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Classification models for subthreshold generalized anxiety disorder in a college population: Implications for prevention

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Abstract

Generalized anxiety disorder (GAD) is one of the most common psychiatric disorders on college campuses and often goes unidentified and untreated. We propose a combined prevention and treatment model composed of evidence-based self-help (SH) and guided self-help (GSH) interventions to address this issue. To inform the development of this stepped-care model of intervention delivery, we evaluated results from a population-based anxiety screening of college students. A primary model was developed to illustrate how increasing levels of symptomatology could be linked to prevention/treatment interventions. We used screening data to propose four models of classification for populations at risk for GAD. We then explored the cost considerations of implementing this prevention/treatment stepped-care model. female), 8.0% (198/2489) met DSM-5 clinical criteria for GAD, in line with expected clinical rates for this population. At-risk Model 1 (subthreshold, but considerable symptoms of anxiety) identified 13.7% of students as potentially at risk for developing GAD. Model 2 (subthreshold, but high GAD symptom severity) identified 13.7%. Model 3 (subthreshold, but symptoms were distressing) identified 12.3%. Model 4 (subthreshold, but considerable worry) identified 17.4%. There was little overlap among these models, with a combined at-risk population of 39.4%. The efficiency of these models in identifying those truly at risk and the cost and efficacy of preventive interventions will determine if prevention is viable. Using Model 1 data and conservative cost estimates, we found that a preventive intervention effect size of even 0.2 could make a prevention/treatment model more cost-effective than existing models of “wait-and-treat.”

Keywords

Generalized anxiety disorder; College health; Prevention; Screening; Stepped-care models; Self-help interventions; e-Health

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1. Introduction

Generalized anxiety disorder (GAD) is one of the most common psychiatric disorders among college students, with 7% prevalence in 14,175 students across 26 college campuses (Eisenberg, Hunt, & Speer, 2013). Onset occurs at approximately 20 years of age for most individuals (Brown, O’Leary, & Barlow, 2001; Yonkers, Warshaw, Massion, & Keller, 1996). Therefore, a college sample is an ideal group within which to examine models of prevention.

Preventing and treating GAD among young people has tremendous public-health significance. Left untreated, GAD has a chronic course and persistent symptoms (Yonkers, Bruce, Dyck, & Keller, 2003) and, in young people, tends to persist into adulthood (Costello, Foley, & Angold, 2006). Untreated GAD is also very costly in terms of distress, disability, quality of life, and medical problems (Newman, 2000). Even individuals who do not meet the full criteria for GAD (i.e., subthreshold cases) have demonstrated important similarities to those with the full GAD syndrome in functional impairment, medically unexplained symptoms (Beesdo et al., 2009), quality of life (Mendlowicz & Stein, 2000), socio-demographic features, and other key correlates (Beesdo et al., 2009; Bienvenu, Nestadt, & Eaton, 1998; Carter, Wittchen, Pfister, & Kessler, 2001; Hunt, Issakidis, & Andrews, 2002; Kendler, Neale, Kessler, Heath, & Eaves, 1992; Kessler et al., 2005; Maier et al., 2000; Ruscio et al., 2005; Wittchen et al., 2002).

GAD and subthreshold GAD are also significant predictors of first onset of later mood disorders as well as later anxiety disorders, substance-use, and impulse-control (Kessler, 2000; Ruscio et al., 2007). The presence of GAD symptoms increases the cost of healthcare from twofold to greater than fourfold (Bereza, Machado, & Einarson, 2009), with disorder severity positively correlated with total medical costs (Marciniak et al., 2005). Furthermore, those with clinical and subthreshold GAD often score similarly on measures of disability and help-seeking (Kessler et al., 2005; Ruscio et al., 2005).

However, Hunt and Eisenberg (2010) demonstrated that a majority of affected college students did not receive treatment for a variety of reasons. For example, students were often uninformed about their disorder or available treatment options. In addition, many were reluctant to seek treatment due to barriers such as time, stigma, or cost. Finally, inadequate counselor availability prevented even those who sought help from getting it.

In an attempt to address these barriers, researchers have developed and tested technology-based solutions. For instance, low intensity pure self-help (SH) interventions have proven efficacious for treating individuals diagnosed with anxiety disorders including GAD (Al-Asadi, Klein, & Meyer, 2014; Christensen, Mackinnon, et al., 2014; Lewis, Pearce, & Bisson, 2012; Newman, Szkodny, Llera, & Przeworski, 2011). In addition, Lewis et al. (2012) conducted a meta-analysis of 31 randomized controlled trials (RCTs) that included SH interventions for anxiety disorders. When comparing SH with wait list, they found a significant effect size of 0.84 favoring SH. When comparing SH with therapist-administered treatments, there was a significant difference in favor of therapist-administered treatment with an effect size of 0.34. In another study, individuals identified as having clinical GAD

received a fully-automated SH anxiety program and achieved significant improvements across primary symptom severity measures as well as secondary measures such as self-confidence in managing mental health issues and quality of life (Al-Asadi et al., 2014). These findings suggest that purely SH interventions for anxiety, although less efficacious than therapist-administered treatments, are less resource intensive yet still efficacious.

