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SPECIAL ARTICLE

The global burden of mental and substance use disorders: changes in estimating burden between GBD1990 and GBD2010

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Background. The main aim of this paper is to compare and contrast the methodological approaches of the new Global Burden of Disease 2010 Study (GBD 2010) with the original study conducted for 1990 (GBD 1990), in terms of calculating burden for mental and substance use disorders.

Methods. We reviewed the conceptual and methodological changes to GBD burden calculations in the GBD 2010 study, compared with previous studies. We then discuss the possible implications of these changes with respect to burden estimates for mental and substance use disorders.

Results. It is not possible to compare burden estimates arising from the GBD 1990 study with the most recent burden estimates. There have been important advances in the categorisation and definition of mental disorders, and the input and computation of epidemiological models for disease distribution. There have also been major changes to conceptual and social value choices aimed at addressing concerns that arose following publication of earlier GBD studies.

Conclusion. Advancements to the GBD conceptual framework and method of calculating burden estimates has led to more accurate and equitable consideration of the burden for mental and substance use disorders. Proposed annual updates of GBD estimates by the Institute of Health Metrics and Evaluation provide an opportunity to continue to advance the evidence base that underpins the quantification of disease burden.

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Introduction

The first Global Burden of Disease study (GBD 1990) found that a large, previously under-recognised proportion of premature mortality and disability, aggregated as disability-adjusted life years (DALYs) was attributable to neuropsychiatric disorders. This grouping of disorders, comprising mental, neurological and substance use disorders, accounted for more than 8.5% of the entire global burden (DALYs) in 1990 and more than one-quarter of all years lived with disability (YLD) (World Bank, 1993; Murray & Lopez, 1996). These findings were highly influential, leading to increased attention to mental disorders on the global health agenda (Whiteford, 1999; World Health Organization, 2001) and a renewed impetus for mental health research (Kessler & Ustun, 2008). Estimates for selected mental disorders were revised in the early 2000s by the World Health Organization using updated epidemiological evidence and, for some disorders, modified health states and disability weights (Mathers *et al.* 2002; World Health Organization, 2008).

The GBD approach to assessing health loss has evoked considerable debate, around both methodological aspects of the burden calculations and concerns specific to particular disease groups, including mental disorders. The empirical data available in 1990 to inform mental disorder epidemiology was limited (Brhlikova *et al.* 2010). Some of the more common mental disorders (e.g., generalised anxiety disorder (GAD) and social phobia), those associated with premature mortality (e.g., anorexia nervosa) and disorders which typically commence in childhood (e.g., autism spectrum disorders) were noticeably absent (Andrews

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et al. 2000; Vos, 2006). Disability estimates were reliant on expert judgement rather than representative of community beliefs (Andrews *et al.* 2000; Kessler & Greenberg, 2002). Many considered the use of other social value choices such as age-weighting and discounting to be inequitable (Anand & Hanson, 1998; Williams, 1999; Arnesen & Kapiriri, 2004).

In 2007, a new study (GBD 2010) was launched. This was a comprehensive re-analysis of burden for 291 causes, 20 age-groups, for males and females separately in 187 countries, across 21 world regions for 1990, 2005 and 2010 (Murray *et al.* 2012). New burden estimates from the GBD 2010 study have been published for mental disorders (Whiteford *et al.* 2013*a*) and illicit drug use disorders (Degenhardt *et al.* 2013), showing that, together, mental and substance use disorders account for 7.4% of all burden worldwide. It is natural to draw comparisons between the findings of the first GBD study, subsequent updates and those produced for GBD 2010. However, there have been major conceptual and methodological changes to calculating burden estimates in GBD 2010 and this prevents the comparison of GBD 2010 burden estimates with previous studies. This paper describes some of the major methodological advances in GBD 2010 and the implications of these changes with respect to burden estimates for the mental and substance use disorders.

