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Internet-Based Depression Prevention over the Life Course: A Call for Behavioral Vaccines

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Background

Significance

Major depression is the number one cause of disability worldwide.¹ The lifetime prevalence of major depression in the United States is 16.6%, but is as high as 19.8% for those in more recent birth cohorts.² Depression, known as a “life course” disorder, usually has its first onset in mid-adolescence, and recurs every five to seven years in 80% of individuals.³ Most people with major depression do not obtain treatment⁴; of those who do obtain evidence-based treatments, approximately one-third do not improve.^{5–6} Depression is associated with substantial impairment both during and after the episode. Many who suffer from depression

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face difficulties in various areas, including school, interpersonal relationships, occupational adjustment, and behavior (e.g., substance abuse, suicide attempts). Depression affects both the individual and the nation, with a loss of \$77.4 billion dollars/year in the United States alone attributed to depression.^{7-9 10}

Need for preventive interventions

There are 121 million people with depression worldwide, yet fewer than 25% of them have access to effective treatments, and many of those in the developed world who do have access do not seek treatment.¹¹ For example, even in study settings such as Youth Partners in Care (YPIC) where youth received a comprehensive primary care intervention to facilitate treatment, less than one-third of depressed adolescents in primary care attended counseling referrals to mental health specialists.¹² Even within structured study settings, most individuals do not make full functional recoveries, warranting use of both effective treatment and prevention strategies.¹³⁻¹⁴ Prevention-focused efforts have the potential to make a major impact on global public health, particularly if they are highly scalable and easily disseminated.¹³ Two recent meta-analyses indicate that clinical episodes of depression can be prevented, with a demonstrated mean incident rate ratio of 0.78 (22% risk reduction) for all interventions.^{15 16}

Value of Technology-Based Approaches in Preventing Depression

The Institute of Medicine (IOM) has published two major reports on the prevention of mental, emotional, and behavioral disorders¹⁸⁻¹⁹ and has called for the development and rigorous evaluation of new technology based on new prevention strategies. Technology-based delivery offers considerable benefits including easy access (time and space), patient autonomy, and “non-consumable” services that are autonomous from traditional (face-to-face) interventions.^{13, 20} In the IOM model (Figure 1, interventions are deployed to prevent the onset of illness in individuals who do not already meet diagnostic criteria for these disorders. Such interventions can be universal (applied to the entire population), selected (applied to those with a risk factor for disorder), and indicated (applied to those with early symptoms of disorder). Ritterband and others have summarized key components for Internet interventions, such as the importance of the motivation of participants, participant use of interventions, website design, and support for participation.²¹⁻²³ However, technology-based interventions have important limitations, such as the difficulty motivating participants to completion, stigma, and limited availability of Internet access in economically distressed settings.²⁴⁻²⁵

"Behavioral Vaccine" Model

Effective vaccine strategies include several key components that relate closely to Internet-based prevention (Figure 2). These elements include: (1) a schedule of vaccines across the lifespan to address specific threats; (2) an active ingredient (e.g., an antigen or live attenuated organism) that is intended to protect against the disease; (3) an adjuvant to boost the immune system's natural response to active components; and (4) a structured implementation and delivery schedule that optimizes immunity. We have previously worked to develop Internet interventions based on the frameworks proposed by Nation²⁶ and Wandersman²⁷ for conventional, face-to-face effective community-based interventions,²⁸⁻²⁹ and propose to integrate these models into a “behavioral vaccine model” which we believe is aptly applicable to technology-based delivery. Like vaccines, “behavioral vaccines” require four key components: (1) a *life course schedule* that is theory-driven and includes booster doses; (2) information and training (active components) to encode responses to future threats that is theoretically and empirically grounded; (3) a *motivational framework* to boost response to behavior prescription (“motivation”, “positive

relationships”, and “dose”); and (4) a *structured implementation strategy*, as we must intervene before the onset of disorder (“website design”, “varied teaching methods”, “effective training”, “practitioner control.”) ^{23, 26–27}

Presently, we will review the literature on Internet-based depression prevention programs using this “behavioral vaccine” development model, reviewing literature relevant to each component of the model in turn. Specifically, we will look at literature on effective components of Internet-based depression prevention programs across the life-course, followed by a review of frameworks for motivation. Finally, we will discuss the literature pertaining to implementation strategies associated with these Internet-based prevention programs. Cohen’s D effect sizes (based on self-report symptoms) and number needed to treat (based on clinical assessments) were calculated for each age group.