More intensive guided self-help (GSH) interventions have proven even more effective than pure SH interventions (Cuijpers, Donker, van Straten, Li, & Andersson, 2010; Paxling et al., 2011). GSH interventions comprise the psychoeducational content in SH interventions and the support of a program guide or “online coach” who provides encouragement, monitors progress, and gives feedback typically via messaging within the program. In an RCT for the treatment of GAD comparing GSH to a wait-list control condition, there were large effect sizes (Cohen’s $d > 0.8$) both within the treatment group and between the groups in favor of GSH on measures of worry, anxiety, and depression (Paxling et al., 2011). Furthermore, at one and three-year follow-ups, symptoms had improved further or were sustained. GSH interventions were also as or more efficacious than in-person therapy for clinical levels of anxiety and depression in a meta-analysis of 21 RCTs ($N = 810$). The overall effect size at post-test was $d = -0.02$, in favor of GSH. However, there was no significant difference at one-year follow-up or between dropout rates (Cuijpers et al., 2010). These findings suggest that less costly GSH interventions may be an adequate substitution for traditional in-person therapy.

Low cost technology-based interventions might prove even more cost-effective if used in a stepped-care fashion. A stepped-care model of service delivery, in which increasing levels of symptomatology are aligned with interventions of increasing intensity, can be developed to prevent and treat GAD. The UK has demonstrated the feasibility and scalability of stepped-care models integrating such technology-based, self-help interventions via the Improving Access to Psychological Therapies (IAPT) initiative (Gyani, Shafran, Layard, & Clark, 2013). In its first three years of operation (ending March 2012), the new program served more than 1 million people, achieved recovery rates above 45%, and helped move 45,000 people off sick pay and/or other disability benefits. Although IAPT’s early success demonstrated that stepped-care models could improve issues of accessibility, the treatment primarily focused on clinical disorders and did not address sub-threshold disorders or prevention.

Historically, universities have focused on populations with acute, disabling symptoms. However, from a public health perspective, the optimal goals in a college population are to reduce the prevalence and incidence of GAD and to increase the availability of effective treatments. Thus, an intervention that reduced symptom progression and prevented onset would reduce the incidence of developing GAD.

Preventive interventions are generally classified as either universal interventions delivered to the entire population, including those at risk, or selective interventions delivered to those with known risk, or indicated interventions delivered to those who are symptomatic but subthreshold (Gordon, 1983). Studies of possible GAD risk factors have suggested that subthreshold symptoms might predict onset (Karsten et al., 2011; Kessler et al., 2003;

Ruscio et al., 2007). In the prevention nomenclature, individuals with subthreshold GAD might be appropriate for selective/indicated preventive interventions that aim to reduce symptoms and halt symptom progression.

University population-based intervention for GAD would then focus on two general strategies: reducing symptom progression in symptomatic but not yet clinical individuals who are classified as “at-risk” and reducing symptoms in clinical individuals. Thus, the goal of the present research was to evaluate results from a population-based screening of college students to inform a stepped-care model of service delivery. A primary model was developed to illustrate how increasing levels of symptomatology could be linked to prevention/treatment interventions. Whereas the well-defined and highly restrictive criteria detailed in the fifth edition of the Diagnostic and Statistical Manual (DSM-5) can identify those most in need of treatment, determining how to relax these criteria to identify those most at-risk for developing GAD and/or those suffering most from subthreshold symptoms is required to design a stepped-care model. Unfortunately, little prospective data is available to determine who is at risk. To explore how universities might identify those who are at risk, we proposed four models that used different criteria for allocating students into this at-risk category. Each of the four criteria reflects a unique domain of severity and/or impairment that might reasonably merit early intervention. Following, using conservative assumptions about the cost, efficacy, and feasibility of delivering self-help indicated preventive interventions, we also estimated costs. Thus we aimed to explore the feasibility and cost-benefit considerations of implementing a prevention/treatment stepped-care model.

2. Methods

2.1. Procedure

College students were recruited to participate in this study through the university’s research participation program. Students completed a battery of self-report measures among a larger pool of assessments and received partial course credit for their participation. The university’s institutional review board approved all study procedures.

2.2. Participants

Participants were undergraduate students ($N = 2489$) enrolled in introductory psychology courses at a large, public university in the northeast who completed an anxiety screen in 2014. The majority of the sample was female (67.4%), and the mean age was 19.1 years ($SD = 2.9$). 76.1% of participants self-identified as White/Caucasian, 11.0% as Asian/Asian American, 3.8% as Hispanic/Latino, and 3.5% as African American/Black, 3.1% indicated other, and 2.6% chose not to respond to this demographic question.

2.3. Measures

2.3.1. The fourth edition of the Generalized Anxiety Disorder Questionnaire (GAD-Q-IV)—The GAD-Q-IV (Newman et al., 2002) is a nine-item self-report measure designed as an initial screen for the presence of GAD based on the DSM-IV. The GAD-Q-IV showed 89% specificity and 83% sensitivity when compared to structured interview diagnoses of individuals with GAD, Social Phobia, Panic Disorder, and a non-anxious

comparison group. The GAD-Q-IV has demonstrated good retest reliability in a college sample over a two-week assessment, with 92% of the sample showing stability across time with respect to GAD diagnosis. They found strong inter-rater agreement with a structured diagnostic interview (Cohen's $K = 0.67$).

2.3.2. The Depression Anxiety Stress Scales (DASS)—The DASS (Lovibond & Lovibond, 1995b) is a 42-item self-report inventory designed to measure negative emotional states of depression, anxiety and tension or stress. The DASS is divided into three self-report scales, each containing 14 items, divided into subscales of 2–5 items with similar content. The Depression Scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia, and inertia. The Anxiety Scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The Stress Scale is sensitive to levels of chronic non-specific arousal, assessing difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient. All scales have been shown to have high internal consistency and to yield meaningful discriminations in a variety of settings.

