Predictors of Persistence After a Positive Depression Screen Among Adolescents

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KEY WORDS

adolescent depression, screening, primary care

ABBREVIATIONS

GH—Group Health

PHQ-9—Patient Health Questionnaire 9-item screen

PHQ-2—Patient Health Questionnaire 2-item screen

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WHAT'S KNOWN ON THIS SUBJECT: Adolescents have high placebo response rates in depression treatment trials. Screening for depression will likely detect youth with a broad range of symptom severity, including some who would benefit from watchful waiting but might not require active treatment.

WHAT THIS STUDY ADDS: The strongest predictors of symptom persistence are depressive symptom severity at presentation and continued symptoms on repeat screening 6 weeks later. These results provide important information for the development of postscreening management protocols in the primary care setting.

abstract

OBJECTIVE: To examine predictors of depression persistence after a positive screening test to inform management protocols for screened youth.

METHODS: We conducted a cohort study of 444 youth (aged 13–17 years) from a large health care delivery system. Youth with depressive symptoms, based on a 2-item depression screen, were oversampled for the baseline interview. Baseline assessments included the Patient Health Questionnaire 9-item (PHQ-9) depression screen as well as clinical factors that were hypothesized to influence depression persistence (family history of depression, functional impairment, perceived social support, anxiety symptoms, externalizing symptoms, and medical comorbidity). Logistic regression analysis was used to examine factors associated with the persistence of depression at 6 months postbaseline.

RESULTS: Of 113 youth with a positive baseline screen (PHQ-9 ≥ 11), 47% and 35% continued to be positive at 6-week and 6-month follow-up, respectively. After controlling for treatment status, only 2 factors were significantly associated with depression persistence at 6 months: baseline depressive symptom score and continuing to have a positive screen at 6 weeks. For each 1-point increase on the PHQ-9 score at baseline, youth had a 16% increased odds of continuing to be depressed at 6 months (odds ratio: 1.16, 95% confidence interval: 1.01–1.34). Youth who continued to screen positive 6 weeks later had almost 3 times the odds of being depressed at 6 months (odds ratio: 2.89, 95% confidence interval: 1.09–7.61).

CONCLUSIONS: Depressive symptom severity at presentation and continued symptoms at 6 weeks postscreening are the strongest predictors of depression persistence. Patients with high depressive symptom scores and continued symptoms at 6 weeks should receive active treatment. *Pediatrics* 2012;130:e1541–e1548

The US Preventive Services Task Force recommends screening for depression among adolescents in primary care when systems are in place to ensure accurate diagnosis, treatment, and follow-up.¹ However, few studies have been conducted examining the psychometric properties of depression screening tests in primary care,^{2–5} and no studies have been conducted examining the course of depression among youth in primary care who screen positive.

There is evidence that, for many youth, depressive symptoms resolve without active treatment. Antidepressant medication trials have consistently demonstrated high placebo response rates (50%–60%), with the steepest decline in depressive symptoms during the first 6 weeks of treatment.^{6–8} Placebo response rates have also been shown to be inversely correlated with depression severity in the population studied,⁹ suggesting that some placebo response may be due to spontaneous recovery in less severely affected individuals. To avoid potentially unnecessary treatment and to target treatment of youth who would most benefit, providers need strategies to identify youth who are likely to have persistent symptoms as well as those who are likely to have spontaneous symptom resolution.

The purpose of this study is to identify clinical and demographic predictors of depression persistence after a positive depression screen among adolescents in primary to develop strategies to identify youth who would most benefit from early engagement in active treatment versus watchful waiting.

METHODS

The AdoleSCent Health Study was developed by researchers at the University of Washington and the Group Health (GH) Research Institute. The main purposes were to evaluate the performance of depression screening instruments and to examine predictors of persistence

of depressive symptoms after a positive screen. All procedures were approved by the GH Institutional Review Board.

Survey Methods

Between September 2007 and June 2008, study staff randomly selected 4000 13- to 17-year-olds who had seen a GH provider in the previous 12 months. GH is a nonprofit health care organization that serves >660 000 residents of Washington State and Idaho. The parents/guardians of selected enrollees received an invitation letter, a consent form, and a brief survey. Parents were asked to sign the consent form and give the survey to their child to complete privately. The child received a \$2 preincentive. Completion of the survey was considered assent to participate by the child. Parents of youth who did not respond received a second mailing and follow-up phone calls.