The studies reviewed here were identified through a systematic search of Medline and PsycInfo databases for unique Internet depression intervention papers that met our inclusion criteria. The great majority of papers identified did not meet the IOM criteria for a prevention study. Most of the studies were best characterized as “early intervention,” encompassing mixed populations of those just below (indicated prevention) and above (case identification treatment) diagnostic threshold. Because only a limited number of true “prevention” studies are available for review, we included early intervention studies that reported at least 6 months of follow-up to provide a broad overview of this field.

Life Course Schedule

The first component of an effective vaccine is a life-course schedule that is theory driven. We review interventions in light of timing, life-course stage, and theoretical grounding of the intervention components (e.g. problem-solving therapy versus cognitive behavioral psychotherapy).

Interventions involving Mothers, Infants and Children

While we did not identify a published intervention, we are aware of several unpublished projects that suggest the prospect of progress in this life course period, including Mothers and Babies, Legend of the Snow Orchid, and the Pennsylvania Optimism Study, for which some limited information is available.

The Mothers and Babies Internet Project (HealthyPregnancy.ucsf.edu and EmbarazoSaludable.ucsf.edu) is an unpublished pilot randomized controlled trial (RCT) examining an intervention intended to prevent postpartum depression in an international sample of pregnant women. The program utilizes an automated, self-help, web-adapted, cognitive behavioral therapy (CBT)-based intervention³⁰ and recruited participants online using sponsored links over a six month period (January – July 2009). Participants were subsequently stratified based on depression status as baseline (“prevention” or “treatment” – depending on whether they are above or below the diagnostic threshold) and randomized to either the Mothers and Babies or information condition. Using automated email messages, depression status was assessed monthly up to six months postpartum, with subsequent deployment of a CBT-based intervention components focusing on reducing risk of depression during the peri-partum transition. The sample, currently N>1000, consisted of primarily Latino women (81%) from 45 countries in their late twenties (M= 27.6 years, SD = 5.6). Half of the participants were married (50%), the majority were educated (83% completed college degrees or above), most were employed (60%) and many had no history of major depressive episodes (69%). Another novel project is the Legend of the Snow Orchid Internet site, (<https://www.roc-n-ash.com/imheportal/welcome/>) developed by Dr. Daniel Fung for the Department of Mental Health Singapore. The site uses a fantasy-based

game to reduce anxiety and depressed mood.³¹ The Pennsylvania Optimism Study program has been developed and deployed in multiple settings. The program focuses on creating a more favorable attributional style and plans are underway to develop an Internet application.³²

Adolescent and Emerging Adulthood Studies

Six Internet-based studies were identified that focused on the prevention of depression in adolescents and/or emerging adults. Combined, these sites observed a mean effect size of 0.32 between randomization groups, and a pre/post effect size of 0.65 at the latest follow-up.^{33–38}

In a study of a problem-solving therapy (PST), which currently has no available data, approximately 210 participants between the ages of 12 and 18 with mild to moderate depressive symptoms will be randomized into an active group and a control group.³⁴ This PTS intervention uses a step-by-step approach to first triage problems based on their importance, and then to generate, implement, and evaluate trial solutions. The control group will receive no treatment except a link to a website with general information about depression and anxiety. The active group will undergo a PST Internet intervention for a total of 5 weeks, and follow-up assessments will occur at 3 weeks, 5 weeks, 4 months, and 8 months.

The program MoodGYM (moodgym.anu.edu.au) consists of five modules, ranging between 30–45 minutes each, that focus on prevention, education, and treatment using CBT. An observational study of 2909 registrants (mean age=35.5, SD=13) and 71 university students demonstrated that the participants who completed more modules exhibited the best results, suggesting that more time on the site yields better outcomes. Its effectiveness in preventing depression was demonstrated through three randomized clinical trials that compared MoodGYM to the participation in a health class, using a universal prevention model. Initial early intervention studies were completed in two single gender schools (baseline depressed: male=19.5%; female=25%). In the single gender study, males showed a lower likelihood of becoming depressed, and in the female-only study, those in the intervention group were less depressed than the control group at 20 weeks (moderate effect size).^{36–39} In the larger RCT (N=1477, mean age=14.34; SD=0.75; baseline depressed=10.1%), the effectiveness of MoodGYM was compared to that of a wait-list control group who received a typical school curriculum's health class. Only male participants showed a reduction in risk of depression (36.9% intervention, 48.5% control).³³

