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## Development of a technology-based behavioral vaccine to prevent adolescent depression: A health system integration model☆☆☆



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### ABSTRACT

Efforts to prevent depression have become a key health system priority. Currently, there is a high prevalence of depression among adolescents, and treatment has become costly due to the recurrence patterns of the illness, impairment among patients, and the complex factors needed for a treatment to be effective. Primary care may be the optimal location to identify those at risk by offering an Internet-based preventive intervention to reduce costs and improve outcomes. Few practical interventions have been developed. The models for Internet intervention development that have been put forward focus primarily on the Internet component rather than how the program fits within a broader context. This paper describes the conceptualization for developing technology based preventive models for primary care by integrating the components within a behavioral vaccine framework. CATCH-IT (Competent Adulthood Transition with Cognitive-behavioral, Humanistic and Interpersonal Training) has been developed and successfully implemented within various health systems over a period of 14 years among adolescents and young adults aged 13–24.

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### 1. Introduction

Healthcare organizations are increasingly being required to both improve outcomes and reduce costs (McClellan, 2011). Mental disorders in adolescence, which are the single greatest hospitalization cost and source of disability in this age group, will soon be a major target for intervention within child health systems (Bardach et al., 2014). Depression in particular is a common disorder with episodic and chronic courses, marked by considerable impairment that accounts for a substantial proportion of costs incurred. Adolescent depression also accounts for a substantial proportion of future psychiatric, social and medical morbidity (Gladstone et al., 2011).

Reducing the incidence of mental disorders, including depression, in children and adolescents could substantially improve social and developmental factors such as high school graduation rates, work force participation, and relationship functioning in the future (Weisz et al., 2005). Preventive interventions targeting depression have been described as an economically efficient way to effectively reduce the incidence of the disease (Van Zoonen et al., 2014). However, creating models that prevent youth depression proves daunting because of the need to both develop an effective model that improves outcomes and

costs, as well as the challenge of implementing such a model within a specific context (Gillham et al., 2000; Hoek et al., 2009).

Internet-based behavior change strategies have been proposed as one method that may facilitate a resolution of the cost and outcomes paradox. Several models of Internet- and technology-based learning to prevent or treat psychiatric and medical disorders have been developed as “stand alone entities”. Some emphasize the content and importance of taking into account the psychological factors that influence health outcomes (Ritterband et al., 2009), while others focus on the factors related directly to the websites, that impact the “user experience” (Crutzen et al., 2009). Researchers have proposed the need to evolve and test intervention versions using randomization designs to optimize performance (Mohr et al., 2011), as well as consider specific implementation factors that are necessary for treatment efficacy (Durlak and Dupre, 2008).

In this paper, we describe the research and development process of CATCH-IT (Competent Adulthood Transition with Cognitive-behavioral, Humanistic and Interpersonal Training), a web-based depression prevention program designed for adolescents. We outline the scientific and practical steps required to develop an Internet-based prevention for health systems, or an integrated development model. We have previously posited that “technology-based behavioral vaccines” provide the optimal framework necessary to implement an Internet-based prevention program within a healthcare setting (Van Voorhees et al., 2011). Similar to the steps involved in the development of biological vaccines, the development of CATCH-IT incorporated specific preventive components that began with exploratory research, moved through pre-clinical research, and involved 3 clinical trials over a period of 14 years. The goal for CATCH-IT is to become a universal public health strategy, or behavioral vaccine, for the prevention of major depression among adolescents.

The development of a technology-based behavioral vaccine requires an extensive process to ensure each component is thoroughly developed in order to create the appropriate implementation that can maximize outcomes (i.e. reduce symptoms or prevent depressive episodes) (Van Voorhees et al., 2011). Much like the development of biological vaccines, the development of behavioral vaccines requires time, effort, and scientific expertise. Vaccine development is a multi-step process that can take years and in some cases, several decades. The research and development process moves through defined stages that take a candidate, such as CATCH-IT, from a concept to a licensed product (Collins, 2005). These processes include exploratory and pre-clinical phases. In this paper, we describe the current intervention, CATCH-IT 3, which is being evaluated presently through a grant from the US National

Institute of Mental Health (Van Voorhees et al., 2011). We describe the process of developing the intervention, from exploratory research (1998–2006), to pre-clinical research (2002–2011), and then through the development and delivery of the program with revisions based on clinical research (2004–present).

## 2. Material and methods

### 2.1. Behavioral vaccine framework

The behavioral vaccine concept (Embry, 2002) provides a framework to develop and understand the model for what we call a technology based behavioral vaccine (Van Voorhees et al., 2011). We have described four key components of a behavioral vaccine that take into account both therapeutic and contextual factors. The therapeutic elements (see Fig. 1 below) include (1) a *life course schedule* that is theory-driven and includes booster doses and (2) active *effective components* of information and training to encode responses to future threats that can then be deployed at some future point. The contextual elements involve (3) a *motivational framework* to boost response to behavior prescription and (4) a *structured implementation strategy* to optimize intervention effectiveness (Van Voorhees et al., 2011). Below we use the behavioral vaccine framework to describe the revision process for the CATCH-IT model. Specifically, for each therapeutic element of the behavioral vaccine model (i.e., life course schedule, effective components, motivational framework, structured implementation strategy), we provide details about intervention development, and about the use of that element within the CATCH-IT 3 program.

In addition, we present a discussion of regulatory and administrative issues involved in the development and implementation of the CATCH-IT intervention.