2.3.3. The Penn State Worry Questionnaire (PSWQ)—The PSWQ is a 16-item self-report measure of the frequency and intensity of worry (Meyer, Miller, Metzger, & Borkovec, 1990). The PSWQ has been shown to distinguish individuals with GAD from individuals with other anxiety disorders (Brown, Antony, & Barlow, 1992).

2.4. At-risk criteria

As no universally accepted standards exist for what constitutes significant levels of subthreshold symptoms indicating risk and necessary intervention, our boundaries for at-risk in this paper were exploratory. We chose four criteria reflecting four different domains of severity and impairment that might merit early intervention.

2.4.1. GAD diagnosis—DSM-IV criterion-based scoring of the GAD-Q-IV was used to diagnose GAD. Given that the diagnostic criteria have not changed from DSM-IV to DSM-5, we will refer to this as DSM-5 criteria. Using this criteria, students were required to positively endorse items 1–4 and 6, endorse two or more worry topics in item 5 and three or more symptoms in item 7, and select four or more on items 8 or 9 (Moore, Anderson, Barnes, Haigh, & Fresco, 2014).

2.4.2. Model 1: subthreshold, but considerable symptoms of anxiety—This model was based on the assumption that subthreshold symptoms of anxiety might confer risk or warrant intervention. Our assumption was based on a prospective risk study demonstrating that subthreshold symptoms of anxiety, as measured by the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988), can predict the occurrence of an anxiety disorder within two years (Karsten et al., 2011). As a proxy for subthreshold anxiety as measured by a score of 11 or greater on the BAI, which was missing from this screen, *above normal stress* as measured by a score of 15 or greater on the Stress subscale of the DASS (Lovibond & Lovibond, 1995b) was used to distinguish the at-risk group. We chose this measure because the BAI positively correlated with the DASS. Although it had a

slightly stronger positive correlation with the Anxiety subscale ($r = 0.81$) than with the Stress subscale ($r = 0.64$) (Lovibond & Lovibond, 1995a), we deemed the Stress subscale a potentially more accurate predictor of GAD. The Stress subscale was designed to capture emotional disturbance of stress and anxiety and correlated strongly with GAD, whereas the Anxiety subscale was designed to capture symptoms such as autonomic arousal and skeletal muscle effects and correlated well with most anxiety disorders but not GAD (Brown, Chorpita, Korotitsch, & Barlow, 1997). Students were required to score 15 or above on the DASS Stress subscale but not be categorized as clinical using DSM-5 criterion-based scoring of the GAD-Q-IV.

2.4.3. Model 2: subthreshold, but high GAD symptom severity—This model was based on the assumption that high severity of subthreshold GAD symptoms might necessitate intervention. Newman et al. (2002) proposed that a cut-score of 5.7 could distinguish those with clinical GAD. However, subsequent research (Moore et al., 2014) proposed that the cut-score of 5.7 was too sensitive and that a higher cut-score of 7.67 would more accurately distinguish those who truly had GAD. Therefore, students were required to score 5.7 or above on the GAD-Q-IV but not be categorized as clinical using DSM-5 criterion-based scoring of the GAD-Q-IV to be considered at risk.

2.4.4. Model 3: subthreshold, but symptoms were distressing—This model was based on the assumption that greater experienced distress from GAD symptoms might indicate greater risk. Thus, individuals who reported that symptoms caused distress or interfered with life, work or social activities were deemed appropriate to target for preventive interventions. Students were required to respond “moderately” or greater to questions on the GAD-Q-IV assessing “interference of” or being “bothered by” physical symptoms and worry but not be categorized as clinical using DSM-5 criterion-based scoring of the GAD-Q-IV.

2.4.5. Model 4: subthreshold, but considerable worry—This model was based on the assumption that worry might confer risk. Excessive and uncontrollable worry is the primary feature of GAD (Borkovec, Hazlett-Stevens, & Diaz, 1999). Research has also demonstrated that among those with clinical GAD, those with excessive worry experience earlier onset, a more chronic course, and greater symptom severity (Ruscio et al., 2005). Thus, a screen for worry was viewed as a potential way to screen for those at risk for GAD. Students were required to score 62 or above on the PSWQ, a cutoff score determined by Behar, Alcaine, Zullig, and Borkovec (2003) to adequately distinguish those with GAD from those without it with high negative predictive power but low positive predictive power, but not be categorized as clinical using DSM-5 criterion-based scoring of the GAD-Q-IV.

2.5. Cost analysis approach

The viability of a stepped-care model of prevention/treatment is influenced by four main factors: (1) the availability of near universal and efficient screening, (2) the rate of onset of GAD in the at-risk population, (3) the cost and (4) the efficacy of each intervention: SH, GSH, and in-person therapy. Estimating costs of delivering preventive interventions is complicated. Sophisticated models include many variables, such as cost of lost opportunity

(e.g., time to drive to therapy), decreased/loss of productivity, and system maintenance costs (e.g., staff, facility benefits). We pursued a model in which the services would be purchased at known prices (e.g., from online services, face-to-face providers, etc.), following the suggestion that cost analysis should assess the value of resources consumed in each procedure (Yates, 1997).

