What is needed to eradicate the depression epidemic, and why

Johan Ormela,⁎ Pim Cuijpersb, Anthony Jormc, Robert A. Schoeversd

a University of Groningen, University Medical Center Groningen, Hanzeplein 1 9700RB, the Netherlands
b Vrije Universiteit (VU) Amsterdam, the Netherlands
c University of Melbourne, Australia
d University of Groningen, University Medical Center Groningen, the Netherlands

ARTICLE INFO

Keywords:
Prevention
Depression
Structural Embedment
Treatment effectiveness
Etiology
Environmental risks
Parenting
Personality Traits

ABSTRACT

Despite substantial investments in the treatment of major depressive disorder (hereafter ‘depression’), especially antidepressant medications and cognitive behavioral therapy, epidemiological data do not indicate that depression burden, as measured by the period prevalence, has decreased in recent decades.

Although improving the delivery and quality of treatment will undoubtedly reduce episode duration and recurrence risk, and thereby reduce depression burden, the effect is probably limited because treatment does not always improve long-term outcomes. To further reduce the burden, prevention of depression episodes is crucial. Unfortunately, so far preventive efforts have not succeeded in reducing depression burden either. This, we argue, arises from a lack of socially-embedded structural prevention efforts and the difficulty of reducing the impact of major determinants.

First we summarize the evidence on period prevalence and treatment trends and the limitations of current prevention strategies that have hampered both their effectiveness and large-scale implementation. Then we analyze the modifiability of major determinants of depression and identify the prerequisites for effective prevention to reduce depression burden and explain their importance. Prerequisites include embedment in major social institutions, structural funding, legal consolidation, starting early in life, simultaneous targeting of major personal and environmental determinants and their interactions. This includes addressing both poor parenting and children's maladaptive personality traits and insufficient life skills, and combining universal, selective, and indicated prevention strategies with an emphasis on universal prevention. Although it is necessary to determine the feasibility and cost-effectiveness of the proposed prevention strategy, we think that without it, the depression epidemic will not subside.

1. Introduction

Major depressive disorder (‘depression’) as operationally defined by the Diagnostic and Statistical Manual of Mental Disorders (APA, 1994) during recent decades is a common, highly heterogeneous disorder category with a 12-month prevalence of about 5% in Western countries (Bromet et al., 2011; Ferrari et al., 2013). About 150 million people worldwide are affected with depression at any moment, and one in every five women and one in every eight men experience an episode of major depression over the course of their life (Bromet et al., 2011; Ferrari et al., 2013; Kessler & Bromet, 2013). Depression is associated with disability, loss of quality of life, increased service use, considerable productivity losses, and increased mortality (Erskine et al., 2015; Ormel et al., 1994; Vos et al., 2017; Whiteford et al., 2013). Depression is projected to become the single leading cause of disease burden in high-income countries by 2030 (Mathers & Loncar, 2006).

Despite substantial increases in expenditures on mental health care and treatment (Jorm, Patten, Brugha, & Mojtabai, 2017; Saxena, Sharan, & Saraceno, 2003), especially antidepressant medication (Marcus & Olsson, 2010; Olsson, Marcus, Druss, & Pincus, 2002; Olsson, Blanco, Wang, Laje, & Correll, 2014), epidemiological data since the 1980s do not indicate that the burden of depression has decreased, as indexed by 1-month or 12-month prevalence of depression in the general population (Ferrari et al., 2013; Kessler & Bromet, 2013). Although it is possible that depression burden would have gone up without this increase in treatment, stable prevalence rates suggest a limited impact of treatment at the population level.

These findings also raise the question: what is needed to reduce the...
depression burden in the near future? Some reduction could be achieved with more effective treatments and smaller treatment gaps (Chisholm et al., 2016). However, since the 1990s there have been few new drug therapies for depression and newer psychological treatments appear not more effective than already existing ones (Barth et al., 2013). Even with optimal treatment delivery of currently available treatments, other approaches are necessary to reduce the burden (Andrews, Issakidis, Sanderson, Corry, & Lapsley, 2004).

Prevention is a very interesting option to reduce depression burden, but it has its own complexities. Universal, selective, and indicated prevention trials report small to occasionally moderate effectiveness, but they often involve psychological therapies administered to motivated people with sub-threshold symptoms, rarely target the strongest determinants of risk upfront, are often limited to short-term outcomes (rarely exceeding 1–2 years), and their effects tend to decrease over time (Jorm & Mulder, 2018). In addition, prevention has not been widely implemented and, when implemented, adherence is far from optimal. Populations at the highest risk are often the least motivated to participate (Cuijpers, van Straten, Warmerdam, & van Rooy, 2010).

In this article, after summarizing the evidence on the increases in treatment and prevention without corresponding reductions in depression, we discuss its implications and the conditions that prevention has to meet in order to substantially reduce the burden of depression. These include political and social embedment in major social institutions, structural funding, consolidation in the law, starting early in life, simultaneously targeting major personal and environmental determinants and their interactions, and combining universal, selective, and indicated prevention with an emphasis on universal prevention.

