



# Preventive strategies for mental health

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Available treatment methods have shown little effect on the burden associated with mental health disorders. We review promising universal, selective, and indicated preventive mental health strategies that might reduce the incidence of mental health disorders, or shift expected trajectories to less debilitating outcomes. Some of these interventions also seem to be cost-effective. In the transition to mental illness, the cumulative lifetime effect of multiple small effect size risk factors progressively increases vulnerability to mental health disorders. This process might inform different levels and stages of tailored interventions to lessen risk, or increase protective factors and resilience, especially during sensitive developmental periods. Gaps between knowledge, policy, and practice need to be bridged. Future steps should emphasise mental health promotion, and improvement of early detection and interventions in clinical settings, schools, and the community, with essential support from society and policy makers.

## Introduction

Although interest in early detection to prevent progression to severe mental health disorders such as schizophrenia and recurrent major depression is increasing, knowledge of risk factors and developmental trajectories has not yet been widely applied to clinical practice and public health.<sup>1</sup> Psychiatry has traditionally been based on treatment and prevention of progression and disability in individuals with established illness (ie, tertiary prevention). Although many medical specialties have joined forces with public education and health associations to reduce risk factors for diseases such as myocardial infarction,<sup>2</sup> preventive initiatives for mental health have received far less attention. Scientific evidence gathered from other areas of medicine, along with increasing knowledge of developmental risk factors preceding psychiatric illness, and preliminary findings supporting preventive interventions, indicate that our field could move toward the more ambitious goals of universal prevention of vulnerability, selective prevention in high-risk subgroups, and indicated prevention of full or more severe expression of illness in individuals already showing early manifestations.<sup>3</sup> The reality is that less than 5% of mental health research funding goes on prevention research, even in countries that invest in prevention.<sup>4</sup>

In this Review, we will first summarise the various possibilities for mental health prevention throughout development, and the evidence supporting them. We will then review the potential limitations associated with these approaches, and potential ways to overcome them.

## Prevention in mental health

### Preventive interventions

Prevention in mental health aims to reduce the incidence, prevalence, and recurrence of mental health disorders and their associated disability. Preventive interventions are based on modifying risk exposure and strengthening the coping mechanisms of the individual.<sup>5</sup> Effective interventions require the identification of causal risk factors<sup>6</sup> and can target both generic risk factors, which are likely to be shared by different disorders, and

disease-specific factors. Most preventive programmes will involve a combination of strategies for reducing exposure to risk factors, enhancing protective factors, and targeting putative mediating causal mechanisms, such as cognitive schemas or neurotransmitter imbalances. Primary preventive interventions in mental health target risk factors and promote mental health in individuals without a clinically diagnosable mental disorder. Such interventions could target a whole population regardless of individual risk (universal prevention), a subpopulation known to be at increased risk for mental disorders (selective prevention), or individuals already showing subthreshold clinical manifestations (indicated prevention).<sup>5</sup> Table 1 provides an overview of the different kinds of preventive interventions in mental health with examples of each. This Review will focus mostly on primary preventive interventions.

### Risk factors increasing vulnerability to mental disorders

Mental disorders have different degrees of heritability, with pathogenic genetic variation being a major

#### Key messages

- Increasing evidence supports the efficacy of universal and selective preventive interventions to promote mental wellbeing and prevent mental disorders throughout development
- Indicated prevention in individuals showing subthreshold manifestations of vulnerability can shift expected trajectories towards less debilitating outcomes, or delay the onset of severe mental disorders
- Ethical and safety considerations should guide the implementation of preventive interventions in mental health, especially in young people and at-risk populations
- Mental health professionals should incorporate a focus on prevention into their daily practice and work in close cooperation with other specialties (primary care, obstetrics, and paediatrics) and sectors (education and social services) to increase awareness of the evidence base for preventive interventions in mental health

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|                                            | Population                                                                                                                                                                                                | Aims                                                                                                                                                                                                                                                           | Examples                                                                                                                                                          |
|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Mental health promotion interventions      | General public or whole population                                                                                                                                                                        | Promote psychological wellbeing and increase the ability to achieve developmental milestones. Strengthen abilities to adapt to adversity and build resilience and competence                                                                                   | School-based programmes to foster healthy eating or positive coping skills                                                                                        |
| Universal primary preventive interventions | General public or whole population, regardless of individual risk factors                                                                                                                                 | Target risk factors in the whole population to prevent the development of one or more conditions. Interventions should be effective, safe, and associated with low costs                                                                                       | School-based programmes to prevent bullying                                                                                                                       |
| Selective primary preventive interventions | Individuals or subpopulations with a higher than average risk of developing mental disorders; identification of at-risk groups might be on the basis of biological, psychological, or social risk factors | Target risk factors and strengthen abilities in these individuals or subpopulations to prevent the development of one or more conditions. Interventions should be effective and associated with low risk of adverse events and moderate costs                  | Interventions in the offspring of patients with severe mental disorders                                                                                           |
| Indicated primary preventive interventions | Individuals at high risk with early minimal but detectable clinical manifestations, but currently not meeting diagnostic criteria                                                                         | Treat subclinical manifestations to prevent transition to the full-blown disorder. Target risk factors and strengthen abilities in these individuals to promote resilience. Interventions might be associated with higher costs and some risks can be accepted | Interventions in people at clinical high risk for psychosis (ie, showing attenuated psychotic symptoms and a recent decline in functioning)                       |
| Secondary preventive interventions         | Individuals meeting diagnostic criteria in the early stages of illness                                                                                                                                    | Early detection and intervention in patients already meeting diagnostic criteria for a specific mental disorder. Provide adequate treatment, improve satisfaction with treatment, reduce substance use, and prevent relapses                                   | Interventions to improve early detection and access to services in patients with depression to reduce the duration of untreated depression                        |
| Tertiary preventive interventions          | Individuals with established illness                                                                                                                                                                      | Treat established disease to prevent deterioration, disability, and secondary conditions                                                                                                                                                                       | Interventions for smoking cessation or cognitive remediation in patients with schizophrenia. Prevention of suicide with lithium in patients with bipolar disorder |

Some overlap exists between indicated primary preventive interventions and secondary preventive interventions. Universal primary preventive interventions will frequently use mental health promotion strategies.