### 2.2. Life course schedule

#### 2.2.1. Intervention development

Intervention development first began at Johns Hopkins University, continued at The University of Chicago, and moved to the University of Illinois at Chicago. Van Voorhees led an interdisciplinary team of investigators in a multi-step development process: (1) initial translation by a primary care physician of manuals for face-to-face preventive interventions; (2) Internet-site design using an informal focus group; (3) serial fidelity reviews by a health psychologist, manual authors, and a practicing psychotherapist; and (4) socio-cultural review by an adolescent editor. The prototype intervention included an initial motivational

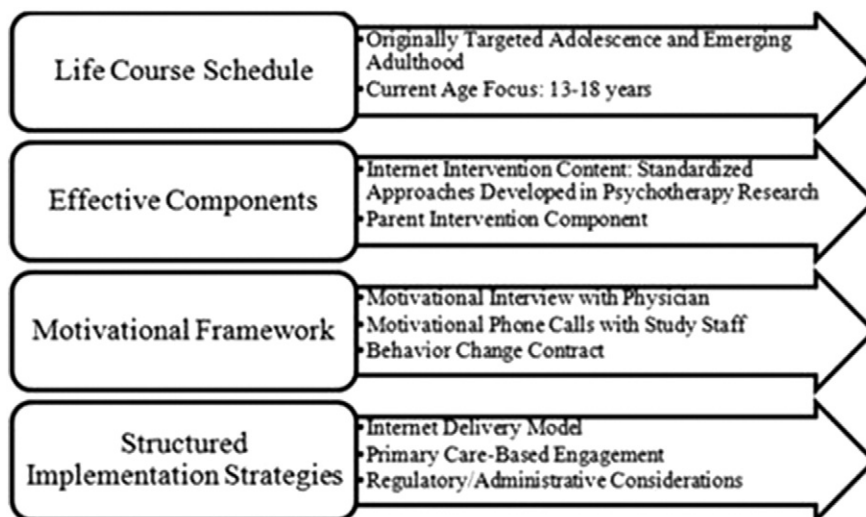


Fig. 1. Components of technology-based behavioral vaccine.

interview (MI) in primary care to engage the adolescent, 11 Internet-based information modules based on cognitive behavioral therapy (CBT) strategies, including behavioral activation, counter pessimistic thinking, and interpersonal training (IPT) strategies, such as interpersonal psychotherapy, activating a social network, and strengthening relationship skills. Additionally, a follow-up MI in primary care was included to enhance behavior change. The CATCH-IT 1 content and pilot study targeted youth aged 18–24.

We elected to focus on the 14–21 age group as the peak at-risk group for the CATCH-IT 2 clinical trial (feasibility and dosing) as opposed to ages 18–24 in the CATCH-IT 1 pilot study. We elected to move into the adolescent age group after consultation with program officers at the US National Institute of Mental Health. For the third clinical trial, CATCH-IT 3, the age range was further narrowed to 13–18 with a nodal age of 15, which is the mean age of onset of a depressive episode (Institute of Medicine, 2009).

### 2.2.2. CATCH-IT 3

Based on promising results from the phase 2 trial of CATCH-IT, a modified version of this primary care/Internet-based preventive intervention was prepared (text revised and edited, Internet design completed, see Appendix 0 for sample page) titled CATCH-IT 3 (using previously published methods (Gagne et al., 1992; Landback et al., 2009; Van Voorhees et al., 2010; Van Voorhees et al., 2007a)). The CATCH-IT 3 intervention has a motivational (3 primary care physician (PCP) MIs at time 0, 1.5 months and 12 months and 3 coaching phone calls at 2 and 4 weeks and 18 months) and an Internet component (with separate adolescent [14 modules, and one optional model on anxiety] and parent [5 modules] programs). This revised and expanded intervention includes a comprehensive approach to reducing modifiable risk factors and enhancing resiliency factors associated with increased or decreased risk of depression, respectively, proposed by Spence and Reinecke (2003). The revised CATCH-IT “Tracker” will monitor time in the study and deploy elements of the intervention based on time since enrollment, including computer and human elements (e.g. calls, doctor visits). Adolescent experience in CATCH-IT 3 is presented in Appendix 0.

The intervention targets the period of peak incidence of new onset major depression, ages 13–18. Materials and stories were built around a nodal point of age 15, the mean age of onset (Institute of Medicine, 2009).

## 2.3. Effective components

### 2.3.1. Intervention development

The revision process of CATCH-IT 2 and CATCH-IT 3 reflected theoretical re-orientation to a comprehensive vulnerability and protective factor model and shift toward actual behavior change rather than simply web-based experiences. With regard to a comprehensive model of vulnerability and protection, a new integrated model was developed that combined Spence and Reinecke's (2003) transactional/multi-factorial model on vulnerability and onset, Compas' model of stage wise progression from depressed mood to depressed syndrome to a depressive disorder (Compas et al., 1993), and the Trans-theoretical Model of Change (Diclemente and Prochaska, 1985). The CATCH-IT 2 intervention included a comprehensive approach to reducing modifiable risk factors and enhancing resiliency factors associated with depression risk (Spence and Reinecke, 2003).

In terms of behavior change orientation, the overarching goal of this intervention experience was to provide a sense of mastery over emotions in a range of domains (e.g., peer, family, school). Using standardized approaches developed in psychotherapy research, the CATCH-IT program teaches adolescents how to reduce behaviors that are associated with increased vulnerability for depressive disorders (e.g., procrastination, avoidance, rumination, pessimistic appraisals, indirect communication style) and increase behaviors that are thought to protect against depressive disorder (e.g., behavioral scheduling,

countering pessimistic thoughts, activating social networks, strengthening relationship skills) (Hankin, 2006; Reinecke and Simons, 2005; Van Voorhees et al., 2008a). Like previous successful chronic disease prevention interventions, the CATCH-IT program emphasizes actual behavior change (Diabetes Prevention Program Research Group, 2002; Wing et al., 2004).

Process evaluation using qualitative methods suggested that perhaps self-efficacy was the mechanism of improvement in the CATCH-IT 2 study. This concept was first proposed by Ricardo Munoz in 1977 (Muñoz, 1977). The CATCH-IT 3 intervention was revised to encourage openness to change and self-affirmation. The assessment process became more extensive to allow for the participants to share their experiences with a semi-structured clinical diagnostic interview (Kaufman et al., 1997). We focused on improving story quality, which we believed to be critical in creating relevance for the lesson and spurring self-efficacy. Additionally, we added a self-efficacy exercise to each module that includes interactive features (re-call of prior goals) (Cuijpers et al., 2009). We also added a “My Progress” component, where the adolescent could track their course throughout the program, including the trajectory of their mood from day one.