2. Evidence that the burden of depression has not fallen despite increased treatment

2.1. Prevalence trends

Since the introduction of operational criteria for mental disorders in the 1970s, there have been many epidemiological studies of mental disorders, most in high-income Western countries. In 2013, Ferrari and colleagues published their meta-analysis of 116 epidemiological period prevalence studies performed between 1980 and 2011 (Ferrari et al., 2013). The point prevalence of depression, adjusted for methodological differences, was 4.7% (95% CI 4.4–5.0 %) globally, 3.7% (3.1–4.3) for North America, and 4.7% (4.2–5.1) for Western Europe. Cross-national differences in prevalence were substantial and, though diminished, these differences persisted after adjusting for study-level determinants of prevalence. The meta-analysis detected a time effect suggesting that the point prevalence of depression had increased over time. This was based on an ecological comparison that used the midpoint of the case ascertainment period as a continuous variable. The authors noted that this finding could be due to methodological or ecological differences across time that they were unable to capture.

More direct trend information was collected in three large repeat cross-sectional surveys that examined trends over periods of 10–12 years in the 1990s and 2000 (Compton, Conway, Stinson, & Grant, 2006; de Graaf, Ten Have, van Gool, & van Dorsselaer, 2012; Kessler et al., 2005). Each survey used face-to-face interviews, the same diagnostic criteria, and consistent assessment instruments over time. Neither of these trend surveys found a significant drop in 12-month depression prevalence when adjusted for demographic differences in the samples. Unexpectedly, the repeat survey reported by Compton and colleagues found the opposite: past-year prevalence had doubled between 1991–1992 and 2001–2002, from 3.3% to 7.0%. Note that the Compton et al. surveys were by far the largest of the three with more than 40,000 respondents at each wave.

Most epidemiological prevalence studies of depression have lower age limits, typically 18 years, but research has generally found stable prevalence estimates for children and adolescents as well (Costello, Erkanli, & Angold, 2006), although some studies report an increase of internalizing problems in adolescents and young adults during the twenty-first century, in particular burnout and depression in females (Bor, Dean, Najman, & Hayatbakhsh, 2014; Keyes, Gary, O'Malley, Hamilton, & Schulenberg, 2019). This increase could be due to increased pressure on achieving a myriad of goals in life and associated perfectionistic concerns (Hill & Curran, 2016).

2.2. Mental health care expenditures

The stability of depression prevalence is at odds with the substantial increase in mental health treatment expenditures since the 1980s in Western countries (Jorm et al., 2017; Saxena et al., 2003). In the Netherlands, for example, the annual growth in mental health expenditures (excluding primary care) was 5.6% between 1982 and 2010 (Niaounakis, 2013; Statline, 2017). Treatment costs of depression increased 240% (Statline, 2017) and full-time jobs in specialty mental health care doubled. In the US, expenditures on mental health increased between 1986 and 2005, with an annual growth of 6.9% (Mark, Levit, Vandivort-Warren, Buck, & Coffey, 2011). In Australia, total government expenditure on mental health increased by 178% in real terms between 1992/93 and 2010/11 (Note 1).

Although the rise in mental health expenditures was driven to a large extent by inflation and salary improvements, it also reflects more mental health care for more people. Most of this increase was spent on antidepressant treatment, but also, to a lesser extent and not in all countries, on psychotherapy (Brugha et al., 2004; Jorm, 2014; Kessler et al., 2005; Niaounakis, 2013; Olsson et al., 2002; Olsson et al., 2014; Olsson, Blanco, & Marcus, 2016; Patten et al., 2016; Spiers et al., 2016; Whiteford et al., 2014). The increase was especially substantial in the 1990s and in general medical settings (Verhaak, van de Lisdonk, Bor, & Hutschemaekers, 2000).

2.3. Has a prevalence drop been masked?

Despite stable depression prevalence, it is possible that a true treatment-driven prevalence drop has been masked by an increase in environmental risk factors or greater willingness to disclose mental health problems during recent decades. Research on such trends is hampered by a lack of statistics, the use of varied data sources and measures, between-country differences, and temporal trends in survey response rates. Averaged across Western countries, the evidence does not suggest a substantial increase in environmental risk (e.g., Jorm et al., 2017; Patten et al., 2016). Likewise, the implications of recent major economic, technological and sociocultural changes for proximal risk factors are difficult to discern. Thus, we cannot rule out that small increases in objective risk, growing mismatches between expectations and reality (visible to all thanks to the internet), increasing inequality, and medicalization of unhappiness have masked a prevalence drop caused by an increased need for treatment. But it is unlikely that this has occurred to an extent that it has masked a large treatment-driven prevalence drop (e.g., Jorm et al., 2017; J. Ormel, Kessler, & Schoevers, 2019; Patten et al., 2016).

2.4. Conclusion

The stable or slightly increased period prevalence of depression suggests a low effectiveness for treatment at the population level. This raises the question of what is needed to reduce the burden of depression in the near future. It is plausible that decreasing the treatment gap will have some impact on the period prevalence (Andrews et al., 2004; Chisholm et al., 2016), but given the limited long-term effectiveness of current treatments, the impact at the population level is probably modest. Andrews and colleagues calculated that even optimal treatment with evidence-based treatments and 100% coverage could prevent ‘only’ 34% of depression burden (Andrews et al., 2004). It is clear that
other approaches are necessary to reduce the burden further. Prevention is a very interesting option, as it has the potential to reduce not only recurrences but also first-ever episodes, and thus reduce both periods and lifetime prevalence. The next section examines preventive efforts undertaken thus far.