Mental disorders in GBD 1990 and GBD 2010

In GBD 1990, burden estimates were presented for 'neuropsychiatric disorders' which included neurological disorders (comprising epilepsy, dementia, Parkinson disease and multiple sclerosis), substance use disorders (comprising alcohol use and illicit drug use disorders) and mental disorders comprising affective disorders (unipolar depression and bipolar disorder), anxiety disorders (panic disorder, obsessive compulsive disorder and post-traumatic stress disorder) and schizophrenia (Murray & Lopez, 1996). The absolute number of DALYs attributed to neuropsychiatric disorders in 1990 was 145 million, 12% of which was attributed to neurological disorders, 17% substance use disorders and 71% mental disorders (unadjusted for comorbidity) (Murray & Lopez, 1996). Two additional disorders (primary insomnia and migraine) were included in revised estimates for 2000–2004, and the effect this had was to increase the proportion of total disease burden attributable to neuropsychiatric disorders from 10.5 to 13.1% (World Health Organization, 2008).

In GBD 2010, neuropsychiatric disorders were disaggregated into two separate groups: (a) neurological disorders and (b) mental and behavioural disorders, which included substance use disorders. Together, these categories captured a more comprehensive list of disorders than what was included in previous iterations. The specific mental disorders (including substance use disorders) captured in GBD 1990 and GBD 2010 are described in Table 1 (note that neurological disorders are not detailed here). To account for variation in burden within depressive disorders, separate burden estimates were calculated for major depressive disorder (MDD) and dysthymia in GBD 2010. For the same reason, burden was estimated for cannabis, amphetamine, cocaine, opioid and alcohol dependence separately rather than a combined estimate made up of harmful use and dependence of selected disorder types as previously reported. Instead of only three individual anxiety disorders, GBD 2010 captured estimates for 'any' anxiety disorder to account for the high co-occurrence of specific disorders. Furthermore, burden estimates were made for eating disorders (anorexia nervosa and bulimia nervosa) and childhood mental disorders, including pervasive developmental disorders (autism and Asperger's disorder) and childhood behavioural disorders (attention-deficit/hyperactivity disorder (ADHD) and conduct disorders).

Changes to the categorisation and inclusion of disorders in GDB 2010 mean that the new burden estimates reflect a more accurate representation of overall health loss caused by mental and substance use disorders and provides a wealth of information on the relative burden at different ages. The inclusion of childhood disorders is a particularly important advancement in GBD 2010 given that in regions such as Africa, children constitute up to 40% of the total population (United Nations, 2011). Together, burden for these early onset disorders accounted for almost 10% of the DALYs attributable to mental disorders. Hence, the exclusion of disorders commencing predominantly in childhood would miss a substantial component of the population burden in these regions.

Epidemiological data

Burden of disease calculations are based on meta-synthesis of available epidemiological data (Murray & Lopez, 1996), and as such, accuracy of burden estimates rely on the quantity and quality of the data identified. There is limited information about the empirical input for mental disorders in GBD 1990 (Vos & Mathers, 2000). In the 2000–2004 revisions, information on prevalence and incidence were ascertained through literature reviews and correspondence with researchers (Mathers *et al.* 2002) and were included if based

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Table 1. *Comparison of mental and substance use disorders included in the GBD 1990 and GBD 2010 studies**

Disorder categories	GBD 1990	GBD 2010
Eating disorders	Not included	• Anorexia nervosa • Bulimia nervosa
Childhood behavioural disorders	Not included	• ADHD • Conduct disorder
Autism spectrum disorders	Not included	• Autism • Asperger's disorder and Pervasive Developmental Disorder NOS
Anxiety disorders	• Panic disorder • Obsessive-compulsive disorder (OCD) • Post-traumatic stress disorder (PTSD)	• 'Any' Anxiety disorder, comprising: separation anxiety disorder, panic disorder, agoraphobia, specific phobia, social phobia, OCD, PTSD, generalized anxiety disorder
Schizophrenia	• Schizophrenia	• Schizophrenia
Bipolar disorders	• Bipolar disorder	• Bipolar disorders, including: bipolar I, bipolar II, bipolar NOS, cyclothymia
Depressive disorders	• Unipolar depression	• Major depressive disorder • Dysthymia
Drug use disorders	• Drug harmful use/ dependence	• Cannabis dependence • Opioid dependence • Cocaine dependence • Amphetamine dependence
Alcohol use disorders	• Alcohol harmful use/ dependence	• Alcohol dependence • Fetal alcohol syndrome
Other mental and substance use disorders	Not included	• Estimated attributable burden within residual categories of other mental and substance use disorders

*Neurological disorders are not included.
NOS, not otherwise specified.

on population-based studies with sample sizes greater than 1000, and used a random or national/regional sampling frame (Ayuso-Mateos, 2006).

