kimhy et al., 2012). For example, subgroups of respondents that have access to this technology can be drawn from samples collected via traditional epidemiological studies for repeated-measure assessments of symptoms, service use, compliance, unmet need etc. These smaller follow-up studies can be very cost-effective and as this technology becomes more widely available, it will probably be a preferred mode of data collection for many individuals with psychosis.

An issue of 'caseness'

In order to count the disorders of interest, it is essential to have reliable diagnostic criteria to define caseness. More than any other disorder, commentators seem to be constantly drawn to debates related to the label schizophrenia. What is it? Should we abandon the name? Would a fresh label reduce stigma? Medicine has many poorly understood syndromes that are known to be heterogeneous. While we wait for the inevitable progress of science, we are forced to make do with interim labels. These diagnostic categories can be reliability measured, despite psychometric weaknesses related to validity, and can guide treatment and allow broad predictions about prognosis. The fact that these debates attract so much attention on a regular basis speaks to the sense of frustration clinicians (and the general population) have with schizophrenia – it is a very disabling and poorly understood group of disorders. Even our best treatments are suboptimal, thus residual stigma is hard to address from community education alone. There is a long and well-rehearsed debate about moving from categorical to dimensional measures of psychosis (Van Os et al., 1999, Potuzak et al., 2012). In more recent years, this has evolved in a call for a shift from the use of unreliable diagnostic criteria during the early phases of psychotic disorders to the use of a

'staging' model. (Scott et al., 2013). This model acknowledges that the early phases of psychosis are 'pleuripotent', and that clinical and service needs are better captured by the purposeful use of interim stage-related classifications (Fusar-Poli et al., 2014). Future epidemiological studies should endeavor to incorporate these concepts, as it will be important to explore if these concepts can be conceptualized within an epidemiological framework.

Common mental disorders such as major depression or generalized anxiety disorders lend themselves to structured questionnaires that can be delivered by well-trained lay interviewers (Kessler and Üstün, 2008, Heeringa et al., 2008). The core features are understood by the general community as anxiety and depression can be conceptualized on a continuum, and mild and/or transient anxiety or depression is universal. In contrast, the symptoms and signs of psychotic disorders are less precise and usually require clinical judgment. The elements that underlie diagnostic criteria cannot be readily operationalized. When is a delusion an overvalued belief? What is a hallucination in the context of a psychotic disorder versus a culturally-understandable event (e.g. transient hallucinations associated with bereavement)?

There has been a shift in our understanding of how to define psychosis in recent years. This has been driven by pragmatic concerns (e.g. the cost of undertaking detailed clinically-informed diagnostic instruments) versus the realization that sometimes 'less is more'. Sometimes called 'shallow phenotyping', there is awareness that simple and imprecise measure of a health outcome can be sufficient for many research questions. For example, asking a simple question such as "Has a doctor ever told you that you have schizophrenia or a psychotic disorder?" may be suitable for concentrating putative cases for two-stage studies. In the past, exhaustive diagnostic interview have been blended with detailed chart reviews and consensus criteria. However, for pragmatic as well as scientific reasons, these time consuming procedures are not suitable for large scale epidemiological surveys.

Future proofing for changes in diagnostic criteria

Changes in diagnostic criteria over time have the potential to significantly influence epidemiological research. There may be changes in the instrumentation that is used for data collection and the estimates themselves may increase or decrease. This also has implications for drawing comparisons in estimates and particularly for longitudinal research where data from different time points may have used different diagnostic criteria. While some changes are terminological, for example Schizophrenia and Other Psychotic Disorders in DSM-IV to Schizophrenia Spectrum and Other

Psychotic Disorders in DSM-5, others add new disorders, for example the move to include Schizotypal (Personality) Disorder from the Personality Disorders chapter.

When changes are made to the diagnostic criteria, the threshold for a case can change. For example, In DSM-5, changes have been made to criterion A for schizophrenia with bizarre delusions and Schneiderian auditory hallucinations have been removed due to poor reliability in differentiating bizarre delusions from non-bizarre delusions and the non-specificity of Schneiderian symptoms. In DSM-5, two Criterion A symptoms are now required for the diagnosis of Schizophrenia (only one was required in DSM-IV) and in addition to Criterion A symptoms, one additional core positive symptom must be present (i.e. a delusion, hallucination, or disorganized speech). Additionally, the diagnostic criteria no longer identify subtypes and a dimensional criterion (measured on a 0–4 point scale) to evaluate severity in Schizophrenia is included in Section III. The implications from changes that raise the threshold needed for a diagnosis is that the number of individuals who meet case definition in a survey might fall but in reality it is unlikely the change will significantly alter demand for psychosis services (though it may decrease the use of antipsychotic medication and this could better align clinical need and pharmacological treatment).