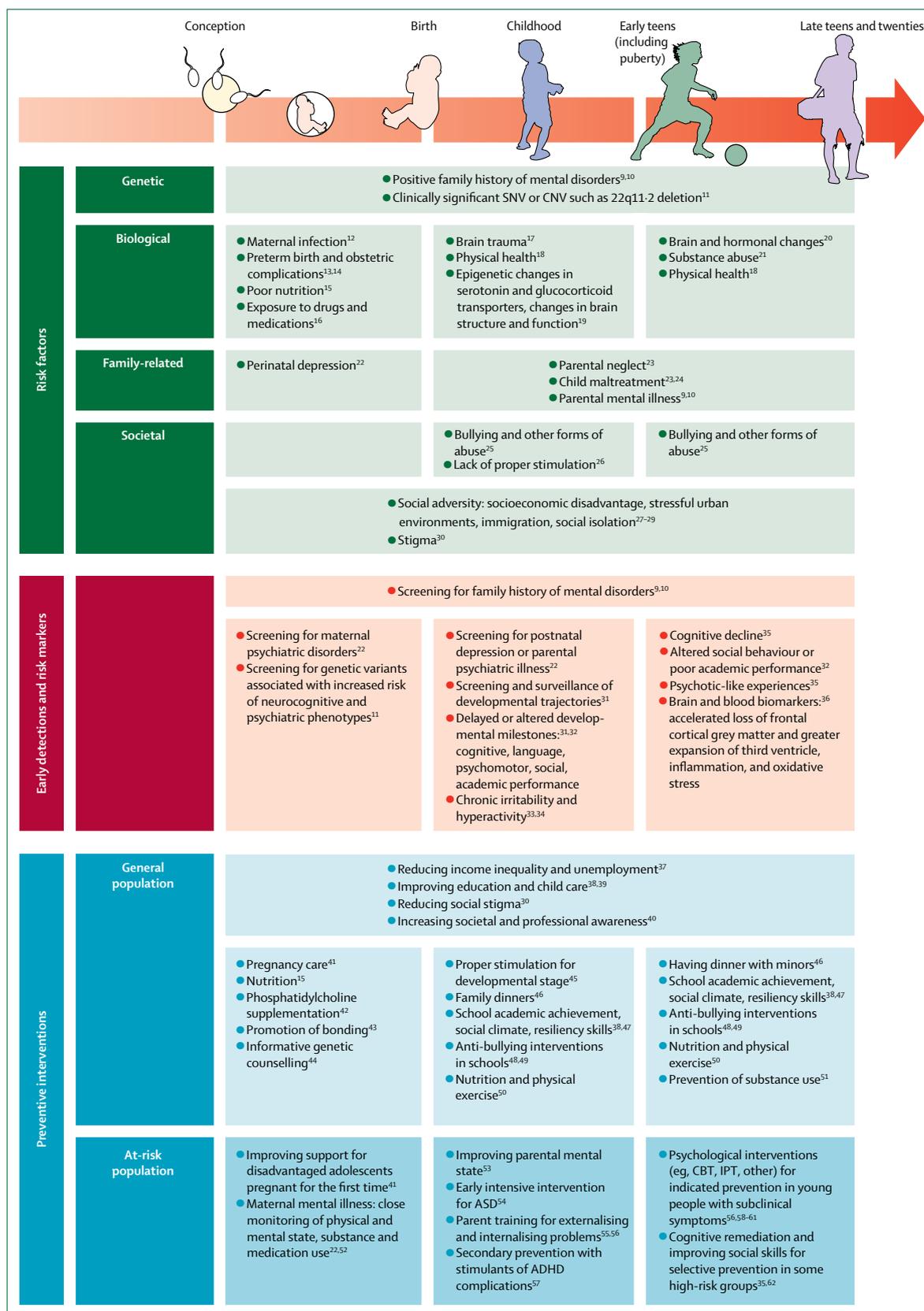
**Table 1: Preventive interventions in mental health**

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risk factor.<sup>7</sup> The cumulative effect of multiple common alleles with small effects, or the relatively high impact of rare pathogenic variants, in combination with environmental risk factors, increases the risk of developing mental disorders; similarly, although some rare environmental risk factors might have large effect sizes, most are characterised by small effect sizes and seem to increase susceptibility, but are not sufficient to explain the occurrence of a disorder.<sup>8</sup> They include, but are not limited to, prenatal environment (eg, poor nutrition, exposure to drugs or toxins, and maternal infections or stress), birth complications, preterm delivery, brain trauma, social risks (eg, socioeconomic disadvantage and poverty, urbanicity, immigration, and social isolation), trauma (eg, parental neglect, physical, emotional, and sexual abuse, and bullying), insufficient stimulation, general adversity and stressful life events, and drug abuse (figure).<sup>23,25,27,35</sup> Many risk factors are interrelated, and tend to cluster and have synergistic effects. For example, immigration often co-occurs with urbanicity and social disadvantage,<sup>28</sup> whereas children who have been exposed to violence are at higher risk of repeated victimisation.<sup>63</sup> People with mental health disorders or disabilities, and individuals who have already been exposed to risk factors, might be less capable of defending themselves than those without these factors and seem to be targeted by bullies and abusers more frequently.<sup>64</sup> Therefore, once an individual becomes vulnerable, they are more likely to experience further risk factors, leading to a vicious cycle. This so-called facilitation effect is supported by epigenetic

changes found in the serotonin transporter and glucocorticoid receptor genes, and subsequent neuroendocrine alterations and changes in brain structure and function, in victims of childhood trauma.<sup>19</sup> Neurobiological changes can lead to maladaptive responses to stress, thus increasing vulnerability to stress-related diseases, and feeding lifetime revictimisation.<sup>19</sup>