The empirical data used in GBD 1990 and subsequent updates reflected the state of the literature at the time, exposing limitations in the epidemiological data for mental disorders. Due to lack of data available for unipolar depression for example, expert advice rather than empirical data was used to determine disorder duration and studies with sub-optimal representativeness, response rates and case definitions were included for other parameters (Brhlikova *et al.* 2010). To provide the best possible data for GBD 2010 epidemiological input was collated by over 50 expert groups through systematic reviews of the literature. The Mental and Substance Use Disorder Expert Group oversaw searches for studies reporting population-representative data for prevalence, incidence, remission/duration and excess all-cause mortality. The protocol and results of these reviews have been described in detail elsewhere (Ferrari *et al.* 2010, 2013; Degenhardt *et al.* 2011; Baxter *et al.* 2013*b*; Charlson *et al.* 2013; Erskine *et al.* 2013; Whiteford *et al.* 2013*b*; Baxter *et al.* 2014). In brief, epidemiological estimates for mental and substance use disorders were identified and extracted from a diverse range of studies, including national mental health surveys, more geographically limited regional and community surveys, health screenings in communities and schools, birth cohort studies and for disorders with higher treatment rates: psychiatric registry data and clinical records.

The final data sources that underpinned GBD 2010 estimates were drawn from 78 countries in 19 of the 21 GBD world regions. In comparison to previous GBD studies these data provided much greater representation of non-western populations, hence regional estimates for disease frequency (e.g., Africa, Central

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and Eastern Europe, South America and Asia) were more strongly based on empirical data with less reliance on extrapolation from West European, Australasian and North American data. Whilst the data still reflects a degree of incompleteness and methodological limitations (Baxter *et al.* 2013*a*), the improved evidence-base for epidemiological estimates in GBD 2010 is reflected in the improved confidence intervals for regions where empirical data were identified.

Disease modelling

Given that epidemiological data (e.g., prevalence and incidence estimates) used in the estimation of non-fatal burden are variable for those countries and regions where data are available, and absent for many countries and age groups, GBD developed disease-specific statistical models to first reconcile limitations arising from the data before YLDs were estimated. A generic disease modelling tool known as DisMod was developed for GBD 1990 to force consistency on the available data and to supplement missing data (Barendregt *et al.* 2003). Linear differential equations were applied to describe the transitions between major health states 'healthy', 'diseased' and 'dead' based on the transition rates incidence, recovery (remission) and excess mortality (Barendregt *et al.* 2003). Second-generation DisMod modelling (DisMod II) used in the GBD 2000–2004 revisions allowed a wider range of empirical data inputs to be included in the estimation of burden (including prevalence, remission and relative-risk of premature mortality), and was able to apportion different weighting and smoothing algorithms to the various inputs (Barendregt *et al.* 2003; Global Burden of Disease, 2009).

Disease modelling in GDB 2010 was based on a new Bayesian meta-regression tool, called DisMod-MR (Vos *et al.* 2012). This built upon the Incidence–Prevalence–Mortality disease model used in DisMod and DisMod-II and was able to estimate prevalence, incidence, remission, duration and excess mortality for 187 countries, 21 regions, 3 time points, males and females and 20 age groups. A generalised negative binomial model was estimated for all epidemiological data using super-region, region and country random effects as well as two sets of covariates: study level covariates which adjusted for variability in the empirical data arising from differences in the methodology used between studies; and country level covariates, which supplemented the predictive power of the model by adjusting for ecological effects in the data. For example, given the established association between conflict and mental disorders such as depression and anxiety disorder, a conflict-based covariate could be used to impute the prevalence of these disorders in populations exposed to wide-spread conflict. An important improvement in GBD 2010 was the ability for DisMod-MR to also estimate 95% ranges of uncertainty around all modelled epidemiological estimates. This was done by propagating uncertainty from the raw epidemiological data (as standard errors or 95% confidence intervals) and prior model settings through to the final model-derived estimates. Thus users of the burden estimates can identify where there is broad uncertainty around a regional estimate due to limited empirical input.