The United States is a culturally diverse country and Western concepts of mental disorder and the way symptoms of a disorder are expressed can vary between cultures. One US study has shown that differences exist in response to questions in the Composite International Diagnostic Interview concerning depression but these do not account for relatively low-prevalence of depression among minority groups (Breslau J. et al., 2008). These issues are even more pronounced in psychosis research if the category of observation shifts from diagnostic criteria to the level of symptom. Large cross-national studies of hallucinations and delusions confirm prior expectations that cultural factors influence the frequency, age of onset and nature of psychotic experiences (McGrath et al., 2016, McGrath et al., 2015b, Nuevo et al., 2010).

The epidemiology of psychosis; selected examples from recent literature

Finland

One of the most impressive studies in recent decades has come from Finland (Perala et al., 2007). A representative sample (n = 8028) of those aged 30 year or older were screened for psychotic disorder and bipolar disorder (with the Composite International Diagnostic Interview (CIDI)), and with cross-linking with various national registers (hospital discharge records, disability pensions records, and pharmacoepidemiology registers). Screen-positive individuals were then screened with the Structured Clinical Interview for DSM-IV (SCID) (First et al., 2001). Of the various methods used to screen for cases used in this study, the national hospital discharge register was the most reliable (kappa = 0.8).

Australia

The Australian Federal Government commissioned two studies to determine the prevalence and correlates of psychotic disorder. The Low Prevalence Survey of Psychotic Disorders study (Jablensky et al., 2000) was undertaken in 1997, and the Survey of High Impact Psychosis (Morgan et al., 2012, Morgan et al., 2014) was undertaken in 2010. Both studies were based on two-phase surveys. Firstly, catchment areas were defined and known sites of service contact for those with psychosis were enlisted (e.g. hospital, community clinics, primary care physicians, private psychiatrists, non-government organizations). The first phase involved a census month where all contacts with the selected services were screened with a simple check list (Castle et al., 1997) in order to identify those with probable psychosis. The second phase involved re-contacting individuals from the census survey who were screened-positive for a psychotic disorder (and a set of screen-negative individuals in order to define sensitivity and specificity) for a detailed diagnostic interview (Castle et al., 2006) and an assessment of other key areas. In the more recent 2010 study, the second-stage interview focused strongly on issues of concern for the Australian government such as (a) comorbid physical illness, (b) contact with services and types of treatment received, (c) met and unmet needs, (d) employment and measures related to social inclusion. Participants were also invited to provide blood for measures related to diabetes and metabolic syndrome. A separate consent was used to collect and store DNA for future (unspecified) genetic studies. Both studies were designed and conducted by clinical researchers, which maximized service participation and investigator commitment.

Canada

A Federal initiative, the Canadian Community Health Survey (CCHS), is a biennial household survey providing population health estimates representative at the provincial, regional and national level. The CCHS, for which data collection began in 2000, consists of two cross-sectional surveys conducted over a two-year, repeating cycle. The first survey is designed to collect data from a sample large enough to provide information by health region. The second survey focuses on a specific health topic, and provides data at the provincial level (Béland, 2002). Mental health and wellbeing was the health focus of the 2002 (Gravel and Béland, 2005) and 2012 (not published at the time of writing) provincial surveys. The surveys utilized a modified version of the CIDI and provide estimates of bipolar disorder at the regional and national level. Schizophrenia was not included in the CCHS due to challenges with measurement.

The mental health and wellbeing CCHS survey targets individuals aged 15 or older who are living in private dwellings in the 10 Canadian provinces. The 2002 CCHS used the area frame designed for the Canadian Labour Force Survey as its primary sampling frame and set a sample size of 48,000. A multistage stratified cluster design is used to sample dwellings within the area frame with oversampling of youths aged 15-24. People living on Indian reserves or Crown lands, residents of institutions, full-time members of the Canadian Armed Forces, and residents of certain remote regions are excluded (Béland, 2002).

China

China has produced an impressive number of epidemiological surveys covering a range of mental disorders including schizophrenia and bipolar disorder. The majority of these population surveys have been at the provincial levels (Xiang et al., 2008, Xiaoyong et al., 2004, Wei et al., 2011, Ran et al., 2003); however, two significant psychiatric epidemiological surveys have been independently undertaken providing nationally representative prevalence estimates for schizophrenia and bipolar disorder. The first was in 1993 (Weixi et al., 1998) and the second in the period of 2001-2005 (Phillips et al., 2009). Both were household surveys and included participants over 15 years of age and 18 years of age, respectively.