3. Preventive interventions to date: unfulfilled potential

Caplan’s 1964 book “Principles of Prevention Psychiatry” marked the introduction of theories of prevention into psychiatry. But it took another two and a half decades before the first randomized controlled trials (RCTs) were carried out to test whether depression could be prevented. Since the 1980s, a large number of RCTs of preventive interventions have been published; including universal, selective, and indicated prevention; targeting parents, children, adolescents, or adults (Munoz, Cuijpers, Smit, Barrera, & Leykin, 2010). Most programs were based on psychological (Cognitive Behavioral Therapy, CBT), educational, and behavioral (activation) principles and delivered in a variety of settings, such as schools, general medical care, and pregnancy-related settings (Jorm & Mulder, 2018). Initially, efforts to prevent major depression targeted individuals, but more recent research has emphasized the need to address family, community, and social levels of intervention (Note 3). Internet- and mobile-phone-based interventions for preventive purposes are increasingly examined (e.g., Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Buntrock et al., 2016; Cuijpers, Donker, van Straten, Li, & Andersson, 2010; Jacka et al., 2013).

Systematic reviews and meta-analyses of up to 156 trials consistently report small to modest overall effectiveness for psychological and/or educational interventions to prevent depression in a variety of settings (including health care and primary care, schools, and community settings) and populations (including students, pregnant women, young mothers, and others) with a pooled SMD of 0.16 (0.07–0.26) e.g., (Calear & Christensen, 2011; Christensen, Pallister, Smale, Hickie, & Calear, 2010; Conejo-Ceron et al., 2017; Cuijpers, 2008; Kavanagh et al., 2009; Munoz et al., 2010; van Zoonen et al., 2016; Werner-Seidler, Perry, Calear, Newby, & Christensen, 2017). Universal depression prevention programs were less numerous and often had smaller effect sizes relative to more targeted programs that utilized selective or indicated prevention.

These meta-analyses show that the efficacy of most psychological and educational interventions to prevent depression is a robust finding, especially in high-risk populations, even though effect sizes are typically small (incidence risk ratios in the range of 0.7–0.8 corresponding to numbers needed to treat [NNT] around 21; incidence drops of 20% to 25%; and SMDs around –0.16 with ORs ~0.75). Note that these NNTs are comparable to the NNT = 21 observed for the use of statins over 5 years to prevent recurrence of acute myocardial infarction (Cuijpers, van Straten, Smit, Mihalopoulos, & Beekman, 2008). Regarding internet- and mobile-phone-based interventions, a recent meta-analysis of 10 RCTs testing CBT-based preventive eHealth interventions found a pooled mean difference of 0.25 (95%CI 0.09, 0.41) for short-term outcomes, but no effect on long-term disorder incidence rates (Deady et al., 2017).

There is strong evidence that prevention of depression and other common disorders can be cost-effective, at least in the short-term. This holds for children(Heckman, 2011), adolescents in schools(Lee et al., 2017), and adults (Knap. McDaid, Parsonage, 2011; McDaid, Park, & Wahlbeck, 2019). For instance, Lee and colleagues identified two types of intervention with sufficient evidence of efficacy: universal prevention involving group-based psychological interventions delivered to all participating high school students and indicated prevention involving group-based psychological interventions delivered to students with subthreshold depression (Lee et al., 2017). They estimated the averted cost per disability-adjusted life year at about $5500 for universal prevention and $13,500 for indicated prevention.

3.1. Preliminary conclusions and cautionary notes

Apart from the robustly demonstrated, though limited, effectiveness of depression prevention, the meta-analytic evidence suggests at least 10 additional points that contextualize the promising efficacy findings. These points qualify the implications of prevention for the reduction of depression burden, making current prevention less straightforward than it might otherwise seem.

(1) A substantial minority of trials, about 24% of the 156 included in Bellon’s review, did not report statistically significant differences. In addition, only 24% had follow-ups exceeding 12 months.

(2) In general, effect sizes seem to depend on the risk gradient, with the lowest effect sizes typically found among universal samples and the highest among indicated and selective samples (Horowitz & Garber, 2006; Jane-Llopis, Hosman, Jenkins, & Anderson, 2003; Munoz, 2010; Stice, Shaw, Bohon, Marti, & Rohde, 2009). This might explain why the effects of selective and indicated prevention are often larger than the less common universal preventions, although it may partially also be an artifact, because universal interventions need much larger sample sizes, and such studies have hardly been done (Cuijpers et al., 2008).

(3) Trials with long-term follow-ups tend to find that effect sizes drop over time, perhaps due to a natural decay process (e.g., Kavanagh et al., 2009; Merry et al., 2011; Stice et al., 2009). For instance, Merry’s review of 16 studies including 3240 participants reported outcomes on depressive diagnosis found that the risk of having a depressive disorder post-intervention, expressed as risk difference (RD), dropped from −0.14 to −0.06 at three and 12 months. Hence, it is unclear how long the observed preventive effects will last. A notable exception are RCTs of preventive parenting interventions (Kaminski, Valle, Filene, & Boyle, 2008; Sandler, Schoenfelder, Wolchik, & MacKinnon, 2011; Yap et al., 2016). A substantial number of these trials have found long-term effects on a variety of child outcomes, typically in the domain of externalizing problems. However, it is unclear how well these findings generalize to depression.

(4) Due to a lack of RCTs using active comparators (e.g. placebo attention), it is unclear whether RCTs using passive comparators (e.g. waiting lists) overestimate efficacy, as has been observed for psychological and pharmaceutical treatment of depressed patients (Cuijpers & Cristea, 2015).