Prevalent burden *v.* incident burden

Burden of disease has traditionally been viewed from the perspective of incident cases, based on the premise that deaths are an incident occurrence (World Bank, 1993). This approach was said to be 'forward looking' as it focused on the future burden arising from new cases in a given year (World Bank, 1993; Global Burden of Disease, 2009). Previous GBD estimates are therefore considered incident as burden, within the context of YLD, were based on incident cases.

In GBD 2010, YLDs (and consequently DALYs) are considered prevalent. This means that the estimate reflects the burden for a specific year (e.g., 2010), regardless of when the disease commenced. Prevalent YLD calculations reflect the current disability in a population, which is particularly relevant for chronic disorders as the onset of many of these disorders occurred years earlier (Garcia-Fulgueiras *et al.* 2011). Moreover, prevalent YLD are more sensitive to time-trends, such as changes over time due to policy changes or new interventions. For example, incident cases of cervical cancers are predicted to fall over time due to the advent of the human papillomavirus (HPV) vaccine (Munoz *et al.* 2010) However, prevalence reduction will take longer due to the number of people who already have the virus. As such, it is vital not to overlook these already present cases when considering health-care priorities.

An additional benefit of prevalent YLDs is the greater availability and arguably better accuracy of data available for prevalence *v.* incidence in mental disorders (Hoek & van Hoeken, 2003). This is apparent in low and middle income countries (LMIC) where cohort studies are rare. To illustrate, prevalence data for anorexia nervosa were identified from 22 studies in 15 countries, whereas only five studies in the same number of countries, all high income (HI) countries, reported incidence. For ADHD there were no nationally comparable incidence studies found.

The use of prevalent, as opposed to incident, YLDs will therefore better represent burden attributable to

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mental and substance use disorders. The consideration of current disability means that disorders which often begin early in life and take a chronic course, such as depression, will not be under-represented by only considering incident cases. Furthermore, the use of prevalence data will allow more accurate burden estimations to be made given that this is the most available type of data particularly in LMICs where the cost and resources required for incidence studies are often prohibitive.

Disability weights

Beyond the epidemiological issues in compiling burden estimates, methods for estimating the extent of health loss, or disability have been controversial (Williams, 1999; Sanderson & Andrews, 2001; Mont, 2007). Disability weights used in the GBD 1990 study were derived by an international group of health care providers by calculating weightings for 22 indicator conditions using the person-trade off method (Murray & Lopez, 1996). These weights were then used to define seven disability classes ranging from perfect health to death and group consensus then determined distribution of the remaining conditions across the seven classes using the indicator conditions in each class as markers. The 2004 revision largely used the same disability weights, except for a few disorders (e.g., MDD) where weights from the Netherlands disability weights study were conducted (Stouthard *et al.* 1997; World Health Organization, 2008).

In response to increasing literature and debate on the definition and measurement of disability (Salomon *et al.* 2003; Mont, 2007; Salomon, 2010) certain aspects of the methodology used to generate previous disability weights were refined in the GBD 2010 study: (1) disability weights were estimated for a more comprehensive group of indicator conditions (230 health states); (2) multiple disability weights were allocated to schizophrenia, bipolar disorder, MDD and anxiety disorders to more accurately represent variability in severity and disability throughout the course of the disorder; and (3) rather than using an expert panel to derive disability weights, community representative surveys were used (Global Burden of Disease, 2009; Salomon, 2010; Ferrari *et al.* 2012).