The brief survey included 10 items about age, gender, weight, height, sedentary behaviors, overall health, functional impairment, and depressive symptoms (the Patient Health Questionnaire 2-item Depression Scale [PHQ-2]). In a previous study using these same data, we found that a score of ≥ 3 on the PHQ-2 had a sensitivity of 73% and a specificity of 75% for detecting major depression compared with structured psychiatric interviews among adolescents.³

Figure 1 details study enrollment procedures. Of the original 4000 invited youth, 3775 were eligible and 2291 completed the brief survey. A subset of youth ($n = 499$) was invited to participate in a longitudinal phone interview study, including assessment of depressive symptoms, functional impairment, and health behaviors. Youth with a PHQ-2 ≥ 3 ($n = 271$) and an age and gender frequency-matched sample of youth with a PHQ-2 ≤ 2 ($n = 228$) were invited to participate. Consent for the longitudinal phone study was obtained from both the parent and the child.

Phone interviews were conducted at baseline, 6 weeks, and 6 months. Youth received \$20, \$10, and \$15 for completion of the baseline, 6-week, and 6-month interviews, respectively.

Youth who indicated “thoughts of death or dying” more than half the days in the past week on the PHQ-9 received additional assessment by a study clinician. For youth who were judged to have an elevated risk for suicide, the study clinician helped connect the youth and parent with treatment resources. No other treatment or feedback on screening was provided through this study.

Baseline phone interviews were completed with 444 youth (89.5% of invited youth). Of the 444 youth in the baseline sample, 436 (98%) completed the 6-week assessment and 433 (97.5%) completed the 6-month assessment. Given the low level of missingness, only youth with complete data at the relevant time points were included in analyses.

Depression Measures, Baseline

The baseline child phone interview included the Patient Health Questionnaire 9-item (PHQ-9) screener and the Diagnostic Interview Schedule for Children depression modules. The PHQ-9 is a self-administered version of the PRIME-MD depression interview,¹⁰ which uses *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria to assess for depression.¹¹ In a previous study using these data, we found that at a score of ≥ 11 , the PHQ-9 had a sensitivity of 89.5% and a specificity of 77.5% for detecting youth with major depression.⁴ To assess for persistence of depressive symptoms, the PHQ-9 was repeated at both the 6-week and 6-month follow-up assessments.

Other Predictors of Persistence

Potential predictors were selected based on literature review of factors associated with depression persistence. Because there have been no previous longitudinal studies of depression persistence

FIGURE 1
Study enrollment flow diagram.

among adolescents in primary care, potential predictors were selected based on the results of studies among adults in primary care and adolescents in specialty settings. In primary care samples of adults, predictors of persistent disorder include increased initial severity, comorbid anxiety disorder or medical disorder, duration of depressive symptoms, and previous history of recurrent depression.^{12–16} Predictors of depression persistence in adolescent specialty samples include older age,¹⁷ female gender,¹⁸ presence of comorbid anxiety disorder^{17,19} or substance abuse,¹⁷ poor quality of friendships,²⁰ higher depression severity at baseline,¹⁸ and poor parental relationships.^{17,21} We also included externalizing symptoms based on the high prevalence of externalizing and depression comorbidity in this age group. Specific measures for each of these constructs, all collected at the baseline interview, are outlined in the following subsections.

Functional Impairment

The 13-item Columbia Impairment Scale was used to measure impairment in

school, family, and peer relationships and has been shown to correlate with the clinician-rated Children's Global Assessment Scale.²²

Comorbid Mental Health Disorders

The 5-item youth self-report version of the Screen for Child Anxiety Related Emotional Disorders was used to screen for anxiety comorbidity.²³ A cutoff of ≥ 3 on the brief version of this measure has been shown to have a sensitivity of 74% and a specificity of 73% for identifying youth with clinically significant anxiety.²³

To assess for externalizing symptomatology, parents were asked to complete the Brief Pediatric Symptom Checklist. The externalizing component (at a cut point of ≥ 7) has a sensitivity of 62% and a specificity of 89% for detecting youth who met criteria for an externalizing disorder.²⁴

To assess for problem substance use behavior, youth were asked to complete the CRAFT screen, a validated measure that includes 6 yes/no items on risky substance use behaviors.²⁵ A score of ≥ 2 has been shown to have a sensitivity

of 76% and a specificity of 94% for identifying problem alcohol or substance use.²⁵

Perceived Social Support

To assess current perceived support from friends and family, youth were asked to complete the Perceived Social Support Scale, which was included in analyses as a continuous measure.²⁶ Higher scores indicate higher levels of support.

Family History of Depression

Youth were considered to have a family history of depression if there was a history of depression in any first-degree family member based on parent report.