(5) Larger samples tend to have smaller effect sizes (Slavin & Smith, 2009).

(6) Some RCTs of selective/indicated preventive interventions are perhaps more accurately described as treatment that sought to prevent relapse or recurrence in remitted individuals (Jorm & Mulder, 2018). It is not clear whether such RCTs have been excluded from the meta-analyses (which is important because they may have relatively large effect sizes). In addition, extending this same sort of treatment approach further down the continuum of severity may not be a cost-effective way to improve public mental health.

(7) While the methodological quality of RCTs has steadily improved, there are often still problems with random assignment, blinding, and active controls (Cuijpers, Smit, & Beekman, 2010; Stockings et al., 2016; van Zoonen et al., 2014). Higher-quality studies report substantially smaller effects (Araya et al., 2013; Merry et al., 2011; Stallard et al., 2012; Stockings et al., 2016).

(8) Most meta-analyses, but not all (e.g., van Zoonen et al., 2014), found significant heterogeneity and methodological weaknesses, reducing the validity of their conclusions of efficacy (e.g. Merry et al., 2011; Stockings et al., 2016; Werner-Seidler et al., 2017).

(9) Internet- and mobile-phone-based interventions supported by an online trainer or coach yield better outcomes and retention rates.
than unguided interventions (Bennett et al., 2019), as has also been found for computer-based treatment of depression (Ebert et al., 2016; Johansson & Andersson, 2012). A recent high-quality RCT without support was negative (Whittaker et al., 2017).

(10) It is not clear whether the cost-effectiveness studies used realistic effectiveness estimates adjusted for the limitations listed above.

These 10 issues, in particular the small effects, their decay over time, the paucity of long-term follow-ups, and the potential for bias, reduce the hope that current preventive programs have substantial positive effects that persist long-term (> 2 years). Consistent with this concern is the drop in effectiveness observed with higher methodological quality, in particular when trials used active comparators (e.g. placebo attention) or examined outcomes at 12 months or longer (Araya et al., 2013; Cuijpers & Crisitea, 2015).

3.2. Prevention to date is not sustainably implemented and has limited reach

Prevention is still not widely implemented and, if implemented, is not much used by those who might benefit most (Cuijpers, van Straten et al., 2010; McLaughlin, 2011). A variety of hampering factors may play a role, including doubts about long-term effectiveness, difficulties in doing trials on the strongest risk factors, costs, stigma, and a lack of long-term public health perspective and imagination. As indicated above, doubts about long-term impact are not unreasonable. Uncertainties also exist regarding the best intervention methods given the few trials that examined interventions based on problem-solving and interpersonal therapy (IPT) principles. Cost is a major barrier as well (McLaughlin, 2011). Many health systems have limited resources for prevention because they give priority to treatment services. In the Netherlands, for example, patients have a legal right to treatment. As a result, resources for prevention are very limited and it is difficult to redirect part of the budget to prevention. Furthermore, as prevention may be ‘anonymous’, the costs of such interventions are not covered by individual health insurance policies. In times of recession and public budget constraints, prevention is typically the first victim. To reduce the costs of expensive intervention, technology-based interventions and administration by lay-personnel hold some promise (Munoz, 2010; Patet et al., 2017).

Perhaps the largest obstacle for sustainably implemented prevention is the lack of a long-term perspective and imagination. Politicians’ perspectives are often dominated by short-term concerns, i.e., until the next election. Because of this time frame, it is difficult for politicians to embrace and support the long-term (i.e., life-long) benefits of prevention and endure the long wait for a return-on-investment that might take years to completely accrue. In addition, the benefits of such interventions are typically widespread across all sorts of departments and sectors, benefitting mostly sectors other than those who funded the prevention in the first place.

3.3. Lessons learned

What lessons can be drawn, either from the available evidence on prevention or from common sense? What seems to work and what does not? First, and most importantly, to realize sustainable large-scale implementation of prevention, structural social embedding of prevention is essential. Second, it is important to learn from other fields, in particular public health approaches to reduce smoking and improve physical activity and diet (Jacka et al., 2013). Population-level prevention strategies to reduce cardiovascular disease and cancer mortality have been rather successful (Eheman et al., 2012; Mendis, 2017). Their experiences suggest better prevention results with longer-term, more structural, more intensive programs, with multiple components and multiple targets (at a variety of levels, e.g. individual, class, school, curriculum, and community) (Jacka et al., 2013). Third, integrate depression prevention with public (mental) health promotion and prevention. In particular, integrate population-wide preventive interventions for depression with those for other (physical) disorders that share lifestyle behaviors with depression. Fourth, strengthen the evidence base by addressing the limitations and unanswered questions of previous RCTs, notably long-term outcomes and improving methodological rigor. These issues continue to fuel doubts and reservations about the effectiveness and cost-effectiveness of prevention. Fifth, prevention programs for heart disease and cancer have targeted major risk factors, which psychiatry has shied away from, perhaps because it was perceived as too difficult, and instead focused on adapting psychological therapies for prevention. However, to be truly effective, prevention should target strong but modifiable determinants.