Identification of specific risk and protective factors for mental health disorders is challenging because of person–environment interactions and correlations. Individuals are not passive recipients of events and process their experiences according to their personal history and social environment, thus influencing their ability to adapt to events, and modifying how they interact with the environment to shape and select their future experiences.<sup>65</sup> Interaction with the environment is also subject to genetic influence; genetic factors could affect the sensitivity of the individual to particular environmental risks and contexts (ie, gene–environment interactions)<sup>8,66</sup> and modulate exposure to certain risk and protective factors (ie, gene–environment correlations).<sup>67</sup> Furthermore, exposure to the environment and life events, as well as interventions (both pharmacological and psychosocial), can induce biological changes at different levels (eg, epigenetics, neurotransmitters, and brain connectivity), thus modifying the ability to adapt to further stressors. These processes complicate the situation, but also afford an opportunity for different levels of intervention (eg, biological, psychological, family-related, or societal), at different developmental stages to lessen risk or increase protective factors.



**Figure: Risk factors for mental disorders in sensitive periods of intervention**  
 SNV=single nucleotide variant. CNV=copy number variant. ASD=autism spectrum disorders. ADHD=attention-deficit hyperactivity disorder. CBT=cognitive behavioural therapy. IPT=interpersonal therapy.

### Opportunities for prevention during development

The cumulative effect of risk and absence of protective factors during development can lead to a transition from health to mental illness.<sup>68</sup> Even if early risk factors (eg, genetic risk or early environmental factors such as severe deprivation) are present, without additional so-called hits, a disorder ultimately might not develop. The presence of multiple hits is especially important in the development of disorders such as schizophrenia and bipolar disorder,<sup>69</sup> and offers a unique opportunity for targeted prevention in high-risk individuals by reducing exposure to further risk factors and enhancing protective factors.<sup>35</sup> Among possible additional risk factors, bullying victimisation has been strongly associated with short-term and long-term vulnerability to mental illness.<sup>25</sup> Ceasing exposure to bullying and maltreatment during childhood has been shown to reduce the incidence of psychotic experiences after 12 months.<sup>70</sup> Effective strategies to reduce bullying, such as school-based anti-bullying programmes, have also proved effective in reducing subsequent aggression or internalising problems in adolescents.<sup>48</sup> Similarly, strategies such as providing comprehensive educational and family support to economically disadvantaged children, could be effective in preventing other risk factors such as child abuse; one study<sup>38</sup> reported a 52% reduction in the incidence of maltreatment in participants compared with children not participating in the school-based intervention.

Even when there is a first hit or further hits, the effect could be lessened by enhancing protective factors such as family and social support, and promoting resilience.<sup>71</sup> Resilience is a multidimensional construct that can be conceptualised as the ability to adapt well after experiencing adversity, trauma, or other stressors.<sup>71</sup> Many effective interventions have been developed to promote resilience, especially in children and adolescents.<sup>47</sup> Their core elements include enhancing social and emotional competence skills, and promoting self-efficacy, adaptability, and social connectedness in young people, as well as fostering positive parenting, and facilitating family communication and problem solving.<sup>47</sup> For instance, in children exposed to risk factors such as low birthweight or bullying, a positive family environment increases resilience to these risk factors.<sup>72,73</sup> Although prevention of bullying primarily involves addressing factors in the community and schools that foster bullying behaviour, family interventions and other strategies to promote individual resilience could be helpful in improving outcomes in individuals who have already been victimised.<sup>74</sup>

From a developmental psychopathological perspective, mental disorders appear to be the result of a dynamic process of repeated environmental maladaptation, leading to progressive deviation from normative development. Multiple pathways can lead to similar outcomes, whereas the same deviant developmental pathway can lead to

different psychopathological outcomes. Although change can be constrained to some extent by previous adaptation, especially during sensitive developmental periods, the pluripotentiality of early trajectories of vulnerability suggests that change is possible at many points during development.<sup>75</sup> This developmental psychopathology model is compatible with a staging model similar to models developed in other areas of medicine, which suggests that severe mental disorders develop from at-risk preclinical states, pass through undifferentiated general symptoms, and lead to increasing clinical specificity and functional decline.<sup>76</sup>

Both models have an optimistic outlook for a preventive approach, suggesting it would be possible to intervene in the developmental process of any mental condition, or shift the psychopathological expression towards less debilitating disorders, by intervening in people with risk factors, or people who are already showing subtle abnormal development.<sup>77</sup> Early risk markers of developmental deviance that can precede severe disorders in adulthood include subtle language and motor delays, extreme temperament traits, irritability, subthreshold hyperactivity and conduct problems, low cognitive performance, decline in intelligence quotient, and social difficulties in childhood.<sup>32-34</sup> These markers could help characterise subpopulations with increased developmental vulnerability to guide targeted intensive interventions.