Other Covariates

All multivariate models were adjusted for gender, age, and race (white vs nonwhite). To control for the presence of chronic illness, we used the Pediatric Chronic Disease Score, a classification scheme using automated pharmacy data that has been shown to be a significant predictor of 1-year health utilization and costs.²⁷ To account for potential confounding by treatment status, multivariate models included an indicator for whether the youth had received any treatment of depression (based on self-report of any receipt of psychotherapy or medications for depression in the 6 months after baseline assessment).

Statistical Analysis

Descriptive analyses were conducted by using the entire sample ($n = 444$) examining bivariate associations between each of the potential predictors and likelihood of screening positive for depression at baseline. Flowcharts were developed to describe the distribution of PHQ-9 scores at each assessment relative to the results at the previous assessment.

All subsequent regression analyses focused specifically on persistence and

were conducted only among youth who screened positive for depression at baseline assessment (PHQ-9 ≥ 11). By using multivariate logistic regression modeling techniques, 2 sequential models were constructed examining the association between baseline predictors and depressive symptom status at 6 months. The first model included all of the clinical predictors plus the baseline PHQ-9 score. In the second model, depressive symptom score status at 6 weeks, was added to assess the additional benefit of repeat assessment. Because of concerns that there would be significant collinearity between depressive status at baseline and potential predictors, we also conducted a sensitivity analysis examining a model with only nondepressive measures (eg, family history) as predictors of persistence of depression. In this model, there were no significant predictors of depression persistence (Model 1, Table 2).

RESULTS

Of the 444 youth in the full sample, 113 (25.5%) had a PHQ-9 ≥ 11 at the baseline assessment. Among those with a PHQ-9 ≥ 11 at baseline, 47.7% ($n = 53$) continued to have a PHQ-9 ≥ 11 at 6 weeks and 35.3% ($n = 40$) either remained positive or were positive again at the 6 month assessment (Fig 2). Two-thirds of the youth with a PHQ-9 ≥ 11 at 6 months ($n = 27$) were also positive at 6 weeks. Among the 331 youth with a negative baseline screen (PHQ-9 < 11), 94% ($n = 311$) were also negative at 6 weeks, and 94% ($n = 312$) either remained negative or became negative again at the 6-month assessment. Youth who screened positive at baseline (PHQ-9 ≥ 11) were more likely to receive treatment for depression during the subsequent 6 months (42% vs 8% of youth with a PHQ-9 < 11 , $P = .007$). Among youth with a PHQ-9 ≥ 11 at baseline, those who were also PHQ-9 positive at 6 months were significantly more likely

FIGURE 2

PHQ-9 depression status at 6 weeks and 6 months among youth who screened positive (PHQ-9 ≥ 11) and negative (PHQ-9 < 11) for depression at baseline.

to report having received treatment than those who were PHQ-9 negative at 6 months (50% vs 27%, $P = .004$).

In bivariate analyses, each of the potential nondepressive clinical predictors of interest (eg, female gender, family history of depression, anxiety symptoms) were significantly associated with being depressed at baseline (Table 1, first column). However, when the sample was limited to youth with a PHQ-9 ≥ 11 at baseline, none of these factors were significantly associated with depression status at 6 months (Table 1, second column), suggesting

that they were co-occurring with depression but not predictive of depression persistence.

The results of the 3 sequential regression models are presented in Table 2. Among youth with a PHQ-9 ≥ 11 at baseline, the only factors significantly associated with depression persistence at 6 months were depressive symptom score at baseline and depression screen status at 6 weeks. Each additional point increase on the PHQ-9 at baseline was associated with a 16% increased odds for continuing to meet PHQ-9 criteria for depression at 6

TABLE 1 Distribution of Potential Predictor Variables by Baseline Depression Status and Depression Persistence

	Baseline Depression Status (<i>n</i> = 444)			Depression Persistence at 6 mo Among Youth With PHQ-9 ≥ 11 at Baseline (<i>n</i> = 110) ^a		
	Not Depressed (<i>n</i> = 331), % or M (SD)	Depressed PHQ-9 ≥ 11 (<i>n</i> = 113), % or M (SD)	<i>P</i> Value ^b	Not Depressed (<i>n</i> = 70), % or M (SD)	Depressed, (<i>n</i> = 40), % or M (SD)	<i>P</i> Value
Age	15.3 (1.2)	15.2 (1.4)	.82	15.2 (1.2)	15.3 (1.3)	.76
Female	56%	70%	.01	73%	68%	.55
White	73%	66%	.18	66%	69%	.75
Parent any college	86%	87%	.81	87%	90%	.65
Two-parent home	79%	75%	.29	74%	79%	.49
Family history of depression	48%	60%	.04	61%	59%	.86
Anxiety symptoms	1.5 (1.5)	3.0 (2.0)	<.001	3.0 (1.9)	3.6 (2.2)	.09
Externalizing symptoms	3.3 (2.6)	4.3 (3.0)	<.001	4.4 (3.1)	4.1 (3.1)	.60
Problem alcohol or drug use score	0.6 (1.1)	1.4 (1.5)	<.001	1.6 (1.6)	1.1 (1.4)	.11
Functional impairment	11.4 (7.6)	23.5 (7.4)	<.001	23.3 (8.1)	23.8 (6.3)	.82
Perceived social support	32.4 (3.9)	27.9 (5.3)	<.001	28.5 (5.0)	27.2 (5.2)	.13