The Internet-based components now include resiliency building (Bell, 2001), behavioral activation (BA) (Jacobson et al., 2001), CBT (Clarke, 1995), and IPT modules (Mufson et al., 2004; Stuart and Robertson, 2003). Three behavioral activation modules were added in response to comments from the first prototype phase 1 trial suggesting that it focused too specifically on thoughts and not enough on action. We also evaluated the match between themes reported by adolescents, current theories of development, and vulnerability factors models. We concluded that additional materials relating to anxiety should be added, and a much expanded parent program was needed.

We elected to add a parent program to both CATCH-IT 2 and 3. Preventive approaches that do not attend to the family context may be less effective than interventions that address the child and at a minimum treat parent depressive disorder (Clarke et al., 2001). The rationale for the development of the parent intervention was for it to serve as a resource for parents to be well-informed about the intervention, and to enhance family resiliency (i.e., flexibility, shared activities, mutual understanding, and emotional support). In the CATCH-IT 1 study, in at least one case, a participant withdrew after his parents objected to his participation. During the course of CATCH-IT 3 preclinical work, moderation analysis of the Prevention of Depression study suggested that current parent depression interfered with adolescents' response to a CBT based intervention (Garber et al., 2009). Consequently, a parent intervention was developed to encourage depressed parents to seek treatment and be aware of how their actions can affect their child. This reflects research that shows parental depression influences symptoms in teens (Gunlicks and Weissman, 2008). In addition, the information on communication highlights the importance of understanding family conflicts, which can also influence overall mood (Restifo and Bogels, 2009). The program pushes parents to communicate more with the teen and help strengthen their relationship. In CATCH-IT 2, this was provided as a paper workbook; in CATCH-IT 3, this became a web-based program.

### 2.3.2. CATCH-IT 3

Table 1 below describes the modified intervention in terms of theoretical framework, content, exercises and targeted risk factors. Each module has exercises that participants can complete online and print out for review. We have previously described the development of the Internet intervention based on the Instructional Design Model, Trans-theoretical Model of Change, and the Theory of Planned Behavior (Landback et al., 2009). With the exception of cultural modules, all materials have already been developed. To enhance participation, CATCH-IT 3 includes engaging media options such as stories and videos (Landback et al., 2009; Marko et al., 2010; Van Voorhees et al., 2010).

The parent component of the intervention is based on an adaptation of Beardslee and Gladstone's clinician-facilitated and lecture intervention

**Table 1**  
Intervention phases and components of CATCH-IT 3.

Component	Module content and exercises (theoretical model)	Behavioral target
Induction (months 0–2) and maintenance phase (month 2–6) using standard modules		
Motivational component	PCP MI at time 0, 8 weeks and 12 months Phone calls at 2 and 4 weeks and 18 months	Under-attainment of milestones Low motivation for prevention
Modules 2–4	Event scheduling Practicing active behaviors (Behavioral Activation) BA	Loss of response contingent reinforcement
Modules 5–8	Identifying and countering pessimistic automatic thoughts, general beliefs and hopelessness Problem solving (cognitive behavioral psychotherapy)	Cognitive distortions Pessimistic cognitive style/content Poor coping skills
Modules 9–12	Improving communication skills, coping transitions Conflict resolution. Engaging new networks (Interpersonal Psychotherapy – IPT)	Lack of social support Social skills deficits Lack of peer support
Modules 13–14	Flexibility/humor/persistence, Community involvement Barriers to treatment (resiliency concept)	inflexible responses Low levels of pro-social activities
Situational problem solving	Rational appraisal of problems, solutions, plan and execute (problem solving therapy)	Unresolved conflict Low self-efficacy
Cultural personalization	Culture specific issues addressed for African American and Hispanic Youth (Van Voorhees et al., 2009b, 2007b)	Culture specific risk factors

approaches from the Preventive Intervention Project (Beardslee et al., 2003). This intervention helps parents develop the awareness and skills needed to help build resiliency in their children. The intervention also seeks to reduce known risk factors for adolescent depression. Gladstone and Van Voorhees have developed an intervention plan (Table 2). To address the key mediating role of parental depressed mood, a personalized component will be available to parents with depressed mood.

## 2.4. Motivational framework

### 2.4.1. Intervention development

Given higher than expected utilization rates and high drop-out rates in the phase 1 clinical trial, we elected to modify the motivation component. The original MI, which was performed only by the PI (Van Voorhees), was guided by a short manual of 6 pages which provided a variety of approaches and strategies based on participant responses. Feedback from non-completers include reports that (1) they became too anxious, depressed or had other excessive negative affect to complete the program, (2) their parents objected, or (3) they found the material too “boring” to complete, if they were not currently depressed. To address these concerns, we (1) added pull down tabs under “how are you feeling” to enable participants to deal with negative affect in real time, (2) included a parent program, and (3) restricted participation to those who primarily had some current negative affect or confirmed past episode of MDE. There was also a sense from all participants that they wanted to be called while completing the on-line program.

Further steps were also made in CATCH-IT 2 to enhance the overall motivational program. Because the model switched from PI interviews to PCP interviews, a simplified MI script (1 page) was developed with

experts in MI approaches. Additionally, the participants were asked to complete a behavior change contract. Motivation for participation was also enhanced by three separate phone calls from a trained social worker to check on participant progress and to provide encouragement. For CATCH-IT 3, we restructured the motivational component to implement three PCP motivational interviews at 0, 2 and 12 months and a 1-month safety/motivational call from study staff to monitor thoughts of self-harm and encourage website participation through motivational interviewing techniques. Parents also receive a parallel structure of three motivational interviews and one phone call only by study staff. Small \$5 gift card incentives were provided after completion of major module sections.

### 2.4.2. CATCH-IT 3

The intervention uses motivational interviewing, goal-setting, and telephone coaching to enhance each of these change processes and to advance the participants (adolescent and parent, separate interviews) through the stages of change to reduce vulnerability and increase protective factors. (Wing et al., 2004; Group, 2002; Katon et al., 2001; Unutzer, 2004) In the motivational interview (10–15 min duration), the physician seeks to help the adolescent weigh the balance of positives and negatives of undertaking this depression prevention intervention. The coaching phone calls were conducted by study staff, use the same motivational interview approach, and last 5 min or less in duration, solely designed to encourage completion of the intervention and behavior change (not act as psychotherapy). All adolescents completed a motivational interview questionnaire before the physician interview to enhance level of participation and fidelity to the interview (asks questions physician will ask).