4. Causal risk factors and their modifiability

Prevention is a very interesting option for reducing depression burden, but it requires sufficient modifiability of strong causal risk factors. It is well-established that depression has complex multi-factorial etiologies implicating both personal and environmental risk factors as well as interactions amongst these factors, and correlations due to their effects on each other (Brown, Bifulco, & Harris, 1987; Kendler, Gardner, & Prescott, 2006; Kendler & Gardner, 2011; Otte et al., 2016; Rutter, Moffitt, & Caspi, 2006). A number of conceptual models have been proposed to organize this complex interplay; these models often share the diathesis-stress paradigm (Hankin & Abela, 2005; Monroe & Reid, 2009). For example, the Dynamic Transactional Stress-Appraisal-Coping model, schematically depicted in Fig. 1, distinguishes between (i) stress-appraisal-coping processes and (ii) relevant personal and environmental risk and protective characteristics (Ormel & Jong, 1999). The latter are further divided into more proximal determinants versus more distal or upstream determinants. The model shows how personal and environmental risk and protection factors influence mental health via their effects on (i) the occurrence of provoking agents, notably stressful life events and long-term difficulties, and on how people (ii) appraise (provide meaning) and (iii) cope with the provoking agents (Folkman & Lazarus, 1986; Lazarus & Folkman, 1984; Ormel & Jong, 1999).

Tables 1 and 2 present an overview of the risk factors that are generally considered determinants of depression, although conclusive causal evidence is still lacking for some (Copeland et al., 2018; Dobson, Quigley, & Dozois, 2014; Goldberg & Huxley, 1992; Hankin & Abela, 2005; Kendler et al., 2006; Kendler & Gardner, 2011; Kessler et al., 2010; Kohler et al., 2018; Moffitt, Poulton, & Caspi, 2013; Ormel, Neel, & Wiersma, 2001; Otte et al., 2016; Saveau & Nemeroff, 2012; Schakixs et al., 2017; Smit, Beekman, Cuijpers, de Graaf, & Vollebergh, 2004; Uber & Zwicker, 2017; Wray et al., 2018). A crude indication of the strength of evidence is provided by the quantity of evidence, the methodological quality (experimental, prospective, case-control, cross-sectional), and causal plausibility of the relationship. From the perspective of the fraction of risk attributable to personal factors, the most important person-level determinants of depression include high negative affectivity and a related avoidant (emotionally-oriented) coping style, low conscientiousness, and related poor planning (and obviously the genes co-driving these traits). From the environmental side, important factors include: major adverse childhood experiences (physical maltreatment, sexual abuse, neglect, and trauma); stressful life events and difficulties characterized by loss, entrapment, or humiliation; as well as poverty, social isolation and probably social inequality (Pickett & Wilkinson, 2015) as more upstream determinants.

Especially large risks arise from co-occurring and cumulative personal risks and environmental disadvantages. For instance, adverse childhood experiences could result from maladaptive transactions between (a) poor parenting due to genetically driven “difficult” personality traits of parents and (b) problem behavior of children towards their parents and peers due to the same genetically driven “difficult"
personality traits that the children inherited from their parents (Caspi, Bern, & Elder, 1989; Rutter et al., 2006). Such maladaptive transactions can keep feeding “cascading pathways” of risk
For example, poor parental handling of a child’s noncompliance can lead to increases in the child’s noncompliant behavior and the development of aggression, which in turn can lead to more aversive behavior by the parents. In addition, “cumulative continuity” can develop (meaning that people tend to select into contexts that reinforce their personality traits), causing personal and environmental risks to reinforce each other and become entrenched (Caspi et al., 1989; Rutter et al., 2006).

4.1. Modifiability of genetic risk: perhaps in the future

Twin and family studies suggest a heritability of depression between 30% and 40% (Flint & Kendler, 2014). To date, genome-wide association studies (GWASs) for depression have yielded more than 80 replicated loci (Howard, 2018; Wray et al., 2018). The genetic architecture of depression probably consists of hundreds of common single nucleotide polymorphisms, each having a very tiny effect size (< 0.01%), plus additional contributions from rare variants with effect sizes that are probably larger (Ormel, Hartman, & Snieder, 2019; Smoller et al., 2018). The identified loci provide anchors to explore their etiological relevance for depression, but this comes with new challenges (Ormel, Hartman, & Snieder, 2019).

Is the genetic risk associated with these genetic variants modifiable? In theory, genome editing and gene-based prophylactic pharmacotherapy might become options to modify genetic risk in the future. It may sound far-fetched, but genome-editing technology such as CRISPR/Cas9 makes it possible to change or disable genes in living cells in a manner that is probably larger (Ormel, Hartman, & Snieder, 2019; Smoller et al., 2018). The identified loci provide anchors to explore their etiological relevance for depression, but this comes with new challenges (Ormel, Hartman, & Snieder, 2019).

The genetic risk associated with these genetic variants modifiable? In theory, genome editing and gene-based prophylactic pharmacotherapy might become options to modify genetic risk in the future. It may sound far-fetched, but genome-editing technology such as CRISPR/Cas9 makes it possible to change or disable genes in living cells in a precise, cheap, and fast way by cutting, replacing or adding pieces to the DNA (Doudna & Charpentier, 2014; Zhang, Wen, & Guo, 2014). Current and future genomic findings may also have potential for the development of new medications with prophylactic properties (Kathiresan, 2015). The tiny effect size of genetic variants does not a priori preclude that they could be useful for treatment or prevention (Smoller et al., 2018; Sullivan et al., 2018). However, it is highly doubtful whether GWAS-identified genetic variants will soon direct the development of prophylactic drugs or be able to be altered to “fix” depression-associated genes due to the small effect sizes associated with the variants, unknown individual relevance (each individual may carry a unique combination of protective and risk genetic variants), potential lack of causal relevance (too upstream), and unwanted “side” effects of genome-editing (genetic pleiotropy) (Ormel, Hartman, & Snieder, 2019; Visscher et al., 2017).