The website Project CATCH-IT (<http://catchit-public.bsd.uchicago.edu>) provides an alternate source of depression intervention for youth. Project CATCH-IT is a primary care-based website that focuses on the prevention of depression in adolescents through the integration of CBT, interpersonal psychotherapy (IPT), and Behavioral Activation (BA). The website interacts with its users through homework assignments and short narratives. A pilot study of Project CATCH-IT with participants who were emerging adults (age range =18–24 years) demonstrated moderate effect sizes (group effect=0.81) for the site post-intervention. In a preventative RCT study of Project CATCH-IT, 84 participants were recruited via screening in the primary care setting (sub-threshold depressed mood to enter the study, indicated prevention model) and randomized into either a motivational interview group (MI) or a brief advice group as preparation for the Internet component. Those included had a mean age of 17.39 years (sd=2.04) and were from mostly moderate to high income families. The MI group visited the study website more often and had significantly fewer depressive episodes at the 3-month follow-up.^{37–38}

Clarke et al. (2009) conducted an early-intervention (includes those above and below diagnostic threshold) RCT of 160 participants (80% female, mean age = 22.5 (SD=2.5), 44.9% depressed at baseline). The unguided program consisted of 4 main sections with interactive exercises and a CBT tutorial based on the Coping with Depression Course. Internet intervention participants were recruited from a common Health Maintenance Organization (HMO), and demonstrated moderate reductions in depressed mood compared to treatment as usual at 32 weeks after enrollment.⁴⁰

Middle Adult

Nine Internet-based studies were identified that focused on middle-aged adults (mean age=41.8 years), with a mean between group effect size of 0.30.^{41–50} BluePages (<http://bluepages.anu.edu/au>) is a depression literacy website that was designed to provide evidence-based information and treatment to a youth population. An early-intervention study (individuals above and below diagnostic threshold) was conducted to compare the results of using BluePages or MoodGYM. The study consisted of 525 participants (71% female) with a mean age of 36.43 (SD= 9.40). The participants were randomized into three groups: MoodGYM, BluePages, and an attention placebo consisting of a weekly interview to discuss lifestyle factors. Both sites were effective in reducing symptoms of depression, showing similar results, but those with baseline Center for Epidemiological Studies Depression Scales (CES-D) scores above 16 evidenced significantly higher effect sizes.^{43 47}

In a separate study, 299 adults (mean age= 43.3), 74.6% depressed at baseline, were used to measure the effectiveness of an Internet CBT program, ODIN (includes both focus on pleasurable activities and changing pessimistic cognitions), compared to a control group that received access to the Kaiser Permanente Online home page that provided non-interactive information about health concerns. The computer-generated invitation model included a mixed depressed/non-depressed sample (separate samples generated by query of health records), which could be described as early intervention. Of these participants (73% female), 74.6% were depressed at baseline. The 6-month follow-up provided a moderate pre/post effect size, but demonstrated a small between-group effect size compared to the control group. (However, many individuals in both groups were under active treatment.)⁴⁵

Colour Your Life (CYL) is a multimedia, interactive computer program for depression that was intended to intervene to reduce depressed mood in a heterogeneous population (some above and below diagnostic thresholds, early intervention). The program models an existing CWD course in Lewinsohn, which includes CBT-based lessons and incorporates a homework assignment following each of the nine 30-minute lessons. Originally, CYL was designed for a targeted age group of those over-50, but it was later adapted to suit a more expansive adult population (18–65 years). To test the program, 303 participants between 18 and 65 years (M= 44, SD= 11.6) were divided into CYL, treatment as usual (TAU), or CYL +TAU. This was an early-intervention study (mean baseline Beck Depression Index score= 27.8) where 21% of the population had no previous major depressive episodes. The results showed medium to large improvement effect sizes in all three groups at the six-month follow-up.⁴⁶