**Table 2**  
Parent program.

Component	Module Content and Exercises (theoretical model)	Behavioral Target
Modules 1–3 PIP intervention	Activism Connectedness Affect recognition	Cultivating strengths Encourage discussion, behavioral activation resiliency behaviors and expression of emotion
Module 4 and 5 If parental depressed mood	Treatment education Access to MoodGym depression treatment program	Increase likelihood of treatment Self-directed CBT and IPT via MoodGym to change behaviors (Christensen et al., 2004, 2006)

## 2.5. Structured implementation strategy

### 2.5.1. Intervention development

The re-design of the CATCH-IT 2 website aimed to increase socio-cultural relevance, improve the efficacy of the depression prevention exercises, and include more motivational structure. The structure of each module was based on Instructional Design Theory (Gagne et al., 1992). Each module lesson included teen stories, skill building exercises, and behavior change assignments. The teen stories were based on vicarious learning theory and were included to facilitate adaptive learning/behavior change that occurs in self-help groups (Davison et al., 2000; Gagne et al., 1992). However, as we prepared for the development of CATCH-IT 3, we recognized a more dynamic and interactive experience would be required, based on an analysis of the CATCH-IT 2 data that suggested higher levels of interaction (as measured by characters typed in) and more favorable self-rated experiences correlated with improved outcomes (Saulsberry et al., 2013; Van Voorhees et al., 2007a). After extensive consultation and cost analysis, we elected to pursue a model based on narrative learning with video self-diary rather than a more expensive and time-consuming game-based or animation approach.

We also created short videos portraying key issues in the family life of a teen and added them into the parent program to illustrate the appropriate way of handling a stressful situation. Furthermore, we revised all the picture selections and color design to reflect the overall theme of the module, using a media theory called *Synchronization of the Senses* (Kaplan, 2005). Media studies have long analyzed how film can utilize the deployment of multiple sensory inputs (visual and auditory) in order to create a piece that exceeds the sum of its parts. In order to better connect to human sensory and emotional experience, CATCH-IT 3 took this into account in designing the layout for the modules and in incorporating video content into the intervention (see Appendix 0).

Primary care integration was gradually developed and implemented over the three iterations. The CATCH-IT 1 prototype was evaluated by recruiting by flyer and postings in and around one university physician's office site. Thus, the apparatus of the office was not invoked to enable recruitment, as was eventually used in subsequent recruiting models. However, in the CATCH-IT 1 study (Van Voorhees et al., 2005), we identified common barriers to implementation from the physicians point of view including: 1) lack of established procedures for depression screening, 2) low levels of study interest by nursing staff or physician, 3) practice management problems, and 4) need to create new policies. All pointed to the importance of a clear rationale for participation and health care provider endorsement.

A structured engagement and training program was developed to train the entire office staff on the intervention model in CATCH-IT 2 (Eisen et al., 2013) and then was extended in CATCH-IT 3. In CATCH-IT 2, practices screened for future risk of depression and, in about half the practices, the physician performed the motivational interviews. For CATCH-IT 3, practices screened for depression and carried out letter based recruitment (i.e., all teens in a practice received a letter about the study and could call in to be screened for depression risk), and site physicians performed the motivational interviews. At each level of increased involvement, more extensive health system leadership and site involvement was required. Furthermore, analyses demonstrating both potential benefits and greater challenges in practices located in ethnic minority and low income neighborhoods resulted in a choice to modestly over recruit in these environments. After the implementation of the Affordable Care Act in 2012, with the transition to electronic medical records, practice participation became even more difficult to obtain.

Based on fidelity analysis of the physician MI tapes in the CATCH-IT 2 study, we focused on increasing the levels of empathy and overall "MI spirit". A video-based training model was developed to demonstrate this brief MI to physicians. In CATCH-IT 2-R, the training consisted of only one scenario involving a fairly responsive youth. We expanded the physician MI training to include a didactic focus on MI spirit and

an expanded video instruction with 3 interview scenarios ("high achiever", "bored and not motivated", "sports and girls") to allow the PCPs to be able to see a wider range of examples. The hope was the revised didactics, wider range of video examples and initial feedback would provide an expanded experience base to develop MI spirit as opposed to simply completing scripted elements. Similarly, structured feedback was provided by reviewing each physician's initial interviews.

### 2.5.2. CATCH-IT 3

Practice nurse/medical assistant staff members complete the screening process, and study staff collect the screening forms and then conduct eligibility assessments by phone (Van Voorhees et al., 2009a). Consent and baseline assessments are conducted face-to-face in primary care offices.

At each site, primary care physicians participate in training sessions (during lunch) before being recruited to perform adolescent motivational interviews. A brief didactic presentation was complimented with video-based examples of three different adolescent scenarios with all three MIs (1st, 2nd, 3rd modeled). All PCPs are provided with standard scripts to assist them during the interviews, and all interviews are taped and reviewed for fidelity. We aim to assess PCP ability to perform interviews after session three and provide feedback based on review of taped interviews (McCambridge and Strang, 2004; Schoener et al., 2006; Pierson et al., 2007; Moyers et al., 2005). The study coordinator performs the parent motivational interviews while the adolescent meets with the physician, who also performs the three telephone coaching calls with the adolescent.

## 2.6. Regulatory and administrative issues

### 2.6.1. Risk and liability

Over the course of three interventions, concern about risk and liability steadily increased. The initial protocol (CATCH-IT 1) was approved by the Institutional Review Boards (IRBs) of both Johns Hopkins and University of Chicago. The initial participant population consisting of emerging adults facilitated approval. No concerns were raised initially about supervision of the participants or safety. Self-harm risk was not directly addressed.