^a *n* = 110 due to 3 youth with missing data.^b *P* values based on χ^2 test on categorical variables and Wilcoxon test on continuous variables.

months (Table 2, Model 2). Youth who continued to have a PHQ-9 ≥ 11 at the 6-week assessment had 2.9 times the odds of having a positive PHQ-9 at 6 months (Table 2, Model 3). None of the other variables were significantly associated with depression persistence even when depression measures were not included (Table 2, Model 1).

Figure 3 shows the prevalence of depression at 6 months based on the symptom severity cutoffs proposed for adult patients: <10 = mild, 10 to 14 = moderate, 15 to 19 = moderate to severe, and ≥ 20 = severe. We modified these cut points slightly using ≥ 11 as an indication of moderate symptoms

because of previous work by our group showing that a cut point of ≥ 11 has greater specificity than 10 for detecting major depression among adolescents.⁴ At 6 months, 2.5% of youth with a baseline PHQ-9 ≤ 10 were depressed compared with 28.1% of youth with a PHQ-9 of 11 to 14, 37.5% of youth with a PHQ-9 of 15 to 19, and 71.4% of youth with a PHQ-9 ≥ 20 .

DISCUSSION

This is the first study to examine the persistence of depressive symptoms after a positive screening test in a primary care sample of youth. A key finding of

this study is that ~50% of youth who screen positive for depression do not continue to screen positive 6 weeks later. This is consistent with the high placebo response rate in this age group^{6–8} and emphasizes the importance of developing strategies to identify which youth need active treatment versus “watchful waiting” (active monitoring and support from the primary care provider).

Depressive symptom severity has been found to be a significant predictor of depression persistence in pediatric specialty settings.^{18,19} We found a similar pattern in youth in our primary care population: each 1-point increase in the PHQ-9 above a score of 11 was associated with a 16% increased odds of continuing to be depressed 6 months later. When we examined severity categories based on the baseline PHQ-9 score, we also found that risk of persistence increased as severity increased. At 6 months, 2.5% of youth with mild symptoms at baseline were depressed compared with 28.1% of youth with moderate symptoms, 37.5% of youth with moderately severe symptoms, and 71.4% of youth with severe symptoms. These results suggest that the baseline depression symptom score is a strong predictor of depression persistence and that providers should

TABLE 2 Multivariate Logistic Regression Analysis of Predictors of Depression Persistence at 6 mo among Youth With a Baseline PHQ-9 ≥ 11 (*N* = 110)^a

	Model 1, OR (95% CI)	Model 2, OR (95% CI)	Model 3, OR (95% CI)
Age, mean (SD)	1.12 (0.76–1.63)	1.22 (0.82–1.82)	1.28 (0.84–1.93)
Male	1.05 (0.39–2.80)	0.93 (0.34–2.59)	1.12 (0.39–3.19)
White	1.75 (0.66–4.62)	1.90 (0.70–5.16)	1.91 (0.67–5.42)
Family history of depression (yes/no)	1.06 (0.44–2.56)	1.12 (0.45–2.77)	1.08 (0.42–2.72)
Anxiety symptoms	1.11 (0.88–1.39)	1.10 (0.86–1.39)	0.74 (0.53–1.05)
Externalizing symptoms	0.98 (0.84–1.14)	1.01 (0.86–1.19)	0.99 (0.84–1.17)
Problem alcohol or drug use score	0.77 (0.56–1.07)	0.75 (0.53–1.05)	0.74 (0.53–1.05)
Functional impairment score	1.01 (0.95–1.08)	0.99 (0.91–1.06)	1.00 (0.93–1.08)
Perceived social support score	0.93 (0.85–1.03)	0.94 (0.85–1.03)	0.94 (0.85–1.04)
Depression Score at baseline (per 1 unit in score)	—	1.16 (1.01–1.34)	1.09 (0.93–1.26)
Positive screen at 6 wk (dichotomized at PHQ-9 ≥ 11)	—	—	2.89 (1.09–7.61)

Model 1 includes all nondepression predictors; Model 2 adds baseline depressive symptom score to nondepression predictors; Model 3 adds depression status (PHQ-9 ≥ 11) at 6 wk to baseline depressive symptom score and nondepression predictors. In addition to these covariates, all 3 models are adjusted for self-report of any receipt of treatment of anxiety or depression and pediatric chronic disease score. CI, 95% confidence interval; OR, odds ratio.