Cavanagh studied the effectiveness of a self-help online CBT program called Beating the Blues, which consisted of an introductory video and nine 50-minute treatment sessions with corresponding homework assignments (computer based approach in clinic at that time).⁵¹ In an observational study, 219 participants (mean age= 43, 60% female), 32% exhibiting depression symptoms, tested the site and showed significant improvements that were sustained after 6 months.⁴² A separate study was conducted on Beating the Blues using a sample size of 310 participants (mean age= 44.7) with an average of 1.9 episodes of depression pre-treatment. The researchers compared the effectiveness of this program with a

TAU control group comprised of patients who saw general practitioners for anxiety and/or depression (above and below diagnostic thresholds) recruited from seven general practices in London and South-east England. The results showed a significant decrease in scores for depression and anxiety among those assigned to the Beating the Blues condition, and the average of both depression and anxiety scores fell to the near-normal range.⁵⁰

In a larger early-intervention study by Andersson, 117 adults (74% female) with a mean age of 36.1 years (SD= 10.57) and a baseline BDI score of 21.0 were randomized into either a CBT intervention or control group.⁴¹ The active group was directed through email to undergo an Internet self-help CBT program consisting of 5 modules with a total of 89 pages of text and a quiz following each module. Both groups exhibited a reduction in depression symptoms, but the active group showed greater improvements in their mood.⁴¹

In a prevention RCT (263 participants, age 18 and older), CBT and PST programs were compared alongside a wait-list control group who received no treatment until three months after the intervention was completed. Both treatments differed in length (CBT= 8 weeks, PST= 5 weeks), but had similar design formats; only the CBT site offered video and audio options for its users. Both programs rendered moderate to high effect sizes immediately post-intervention, which increased at the 12-month follow-up.⁵²

Older Adult

Only one Internet-based depression prevention study targeting older adults was identified. In an early-intervention study conducted by Spek and colleagues (2007), 301 participants (63.5% female) (mean BDI baseline score= 18.4), with a mean age of 55 (SD=4.6), were randomly assigned to one of three groups: an Internet-based CBT intervention created at the Trimbos University in the Netherlands, a face-to-face CBT group, and a waiting-list control. The CBT site consisted of eight weekly modules comprised of text, exercises, videos, and figures. The intervention produced moderate between-group effect sizes at both post-intervention and after the 12-month follow-up.^{53–54}

Effective Components

In order to gauge the effectiveness of internet-based behavioral vaccines, we first review the active components of these prevention programs by comparing results to similar, more traditional, face-to-face interventions. More specifically, we examine the duration of benefits, the role of various components, mediating and moderating responses, and the ability of included interventions to demonstrate “socio-cultural relevance.”

Comparable Effectiveness

Where data was available, the Internet interventions reviewed demonstrated similar effect sizes to face-to-face interventions using comparable curriculums. The youth Internet intervention studies yielded a mean between group effect size of 0.25^{33, 35–37, 40} with the Van Voorhees study exhibiting an NNT value of 5.26.³⁷ Among face-to-face interventions for adolescents and emerging adults, Clarke and Garber both showed an overall mean effect size of 0.16 and NNT of 5.13 and 8.85 respectively.^{55–56} For adult Internet intervention studies, the mean between group effect sizes at the last follow-up evaluation was 0.28^{41–43, 45–46, 48, 50, 54} with the NNT values in two of the studies calculated to be 30.3 for Patten and 4.26 for Meyer.^{48–49} Two adult face-to-face studies, focused on postpartum depression, produced a mean between group effect size of 0.60 and had a number needed to treat of 5.0 for Elliott⁵⁷, 6.25 for Zlotnick⁵⁸, and 6.66 Lara⁵⁹

Duration of Benefits

Most of the studies continued with a follow-up visit ranging from 2 months to a year later with enduring reductions in depressed mood. When interpreting the effectiveness of Internet interventions, the positive outcomes seen directly after treatment should also be observed at the subsequent follow-up visits. In a study of older adults, the pre/post effect size of the Internet intervention was calculated to be 1.00 immediately post-intervention.^{53–54} Fifty-seven percent of the Internet CBT group completed the one year follow-up, and the pre/post effect size increased to 1.20, providing evidence of long-term effectiveness.⁵⁴ In adult studies of Colour Your Life, MoodGym, and CATCH-IT, depression scores continued to decline at each long-term follow-up.^{35–36, 46, 60} These results are consistent with Clarke's findings of sustained reduction in depressed mood up to one year of follow-up, but whether mood rebounds after one year cannot be known.^{55, 61}