The CATCH-IT 2 study that involved adolescents invoked several new concerns by overseeing IRBs. There were several complex integration issues in this area. First, the IRB required every page of the Internet site to be reviewed and approved once constructed. The institution required more than 12 months for final approval of all related protocols and remained acutely concerned about liability associated with self-harm. Any statements that appeared to be declarative about potential benefits of the intervention were replaced with subjunctive tense statements ("may"). A disclaimer was required to be placed on the Internet site clearly stating that the program was not "treatment" and was not intended to address "self-harm". The IRB also required the provision of an emergency contact number.

Additionally, the IRB required the development of self-harm management protocols. To achieve this, an entire risk prediction model and trained caller and model/tracking system had to be developed to manage contacts and track risk. Formal clinical management of self-harm risk had to be established to address any future presence of suicidal ideation, self-harm, or severe low mood. The depression screening for the study had to be separated from routine office based screening and eliminated from the electronic medical record. Also, parental consent was required before the office-based depression screen could be transmitted to the study office, for phone eligibility assessment and, of course, for actual study participation. This proved complex and time consuming, as in some cases adolescents visited their physician alone or did not want their parent to know they were being screened for risk of a mental disorder.

These challenges increased for CATCH-IT 3 with additional concerns about "over persuasion" in the form of either too many calls for either

recruitment or assessment. This appeared to be a complex question as the idea of the study was early identification of mental disorder risk at a time when baseline motivation may be quite low. In such a setting, not surprisingly, countervailing concern from the DSMB emerged about “insufficient” outreach perhaps to those who had experienced deterioration. These concerns had to be reconciled with numerous IRB amendments. These changes, which had to be put through  $N = 5$  IRBs (most major health systems in the trial have their own IRB process), resulted in considerable time and expense for study staff. Over and above this, substantial staff time was required to manage and follow-up on reported self-harm from adolescents or their parents. Safety costs accounted for 35% of the total cost of implementation, or \$209.12 (Ruby et al., 2013).

### 2.6.2. Construction of sites and ownership

Additional administrative issues throughout the process included issues related to Internet site construction and maintenance, intellectual property concerns, and conflicts of interest. The CATCH-IT 1 Internet site was constructed by the Medical Arts Department at the Johns Hopkins University for a total cost of less than \$40,000. However, the data base functions did not work properly, and all site use data came from diaries. CATCH-IT 2 was constructed by a joint tech-content team at the University of Illinois where interface and database performance were excellent (total cost was \$138,683.03) (Ruby et al., 2013). CATCH-IT 3 was constructed by Thrive, Inc., of California with content and materials and design provided by the University of Illinois and Wellesley College staff. Building on an outside platform resulted in some challenges around integration behind the university firewall and proved costly, if ultimately successful. Total costs have not yet been estimated.

Intellectual property agreements had to be established between all parties developing materials beginning with CATCH-IT 2. All universities had considerable interest in the possibility that the interventions might prove effective. Eventually the University of Chicago requested the development and ownership estimate for all parties. This created new concerns about conflicts of interest between faculty and outside parties and any future ventures. It was eventually decided to offer CATCH-IT 2 to any willing party at no cost or license fee (two such licenses were granted). The PIs limited their involvement with such projects to providing advice for limited cost and payment. Two companies were eventually formed with either a license or advice by the PI (Van Voorhees, which began as mentored project in business school). In the latter case, the University elected only to provide advice from Dr. Van Voorhees rather than providing a license. The University of Chicago maintained the CATCH-IT 2 internet site for public access until the PI (Van Voorhees) left the institution in McClellan, 2011.

## 3. Calculation

The initial conceptual model of CATCH-IT was developed during a phase of exploratory research focusing on the specific behavioral vaccine components: Life Course Model, Effective Components, Motivational Framework, and Structured Implementation Strategy. Exploratory research provided the empirical and theoretical support for each of these components and highlighted the importance of equally incorporating both therapeutic and non-therapeutic aspects to the intervention. Below, we review the foundational work that supported the development of the CATCH-IT intervention. We structured this presentation by addressing the theoretical basis of the behavioral vaccine model.

### 3.1. Life course schedule for depression prevention

The first component of an effective vaccine is a life-course schedule that is theory driven. Understanding depression and its impact is a primary step in developing an appropriate intervention strategy. Adolescent depression is a common disorder with chronic and episodic

courses marked by frequent recurrence and considerable impairment that accounts for a substantial proportion of the health care costs incurred by this age group (Birmaher et al., 1996a; Birmaher et al., 1996b; Kovacs, 2006). One year prevalence rates for major depressive disorder range from 4 to 7% in adolescence (Costello et al., 2002). According to the National Comorbidity Survey (Kessler and Walters, 1998), the lifetime prevalence of major depressive disorder is 12.6% in adolescents aged 15–16, and 15.4% among adolescents aged 17–18. Adolescent depression is recurrent, with as many as 50–70% experiencing a subsequent episode within 5 years (Thapar et al., 2012).

### 3.2. Effective components

Several characteristics of adolescents experiencing depression were taken into consideration to promote intervention effectiveness. These factors include negative cognitions (Lewinsohn et al., 1995; Lewinsohn et al., 1997), stressful events, poorer social skills (Lewinsohn et al., 1994; Liu, 2002), predisposing vulnerabilities/risk factors, and the absence of protective factors that provide immunity to depression (Lewinsohn et al., 1985). Hollon et al. (1990) reported that changes in negative cognitions mediated the relation between cognitive therapy and depression. Substantial epidemiologic work, including that done by the Principal Investigators (PIs), suggests that adolescents' families are a substantial source of vulnerability and protection with regard to future incidence of adolescent depression (Booth et al., 2008; Paunesku et al., 2008; Van Voorhees et al., 2008a, 2008b, 2008c).

Van Voorhees, Gladstone and colleagues conducted an exploratory factor analysis to identify clusters of factors predicting future depressive episodes in adolescents (Paunesku et al., 2008). They found that strong family and interpersonal relations were protective against depression, while avoidant problem solving and low self-worth amplified the risks associated with delinquency and MDD. Van Voorhees and Booth found that active coping and positive self-concept predicted lower risk while poor affect regulation and greater depressed mood predicted higher risk. Similarly, family related exposures and behaviors constituted the greatest portion of attributable risk for future episodes of adolescent depressive disorder (Booth et al., 2008). In another study, they identified individual, family, school/peer and community factors predicting new-onset depressive episodes. Active coping and positive self-concept predicted lower risk, while poor affect regulation and greater depressed mood predicted higher risk (Van Voorhees et al., 2008a, 2008b, 2008c). In a meta-analytic review of attribution style as a risk factor for depression, Gladstone and Kaslow (1995) showed that there is a significant connection between cognitive styles and depressive symptoms in youth. Knowledge developed from these risk studies forms the foundation of the CATCH-IT intervention.