It could be feasible to change trajectories towards a less severe mental disorder, or a less severe form of a given disorder. Psychosocial interventions in people at clinical high risk for psychosis, such as cognitive behavioural therapy (CBT), could lead to a reduction in transition rates to psychosis, or a delay in the onset and amelioration of debilitating symptoms.<sup>78</sup> Although based on a single study<sup>54</sup> that warrants replication, preliminary evidence suggests that an early comprehensive behavioural intervention in toddlers diagnosed with autism spectrum disorder could improve functionality and diminish core symptoms of the disorder. Another example is attention-deficit hyperactivity disorder. Treatment with stimulants in childhood might improve or stabilise social functioning and academic performance in patients with the disorder; subsequently, the rate of secondary drug abuse, conduct disorders, and social problems can decrease in adolescence and adulthood, stopping a potential downward spiral.<sup>57</sup> Similarly, reducing the duration of anxiety or depressive episodes in young people might prevent the development of more severe mental health disorders during adulthood.<sup>79</sup>

During a lifespan, there are sensitive periods when risk and protective factors could have greater effects and long-lasting consequences.<sup>19,80</sup> These periods include the prenatal period, childhood, and adolescence through early adulthood (figure). These intervals of vulnerability largely overlap with periods of major developmental brain changes, such as maturation of several receptors,

myelination, pruning, and development of hub regions.<sup>80</sup> These periods are also crucial for the development of secure attachment; basic schemas related to self, others, and the world; self-esteem and self-integrity; and the adult personality, and they overlap with the peak incidence of major mental disorders.<sup>81</sup> Prevention focusing on these periods might be more effective and have long-lasting benefits.

The prenatal environment can shape gene expression related to fetal brain development, and thus affect the risk of developing mental health disorders.<sup>82</sup> Therefore, providing appropriate screening and care for factors such as maternal nutrition and substance abuse (including smoking) and parental mental health disorders and stress during this period, could contribute considerably to global prevention of mental health disorders in children.<sup>15,16</sup> In the postnatal period and early childhood, exposure to stressors (such as child abuse, neglect, or malnutrition) might interfere with the development of brain regions crucial for the regulation of emotion, leading to poor mental and physical health.<sup>19</sup> Thus, reducing the frequency of child abuse and improving early family and social environments could decrease the occurrence of lifetime mental health disorders.<sup>24</sup> During adolescence, strategies to prevent substance abuse and other risky behaviours, and to promote healthy lifestyles and positive coping mechanisms, could be especially useful.<sup>47,51</sup>

Despite the numerous opportunities for prevention in mental health, some specific factors could hamper the advancement of prevention in psychiatry, and should be considered when designing and implementing interventions (panel 1).

## Evidence supporting primary prevention in psychiatry

### Universal preventive interventions

Universal prevention of mental health disorders addresses generic risk and protective factors in the general population. Such interventions are likely to affect the global probability of developing psychiatric and other disorders in a non-specific fashion. A holistic approach to health, integrating psychosocial and physical aspects of wellbeing, might be especially valuable in this regard. Results from a meta-analysis<sup>89</sup> of 67 cluster trials reported that the WHO Health Promoting School framework, a holistic approach to promoting mental health in schools, had significant positive effects on physical activity, physical fitness, bodyweight, fruit and vegetable intake, tobacco use, and bullying. Despite the small effect sizes, the investigators suggested that these interventions could have public health benefits at the population level. Data also suggest that promotion of healthy lifestyles, including appropriate nutrition and regular exercise, could have positive effects on cognitive development, scholastic achievement, and mental health vulnerability.<sup>5,50</sup> Something as simple as eating dinner as

a family could serve as a venue for parents to promote coping strategies that offset the impact of stressful environmental factors, such as cyberbullying.<sup>46</sup>

Key targets for universal prevention include the prenatal and perinatal periods. Dietary phosphatidylcholine supplementation during the second and third trimesters could prevent cerebral inhibition deficits associated with schizophrenia and attention-deficit disorder.<sup>42</sup> Furthermore, vitamin D supplementation during pregnancy could reduce the frequency of low birthweight and preterm delivery,<sup>85</sup> which have been associated with attention deficits and an increased risk of developing childhood behavioural and emotional disorders.<sup>13,90</sup> Similarly, preliminary data suggest that vitamin D supplementation during the first year of life could reduce the incidence of schizophrenia in men.<sup>91</sup> Other strategies to improve maternal nutrition (fortification or supplementation) have been associated with reduced obstetric complications and improved behavioural outcomes in offspring.<sup>92</sup> Interventions to promote effective parenting in expectant or new parents can also have positive effects on the cognitive, social, and motor development, and mental health of the child.<sup>93</sup>

Schools have a central, universal preventive role during childhood and adolescence. Many school-based anti-bullying programmes have been shown to be effective, reducing bullying by an average of about 20% according to meta-analysis,<sup>49</sup> and might also reduce related mental health symptoms.<sup>48</sup> Universal school-based programmes could also be effective in improving social and emotional skills, attitudes, behaviour, and academic performance, as suggested by the results of a meta-analysis<sup>94</sup> assessing 213 programmes involving more than 270 000 students from age 5 years to 18 years. School-based programmes with self-regulation change techniques, can also improve self-esteem and internalising behaviour in adolescents, with small effect sizes (about 0.20).<sup>95</sup>

Results from meta-analyses and systematic reviews have shown that some psychosocial universal preventive interventions are effective for anxiety and depression,<sup>96,97</sup> eating disorders,<sup>98</sup> and substance use disorders in young people.<sup>51</sup> Restriction of access to lethal means and school-based awareness programmes have been found to reduce suicidality.<sup>99</sup> Preliminary evidence suggests that additional supplementation strategies (eg, *N*-acetylcysteine, sulphoraphane, and probiotics) constitute promising approaches for universal prevention in mental health.<sup>86</sup>

### Selective preventive interventions

Children of parents with mental illness or substance use disorders represent one of the populations at highest risk for psychiatric problems.<sup>9</sup> In children with high familial risk for psychosis, about 10% will develop psychosis, and 50% non-psychotic problems.<sup>9,32</sup> Similarly, children of parents with depression have a three times higher risk of developing anxiety disorders, major depression, and substance dependence.<sup>10</sup>

**Panel 1: Factors that hamper the advancement of prevention in psychiatry****Limitations of using diagnoses of specific mental disorders as outcome measures of preventive interventions**