Moderators and Mediators

Moderators and mediators of effect have rarely been identified in the studies of focus. Higher levels of depressed mood and a greater number of prior episodes may predict poorer outcomes at follow-up, but this has not been consistently found.^{45, 50, 60} In the MoodGym, those who completed a greater number of modules demonstrated larger changes in depressed mood than those who did not, but the relationship between adherence and outcome has been less clear in other studies.^{45, 62–63} Combining Internet-based approaches with other interventions may potentially enhance efficacy. For example, the combination of a motivational interview with an Internet site demonstrated an advantage in preventing depressive episodes.³⁸ Similarly, Andersson reported that CBT combined with a discussion group demonstrated a greater effect size than CBT alone.^{41, 64} In a meta-analysis, guided interventions, CBT-based interventions, and experiencing major or clinical depression were associated with greater effectiveness.⁶³

Socio-cultural Relevance

In all but one mixed gender experiment, a majority of the participants were females. Of the articles that listed gender as part of their demographics, seven contained ratios of females over 60% of the study population.^{36, 41, 43, 45, 49, 53–54, 64} One possible reason for this is that females, in general, account for a majority of the population suffering from depression, so recruitment appears to show a bias toward women. Three studies that provided ethnicity indicated that, overall, approximately 61% of the participants were Caucasian and 25% African American.^{37–38, 65} Also, seven adult studies indicated mostly mid to high levels of education^{41, 43, 45–46, 49, 53–54, 64}, and most of the youth population was recruited from moderate to high income families^{33, 35–38, 65}. The studies spanned over many regions and to an extent reflected national cultures in Canada⁴⁹, the United States^{37–38, 45, 65}, Australia^{33, 35–36, 43}, and Europe^{34, 41, 46, 52–54, 64} (mainly the Netherlands^{34, 41, 46, 53–54, 64} and one in Sweden⁵²). However, the degree to which each intervention was tailored to meet the needs of ethnic minorities or cultural differences within each country was not clearly specified. CATCH-IT included stories intended to reflect the experiences of adolescents in varying social and cultural frameworks.^{37–38}

Tailoring of interventions to personal profiles (ethnicity, form of motivation, attitudes) is supported both by theory and substantial empirical evidence. From the perspective of cognitive psychology, attention is increased with material relevant to either a “current concern” or if presented by a person with a similar life situation.^{14, 66} Several studies have compared tailored and standard depression and CBT-based interventions in ethnic minority populations.¹⁴ Matching of intervention to motivational style, or providing external motivation (e.g. incentives) for those who prefer external motivations and internal motivations (e.g. linking behaviors to personal goals) for those who prefer internal

motivations, may enhance adherence to health and diet recommendations in public health messages.⁶⁷ The PEN-3 (Persons, Environment, and Neighborhood) Model of Health Behaviors has been used to successfully adapt behavior change interventions to meet the needs of diverse populations.⁶⁸ Rule-based or even an artificial intelligence model could be developed to facilitate tailoring.⁶⁹

Framework for Motivation

Like vaccines that have “adjuvant” to enhance immune response, behavior change interventions often have a *motivational framework* to boost response to behavior prescription (“motivation”, “positive relationships” (professional guidance and peer to peer) and an appropriate “dose” (e.g. adherence)).

Degree of Professional Guidance

In most trials, support was provided to the users throughout the online interventions, but the methods varied considerably. Additional support serves several different purposes: 1) monitors user progress on the site; 2) provides weekly lessons; and 3) determines if the users’ emotional safety is maintained.⁶⁰ Support can be provided through email^{34, 41, 52}, by phone^{37–38, 43, 65}, or no support can be given^{45–46, 53–54}. In three MoodGYM studies, support was given in the school environment by a supervising professional (teacher).^{33, 35–36} In Color Your Life, supervision was provided by a trained coach.⁴⁶ One article specified that users received therapist support, but it did not define the manner in which it was provided.⁶⁴