Although universal and efficient screening is the first necessary component of implementing a stepped-care system, we did not include the cost of screening in our model for two reasons. First, university systems make universal student screening feasible, and free online programs (e.g., Mental Health Online, E-couch) make evidence-based screens available at no cost. We assumed screening could be automated and recruitment could be universal (e.g., send a link to an online screen via an email blast to a school-wide listserv). There would certainly be some labor costs associated with setting up the system (e.g., customizing the screen, marketing it to students, developing the database to track student resource utilization and outcomes), but we assumed that these startup costs could be reasonably absorbed by existing staff such that there would be minimal to no additional costs to the university (Wilfley & Taylor, 2014). Second, given that our estimates of prevalence of the at-risk populations are exploratory, we assumed 100% screen efficiency, meaning the individuals identified as at-risk based on a certain criteria are all truly at risk. In practice, however, the efficiency (i.e., sensitivity and specificity) of a screen will never be 100% and, as a result, resource-intensive preventive interventions might be indicated for individuals who are not truly at risk or withheld from individuals who are at risk. To simplify the model for demonstration purposes, screen efficiency was eliminated as a variable and rate of GAD onset in the at-risk population was used to represent the accuracy of at-risk population selection. Only by evaluating various at-risk models in longitudinal prospective studies will we be able to identify those truly most at risk and the screening method with which to identify them.

Our model was based on the following idea: The cost to treat one clinical case of GAD comprises the cost of delivering a GSH program designed to treat clinical GAD plus the cost of delivering in-person therapy if the GSH intervention fails. To express the likelihood of the GSH intervention failing, we used success rate difference (SRD). SRD is defined as the probability that treatment is better than control minus the probability that control is better than treatment (Kraemer & Kupfer, 2006). When the response measure is binary (e.g., success or failure of treatment), the SRD is defined as the success rate of treatment minus the success rate of control. To note, the SRD is the inverse of the number needed to treat (NNT), or the number of patients one needs to treat to have one more success than if the same number were treated with the control intervention. We used $(1 - \text{SRD}_{\text{gsh}})$ to designate the likelihood of the GSH intervention failing. Expressed in a formula, the cost to treat one clinical case of GAD = (\$ GSH program) + $(1 - \text{SRD}_{\text{gsh}})(\$ \text{ in-person therapy})$.

The decision to extend the delivery of a GSH intervention to the at-risk population depends on the efficacy of the intervention to reduce symptom progression and prevent onset. Although there is minimal research on the efficacy of GSH in GAD prevention, research on its efficacy to treat those with clinical symptoms led us to assume it could achieve similar positive results when treating those with subthreshold symptoms (Cuijpers et al., 2010;

Paxling et al., 2011). We proposed that if the cost of prevention was less than the cost of “wait-and-treat,” indicated preventive interventions would be more appropriate.

In the “wait-and-treat” approach, only those individuals who eventually develop clinical symptomatology receive treatment. In an at-risk population, the wait-and-treat approach would cost a system the cost of treating one clinical case multiplied by the number of untreated at-risk cases that escalate to clinical cases. A stepped-care model of prevention/treatment has the potential to reduce costs depending on the cost and efficacy of the interventions and the true risk of the selected at-risk population. In this model, a subthreshold case would first receive a SH intervention and then step up to a GSH intervention if the SH intervention failed and finally step up to clinical treatment if the GSH intervention failed and the subthreshold case progressed to a clinical case.

Prevention would be viewed as more viable than wait-and-treat when $(\$ \text{SH program}) + (1 - \text{SRDsh}) (\$ \text{GSH program}) + (1 - \text{SRDgsh}) (\text{rate of onset in at-risk population}) (\text{cost to treat one clinical case}) < (\text{rate of onset in at-risk population}) (\text{cost to treat one clinical case})$.

3. Results

3.1. General model tested

We created a model to align increasing levels of symptomatology to prevention/treatment programs (Fig. 1). Those who screened negative for GAD without elevated risk status (e.g., asymptomatic for GAD) were categorized as low-risk and viewed as appropriate to receive a universal, free online health education program. For these individuals, progress in the program would not be monitored, and they would not be stepped up to more intensive programs. However, they would be screened the following year to reassess. Those who screened negative for GAD but positive for subthreshold symptoms were categorized as at-risk and viewed as appropriate to receive an indicated online self-help program. Their progress would be monitored; if they did not demonstrate a reduction in symptoms by mid-intervention, they would be stepped up to a more intensive GSH intervention. GSH programs would be extended to at-risk individuals who did not improve using SH, with the hope that more intensive guided interventions could prevent onset of GAD. Finally, those who screened positive for GAD were categorized as clinical and viewed as appropriate to receive a GSH program. Similar to the at-risk group, their progress would be monitored, and they would step up to in-person therapy should they not demonstrate symptom reduction by mid-intervention. Moving to in-person therapy would allow a clinician to assess why GSH might not have worked and provide more personalized treatment.

3.2. Rates of clinical GAD

Among our sample of 2489 college students, 8.0% (198/2489) of the population met DSM-5 clinical criteria for GAD with criterion-based scoring of the GAD-Q-IV, in line with expected clinical rates for a college population (Eisenberg et al., 2013). For these individuals, a GSH program would be provided as the first line of treatment, with in-person therapy reserved for treatment non-responders.

3.3. Rates of subthreshold GAD/at-risk

3.3.1. Model 1: subthreshold, but considerable symptoms of anxiety—21.9% (476/2489) had *above normal stress*. Clinical GAD as indicated by criterion-based scoring of the GAD-Q-IV was classified within 28.4% (135/476) of those with high stress. Removing those threshold individuals, this model would classify 13.7% as at-risk ((476 – 135)/2489).