### 3.3. Motivational framework

Motivational factors are necessary to improve adherence to Internet intervention programs (Neil et al., 2009). Use of Internet interventions without some process of engagement and motivation is lower than in programs that have such processes in place. According to the Trans-theoretical Model of Change (Diclemente and Prochaska, 1985), the process of depression onset may be interrupted with a motivational interviewing strategy (Diclemente and Velasquez, 2002). The hypothesized mechanism of action is increased quantity and quality of motivation by strengthening the internal rationale around innate needs for competence, autonomy and connection (Diclemente and Velasquez, 2002, Miller and Rollnick, 1991, Vansteenkiste and Sheldon, 2006). The CATCH-IT intervention uses our published model based upon the Theory of Planned Behavior and depression help-seeking to engage youth in the intervention and motivate behavior change (Carter, 1990; Halgin et al., 1987; Howland, 1997).

### 3.4. Structured implementation strategy

The Internet was chosen as the most promising modality for the delivery of preventive interventions because it offers advantages such as interactivity, personalization for adolescents, and has wide availability through libraries and schools, for all youth including ethnic minorities (Christensen et al., 2002; Clarke, 2002; Crutzen et al., 2008; Cuijpers et al., 2005; Gillham et al., 2000; Gray et al., 2002; Kaltenthaler et al., 2002; Mains and Scogin, 2003; Merry et al., 2004; Van Voorhees et al., 2007a). Adolescents with obesity, smoking, alcohol use, HIV/AIDS risk, and sexual risk-taking have website visit rates of 45% to 96% and have demonstrated favorable behavior change in studies of motivated volunteers (Crutzen et al., 2008; Kirk et al., 2003; Lou et al., 2006; Patten et al., 2006; Van Den Berg et al., 2007; Van Voorhees et al., 2007a; Walters et al., 2006; Wantland et al., 2004; Ybarra et al., 2006).

Motivational interviewing in primary care offered the prospect of a readily available method of engaging and motivating youth to complete an Internet-based self-directed program. Although adolescents may be unlikely to complete free-standing Internet based interventions (Christensen et al., 2002; Clarke, 2002), when combined with some minimal amount of face-to-face contact and self-directed interventions, they may have higher completion rates and greater reductions in symptoms (e.g. risk). A primary care-based intervention may be more acceptable than specialty mental health services to adolescents and may provide the primary care-based psycho-social guidance many seek (Jaycox et al., 2003; Joffe et al., 1988; Van Voorhees et al., 2003), particularly for ethnic minority youth (Van Voorhees et al., 2007b).

## 4. Results

### 4.1. Phase 1 clinical trial

The first evaluation of the intervention was conducted in a pilot study (Van Voorhees et al., 2005). The intervention included an initial motivational interview in primary care, eleven online modules that focused on CBT and IPT, as well as a follow-up motivational interview. Fourteen emerging adults (aged 18–24) were recruited from two urban primary care clinic settings who had at least one risk factor for a depressive episode (family or personal history of an episode), but who were unlikely to meet criteria for major depression (Center for Epidemiologic Studies Depression Score CES-D < 17) (Van Voorhees et al., 2007a). They evaluated three outcomes: 1) acceptability, 2) adverse effects, and 3) evidence of benefit.

All participants completed the first motivational interview, 13 of the 14 participants engaged the Internet site, and 8 of the 14 participants completed the entire intervention. On a 1 to 5 scale, completers reported high levels of readability ( $M = 4.7$ ,  $SD = 0.5$ ) and ease of understanding ( $M = 4.7$ ,  $SD = 0.4$ ) and low levels of negative emotions ( $M = 2.0$ ,  $SD = 0.8$ ). For completers, favorable trends were noted for the targeted risk factors between the pre/post measures: depressive symptoms decreased, measured by CES-D,  $p$ -value < 0.15 (effect size = 0.43); dysfunctional thinking decreased, measured by ATQ-R,  $p$ -value < 0.51 (effect size = 0.17); and sense of lower social support decreased, measured by SSQ-6,  $p$ -value < 0.13 (effect size = 0.27). Effect sizes were similar to those of other preventive interventions for depression (Jane-Llopis et al., 2003).

### 4.2. Phase 2 clinical trial: CATCH-IT 2

In the phase 2 clinical trial,  $N = 83$  adolescents were randomized into one of two versions of CATCH-IT 2: PCP MI + Internet program versus PCP brief advice + Internet program (BA). The intervention included an initial and follow-up interview in primary care, 14 Internet-based modules, and an accompanying parent program. The MI group demonstrated superiority in adherence with: number of sessions (8.16 versus 6.00,  $p = 0.04$ ), longer duration of session activity (46.2 days versus

29.34 days,  $p = 0.04$ ), and more characters typed into exercises (3532 versus 2004,  $p = 0.01$ ). The MI group demonstrated a trend of increased adherence of use of Internet program and total time on site. Additionally, teens in the MI group reported higher trust in their physician (4.18 versus 3.74,  $p = 0.05$ ), greater satisfaction with the Internet-based component (7.92 versus 6.66,  $p = 0.01$ ), and lower levels of hopelessness (MI group of 2% versus 15% for the BA group,  $p = 0.044$ ). Both groups demonstrated lower depressive symptoms (CES-D scores) from baseline to one-year follow-up (MI:  $ES = 0.84$ , 95% CI: 0.39, 1.27; BA:  $ES = 1.08$ , 95% CI: 0.60, 1.54), along with lower reports of loneliness from baseline to follow up ( $ES = 0.43$ , 95% CI: 0.00, 0.85). Similarly, they found that all adolescents showed improvements in peer social support and ratings of motivation, as well as declines in perceived impairment of school performance (Van Voorhees et al., 2008b). Furthermore, MI group participants were less likely to be diagnosed with a depressive episode by their physicians and/or in the course of assessments provided to the physicians (32.5% vs. MI: 11.6%,  $P = 0.03$ ) (Saulsberry et al., 2013).