Peer-to-peer supports

Internet-based social groups (ISG) support offers the prospect of enhancing curricular-based interventions by one of several mechanisms: 1) increasing use of the curricular based prevention; 2) providing opportunities to discuss contents and increase socio-cultural relevance; and 3) directing action of social support.⁷⁰ The experience of ReachOut in Australia suggests that sites that incorporate peer-based social support have considerable appeal to the public and may perhaps increase use of other more traditional learning venues.⁷¹ Online groups often sustain individual membership **from for as long as 12 months** (72.6% retention) and some participants experience resolution of depression symptoms after one year of participation (33.8%).⁷² Likewise, in a study of five online one-on-one male-to-female or female-to-female chat sessions, Shaw found some evidence that participation in Internet-based peer support groups may reduce depressed mood.^{72–73} However, Takahashi suggested that ISGs could have negative effects on a person’s depressive tendencies, due to the influence of participants with depressive symptoms.⁷⁴ With regard to enhancing social support, factors such as subjective view of social support system, belongingness, and self-esteem may improve with ISG participation.⁷³

Adherence

Completion rates, and even the definition of completion, varied across interventions. Overall, half of the guided study participants completed about half the modules, while only about one-fifth to one-tenth of those who had unguided interventions met this mark. Participation in intervention conditions, particularly those including psychotherapy, increased attrition. For example, during the Colour Your Life trial, participants completed a mean of only 3.7 of 9 sessions.⁴⁶ In a Swedish study, psychotherapy-armed participants experienced more withdrawals than the control group (psychotherapy= 37%, control= 18%).⁴¹ When MoodGYM (self-directed psychotherapy) and BluePages (psychoeducation) were compared, drop rates were greater for the psychotherapy group (MoodGYM: 25.27%, BluePages: 15.15%).^{43 47} A structured setting with phone follow-up may reduce dropouts.

Phone calls can be for motivation, safety assessments, or education purposes.⁶⁰ For example, in the primary care CATCH-IT study, only 7% dropped out at 3 months when phone follow-up was added⁶⁰, while 43% dropped out in an earlier study without phone follow-up.⁶⁵ Similarly, in the Colour Your Life trial, the authors reported receiving numerous contacts from their participants and provided regular guidance, and reported only a 5% drop out rate. Further, at the 2- and 3-month follow-ups, the authors reported 95% participation in the intervention group and 91% at the 6-month follow-up.⁴⁶ In terms of intervention adherence (modules completed, time on site), baseline factors (younger age, higher education, higher illness severity, favorable attitudes toward the intervention), implementation factors (any structured setting), and intentional use of motivational approaches (referral by mental health specialist, use of brochures, or motivational interview by their primary care physician) may influence degree of participation in Internet Interventions.^{35–36, 75–77}

Implementation Structure

A proper behavioral vaccine requires a well-thought-out implementation structure, which includes website design, varied teaching methods, and effective training.

Delivery mechanisms

Behavior change sites must balance education, behavior change, and entertainment functions in order to retain the audience, using approaches such as instructional design.⁷⁸ Most of the sites providing information primarily in text format were adult intervention studies^{41, 43, 45–46, 49, 53–54, 64}, and most were tested on individuals with moderate to high levels of education.^{41, 43, 45–46, 49, 53–54, 64} Supplying fewer interactive exercises and more textual information could possibly yield lower participation rates due to decreased participation, which could cause lower effect sizes.⁴⁴ Conversely, the use of a range of media experiences including, games, music, video, stories, photography, virtual reality, and in-the-moment cell phone interactions may substantially enhance the intrinsic appeal of sites (*e.g.*, *ReachOut*⁷¹ and *YooMagazine*⁷⁹). However, we must consider the technical infrastructure available in developing countries, which may not support broadband applications.

Delivery Context

The depression interventions and Internet sites were provided at several locations, depending on the study. Three of the interventions, all MoodGYM, were offered in a school setting^{33, 35–36} while the other interventions were accessed at the users' homes,^{34, 37–38, 40–42, 45–50, 52–54, 65} which required home Internet access to participate in the research.

However, the main form of variation between most of these studies existed in the form and location of the initial interview and assessment. Five studies conducted the first interview and assessment within a primary care facility^{37–38, 46, 53–54, 65}, three in a school environment^{33, 35–36}, three by Internet and e-mail^{41, 52, 64}, and three by brochures.^{34, 45} Two assessment strategies producing the best participation were Internet and primary care. In a study of a CBT intervention program with an initial Internet assessment, all participants reached 4 of the 5 modules.^{41, 40} In the Clarke HMO studies^{40, 45}, recruitment via search of medical records was used, which may herald future integrative technologies. Integrative technologies such as rule-based algorithms or even artificial intelligence may be able to link interventions to medical records as well as various delivery platforms such as cell phones.