4.2. Modifiability of personality traits and life skills

Two important domains of personal factors are personality traits and life skills. The Five Factor Model of personality (Big Five) distinguishes Neuroticism or Negative Affectivity (vs. emotional stability), Conscientiousness (vs. disinhibition), Extroversion, Agreeableness (vs. antagonism), and Openness (McCrae & Costa, 1999). Personality traits, in particular neuroticism and conscientiousness, predict not only depression but also life outcomes in other domains, such as externalizing problems, income and profession, well-being, relationship success, and health (Hampson, Goldberg, Vogt, & Dubanoski, 2006; Kuncel, Ones, & Sackett, 2010; Moffitt et al., 2011; Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007). Although personality traits used to be defined as stable lasting characteristics, they do change, not only during childhood and adolescence but also in adult life. Such changes not only occur in response to ageing (Caspi, Roberts, & Shiner, 2005; Roberts, Walton, & Vuchtbauer, 2006) but also in response to major life changes and far-reaching experiences (Schecht, 2017) and, importantly, targeted interventions (Roberts, Hill, & Davis, 2017). The impact of interventions varies across traits, with modest effects on neuroticism, but weaker effects on conscientiousness. Some uncertainties remain, in particular regarding the persistence of such trait changes (Ormel, VonKorff, & Riese, 2017). Nonetheless, it seems safe to conclude that personality is modifiable, at least to some extent, especially at younger ages, although persistent change probably requires “consolidation” by cumulative and interactional continuity (Caspi et al., 1989; Rutter et al., 2006).

Life skills are typically defined as abilities for adaptive and positive behavior that enable individuals to deal effectively with the demands and challenges of everyday life (Danish, Forneris, Hodge, & Heke, 2004). These skills are behavioral (e.g., communicating effectively with peers and adults), cognitive (e.g., making effective decisions), interpersonal (e.g., being assertive), or intrapersonal (e.g., setting goals). Two main categories of life skills are often distinguished: self-management and social skills (Greenberg et al., 2003). Like personality traits, life skills predict life outcomes in multiple domains including internalizing and externalizing psychopathology (Smithers et al., 2018; Steptoe & Jackson, 2018). Life skills are also responsive to interventions such as the Life Skills Training program (LST) (Botvin & Griffin, 2004). The evidence from RCT’s is generally positive but mixed. For instance, Botvin and Griffin concluded that LST trials have demonstrated small significant behavioral effects on smoking, and use of alcohol, marijuana, and other illicit drugs, with prevention effects lasting up until the end of high school (Botvin & Griffin, 2004). On the other hand, Sancassiani and colleagues concluded that methodological limitations hamper final conclusions on the effectiveness of school-based interventions to enhance emotional and social skills (Sancassiani et al., 2015). To have lasting effects, sustained exposure to LST programs and their integration in the school curriculum seem very important, in addition to improvement of the school environment itself (Greenberg et al., 2003).

4.3. Modifying environmental risk: difficult and hard to sustain

In theory, most environmental risk factors are modifiable. Even distal upstream determinants are in principle modifiable, in particular by policies at local, national, and international levels, consistent with a public health model of mental illness. However, in practice, substantial risk reduction turns out to be difficult. Few if any of the major risk factors for depression have been eliminated or drastically reduced in recent decades, despite urgent calls (e.g., World Health Organization, 2005).

At least three reasons may account for limitations in modifiability.

1. Many environmental risk factors, especially stressful events and difficulties, are inherent to life itself (e.g., disease, aging, natural disasters, loss of loved ones by death, etc.).
2. Other risks are the unintentional consequences of our way of living (e.g., traffic accidents, relationship misery, work stress, failures, and competition).
3. Yet other risks are indirect consequences of local, national, and international policies; multinational profit-driven corporations; and major socio-economic, geopolitical, and technological developments (e.g., unemployment, poverty, war, migration, technological changes affecting work).

Hence, it is difficult to reduce environmental risk. We think it is unlikely that large-scale and long-term modification of environmental causes of depression will occur in the foreseeable future. There have been, however, some positive environmental developments, for instance in the domains of work stress and bullying. There is considerable evidence that workplace and school-based anti-bullying programs work (Ttofi & Farrington, 2011; Wang et al., 2007).

We posit that indirect approaches to environmental change are probably the way forward, in particular by targeting poor parenting and children’s life skills and maladaptive personality traits. In their turn, these improved skills and traits may enhance the ability to reduce environmental risks other than those related to poor parenting. In the next section, we will examine how environmental risk factors can be modified on a large scale if a number of crucial conditions are met, notably...
social embedment and structural funding.

5. The way forward: socially embedded long-term prevention to break maladaptive interactional and cumulative continuity of poor parenting and children's personality and life skills

We posit that the capacity of prevention to be effective at the population level depends on the extent that it meets the following conditions:

1. Embedded in major social institutions, structurally funded, and consolidated in laws.
2. Starts early in life and simultaneously targets interacting personal and environmental factors.
3. Addresses major determinants, preferably upstream.
4. Combines universal, selective and indicated prevention, with emphasis on universal.