During the second clinical trial, specific aspects of the primary care setting also were evaluated. Using questionnaires given to the primary care physicians and office staff involved in the study, several key findings were discovered. Providers were able to implement the intervention with adequate competence. In general, both physicians and medical staff found the Internet prevention model valuable and sustainable. The motivational interview performance scores marginally showed that physicians could gain basic minimal proficiency in motivational interviewing after just a 1-h instruction session. Specifically, PCPs were able to complete the basic scripts and components (e.g. open ended questions and reflections), but often lagged on demonstrating “MI spirit”, which rests heavily on an assessment of the relationship between the participant and interviewer in service of behavior change (i.e., empathy, power sharing and eliciting motivational statements). Clinical practices varied considerably in their ability to perform the intervention, and this variability affected the potential public health impact. In an analysis of screening and recruiting, smaller practices and ones where there was a nurse in a leadership role may be more effective in implementing the model (Van Voorhees et al., 2010). We conducted a RE-AIM analysis to examine contextual and practice factors. Lower neighborhood median income was associated with greater efficacy in terms of pre/post changes in depression scores more effective implementation, but because initial reach and maintenance was lower, public health impact declined with median neighborhood income (Eisen et al., 2013).

### 4.3. Phase 3 clinical trial: CATCH-IT 3

A third clinical trial is presently being conducted in Boston and Chicago. All adolescents aged 13–18 visiting the  $N = 33$  practice sites ( $N = 25$  Chicago,  $N = 8$  Boston) in  $N = 8$  major health systems are screened for future risk of depression (after brief consent). If at-risk, they are offered enrollment into the trial and assigned either the HE website or the CATCH-IT website with motivational interviews. This is a diverse sample:  $N = 232$  adolescents were enrolled and randomized ( $N = 138$  Chicago,  $N = 94$  Boston). For the data currently accrued and evaluated, teen mean age is 15.004, with females comprising 71% of the sample, and racial minorities comprising 50% of the sample. The mean CES-D 20 (adolescent) is 17.27 ( $SD = 8.95$ ), suggesting elevated depression risk (moderate depressed mood) and substantial impairment. For parents, the CES-D 20 (adult) is 10.40 ( $SD = 8.52$ ), which also demonstrates a slightly elevated depressed mood.

Adherence to the CATCH-IT 3 intervention is strong in both arms of the program. The mean number of modules started or completed for teens enrolled in HE ( $M = 6.98$ ,  $SD = 6.37$ ) is greater than those in CATCH-IT ( $M = 4.14$ ,  $SD = 4.60$ ;  $p < .001$ ). Although the control group is starting or completing more modules, the mean number of minutes spent on-line is significantly higher for the CATCH-IT teens

( $M = 103.66$ ,  $SD = 115.11$ ) than for the HE teens ( $M = 20.94$ ,  $SD = 19.11$ ,  $p < .001$ ). CATCH-IT teens also are typing an average of 4422.823 ( $SD = 1038.092$ ) characters. Based on these findings and prior CATCH-IT 2 study results, typing an average of more than 3000 characters may be a sufficient dose, and completing  $N = 4.13$  modules, or one therapeutic section (e.g. CBT or IPT), may provide the minimum dose associated with a positive outcome.

Parents in both the CATCH-IT and HE groups also are adhering to the program, as usage (the mean number of modules started or completed) is similar between the groups (CATCH-IT:  $M = 2.43$ ,  $SD = 2.04$ ; HE:  $M = 2.27$ ,  $SD = 1.90$ ). CATCH-IT parents are also showing substantial use of the site by typing in an average of 1212.58 ( $SD = 666.95$ ) characters. Because this parent program participation was only through a short parent program, we believe in total, that the family exposure (in terms of modules started or completed, time spent on line, and characters typed) is greater than in the original CATCH-IT 2 study.

## 5. Discussion

This is the first report we are aware of that documents a decade long technology-based prevention intervention development process in a health system context. The development and modification of interventions, such as CATCH-IT, require multiple iterative steps that involve the modification and strengthening of prevention components, building on lessons learned, and using feedback from participants to inform and guide development.

The current CATCH-IT 3 intervention incorporates all of the important elements that previous studies have highlighted for Internet interventions such as substantial depression prevention content with several modules (Jane-Llopis et al., 2003), program characteristics that focus on the motivation of participants as well as their use of the intervention (Bendelin et al., 2011), enhancement of website design through Instructional Design Theory (Gagne et al., 1992) and Synchronization of the Senses (Kaplan, 2005), as well as support for participation through follow up calls (Ritterband et al., 2009). The web-based approach provides a cost-effective way to prevent depression among teens (Mihalopoulos et al., 2012). We are currently investigating the effectiveness of CATCH-IT 3 in reducing depression symptoms.

A range of models have been developed for understanding how to create the effective components of community- and technology-based interventions for behavior change. Frameworks by Nation et al. (2003) provide models of conventional, face-to-face effective community based interventions. These models focus primarily on structural elements of interventions and teams, but do not include the multiplicity of delivery options evinced by technology or the need to refine technology across time. The Fogg Behavioral Model (Fogg, 2009) explains how technology can be used to aid in small behavior changes, but it is limited when applied to greater impact such as reducing depressive symptoms. Mohr et al. (2014) offer a Behavioral Intervention Technology Model that details the conceptual, technical, and timeline aspects, but like the other models, does not have a specific implementation structure.

The behavioral vaccine model used for CATCH-IT differs from other major models of Internet intervention development in that it integrates both therapeutic and contextual factors within one organized framework using an existent model of community intervention. It links back more closely to epidemiological approaches and incorporates systematic quantitative and qualitative analyses to better understand how the effective components of the model create a combined experience and how they may relate to eventual outcome.