To derive the disability weights face-to-face surveys were administered in Bangladesh, Indonesia, Peru, Tanzania and telephone surveys were conducted in the USA. In addition an online (open-access web-based survey) was conducted (Salomon *et al.* 2012). There were over 30 000 responses to questions in which participants were asked to nominate which vignette of a health state they deemed 'the healthier'. This required respondents to choose for instance whether a person who was deaf was in a less or more healthy state than a person with severe depression. Different combinations of health states were used for every participant. The pair-wise comparison responses were converted into discrete values and anchored between 0, representing perfect health, and 1 representing death (Salomon *et al.* 2012). Some disorders had several health states (e.g., mild, moderate and severe) designed to capture the difference in severity of symptoms associated with the disorder. The disability weights attributed to symptomatic health states have been published (Salomon *et al.* 2012). The health state specific disability weights were aggregated into an overall disability weight taking into account the proportion of cases in each health state. Capturing the complexity of health states in lay descriptions and the extent to which the loss of health attributable to mental and substance use disorders was communicated in these descriptions is one field of research that requires further consideration.

The highest disability weighting given to health states in GBD 2010 was that for acute schizophrenia (Salomon *et al.* 2012). Some of the new mental disorder weights were unexpected. For example, anorexia nervosa and bulimia nervosa were given the same disability weighting (0.223) while autism was considered less disabling than cannabis dependence (0.259 and 0.329, respectively).

Given the high comorbidity between mental and substance use disorders (and other health conditions) GBD 2010 made adjustments for independent comorbidity using microsimulation methods which are described separately (Whiteford *et al.* 2013*a*).

Discounting and age-weighting

Given that the DALY is a generic metric that can be calculated across all disease and injuries, it has important applications for comparative cost-effectiveness analyses between different health conditions (i.e., dollar per DALY averted) and this provides valuable input to decision-making in health service planning. Traditionally economic models have used a discounting method that reflects societal preference for a year of life now compared to a year of life at some time in the future. In previous GBD studies, DALYs were discounted at 3% in line with recommendations from the Panel on Cost-Effectiveness in Health and Medicine (Weinstein *et al.* 1996) and as used by the World Bank (Jamison *et al.* 1993). Results of sensitivity analyses from GBD 1990 suggest that use of different discount rates did have an effect on non-fatal burden, in terms of the proportion of total burden due to

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disability and the age distribution of burden (Murray & Lopez, 1996). The higher the discount rate is set, the greater the weighting given to YLDs. Murray and Lopez found that, with zero discounting, YLDs accounted for less than 25% of all disease burden whereas using a discounting rate of 10% resulted in YLDs making up more than 40% of all burden (Murray & Lopez, 1996). If a discount rate of zero were applied, the importance of burden in children less than 4 years of age was emphasised while a high discounting rate enhanced the importance of burden in groups over the age of 45 years.

A second adjustment common in cost-effectiveness analyses is age-weighting. Intended to capture the greater social responsibility of people in young and mid-adult life, its use results in a higher weighting and time lost due to premature mortality or disability between the ages of 9–55 years (Murray & Lopez, 1996). Use of age-weighting enhances the importance of disability (as opposed to mortality) because the majority of disability occurs in adulthood for which age-weights are greatest (Murray & Lopez, 1996). The important implication of age-weighting in burden of disease analyses is that it places greater emphasis on long-term chronic disabilities at younger ages, and ultimately, increases the proportion of burden due to YLDs.

Following GBD 1990, there was extensive debate about the use of these value choices (Anand & Hanson, 1998; Williams, 1999; Arnesen & Kapiriri, 2004). Use of discounting in GBD 1990 was disputed on two counts: first, that the willingness of a community to sacrifice health now for the sake of future health differs between populations, for instance if a community believe their material life is likely to be better in the future they require less inducement to make sacrifices now for future gain (Murray & Acharya, 1997; Williams, 1999). Hence, the discounting rate should vary between populations depending on economic conditions within each country. Secondly, discounting can result in an underestimate of burden due to mortality and morbidity in childhood (Anand & Hanson, 1998; Arnesen & Kapiriri, 2004). Given that age-weighting is intended to reflect the differential social value of people at different ages, this too led to criticism of inequitable burden estimates at different stages of life, with disability in childhood being assigned a lower level of burden, compared to that in adulthood, while conversely mortality in childhood was assigned a higher burden compared with that in adults (Anand & Hanson, 1998; Arnesen & Kapiriri, 2004). The combined effect of discounting and age-weighting was that disease burden attributed to younger age groups and to communicable disease was thought to be under-estimated in GBD 1990 (Anand & Hanson, 1998; Arnesen & Kapiriri, 2004).