Of these conditions, the first two are most important because they facilitate the other conditions.

5.1. Conditions 1: socially embedded, structurally funded, and backed up by the law

For a variety of reasons, it is important that prevention be "institutionalized," here defined as being embedded in major social institutions and organizations, structurally funded, and backed up by the law. These conditions guarantee that prevention will be implemented in a sustainable way that is successful long-term, systematic, subject to ongoing improvement, and resistant to economic ups and downs, changes in policy and administration, and the issues of the day. Too often evidence-based preventive programs have been short-term, without focus on structural embedding or provision for enduring funding if proven cost-effective. Prevention of both minor and major mental disorder has predominantly been too hurried, depending on the temporary availability of funding and highly motivated care-givers, politicians, or administrators. Institutionalization also provides the long timeframe needed to change difficult-to-modify risk factors, evaluate long-term cost-effectiveness, allow the systematic improvement of prevention activities and programs, and facilitate long-term and repeated age-adapted exposure to effective programs. The last two are important because effects of once-only exposure to prevention are small and decay over time, while accumulation of benefits is essential. In addition, changing personality and social skills is not feasible without long-term training. Finally, it is important to lay down in law the rights and duties of stakeholders to secure embedment, structural implementation and funding, and long-term cost-effectiveness.

Two forms of embedment are needed for successful prevention. The first is political embedment, whereby local and national governments implement prevention programs, activities, and strategies in existing institutions such as schools, healthcare facilities, and workplaces. The second form is social-psychological embedment, which involves normalizing prevention activities at a societal and cultural level and integrating them into the social norms of day-to-day life (as is currently happening with smoking prevention efforts). Both forms are of embedment are necessary but the second form is critical for the long-term public acceptance of prevention and its political embedment as it rewards mental health behaviors.

Finally, it should be emphasized that the options for political and social embedment are highly complex and have unproven effectiveness at the level of population prevalence. Thus, it is of utmost importance to establish the long-term cost-effectiveness of these strategies prior to their large-scale implementation.

5.2. Condition 2. Prevention starts early in life and targets both parent and child to interrupt maladaptive continuity

First, retrospective studies have found that chronic-recurrent internalizing problems in adulthood, including depression, often have precursors of emotional problems in childhood and adolescence, notably phobias (Kessler, Petukhova, & Zaslavsky, 2011; Ormel, Raven, & Oldehinkel, 2015). Second, the modifiability of personality traits and potential for improvement of skills is greater during childhood and adolescence than in adulthood (Roberts et al., 2006; Roberts et al., 2017). Third, it is probably easier to interrupt maladaptive interactional and cumulative continuity, as well as to change negative cascading pathways, by addressing both parenting and child personality at the same time during early life (Masten et al., 2005; Rutter et al., 1997). Finally, without breaking maladaptive person-environment transactions early in life, “bad luck” children often end up in intractable person-environment jumbles resistant to change (e.g., Brown & Moran, 1997; Moffitt et al., 2011; Ormel, Oldehinkel, & Brilman, 2001; Yap & Jorm, 2015).

5.3. Condition 3. Target major upstream determinants: poor parenting and children’s maladaptive personality and life skills

It is possible that targeting major domains of determinants has multiple advantages including synergistic effects. We propose targeting the domains of poor parenting and children's maladaptive personality and life skills simultaneously. Both domains encompass major risk factors that tend to reinforce one another, and they are probably sufficiently modifiable when addressed systematically with repetition of age-adapted programs (Jacka et al., 2013; Kristjansson et al., 2019; Munoz, 2010; O'Loughlin, Althoff, & Hudziak, 2017). For instance, as described earlier, some preventive parenting interventions had long-term effects on not only parent behavior but a variety of child outcomes as well (Fukkink, 2008; Kaminski et al., 2008; Lundahl, Rissler, & Lovejoy, 2006; Sandler et al., 2011). However, because the assessed child outcomes targeted mainly externalizing behaviors, it is unclear whether these results generalize to depression.

An advantage of the selected targets is their “medium” upstream position. Although the exact position is dependent on the specific trait or parenting component, it is likely that the targeted determinants also have pleiotropic effects on outcomes other than depression. Prospective research indicates that exposure to poor parenting and a child’s maladaptive personality traits and problem-solving skills impact not only the risk of depression, but also adult mental health in general and even other domains of life (Black et al., 2017; Edwards, Holden, Felitti, & Anda, 2003; Jane-Llopis et al., 2011; Moffitt et al., 2011)

5.4. Condition 4. Emphasis on universal prevention

Besides their impact on vulnerability and resilience, a major advantage of universal programs is that they reduce stigma and normalize prevention activities. Stigma is a nasty and intractable problem that limits participation in preventive programs. If prevention is universal and embedded in systems that are (virtually) mandatory, like the educational system and mother-child health care clinics, all children and parents will be exposed to it. Prevention thereby becomes an accepted, normal part of life. Ceiling effects do exist of course, but even parents and children who do well may slightly benefit from such programs.