Risk or protective factors do not seem to be specific for particular mental disorders. Whether at the level of aetiology<sup>7</sup> or pathophysiology,<sup>83</sup> these factors seem to increase or decrease vulnerability to many mental disorders. Even in genetic conditions, such as 22q11.2 deletion syndrome, pleiotropy is remarkable, and the outcome is highly variable in terms of functionality, intellectual disability, and psychiatric diagnosis, which is true for almost all copy number variations associated with psychiatric conditions.<sup>11</sup> Therefore, fixed pathways do not seem to be leading to each disorder as defined in DSM or ICD.<sup>75,77</sup> Although some interventions could be more specific (eg, some indicated interventions), public health interventions, whether population-wide or in a high-risk subgroup, might have low specificity and reduce incidence or improve outcomes across disorders. Quantification of the effectiveness of such interventions should, therefore, be reflected by global measures of disorders and include other outcomes (eg, education, wellbeing, and use of social and legal services). For mental illness, in many instances, a two-decade delay from birth to emergence of a specific disorder is an additional problem.

**Barriers to identification and care in those at risk**

Without reliable biomarkers for mental disorders, prediction of future illness in individuals and reliable identification of subpopulations at risk for specific disorders is very difficult. The difficulties involved in identifying those individuals at high risk are exacerbated by the fact that families most in need of intervention (eg, families who are disadvantaged) might have the least access to care. Further research is needed on the early stages of mental disorders, with the aim of identifying potential psychological, biological, and social risk markers.

**Methodological and ethical challenges of preventive interventions**

Preventive strategies are associated with some intrinsic difficulties, including the high number of potentially false-positive treatments and the high costs associated with interventions in larger populations. Considering the potential for ineffective, or even iatrogenic interventions, doing rigorous research on preventive interventions is crucial. Since a high proportion of the population, not necessarily at risk, could be exposed to these kinds of interventions, safety should guide the implementation of primary universal interventions. Strategies to promote mental wellbeing, healthy eating and physical activity, reduce bullying and other forms of child abuse, and improve workplace conditions are associated with very low risks and could be prioritised. Although supplementation strategies during pregnancy or the neonatal period could become useful preventive strategies, they should be further studied considering their potential risks. Nevertheless, the association of reduced vitamin D during pregnancy and the neonatal period with neurodevelopmental disorders,<sup>84</sup> preliminary data

suggesting a beneficial effect of vitamin D supplementation on birth outcomes in offspring and low risk of side-effects,<sup>85</sup> suggests that supplementation strategies could be carefully implemented, at least in high-risk subpopulations (ie, pregnant women or neonates with vitamin D concentrations in the lowest percentiles). Low sensitivity for the identification of individuals with subthreshold symptoms could limit indicated preventive interventions; it has been estimated that well established clinical high-risk services might miss 95% of people who will develop a psychotic disorder.<sup>86</sup>

Implementing early-stage detection and intervention strategies in a clinical context for indicated and selective prevention has clear ethical implications. It seems feasible (and crucially important) to identify people at high-risk for whom health systems are equipped to provide proper care (eg, young people showing mild symptoms or behaviours suggestive of clinical high-risk, and healthy individuals with known genetic risk). Disclosure in these instances could be beneficial for both patient and family by providing understanding, perspective, and advice for reducing risk, promoting resilience, and orienting future actions in case of progression; however, this process could also be stressful and raise concerns regarding stigma. Disclosure should be done with great caution so as not to decrease self-esteem and hopes or aims for the future. Rather, interventions in at-risk individuals should be framed as encouragement for a better future. Safety should guide clinical decision making in those individuals identified as being at risk, and lower-risk interventions should be prioritised, especially in young people.

**Long-term benefits do not seem to motivate health authorities or political decisions**

Lack of awareness of the substantial economic savings from preventive interventions for mental disorders, the need for an initial investment in training and investment of time by professionals (often with no short-term return), and stigma, partly explain the lower interest in mental health prevention than in other areas of medicine. It might take more time to realise the benefits of investing in prevention for mental health than in other areas of medicine (eg, oncology or cardiovascular disease), which is problematic when politicians need to prioritise their health actions on the basis of what can be communicated to future voters in 4–5-year election cycles. A focus on prevention and public health requires a long-term view that is sometimes not possible in politics because of politicians' short terms in office, and subsequent shifts in priorities for health and education when a different party comes to power (potentially without regard for the benefits of previous approaches). National and international funding agencies could play an essential part in providing the required long-term support to assess and implement preventive interventions appropriately. Additionally, prevention and early detection of mental disorders might be perceived as more complex than in other areas of medicine because of the false

(Continues on next page)

(Panel 1 continued from previous page)

perception that mental disorders are not associated with mortality, with resources more easily directed toward health conditions that are considered fatal (especially in the short term). To overcome these difficulties, politicians and society should become aware of the high morbidity and mortality associated with mental disorders,<sup>87</sup> and the economic return on investment in mental health research, which is similar to research in cardiovascular disease.<sup>88</sup>

Some preventive interventions could be delivered by sectors other than health care. Support and funding from other institutions, including education authorities, might be required for improving health literacy and developing interventions targeting children and adolescents, especially in schools. An economic argument can be made to employers to motivate them to intervene proactively to reduce stress and improve working environments in their companies. Therefore, research on potential short-term benefits of interventions needs to look beyond impacts on the health system (eg, for school-related outcomes such as academic achievement, reduced truancy, and teacher stress, or potential employer benefits of improved worker mental health) to involve these additional sectors, which also opens up opportunities for additional sources of funding and support.

#### **Challenge of rebalancing investment in prevention and treatment of mental disorders**

Although the costs associated with some preventive interventions are not necessarily high, choices and trade-offs are required between investment in prevention and investment in

treatment of existing conditions. Mid-term to long-term cost-effectiveness arguments should be made. Multisectorial investment also becomes feasible if economic benefits to other sectors (eg, education) can also be identified.