The 1993 survey utilized the Chinese Classification of Mental Disorders (CCMD) which is similar in structure and categorisation to the ICD and DSM. The 2001-2005 survey conducted a vigorous 2-stepped diagnostic assessment by utilizing the 12-item General Health Questionnaire as a screener on a sample of over 66,000 participants followed by the psychiatrist-administered SCID on all those

with identified risk of a disorder. This approach, although more resource-intensive, has several major benefits including the inclusion of Psychosis 'not otherwise specified' category and the ability of skilled interviewers to rephrase standard SCID questions about symptoms if respondents were uncertain about the meaning of the initial question (which can happen when respondents with different educational levels and language skills are interviewed). In fact, prevalence estimates in this study by Phillips band colleagues were substantially higher than those reported in other studies done in China from 1982 to 2004 in which different methods were used.

United Kingdom

The National Psychiatric Morbidity Survey was a household survey representative nationally, with the exception of the Highlands and Islands of Scotland (Jenkins et al., 1997a, Jenkins et al., 1997b). Nearly 13,000 adults aged 16-65 were selected for interview. Psychiatric assessment was carried out by lay interviewers using the Revised Clinical Interview Schedule (CIS-R) (Lewis et al., 1992). Measurement of psychosis was distinct whereby all subjects were additionally screened for psychosis using the Psychosis Screening Questionnaire (Bebbington and Nayani, 1995), and screen-positive individuals were examined by psychiatrists using SCAN (Wing et al., 1990). Seven hundred and forty-nine subjects were positive on the psychosis screen. Of these, 473 were successfully interviewed by psychiatric registrars using SCAN, that is, 63% of those who were positive on the psychosis screen.

Netherlands

The Netherlands Mental Health Survey and Incidence Study, or NEMESIS, was a large prospective cohort study that has been conducted (Bijl et al., 1998a, Bijl et al., 1998b). The first phase was a cross-sectional, multistage household survey in 1996 which interviewed over 7,000 participants from the general Dutch population aged between 18 and 64 using the CIDI. Those with psychotic experiences were followed up with a telephone interview with an experienced clinician (van Nierop et al., 2012). Follow-up measurements in the same sample were conducted twice at 12 and 36 months facilitating the estimation of disorder incidence. Noteworthy were the additional measures included in the survey which included subthreshold presentations of symptoms that were considered potentially clinically relevant but that fail to satisfy the DSM criteria for a disorder; the consequences of mental disorders in terms of care use and care needs; quality of life and functional impairments; and determinants of the emergence and the course of mental disorders. A second study has also commenced (NEMESIS 2) (de Graaf et al., 2010), with the baseline study (n = 6646)

sample followed up with two additional waves of interview (at three year intervals). DNA has been collected from saliva in 76.4% of the baseline sample.

Conclusions

Psychotic and bipolar disorders are associated with persistent symptoms, high levels of disability, premature mortality, high health care costs, need for long-term community support, impaired social functioning and low employment rates. A recent study estimated the economic burden of schizophrenia in the US at $155.7 billion for 2013, of which 24% were excess direct health care costs ($37.7 billion), 6% direct non–health care costs ($9.3 billion) and 76% indirect costs ($117.3 billion) compared to individuals without schizophrenia. The largest components were excess costs associated with unemployment (38%), productivity loss due to caregiving (34%), and direct health care costs (24%) (Cloutier et al., 2016).

Information to quantify the size, distribution, functional impairment and service utilization of individuals with these disorders provides important information for health and social service policy and planning. The following should be considered in planning surveys to collect this information:

1. Collect information on symptoms that allow disorders to be measured on a range of diagnostic, symptom-level and clinical-stage related criteria.
2. Collect information on disability and functional impairment and access to services that assist individuals to maximize their quality of life.
3. Collect information on comorbid medical disorders and the extent of access to healthcare for those disorders.
4. Include consumer and, where possible, caregiver perspectives in additional to symptom, disability and service utilization.
5. Using existing data where possible (state and federal registers and health networks).
6. Use innovative methods, including current and emerging social media and communication technology, cross-sectional surveys to identify cohorts for longitudinal follow-up to gain information on the course of illness, including remission and relapse.
7. Incorporate safeguards that respond to the ethical and consent issues necessary to allow biological samples (e.g. metabolic and genetic information) to be collected; information which has the potential to enhance treatment outcomes and help deliver on the potential

identified in the Precision Medicine Initiative (PMI) Cohort Program whose target groups include bipolar disorder and schizophrenia.

The United States regularly collects epidemiologic and related information, including from high quality surveys, about most of the major contributors to the burden of disease (e.g. cancer, cardiovascular disease and substance use disorders) and has world class psychiatric epidemiology expertise and experience. The US is ideally placed to be able to assemble and analyze the necessary information about psychotic and bipolar disorders to improve health and social outcomes for individuals with these conditions.

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