Safety

One challenge to Internet-based depression prevention is the risk of self-harm or progression to major depression among those who are at risk by virtue of sub-threshold depressed mood.^{60, 80} Specifically, the participant may not be observed for extended period or have

meaningful interaction with a experienced care provider. Under these circumstances, the underlying depressive illness can progress as well as self-harm intent. Three studies reported that after becoming aware of such depression scores, the participants were recommended to consult their physician.^{34, 52–54} Increased monitoring was another method used including “checking up” on their participants via e-mail, phone, or direct contact to discuss progress and/or concerns.^{34, 37–38, 43, 49, 52} However, most articles either did not assess self-harm risk and/or did not report additional safety precautions. A comprehensive, standard approach to safety management approaches does not appear to have been developed.

Conclusions

Considerable progress has been made in developing prototype “behavioral vaccines” for depressive disorders across the life course that include effective components, frameworks for motivation, and a structured implementation strategy. The greatest number of interventions has been developed for middle-aged adults and, to a lesser extent, for adolescents and emerging adults, while no interventions have been developed and published for children or post-partum depression. With regard to effective intervention components, there is substantial evidence that CBT-based interventions can achieve comparable results to face-to-face interventions with benefits sustained one year following treatment. However, the vast majority of studies were not formal prevention studies, so we cannot fully know if components deployed in “treatment” studies would be as effective in prevention. Also, most studies enrolled primarily educated populations of “European ethnic decent”; there is a dearth of research on Internet interventions with ethnically diverse populations. Internet support or peer-to-peer contact offers the promise of both providing a “draw” to the interventions while also potentiating the effects of curricular program elements. As with vaccines, schools and primary care may be auspicious environments to implement these interventions and such settings may engender higher levels of uptake of “behavioral vaccines.” In the future, artificial intelligence-driven risk monitoring in schools, work places, and primary care could deploy personalized “behavioral vaccines” to alter illness trajectories and consequently reduce morbidity while enhancing positive development.

Future Directions

Interventions over the life course—In order to determine if current interventions are effective in the prevention of depression, formal study designs are needed with structured psychiatric interviews and longitudinal data analysis to examine survival curves (dichotomous outcomes).^{18–19} Appropriate comparison groups need to be determined with reference to research ethics and the *de facto* mental health care system.⁸¹ “Behavioral vaccines” need to be compared to effective face-to-face preventive strategies that are often unavailable, too complex, and too expensive for general distribution. We need to broaden assessed outcomes to include achievement of developmental milestones in youth and measures of well-being, resiliency, productivity, and functional status in adults to enhance relevance to policy makers. Furthermore, the cost effectiveness of such programs needs to be addressed, and the optimal schedule for each intervention, and booster sessions within each intervention, needs to be defined.

Effective Intervention Components—For “behavioral vaccines” to develop, we need to identify the key effective content and delivery mechanisms. In addition to dismantling studies, formal moderator and mediator analyses and factorial study designs could facilitate this goal. Methods to inexpensively adapt standard interventions to specific cultural settings worldwide need to be determined. Specifically, we must determine which elements can be shared across large cultural areas and which must be adapted locally. Combining interventions with other modalities, with differing mechanisms of action such as nutritional

supplements (e.g. essential fatty acids) and exercise, could increase the efficacy of interventions.^{82–83}

Framework for Motivation—Current interventions may lack sufficient appeal to attain their public health value because relatively few people are “ready” and willing to participate in such self-directed curricular programs.⁸⁴ Combinations of education, behavior change, and entertainment need to be created (REACH OUT⁷¹ and YooMagazine⁷⁹), and/or social media experiences need to be developed, such as peer-to-peer Internet support groups.^{41, 72–74}

Implementation Structure—It is essential that implementation models be developed that allow these interventions to be effectively delivered to defined populations whereby full public health impact can be assessed.⁸⁵ More engaging delivery mechanisms would integrate multiple elements together, including peer-to-peer support, games, music, video, advanced technology platforms (e.g., virtual reality experiences), cell phone-based guidance and feedback, and integrative technologies (e.g., rule based programs and true artificial intelligence).

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Figure 1.
Institute of Medicine Prevention Diagram.