3.3.2. Model 2: subthreshold, but high GAD symptom severity—13.7% (341/2489) would be considered at-risk (21.7% (539/2489) minus 8.0% who are clinical and 5.7).

3.3.3. Model 3: subthreshold, but symptoms were distressing—20.2% (504/2489) reported “interference of” or being “bothered by” physical symptoms and worry as moderate or greater. Excluding clinical diagnoses, the at-risk population was 12.3% (306/2489).

3.3.4. Model 4. subthreshold but considerable worry—17.9% (445/2489) of students had scores of 62 or greater on the PSWQ. Only 12 of those individuals met clinical criteria, leaving 17.4% ((445–12)/2489) as at-risk. To note, this small overlap aligns with Behar et al. (2003) analyses yielding low positive predictive power (PPP = 0.27), indicating a low probability of an individual having a GAD diagnosis if the PSWQ classified him/her as such. However, as the purpose of this model was to identify those at-risk, this low PPP was not cause for concern.

3.3.5. At-risk model overlaps—The four models produced different subthreshold risk prevalence rates ranging from 12.3% to 17.4%. As can be seen in Table 1, simultaneously being at-risk on all four models captured only 0.2% (6/2489) of the population. Although there was little overlap among the population estimates for all four models, there was overlap among a few. For example, 4.6% (114/2489) of students were classified as at-risk by Model 2 and Model 3, and 3.6% (89/2489) were classified as at-risk by Models 1, 2, and 3. Of note, Model 4 alone captured 15.3% and had little overlap with the other models, suggesting that Model 4 might have captured a unique subset of the population in comparison to the other models. In total, 39.4% of the population was classified as at-risk by at least one of the models. The high percentage of students captured by one or more of the four models suggested that the criteria for being at-risk was diverse, and one or a combination of the models likely had higher specificity to identify those truly at risk and in need of an intervention than the others.

3.4. The cost of prevention

Assuming a cost of \$100 for a two-month GSH treatment program (e.g., goLantern.com, an online GSH program), a success rate difference (SRD) of the GSH treatment program of 0.428 (Paxling et al., 2011), and a cost of \$2000 for a typical course of in-person therapy (Newman, Przeworski, Consoli, & Taylor, 2014), it would cost \$1244 to treat one clinical case of GAD.

$$(\$100) + (1 - 0.428)(\$2000) = \$1244$$

To evaluate whether prevention might be more cost-effective than waiting to treat the clinical cases that develop, we made several assumptions. We assumed a cost of \$0 for a SH prevention program (e.g., Mental Health Online and E-couch, free online SH programs), given university-sponsored Internet connectivity and the prevalence of smart devices among college students. Of note, although the SH interventions are themselves free, there would be some nominal costs associated with developing the infrastructure to make these programs available to students. We assumed these labor costs could be categorized under a one-time startup cost associated with the implementation of this new program on a college campus; therefore, we did not include these costs in the model. We estimated a success rate difference (SRD) of the SH program of 0.112, assuming a low effect size typical of pure SH interventions (Cohen's d , $0.2 = \text{SRD}$, 0.112, Kraemer & Kupfer, 2006). To estimate the rate of onset in the at-risk population, we used data from the risk study that informed Model 1. Karsten et al. (2011) found that individuals with subthreshold anxiety have a 25% chance of developing an anxiety disorder within two years. Finally, as detailed previously, we used a cost of \$100 for an indicated preventive GSH program (e.g., goLantern.com), assuming the cost of GSH will be the same regardless of whether the program is designed for treatment or prevention. We found that the indicated preventive GSH intervention should have a success rate difference of 29% or above (i.e., number needed to treat (NNT) = 3.125 or Cohen's $d = 0.5$, Kraemer & Kupfer, 2006) to make prevention more cost-effective than wait-and-treat.

$$(0) + (1 - 0.112)(100) + (1 - \text{SRD}_{\text{gsh}})(0.25)(1244) < (0.25)(1244)$$

$$1 - \text{SRD}_{\text{gsh}} < 0.71$$

$$\text{SRD}_{\text{gsh}} > 0.29$$

Under these assumptions and assuming $\text{SRD}_{\text{gsh}} = 0.29$, the total cost of implementing a prevention/treatment stepped-care model in Model 1 (in which the population has 8% clinical and 13.7% subthreshold) would be \$105,577, as compared to \$106,051 for wait-and-treat. As we vary parameters of the estimation, the cost differential between prevention and wait-and-treat would change. For example, if the $\text{SRD}_{\text{gsh}} = 0.428$, the effect size of GSH interventions for the treatment of clinical GAD, the cost of prevention using Model 1 would reduce to \$90,941 vs. \$106,051 for wait-and-treat.

To note, using our formula, the size of the at-risk population did not influence whether prevention was cheaper than wait-and-treat. A larger at-risk population would increase the total cost, but the comparison of prevention vs. wait-and-treat would remain constant. What did influence the comparison was the rate of onset in the at-risk population (Table 2). We assumed a 25% rate of onset in the at-risk population defined by Model 1 based on research by Karsten et al. (2011), given the availability of that data. For 100 students, Model 1 would

identify 13.7 students as at-risk. Of those students, 25%, or roughly 3.4 students, would be expected to develop an anxiety disorder. However, if the other risk factors are valid, up to 39.4 students could be considered at-risk, with at-risk subpopulation-specific onset rates determining total number of expected clinical cases. It will be important to evaluate and prioritize true risk factors to determine who should receive a preventive intervention and realistically estimate the total cost to a university.