An interesting question is whether universal prevention programs that are structurally embedded in regular care programs and curricula should still be considered as specifically preventive for depression or much broader as they seek to improve children's resilience and capacities to succeed in life (Jacka et al., 2013; Kristjansson et al., 2019; Munoz, 2010; O'Loughlin et al., 2017). Ideally, both forms of embedment of universal prevention should become so normal that it is not
recognized anymore as prevention of depression or even mental disorder.

5.5. Three desiderata

Although they do not have the status of condition, three important desiderata are cost-effectiveness, integration of universal and targeted prevention, and integration of prevention of depression and non-infectious physical disease. An interesting approach that combines these three desiderata is perinatal depression (Brugha, Morrell, Slade, & Walters, 2011; Henderson et al., 2019). By targeting all expectant mothers it is universal; by using massive open online intervention (MOOI), it can be cost-effective; by providing group or in-person sessions with counselors, it can target expectant mothers with very high risks or reluctant to participate in on-line prevention; and by focusing on both depression and physical health of mother and child, the integration of physical and mental health is achieved.

5.6. How to fund the first decade

Political embedment in existing institutions, such as healthcare, schools, and workplaces, is important to obtain structural funding for prevention activities. But what is the best way to induce these institutions to invest structurally in prevention? It could be stated that, ultimately, the budgets (departments and organizations) that harvest the fruits of prevention should pay for prevention. However, the first fruits of the proposed universal prevention will take at least a decade to ripen. To cover this period, an option could be to earmark a tiny percentage of total health care costs for preventive activities targeted at parenting (in a manner anchored by law, i.e., that by law funding and provision are guaranteed). The other part, needed for the school-based activities (also anchored by law and including smaller classes amongst others, at least in high income countries), could be provided by the central government from its tax income, as part of its regular budget for educational expenditures.

5.7. Concluding comments

We are confronted by remarkable paradoxes. On the one hand, stakeholders (consumers, insurance companies, professional organizations, administrations, and researchers) consider prevention of depression to be a top priority (Christensen, Batterham, Griffiths, Gosling, & Hehir, 2013). On the other hand, compared to the spending on mental health treatment or prevention of cardiovascular disease, preventive activities and prevention research in the mental health field are limited.

However, times are beginning to change. Some countries are undertaking promising initiatives of political embedment of preventive programs. In England for instance, schools will begin offering training on mental health and relationships as part of a revised health education curriculum coming into effect (Note 2). In Australia, the government invests millions of dollars into the “Triple P” and “Be You” initiatives to strengthen the capacity of parents and educators to create mentally healthy learning environments (Sanders, Kirby, Tellegen, & Day, 2014). Likewise, the 2019 US National Academy of Medicine consensus report “Fostering Healthy Mental, Emotional, and Behavioral Development in Children and Youth: A National Agenda” is suggesting an increase in preventive efforts through promotion and community embedding (Note 3). At the EU level, initiatives are being developed to evaluate the mental health implications of all sorts of EU policies (Note 4). The Netherlands has recently introduced a physician-assistant mental health provider in primary care settings (often a psychiatric nurse, social worker, or psychologist) to assist the GP and provide various brief psychosocial treatments designed to treat psychological distress and prevent the development of full blown mental disorder. The proportion of general practices with this type of assistant increased from 27% in 2012 to 87% in 2015, indicating its popularity amongst GPs (Magnée, de Beurs, Schellevis, & Verhaak, 2018). Increased public awareness of the need for prevention of depression is important for embedment of preventive practices. In this respect it is hoped to see the change in public discourse surrounding depression through public figures and mental health professionals advocating awareness of mental illness and reduced social stigma (Hegerl, Rummel-Kluge, Vaernik, Arensman, & Koburger, 2013; Thornicroft et al., 2016).

We have argued that the only way to substantially reduce initial and recurrent episodes of depression is large-scale, socially embedded, structurally funded, and universal prevention supplemented with remedial selective/indicated prevention for those who need more. We do realize that this will not be easy to achieve. A first step in that direction would be regional experiments to test whether the proposed embedded structural prevention works and is cost-effective. Currently, our proposal is speculative, as strong evidence is lacking that the proposed embedded universal prevention works in the long run, though the prospect of prevention of mental illness seems cost-effective (Knapp et al., 2011; McDaid et al., 2019).

Our proposal targets parents and children, and thus focuses largely on individual vulnerability and resilience, and not directly on the larger macro environments. We think that improved resilience and life skills will benefit efforts to improve macro environments so that they have a more positive impact on mental health, such as regenerating neighborhoods (White et al., 2017). This paper examines depression. However, its arguments are relevant for prevention of other common mental disorders as well.

Prevention of depression is, as Jorm put it, “all a matter of political will” (Jorm, 2014). Why has this will failed to materialize? Perhaps because our professional organizations have not successfully persuaded politicians and the public to structurally embed mental health promotion and prevention into our institutions.

Notes (1–4)

pdf)


Reports on prevention of mental disorders published by the United States Institute of Medicine in 1994 and 2009, and by the National Academy of Medicine (the Institute of Medicine’s new name since 2015) in 2019.

https://www.mentalhealthandwellbeing.eu/mental-health-in-all-policies/

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

All authors declare to have no conflict of interest.

Supplementary materials


References


Author/s:
Ormel, J; Cuijpers, P; Jorm, A; Schoevers, RA

Title:
What is needed to eradicate the depression epidemic, and why

Date:
2020-03-01

Citation:

Persistent Link:
http://hdl.handle.net/11343/241356

File Description:
Published version