

Screening for depression: the global mental health context

Depression is the leading mental health related cause of the Global Burden of Disease. The sequelae of depression contribute further to its immense public health burden, including impact of maternal depression on child growth and development, and increased risk for dementia, suicide, and premature mortality from co-occurring physical disorders. The World Health Organization (WHO)'s Mental Health Gap Action Programme (mhGAP) guidelines recommend antidepressant medication or brief psychological treatments for moderate to severe depression, and there is a mounting body of evidence from trials on how these treatments can be delivered in real-world primary care settings in low resource contexts by relying on lay health workers and primary care practitioners¹.

Despite this evidence on cost-effective and scalable models of depression care, the vast majority of people suffering from this condition – for example up to 90% in India and China – do not receive treatment. A major barrier to receiving treatment is the low detection rate in primary care. To date, virtually all efforts to improve detection have focused on training of general practitioners, and this is also the approach adopted by the mhGAP guidelines. Yet, the evidence in support of training is weak. In an early WHO Collaborative Study, following training of primary care workers in four countries (Colombia, India, Sudan and Philippines) to detect mental disorders, detection rates barely increased from 2.4% to 2.6%². In a Kenyan study, detection rates post-training did not significantly differ between the trained and the control group³. In a cluster randomized controlled trial conducted in Malawi, while there was a significant difference between the 5-day mental health trained primary care workers and workers in the control condition, the training arm failed to detect 90% of patients with depression⁴. In short, training alone has a negligible or, at best, a small impact on detection rates.

It is in this context that screening should be considered as a cost-effective supplementary strategy to improve the detection of depression in routine care settings and translate the evidence of effective interventions to reduce its global health burden. Many of the trials in low and middle income countries, as well as US-based studies such as IMPACT⁵ and PROSPECT⁶, have shown that lay workers or general medical ancillary personnel (e.g., nurses and social workers) can be taught to screen for depression and other common mental disorders effectively using brief questionnaires with a high degree of acceptability.

We emphasize that the use of such questionnaires also meets the criteria recommended for screening tests, for example, that the test is valid, feasible at a very low resource cost, and that there are cost-effective interventions to follow. Additionally, screening using symptom measures avoids the complexity of diagnosis, and the same measure can be used for monitoring of clinical progress and outcomes, as in the Improving Access to Psychological Treatments national program in England⁷. Based on these experiences, and the recent recommendations of the

US Preventive Services Task Force⁸, we propose steps regarding the implementation of screening for depression in routine care.

The first consideration is *what* measure should be used for screening for depression. Experience supports the use of brief, self-report questionnaires, such as the Patient Health Questionnaire (PHQ-9)⁹, which has been widely used internationally, takes a few minutes to complete, can be used to generate a diagnostic outcome, and shows sensitivity to treatment response. One caveat, however, is that, because depression and anxiety frequently co-exist, additional brief screening for anxiety may also be appropriate, using such measures as the Generalized Anxiety Disorder 7 (GAD-7)¹⁰.

The second consideration is *how* screening should be done. These questionnaires can be delivered either in self-report or health worker delivered formats and, with the growing use of digital technologies, can also be used on devices to allow for self-screening and remote monitoring of clinical progress. Stepped approaches to screening, for example using the two-item version of the PHQ routinely for all attenders, followed by the remaining seven items for those who screen positive on at least one question, may also be a cost-effective approach.

The third consideration is *who* should be screened. Given the high prevalence of depression and other common mental disorders in primary care populations, one option is to routinely screen all adult attenders. However, this may not be feasible in the very low resource settings, where the possible yield of cases may greatly exceed the feasibility of delivering effective interventions. This challenge may be partly addressed by calibrating the screening questionnaire cut-point to a higher level, so that only more severe presentations are identified. An alternative approach is to screen high-risk or vulnerable groups such as mothers with newborn children, people with chronic diseases, people with chronic sleep disturbances or medically unexplained somatic complaints or severe social stressors.

The fourth consideration is *when* screening should take place. Since depression is frequently a recurring condition, annual screening, in particular for individuals with a prior history, would seem sensible.