3.5. Accounting for the benefits of prevention

A combined prevention/treatment model appeared to be an even more viable strategy when the benefits of this approach were included. Cost-effectiveness analysis should quantify relationships between not only costs, but also procedures, process, and outcomes in order to accurately evaluate and improve the cost-effectiveness of psychotherapy (Yates, 1997). As mentioned earlier, several studies suggested that subthreshold symptoms of GAD were just as debilitating as threshold symptoms and could similarly lead to higher medical utilization and lower productivity (Kessler, 2000; Newman, 2000). These findings suggest that targeting symptom reduction among subthreshold cases as well as clinical cases might reduce costs. Additionally, a focus on preventing case onset might also lead to cost savings by impacting the total number of clinical cases that required treatment. On average, only 50% of clinical cases of GAD treated with CBT achieve high end-state functioning whereas the other 50% require further intervention (Borkovec & Whisman, 1996). Assuming that treating subthreshold symptoms/preventing case onset would be more feasible than treating clinical symptoms, employing preventive interventions might reduce total costs. Finally, inadequate treatment due to capacity limitations (e.g., as is the case in many university counseling centers) might also instigate additional necessary and costly treatment. Factoring in even a few of these cost-offsets significantly relaxed the criteria necessary to prioritize a prevention/treatment model.

$$(\$0) + (1 - 0.112)(\$100) + (1 - \text{SRD}_{\text{gsh}})(0.25)(\$1244) < (0.25)(\$1244) \\ + (\text{cost of medical utilization for those symptomatic}) + \\ (\text{cost of further treatment for clinical treatment non-responders})$$

Assuming a very conservative average cost of \$50 for supplementary medical utilization by those at risk and that at-risk individuals who received self-help programs would no longer incur supplementary medical care costs, the GSH preventive intervention might have a success rate difference of 13% or above, roughly an effect size of 0.2 typical of low intensity public health interventions, to prioritize prevention. If we also accounted for further treatment for non-responders, the necessary effect size for preventive interventions would decrease and the cost differential between prevention and wait-and-treat would become even more apparent in favor of prevention. Our estimates suggested that universities could redistribute existing (or even fewer) resources to SH and GSH interventions to increase the reach of services to a greater proportion of students struggling with symptoms of anxiety, including those at-risk, to reduce the prevalence and incidence of GAD.

4. Discussion

Given the high incidence and prevalence of GAD on college campuses, there is a need to consider ways to deliver interventions that both reduce symptom progression in subthreshold at-risk groups and reduce symptoms in clinical populations. Using reasonable assumptions for who might be at risk and in need of early intervention, we applied four possible models for identifying those at risk. In addition, we explored the cost of implementing a stepped-care model of service delivery. Surprisingly, we found that there was little overlap among the subthreshold populations captured in the four models, and 39.4% of the sample had one or more “risk factors.” This suggests that including all of our at-risk models is likely to be very sensitive, but poorly specific, in predicting the onset of GAD. Additional studies investigating longitudinal risk factors are warranted.

Additionally, we found that the cost of deploying preventive interventions in a stepped-care model depended on the effect size and cost of preventive interventions as well as the rate of onset in the at-risk population. After factoring in the potential benefits of prevention (e.g., reduced medical utilization among those with subthreshold symptoms), a stepped-care model appeared to be a more cost-effective approach to university-based psychotherapy than wait-and-treat. Increasing the PPP of risk factors will be a critical step in developing a more cost-effective stepped-care model that achieves reduction in risk factors such as subthreshold symptoms and subsequently onset of disorder.

Of note, our cost calculations are based on only one model of risk, as Model 1 was the only model based on a risk study that determined expected rate of onset (Karsten et al., 2011). Our data suggest that other potential risk factors do not necessarily overlap and, to the extent that they do represent true risk factors, the total prevention costs for a college population would need to account for preventive interventions addressing each of the important risk factors. Furthermore, from a population standpoint, the cost of prevention needs to account for the efficiency (i.e., specificity and sensitivity) of a screen, since any screen is likely to identify individuals who are not actually at risk but might be allocated a preventive intervention (Jacobi, Abascal, & Taylor, 2004; Offord, Kraemer, Kazdin, Jensen, & Harrington, 1998). Although prospective risk factor studies would help clarify this, another approach is to apply a preventive intervention designed to reduce all the risk factors identified and then use moderator analyses to make future intervention allocation more efficient (e.g., Jacobi, Bryson, Wilfley, Kraemer, & Taylor, 2011).

Our findings also highlight the problems of basing effectiveness of prevention on reducing case onset. As mentioned, an alternative or additional strategy would be to focus on reducing any symptom progression and/or impairment (van der Aa et al., 2013). This approach makes particular sense for GAD. GAD is one of the least reliably diagnosed anxiety disorders (Brown, Di Nardo, Lehman, & Campbell, 2001; Di Nardo, Moras, Barlow, Rapee, & Brown, 1993), suggesting that the boundaries of prevention/treatment are unclear. Even more importantly, GAD symptoms exist on a continuum (Newman et al., 2002). Since effectiveness data are traditionally based on clinical cases (Christensen, Batterham, et al., 2014), the effectiveness of indicated preventive interventions to reduce subthreshold symptoms or symptom progression can only be assumed based on demonstrated efficacy to

reduce symptoms in clinical cases (Christensen, Mackinnon et al., 2014). However, factors such as the cost of successfully treating subthreshold symptoms also influence the risk from a cost perspective, and studies evaluating the ability of indicated preventive interventions to reduce subthreshold symptoms are necessary to develop more accurate models.