#### **Stigma**

General stigmatisation of mental illness implies an underestimation of the need for prevention in psychiatry on the part of the general population. The risk of a heart attack seems plausible to most of us, but many will not believe they need to be protected against suicide or self-harm. Personal and community stigma, and lack of insight, could also hinder indicated prevention in people with early manifestations of mental illness, more than for other medical conditions, by delaying help-seeking behaviour as a result of anticipated discrimination.<sup>30</sup> Evidence-based interventions to tackle stigma and improve access to care in individuals already experiencing mental distress should be prioritised.

#### **Additional factors**

Additional factors include poor insurance coverage in some countries, the need for multilevel and multisectorial intervention when services are usually compartmentalised, low perception of risk when early manifestations of mental illness are subtle (especially in children and adolescents), high variability of behavioural manifestations during infancy and adolescence, and paucity of validated screening tools and treatment for conditions first evident in infants. These factors should be considered when designing preventive interventions.

Genetic vulnerability aside, several studies<sup>100,101</sup> have found an association between childhood risk and parental mental health status, suggesting that successful management of parental psychopathology could improve outcomes in their children. Outcomes of a meta-analysis<sup>53</sup> have indicated that preventive interventions targeting parents with mental illness could reduce the risk of mental disorders in their children by 40%.

Other at-risk populations include children with genetic disorders associated with an increased risk for early developmental deficits and psychiatric symptoms. In these at-risk populations, universal school-based or community-based preventive interventions against bullying and abuse might be especially helpful in preventing mental disorders, by reducing exposure to these frequent risk factors. Selective preventive interventions in at-risk populations should target social stress and emotional problems, promote resilience, and facilitate early identification and access to services in individuals already in need of care.<sup>35</sup> Compensatory approaches to social and cognitive problems could provide additional benefits to interventions aimed at improving resilience in at-risk populations.<sup>62</sup>

Evidence also supports the efficacy of some psychosocial selective interventions to prevent externalising disorders in children reared in disadvantaged environments<sup>102</sup> or exposed to violence within the family context,<sup>103</sup> post-traumatic stress disorder (PTSD) in children and adolescents exposed to traumatic events,<sup>104</sup> eating disorders in young people belonging to high-risk groups (eg, female athletes or adolescents with body image issues),<sup>98</sup> post-partum depression,<sup>105</sup> and depression or anxiety disorders in young children of patients with depressive disorders<sup>106</sup> and other high-risk populations.<sup>96,107</sup> Additionally some pharmacotherapy strategies (eg, hydrocortisone) have been shown to be effective for the prevention of PTSD.<sup>108</sup> Most effective interventions had small to medium effect sizes relative to control conditions.

#### **Indicated preventive interventions**

Indicated preventive interventions are used for individuals showing subthreshold manifestations of mental health disorders. Interventions in these subgroups might be more cost-effective, and therefore efficient, because they minimise the number of

|                                                         | Sources of evidence                    | Efficacy results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cost-effectiveness data (2016 US\$)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Preventive strategies for post-partum depression        | Meta-analysis, systematic review, RCTs | Roughly a 20% reduction in rates of maternal depression during the first months after birth. <sup>105</sup> Improvement in mother–infant interaction and child developmental functioning. Reduction of child abuse and neglect. <sup>51</sup> Universal preventive interventions found to be most effective in reducing 12-month depression scores (Edinburgh Postnatal Depression Scale) were midwifery redesigned postnatal care, person-centred approach interventions, and cognitive behavioural therapy-based interventions. <sup>122</sup> | In the UK, home health interventions were associated with a cost of about \$7281 to \$7928 per quality-adjusted life-year gained, as compared with routine care. <sup>109,120</sup> In Canada, trained telephone peer support had a 95% chance of a cost per case of averted maternal depression of less than \$17 446. <sup>123</sup> These examples are conservative because long-term effects on the child, siblings, and fathers are not considered. A study <sup>124</sup> in Australia suggested that psychoeducation could be cost-effective in preventing post-partum depression and anxiety. |
| Parent training for prevention of behavioural disorders | Meta-analysis, systematic review, RCTs | Reduction in child conduct problems, improvement in parental mental health, and a reduction in negative and harsh parenting practices. <sup>55</sup>                                                                                                                                                                                                                                                                                                                                                                                             | 60% of programme investment would be recovered because of costs averted within 2 years and 100% in 5 years. <sup>55</sup> Cost savings after 8 years and total savings over 25 years of at least \$15 028 from the public purse and a societal perspective would be made. <sup>109</sup>                                                                                                                                                                                                                                                                                                              |
| School-based interventions to prevent bullying          | Meta-analysis, systematic review, RCTs | About a 20% reduction in prevalence of peer victimisation. <sup>49</sup> Reduction in aggression and internalising symptoms. <sup>48</sup>                                                                                                                                                                                                                                                                                                                                                                                                       | In the UK, a universal programme would show cost savings after 3 years and generate expected mid-term return on investment through reduced health costs, improved education outcomes, and possible higher earnings of \$10.67–16.79 per dollar invested per pupil by age 21 years. Further savings could be made because of a potential reduction in adulthood depression. <sup>112</sup>                                                                                                                                                                                                             |

RCTs=randomised controlled trials.