In conclusion, now that we have strong evidence on how we can effectively treat patients with depression in a cost-effective way using locally available resources, it is time to scale up this evidence through addressing the barrier of low detection rates by instituting routine screening. This recommendation to improve detection needs to be accompanied by a research agenda addressing many of the considerations outlined above regarding the implementation of screening, such as the measure to be used, the frequency, the method of delivery and the target group.

Routine screening for depression in adult primary care attenders is a vital milestone in the journey towards reducing the very large treatment gaps globally and scaling up the robust evidence on cost-effective interventions for this common mental disorder.

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Antidepressants and suicide risk in depression

The last years have witnessed a controversy about antidepressant use that is still in the balance. On one side, treating depression with antidepressants seems to reduce the risk of suicide at an epidemiological level¹. This is in accord with the high population attributable risk for a first occurrence of suicidal ideation and suicide attempts in people with mood disorders, which has been estimated at 51% and 44% respectively², and with the finding of a history of depressive episodes in most completed suicides (approximately 60%). On the other, the possible emergence or worsening of suicide risk at the beginning of treatment, at least among the young, has led regulatory bodies to issue specific warnings. Antidepressant prescriptions fell as an effect of these warnings, also in adult populations, and research about the *suicidal effect* of antidepressants was fostered. Doubts about the usefulness of antidepressants in the treatment of depressed patients who are or become suicidal need an urgent response.

The controversy began in 2003, when re-analyses of data from randomized controlled trials (RCTs) found that the risk of suicidal ideation or suicidal attempts among youth treated with antidepressants was doubled compared with those treated with placebo (4% vs. 2%), independently of the indication (see Brent³ for a review). Later, a meta-analysis of RCTs across the life span reported an increased risk of “suicidality” with antidepressants under the age of 25 years. Of note, this risk was found only in patients with psychiatric indications other than depression, while antidepressants showed a protective effect in depressed elderly subjects⁴. Reporting about suicidal events in RCTs, most of which are not aimed at examining suicidality, is limited by important shortcomings. Anyway, the warnings – amplified by the alarming media coverage – led many physicians to decrease antidepressant prescriptions, even when no alternative was available⁵.

The use of antidepressants to prevent suicidal behaviour is supported by several facts. First, most pharmacoepidemiologic studies, which are more representative of patient populations than RCTs, show a protective effect of antidepressant use with respect to suicide¹. Second, although observational studies suggest an increased risk of suicidal ideation or suicide among young people receiving antidepressants, antidepressants actually seem to reduce the risk when confounding by indication is accounted for³. Third, post-mortem studies with toxicological

detection of antidepressants indicate that suicides in depressed patients occur more often among those who are not taking an antidepressant¹.

Furthermore, treatment-related suicidal events can be minimized. The guidelines produced by the US Food and Drug Administration and the UK National Institute for Health and Care Excellence recommend a closer monitoring of antidepressant treatment in suicidal patients or those younger than 30 years, with a follow-up visit one week after the start of a new antidepressant. Web-based tools and smartphone apps may help in the near future to improve the monitoring of patients at risk. On the other hand, depressed patients are frequently non-adherent to treatment, which has made some authors wonder if antidepressants have actually any effect, positive or negative, on suicide rates at the level of the general population⁶.

This controversial context has also fostered research, but only some observational studies have investigated the predictors of *de novo* suicidal behaviour in depressed patients starting an antidepressant^{5,7}. In general terms, treatment-emergent suicidal ideation is infrequent in adults and tends to disappear progressively in the first 4-6 weeks of treatment. The lack of response to treatment, a history of previous suicide attempts and a history of substance use disorders are the best predictors of the emergence of new suicidal ideation or attempts. Of note, starting treatment with high doses of antidepressants (beyond the recommendations) seem to increase the risk of suicidal ideation or attempts⁵.

Suicidal events at the onset of antidepressant treatment may also be associated with an undiagnosed bipolar disorder, whose presence may be suggested by early onset of depression and atypical depressive episodes. Moreover, the age effect in treatment-emergent suicidal ideation or attempts is probably influenced by the more frequent association of substance abuse and impulsive aggression with depression in the youth.

All these findings sum up to the general need of a paradigm shift in the treatment of suicidal patients. The clinical response to antidepressant treatment is poorer in subjects presenting suicidal ideation or a history of suicide attempts, independently of clinical confounders or the type of antidepressant⁷. Those who are most in need of an efficient treatment respond less well. The