The behavioral vaccine model follows the biological vaccine structure and creates a scheme that considers all the necessary disease characteristics to inform content development, along with important implementation factors that maximize prevention efforts. The *life course schedule* involves understanding the prevalence and

recurrence rate of depression among this particular age group. The *effective components* are based on theoretical and empirically grounded knowledge regarding risk and protective factors of depression, including the focus on parents as having an influential role. The *motivational framework* enhances behavior change through motivational interviewing within the primary care setting and with follow up calls. The *structured implementation strategy* takes into account the website design, physician training, as well as administrative issues in order to meet the needs of healthcare systems. This led to the creation of a more comprehensive approach involving the adolescent, and family and the health system.

The primary limitations in the development of CATCH-IT relate to the mode of technology needed to access the Internet and the form of content delivery. Since the development of even the CATCH-IT 3 intervention, more and more people have started to access the Internet through mobile phone devices, especially teens (Lenhart et al., 2010). Moreover, mobile applications used for healthcare, and particularly for depression, have increased (Martinez-Perez et al., 2013; Luxton et al., 2011). In addition, social media applications have become extremely popular among adolescents, and the current prevention program does not allow for connecting with other teens. While we recognize the possible safety concerns that may arise if teens enrolled in a depression prevention program are able to connect, we know from interactions with study participants that they want to connect with peers through this intervention. Future development should involve both mobile phone adaptation and some form of monitored online connection opportunities.

## 6. Conclusion

Technology offers a plausible solution to mass distribute prevention for common mental disorders in a cost-effective way; however, like the earlier and contemporary efforts to prevent infectious disease with bio-vaccines, it requires a long term process. Clinicians, public health officials, regulators, and investigators can expect to see continued efforts in this area that will require support, flexibility and adaptation for long term success (i.e., the prevention of common, preventable mental disorders) to be obtained.

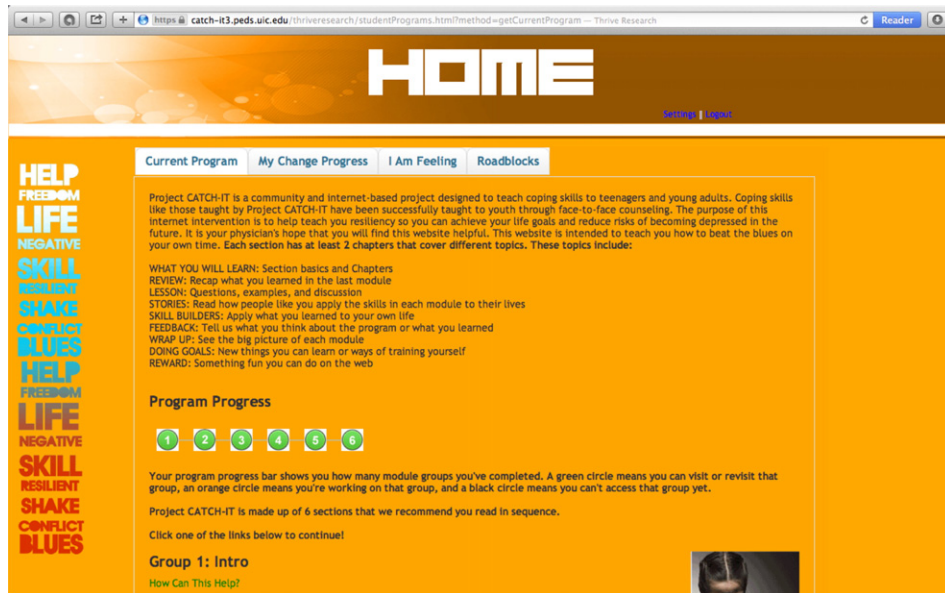
The future of Internet-based behavior change interventions may largely be shaped by the degree to which they actually prevent chronic disease through improving outcome and reducing costs, rather than by how well they manage the disease. To achieve these dual goals, a family of interventions needs to be developed around these focused requirements for prevention within health systems. However, without careful attention to implementation factors, the interventions may not achieve their potential. Funding agencies, investigators and health care organizations will need to consider the importance of investing resources and expanding administrative capacities to manage and develop technology based behavioral vaccines.

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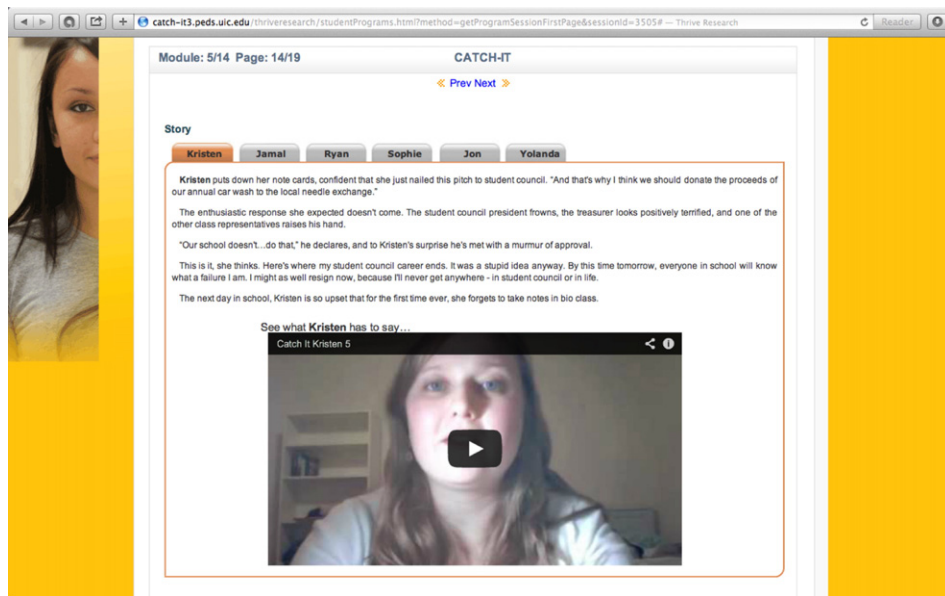
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Appendix A



Screenshot 1 from CATCH-IT website highlighting design features.



Screenshot 2 from CATCH-IT website highlighting video component.

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