**Table 2: Key examples of primary preventive interventions in mental health**

individuals who need to be exposed to the intervention and target individuals who might already be in need of care. Results of meta-analyses<sup>58,97,98</sup> suggest that indicated interventions could have greater effect sizes than universal ones (eg, programmes for eating disorders or depression), although this outcome is not consistent across studies; several meta-analyses<sup>96</sup> report no significant differences or greater effect sizes for universal interventions. Examples of effective indicated interventions, supported by meta-analyses,<sup>55,56</sup> include parent management training to prevent externalising disorders in children with high antisocial behaviour scores, and prevention of depression and anxiety disorders in children showing early manifestations of internalising disorders. CBT in individuals at clinical high risk could lead to a reduction in the transition from clinical high risk to psychosis.<sup>59</sup> CBT-based strategies might be effective for preventing chronic PTSD in patients showing early acute stress symptoms after exposure to a traumatic event<sup>60</sup> and eating disorders in young people with subthreshold symptoms.<sup>98</sup> CBT and interpersonal therapy might also be effective for the prevention of depression and anxiety in young people and adults presenting with subclinical symptoms.<sup>58,61</sup>

### Is it worth investing in mental health prevention?

Despite mounting scientific data supporting the efficacy of early intervention and prevention in psychiatry, a gap still exists between research evidence and clinical and

public health practices. Can this be attributed to economics? Improving long-term outcomes, and reducing long-term adverse consequences of poor mental health (eg, secondary disorders, criminality, and unemployment), make many early mental health interventions cost-effective for society.<sup>35,109</sup> This cost-effectiveness is in light of the high direct and indirect costs generated by neuropsychiatric disorders, which are responsible for 14% of the global burden of disease (disability-adjusted life years) worldwide.<sup>110</sup> The European Observatory on Health Systems and Policies, the Organization for Economic Co-operation and Development, and the WHO Regional Office for Europe have compiled data showing that influencing risk behaviours for chronic non-communicable diseases, including mental health disorders, is an efficient use of government money, and that government policies can have a major impact on risk behaviours for mental health disorders.<sup>111</sup>

In the UK for every US\$1 spent on mental health promotion and prevention, the calculated total societal returns on investment over 10 years (including impacts on health and other sectors, such as education and the criminal justice system) were \$83.73 for whole-school conduct disorder prevention and \$10.27 for early detection services in people with prodromal symptoms of psychosis.<sup>109</sup> An estimate of the benefits of bullying prevention suggested a conservative return of between \$10.67 and \$16.79 per dollar invested by age 21 years, due to higher earnings and better educational outcomes,

**Panel 2: Key messages for prevention of mental health disorders**

- 1 Translate scientific evidence for cost-effective preventive interventions into public health initiatives, clinical practice, and service delivery systems.
- 2 Increase social, professional, and political awareness of advancements and the importance of mental health prevention and promotion.
  - Includes social education campaigns about early signs, risk, and protective factors, and consequences of mental disorders. Claims for societal health investment in preventive psychiatry should be based on personal, family, health, education, and social benefits of reducing mental illness burden, and on long-term and indirect economic savings of mental health prevention programmes by reducing disability.
- 3 Move clinical practice toward at-risk-oriented detection and intervention.
  - Need for clearer and more specific definitions of early clinical stages incorporating neuroimaging, neurocognitive, and biochemical markers into the description of cases, which could help monitor possible trajectories and detect new therapeutic targets.
  - Provide standardised and cost-effective screening measures for the accurate detection of at-risk populations at early stages of development such as patients with perinatal mental illness and developmental disorders, individuals at high risk for psychosis, and children of parents with severe mental illness. In particular, development of screening tools with high sensitivity, specificity, and positive predictive value for toddlers and preschool children is needed.
- Procure standardised and cost-effective preventive interventions such as caring for pregnant adults and adolescents, parental training programmes, cognitive-behavioural therapy, and other psychosocial interventions (for high-risk subjects).
- Promote proper training in standardised and cost-effective preventive interventions for professionals. Since professionals will detect the risk, they should acquire skills for communicating probability, and managing related stress in parents and patients facing uncertainty. In this regard, any decision making should be based on evidence regarding risks and benefits.
- 4 Provide interventions designed for each developmental stage aimed at minimising the impact of risk factors.
- 5 Promote interventions with a multidisciplinary and multilevel (psychological, social, familial, and legal) approach.
  - Requires improving coordination between different institutions.
- 6 Promote healthy lifestyles including nutrition and exercise.
- 7 Encourage school-based interventions (targeting children, parents, and education professionals) for:
  - Early detection of deviation from normal psychomotor development, language delays, abnormal social behaviour, and poor academic performance.
  - Reduction of bullying.
  - Protection and promotion of resilience to peer victimisation and abuse in the vulnerable, and assistance for victims, abusers, and bystanders.
  - Prevention of health risk behaviours, including substance abuse and suicidality, and related burden.
  - Promotion of mental and physical health.

with other savings possibly due to a lower prevalence of adult depression.<sup>112</sup> Similarly, substantial savings could come from investing in home-visiting programmes for disadvantaged pregnant women,<sup>41</sup> early intensive behavioural interventions in preschool children with autism,<sup>113</sup> interventions to reduce truancy and school exclusion,<sup>114</sup> parenting interventions to prevent internalising<sup>115</sup> or externalising disorders in children,<sup>55</sup> and early intervention services for early onset psychosis in children and adolescents.<sup>116</sup> Interventions to prevent the neuropsychiatric consequences of prenatal risk factors, such as folic acid fortification of enriched cereal or grain products for the prevention of neural tube defects,<sup>117</sup> and universal screening in pregnancy for subclinical hypothyroidism,<sup>118</sup> could also be cost effective. For conditions such as maternal depression and suicidal behaviour, improving the ability of professionals to detect and intervene in at-risk groups and at early stages could be beneficial to individuals, relatives, and society.<sup>119,120</sup> The promotion of health literacy in routine educational settings could also be cost-effective for a wide range of health, educational, and social outcomes.<sup>121</sup>

Table 2 provides a summary of the cost-effectiveness analysis of key examples of primary preventive interventions in psychiatry.