^a *n* = 110 due to 3 youth with missing data.

FIGURE 3

Depression severity status on the PHQ-9 as a predictor of persistence at 6 months.

consider initial severity of depressive symptoms when making a decision to recommend active treatment versus watchful waiting.

To decrease the likelihood of recruiting youth with transient symptoms for research studies, investigators commonly use a 2-stage screening protocol with a repeat depression screen at a specified time interval after baseline.^{6,28,29} In our study, we used a 6-week reassessment to evaluate the benefit of a 2-screen strategy to identify youth at highest risk for persistent depression. Among those who

screened positive at baseline, we found that youth who also screened positive at 6 weeks had 2.9-times increased odds for continuing to be depressed at 6 months. This suggests that in cases in which the need for treatment is not clear, providers might consider watchful waiting with a repeat screen at 4 to 6 weeks. Youth who have persistent symptoms at 4 to 6 weeks should then be assisted with starting active treatment.

In regression analyses, the results at 6 weeks were a stronger predictor of persistence than baseline PHQ-9 score. Despite this finding, we would not recommend watchful waiting and a 2-stage screening procedure for all youth. Youth who are clearly at high risk for persistence (eg, those with a PHQ-9 ≥20) as well as those who have a high risk for harm with delay of treatment (eg, youth with suicidal ideation or high degrees of functional impairment) should be assisted in seeking treatment as soon as depression is detected.

Other predictors of persistence that have been identified in at least 1 study of depressed adolescents in mental health specialty settings include female gender,¹⁸ older age,¹⁷ comorbid anxiety,^{17,19} substance abuse,¹⁷ and poor support from peers²⁰ or family.^{17,21} In our study, each of these variables was associated with the presence of a positive depression screen at baseline, but none were associated with depression persistence. There are many possible reasons for this absence of association with persistence in our study. First, because most of these predictors were found to be associated in only a single previous study and some predictors, such as female gender,^{17,18,20} have had conflicting results, there may be no true association between these variables and persistence. Second, diagnosed youth in specialty settings may have greater severity of comorbid disorders, more social stress, and longer history of depressive symptoms than screen-positive

youth in primary care. The absence of association may be due to these underlying differences in frequency and severity of these characteristics in the study population. Finally, because we were interested in measures that could practically be used within the time constraints of a busy primary care practice, our study used brief symptom screens to assess for comorbidity and family and peer support, whereas previous studies have used more detailed peer and family support measures and structured clinical interviews.^{17,20} The decreased specificity in our measures may have resulted in misclassification, and this may have weakened our potential to identify an association. Regardless of the reason, although we encourage providers to assess for comorbidity to help inform appropriate treatment of patients, our findings suggest that these measures are not as helpful as severity of depression in determining which youth will have persistent symptoms.

This study was conducted in an insured, predominantly white population in the Pacific Northwest and may not be generalizable to all settings. Additionally, assessments were conducted at discrete points in time and relied on the PHQ-9, which refers only to symptoms in the previous 2 weeks. It is possible that there may be misclassification of persistence in both directions (ie, patients could have been asymptomatic between episodes but have had a recurrence in the 2 weeks before evaluation, or patients could have been symptomatic in the interval but not in the 2 weeks before evaluation). We did not measure quality or adequacy of depression treatment, making it difficult to draw conclusions regarding the impact of treatment on persistence. In observational studies, treatment is confounded by severity of illness: youth with greater severity are more likely to receive treatment but are no more likely to have improvement (this is because severity

is the best predictor of outcome and, in usual care, few youth actually get guideline-level treatment).^{30–32} Finally, although baseline participation and follow-up rates were high, our screening response rate of 60% may have introduced some response bias.

Despite these limitations, this study has important clinical implications. As we follow the US Preventive Services Task

Force's recommendation and institute broad-based screening of adolescents in primary care settings, we are likely to encounter more youth who have short episodes of depression that resolve with monitoring and support. Given limited resources and potential risks for harm, providers need guidance regarding which youth are most likely to benefit from evidence-based

active treatments versus watchful waiting in the primary care setting. The results of our study suggest that youth with higher severity of depressive symptoms at presentation and youth who continue to meet criteria for depression at a 6-week reassessment are at high risk for long-term persistence and would benefit from early institution of evidence-based treatments.

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