Another limitation to our research was sampling bias. Only students taking introductory psychology courses were screened. Furthermore, our population was predominantly female (67%) and GAD is two to three times more likely in women than in men (Comer et al., 2011), suggesting our model estimates of those at-risk could be inflated as compared to a more gender-balanced population. Similarly, our estimates might lack generalizability to ethnic minorities given the majority (76.1%) of the sample identified as White/Caucasian.

Finally, in our cost estimates, we used a simple formula, excluding factors such as the costs of screening and delivering SH interventions, and relied on untested assumptions of indicated preventive intervention efficacy. First, we did not assign a cost to universal screening, assuming nominal startup costs to adapt and implement an efficient, free, online evidence-based screen. However, there would likely be, at minimum, an additional 0.5 FTE required to oversee the implementation and maintenance of this new program. Ideally, reorganizing existing staff could absorb this labor cost, but sufficient resources may not exist on all campuses. Beyond the cost of successfully achieving universal screening, there might be an unexpected (although not necessarily unwanted) cost associated with successfully increasing the top of the referral funnel, depending on the size of the clinical/subthreshold population and the percentage of referrals that are accepted. Second, we did not assign a cost to delivering SH interventions, given that online, evidence-based programs are already freely available and most campuses have free Internet. However, there would be costs associated with the need to monitor student outcomes in these programs in order to step-up as necessary. Finally, we relied on data from clinical treatment trials to inform our assumptions of preventive intervention efficacy. Measuring the feasibility and value of prevention is difficult and requires different approaches than traditional clinical treatment studies; only longitudinal prospective studies will truly evaluate the efficacy of indicated preventive interventions. Future models should take into account all of these variables.

It is important to consider what data would be needed to further evaluate the viability of prevention on a college campus. Ultimately, researchers must apply exploratory models such as the ones we presented and allow the dynamics of population change to indicate what does or does not work. It would be particularly important to know what happens to individuals over time and to use this data to determine when a “wait-and-watch” program might be useful. In the following section, we suggest what data might be used to determine how a viable GAD prevention/treatment stepped-care model could be developed for college campuses.

4.1. What is required to implement a viable GAD prevention/treatment stepped-care model?

4.1.1. Universal yearly screening linked to evidence-based GAD

interventions—Universities might administer mental health screening to all students at the start of each academic year. Yearly screening both ensures that affected students receive care

and tracks symptoms within a population, enabling identification of risk factors for developing GAD as well as moderators of intervention on outcomes. With increasing ability to monitor the use of online interventions, we can also evaluate mediators as well as use the population to develop and evaluate enhanced interventions that address typical issues of low engagement and cultural competence.

4.1.2. Outcome-focused goals targeting reduction in incidence and prevalence of GAD—Clear targets are necessary to examine the efficacy and cost-effectiveness of this model. Outcomes will indicate whether the step-up rules we have put forth are effective and guide iterative adaptations. Clear goals (e.g., symptom reduction) will also make increasing cost-effectiveness more feasible. For example, there are costs associated with delaying more expensive, intensive care to individuals who will likely not improve in self-help interventions (e.g., student distress, case onset) (Newman, 2000). Defining clear outcome-based goals will allow for the identification of subgroups that might not improve in this model and would instead benefit from immediate designation to a more intensive intervention.

4.1.3. Databases that permit adaptive interventions and new evaluation designs—Given the fluid nature of prevention/treatment, interventions should be able to adapt to the population. A database including screening, intervention, and outcome data would enable this. Adaptive interventions, or individually tailored treatments, are becoming more feasible and opening the door to low-cost yet efficacious public health interventions (Oldenburg, Taylor, O’Neil, Cocker, & Cameron, 2014). To support the development and evaluation of these individually tailored, more potent interventions, adaptive research strategies have been proposed (e.g., the sequential multiple assignment randomized trials (SMART) design (Collins, Murphy, & Strecher, 2007); the continuous evaluation of evolving behavioral intervention technologies (CEEBIT) framework (Mohr, Cheung, Schueller, Hendricks Brown, & Duan, 2013)).

4.1.4. A focus on scalability and sustainability when developing new models—When considering scaling the impact of such a model, screening more generally could enable the development of a more comprehensive system for mental health care treatment. For example, the DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure could be used to screen for 13 psychiatric domains at once (Clarke & Kuhl, 2014). Once disorders and comorbidities have been identified, there would be an opportunity to provide more general, multi-disorder interventions. For example, transdiagnostic programs have been designed for the general treatment of emotional disorders, addressing the dimensional nature of psychiatric disorders and high rates of comorbidity (Boisseau, Farchione, Fairholme, Ellard, & Barlow, 2010). Given the high degree of comorbidity between GAD and other anxiety disorders (Anderson, Noyes, & Crowe, 1984; Barlow, Blanchard, Vermilyea, Vermilyea, & DiNardo, 1986), as well as other psychiatric disorders such as depression, a transdiagnostic approach might be particularly appropriate. Research has already shown that applying CBT for GAD alone reduces comorbid anxiety and depression (Newman, Przeworski, Fisher, & Borkovec, 2010), reinforcing the dimensional and overlapping nature of disorders and suggesting the potential of more general interventions. Furthermore, beyond ameliorating

risk for comorbid mental health disorders, preventive mental health interventions might reduce the incidence of noncommunicable diseases (NCDs) such as diabetes and cardiovascular disease (CVD). Depression, for example, has been shown to be a risk factor for the onset of CVD (Van der Kooy et al., 2007). In our sample, among 198 students classified as clinical GAD, 60% also had above normal depression according to the DASS Depression subscale. Similarly, among 13.7% (341/2489) of the total sample classified as at-risk by Model 1, 43.4% had above normal depression. Such overlap suggests that a transdiagnostic approach could be beneficial for both treatment and preventive interventions.