Given the concerns raised around the inequity of such social value choices, age-weighting and discounting were not used in the GBD 2010 study (Table 2). The effect of this decision was not trivial for mental and substance use disorders. For example, had age-weighting and discounting not been used in the GBD 1990, burden estimates for these disorders were estimated to have been about 30% lower (Vos & Mathers, 2000). It is likely that this change has resulted in lower burden estimates for mental and substance use disorders in GBD 2010.

Discussion

GBD 2010 confirmed the findings of GBD 1990; mental and substance use disorders are major contributors to the global burden of disease, accounting for 7·4% of disease burden worldwide, a greater proportion of the overall global burden than that attributed to HIV/AIDS and tuberculosis (5.3%), diabetes (2%) or, transport injuries (3.3%). The number of DALYs caused by mental and behavioural disorders increased by 37·6% between 1990 and 2010. As there was little change in *per capita* DALYs, the increase of mental disorders was almost entirely attributable to population growth and ageing. Given the rise in life expectancy, one implication of the demographic change is that more individuals will be living with mental and substance use disorders for a longer period of time. For substance use disorders however, the increased burden of alcohol, opioid, and cocaine dependence, between 1990 and 2010 was driven by increasing prevalence of these disorders and less so by demographic transitions (Degenhardt *et al.* 2013).

While GBD 2010 provides the most comprehensive current picture of health loss caused by mental and substance use disorders, some limitations remain to be addressed in future GBD iterations. The limited contribution of YLLs to mental disorder burden, with many deaths coded to the physical cause of death and suicide coded to injuries under self-harm, deserves further consideration. This could be reflected in the comparative risk assessment of the GBD (Lim *et al.* 2012), which has not been discussed in this paper.

Another limitation is the way in which disability is measured and how weights were estimated. Disability as used within GBD is limited to 'within the skin' health loss, which emphasises physical pain and loss of sensory perception rather than the cognitive and emotional impact which is prominent in mental disorders (Salomon *et al.* 2012). In addition welfare loss, both current and future, is not captured by GBD. This is particularly significant for mental and substance use disorders which often impact on an

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Table 2. *Summary of important changes to calculating YLDs for mental and substance use disorders*

Methodological approach	GBD 1990	GBD 2010
Categorisation and definition of disorders	'Neuropsychiatric disorders' category included neurological disorders, mental disorders and substance use disorders	'Mental and substance use disorders' category now excludes neurological disorders and includes eating disorders, childhood behavioural disorders, autism spectrum disorders and a broader range of anxiety disorders
Epidemiological input	Compilation of large-scale study findings, including a mixture of population-based and clinical samples	Systematic reviews of all literature aimed to identify community-representative data on prevalence, incidence, remission/duration and excess mortality
Disease modelling	Linear differential equation modelling (DisMod 1). Required incidence data as input, heavily reliant on transformation of data to satisfy modelling tool parameters	Bayesian meta-regression (DisMod MR). Able to pool multiple data sources, adjust for known variation in the data and propagate uncertainty from a variety of sources
Prevalent YLDs *v.* incident YLDs	YLDs calculated based on incident cases and estimates of duration.	YLDs calculated using prevalent cases
Disability weights	Derived using expert consensus using person-trade-off method	New weights derived using pair-wise comparison based on responses from multiple community surveys
Discounting and age-weighting	Age-weighting and 3% discount rate applied to DALY calculations	Uniform age-weights and zero discount rate used

individual's economic, social and academic functioning as well as that of their family. The method used for estimating disability weights required pairwise comparisons of lay vignettes no more than 35 words in length. While rankings were relatively consistent across different countries, it is possible that stigma and other factors may have influenced which conditions were seen as more 'unhealthy'.

With the continued evolution of the GBD framework, and the proposed annual updates of GBD estimates by the Institute of Health Metrics and Evaluation, there is an imperative to advance the evidence-base that underpins the quantification of the impact of mental and substance use disorders. This will allow the most accurate description of the contribution of these historically neglected disorders and highlight their importance in global public health.

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Conflict of Interest

None.

Ethical Standard

This research did not involve human and/or animal experimentation.

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