Savings made due to the prevention of mental health disorders could be greater than for other medical conditions. Debilitating mental disorders usually have an earlier-onset than many other chronic diseases, increasing the number of years that health and social welfare services and caregiver support are needed. For example, the mean age at onset of diabetes is 52·5 years,<sup>125</sup> and the average age of a first heart attack in men in the USA is 65 years,<sup>126</sup> whereas 50% of mental disorders start before the age of 14 years, and 75% before the age of 24 years.<sup>81</sup> Therefore, we can assume that the direct and indirect savings (eg, higher proportion of employment and higher earnings when employed) to society from the early and long-lasting reduction of the burden of mental illness would be much higher than for many other chronic medical conditions. Furthermore, considering the bidirectional association between mental and physical health, altering risk factors for psychiatric disorders could also help to prevent other

### Search strategy and selection criteria

We identified references for this Review through PubMed searches for articles and previous reviews published from inception to December, 2016, using the key terms "prevention", "high-risk", "risk factors", "promotion", "resilience", "development", "staging", and "early intervention" in combination with the terms "psychiatry", "mental health", and "psychopathology". Articles identified by these searches that related to the main topics covered in the manuscript, and relevant references cited in those articles, were selectively reviewed. We did an additional systematic PubMed search from inception to Nov 6, 2017, to identify meta-analyses assessing primary preventive interventions for specific mental conditions (ie, mood disorders [depression, bipolar disorder], anxiety disorders, post-traumatic stress disorder, externalising disorders [disruptive behaviour disorders (ie, conduct disorders, oppositional-defiant disorder), attention-deficit hyperactivity disorder], eating disorders, psychotic disorders, autism spectrum disorders, and suicidal behaviour; see appendix for additional details). We systematically reviewed these references and included the most recent or comprehensive meta-analyses supporting universal, selective, or indicated preventive interventions for each disorder in the manuscript. We did complementary searches in Google Scholar and PubMed to identify examples of cost-effectiveness studies on preventive interventions in psychiatry.

See Online for appendix **medical conditions in adulthood.** For example, bullying victimisation has been associated with an increased risk of inflammatory disorders.<sup>25</sup> Interventions to prevent bullying are likely to have an effect on the development of both psychiatric and medical disorders, as well as non-medical outcomes (eg, educational attainment and societal benefits).

In light of this evidence, two initiatives in the USA<sup>127</sup> and Europe<sup>128</sup> have included prevention among the top priorities for mental health research. The US group emphasises that it is feasible to achieve these priorities in the next 10 years, but only if funding begins immediately.<sup>127</sup>

### The role of mental health professionals in mental health prevention

Some of the general risk factors for mental disorders, such as social exclusion or economic inequality, cannot be directly addressed by psychiatrists. Universal interventions in the general population require a public mental health approach, and will probably need to be delivered by professionals from other medical specialties, such as obstetricians and general practitioners, or other sectors such as education. We believe that it is the duty of mental health professionals to increase awareness among the general public, politicians, and policy makers of the importance of mental health prevention and promotion, and of the evidence supporting cost-effective interventions. Mental health professionals could also incorporate an at-risk oriented focus into clinical practice by improving definitions for early clinical stages, enhancing screening instruments, developing targeted interventions, and promoting training in prevention for all mental health professionals. The role of clinicians could be especially important for selective and indicated interventions, by providing care to individuals already at

risk in whom periodic specialised monitoring of subsequent mental health problems might be especially useful. Strengthening the coordination between child and adolescent and adult psychiatric services targeting the same areas could be valuable in the management of children of patients with major mental disorders. Furthermore, improved coordination could assist with the transition through services for other high-risk populations, which could be especially useful considering the often large treatment gap during the transition from child and adolescent services to adult services.<sup>129</sup> Improving access to care for people already in need could provide an excellent secondary and tertiary preventive strategy by reducing the duration of untreated illness and its negative consequences. Considering the high comorbidity and bidirectional association of mental disorders with somatic conditions, coordination with primary care is essential. Panel 2 summarises key areas of mental disorder prevention that we suggest should be prioritised.

### Conclusions

Increasing evidence suggests that preventive interventions in psychiatry that are feasible, safe, and cost-effective could translate into a broader focus on prevention in our field. Universal, indicated, and selective prevention strategies might be effective in improving psychological wellbeing or preventing mental disorders throughout development, although further evidence is required. There is a precedent for implementing safe universal interventions, despite incomplete evidence, from other areas of medicine for which data showing benefits were acquired only after universal adoption (eg, folic acid supplementation, fluoride treatment, and measles vaccination). These cases set an example for implementing safe interventions for mental disorders that have preliminary data showing efficacy, especially considering the potential two decade gap between implementation of early preventive strategies and emergence of mental disorders.

Investigations are needed of the early stages of mental disorders integrating different dimensions (genetic, transcriptomic, neurobiological, psychological, and socio-economic), including their complex interactions throughout early developmental periods. Evidence should be gathered on the optimisation of intervention strategies based on developmental timing, while factoring in potential short-term and long-term benefits beyond mental health outcomes (ie, educational, functional, and societal). Because prioritisation of these interventions is needed, we propose that implementation in the area of mental health could start in children with risk factors for developing a mental disorder (eg, offspring of parents with major mental disorders or individuals with genetic risk factors) or children showing non-specific symptomatic manifestations of the early stages of mental disorders or indicators of

early developmental deviation. To achieve these goals, the support of society and public policy makers is essential. Disseminating the potential societal benefits of evidence-based findings could increase community awareness, and stimulate inclusion of cost-effective prevention programmes for mental disorders in political agendas.

#### Contributors

All authors contributed to the conceptualisation of the paper. CA, CMD-C, and ES-D did the literature search and selected the references, wrote the first draft of the manuscript, and were involved in the design of the tables and figure. All authors contributed to the critical review of the scientific literature, revised the manuscript, and approved the final version.

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