Beyond the demonstrated potential of a transdiagnostic approach, a more general program might also be easier to implement and sustain. Training and supervising program guides on one general guided self-help program rather than on several targeted programs is less resource-intensive. Additionally, the demands on the institution might be less (and more likely to be met) if requesting existing staff to learn and integrate just one program (Chorpita, Bernstein, & Daleiden, 2011). Research suggests that modular approaches can be just as effective yet potentially easier to deliver than multiple evidence-based treatments (Chorpita et al., 2013).

Finally, a general program might be more feasible to extend to younger students. Given the average age of onset for and prevalence of anxiety disorders in adolescents is six years and 31.9%, respectively (Merikangas et al., 2010), early intervention at a population level, such as in primary and secondary schools, may be of substantial public health benefit. Among adolescents, research would suggest there is considerable comorbidity of anxiety disorders with other psychiatric disorders (Essau, 2003), increasing the relevance of a more general program, particularly one that might appear less stigmatizing. Following the implementation of a screen-linked-to-intervention system, increasing intervention diversity or inserting personalized modules into one general program would be more achievable.

5. Conclusion

Implementing prevention/treatment programs in a college population (and even in younger school populations) has the potential to reduce the prevalence and incidence of GAD, increase access to services for those affected, and lower the costs of the disorder to the institution and students. Identifying those most at risk by evaluating various at-risk models in longitudinal prospective studies is the first step toward linking a universal screen to a stepped-care model of intervention delivery. Following, through yearly screening and controlled studies, we can determine which interventions work, for which populations, under what conditions, and at what cost.

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Fig. 1.

A model for consideration of how prevention/treatment interventions for generalized anxiety disorder (GAD) might be provided to a college population, using an evidence-based screen to categorize students into levels of symptomatology and associated interventions.

Table 1

At-risk population size based on model(s) used.

At-risk population capture method	Sample size	Percentage out of total sample (N = 2489)
Model 1 alone	137	5.5%
Model 2 alone	75	3.0%
Model 3 alone	57	2.3%
Model 4 alone	381	15.3%
Models 1 + 2	50	2.0%
Models 1 + 3	26	1.0%
Models 1 + 4	29	1.2%
Models 2 + 3	114	4.6%
Models 2 + 4	3	0.1%
Models 3 + 4	6	0.2%
Models 1 + 2 + 3	89	3.6%
Models 1 + 3 + 4	4	0.2%
Models 2 + 3 + 4	4	0.2%
Models 1 + 2 + 3 + 4	6	0.2%
Students captured by at least one of the models (i.e., sum of the above non-overlapping groups)	981	39.4%

Note: Model 1 defines the at-risk population as those who score at least 5.7 on the GAD-Q-IV but do not meet DSM-5 clinical criteria. Model 2 captures those who score at least 15 on the DASS Stress subscale (meaning *above normal stress*) but do not meet clinical criteria. Model 3 captures those who report symptom interference and/or distress are at least moderate, but do not meet clinical criteria. Model 4 captures those who score at least 62 on the PSWQ but do not meet clinical criteria.

Table 2

Comparison of prevention vs. wait-and-treat at different GSH effectiveness, incidence/onset in at-risk, and GSH cost, holding constant SH cost (\$0), SRD of SH (0.112), and treatment cost (\$1244).

Example	SRD of GSH	Rate of onset	Cost of GSH	Cost spent per person in prevention	Cost spent per person in wait-and-treat	Prevention < wait-and-treat
1	0.428	0.25	\$100	\$266.77	\$311.00	TRUE
2	0.428	0.25	\$50	\$222.33	\$311.00	TRUE
3	0.428	0.10	\$100	\$159.96	\$124.40	FALSE
4	0.428	0.10	\$50	\$115.56	\$124.40	TRUE
5	0.276	0.25	\$100	\$313.96	\$311.00	FALSE
6	0.276	0.25	\$50	\$269.56	\$311.00	TRUE
7	0.276	0.10	\$100	\$178.87	\$124.40	FALSE
8	0.276	0.10	\$50	\$134.47	\$124.40	FALSE
9	0.112	0.25	\$100	\$364.97	\$311.00	FALSE
10	0.112	0.25	\$50	\$320.57	\$311.00	FALSE
11	0.112	0.10	\$100	\$199.27	\$124.40	FALSE
12	0.112	0.10	\$50	\$154.87	\$124.40	FALSE

Note: A SRD of 0.428 is equal to a Cohen's d of 0.8, or a large effect size. A SRD of 0.276 equals Cohen's d of 0.5, or a medium effect size. A SRD of 0.112 equals Cohen's d of 0.2, or a small effect size (Kraemer & Kupfer, 2006). Cost spent per person is calculated by dividing the total cost of prevention by the total at-risk population.