Background: There is increasing interest in the extent to which individuals with subthreshold depression face increased risks of subsequent major depression and other disorders.

Objective: To examine linkages between the extent of depressive symptoms (asymptomatic, subthreshold, major depression) at ages 17 to 18 years and mental health outcomes up to age 25 years in a New Zealand birth cohort.

Design: Data were gathered during the Christchurch Health and Development Study, a 25-year longitudinal study of a birth cohort of 1265 New Zealand children (635 males, 630 females).

Setting: General community sample.

Participants: The analysis was based on 1006 participants who represented 80% of the original cohort.

Main Outcome Measures: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition symptom criteria for major depression and anxiety disorder, treatment-seeking, suicidal ideation, and suicide attempt.

Results: There were significant associations (P<.01) between the extent of depression at ages 17 to 18 years and rates of subsequent depressive symptoms, major depression, treatment for depression, anxiety disorder, treatment for anxiety disorder, suicidal ideation, and suicide attempts. After adjustment for covariate factors, the extent of depression at ages 17 to 18 years remained associated with later depression and suicidal tendencies. Planned comparisons showed that sample members with subthreshold depression had a similar prognosis to those meeting criteria for major depression.

Conclusions: Findings suggest that sample members with subthreshold depression are a group with elevated risks of later depression and suicidal behaviors. Current diagnostic procedures, which classify people with subthreshold depression into complex discrete groups, might obscure the fact that depressive symptoms are dimensional and range from none to severe.

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INTRODUCING STANDARDIZED DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSION (MD) HAS OVERCOME MANY ISSUES RELATING TO THE CLASSIFICATION AND TREATMENT OF INDIVIDUALS WITH DEPRESSION.1-4 AT THE SAME TIME, DIVIDING THE POPULATION INTO “CASES” AND “NONCASES” HAS RAISED ISSUES ABOUT THE STATUS OF INDIVIDUALS WITH MINOR OR SUBTHRESHOLD DEPRESSION. THESE INDIVIDUALS HAVE CLINICALLY RELEVANT SYMPTOMS OF MD WITHOUT MEETING THE FULL CRITERIA FOR THIS DISORDER.5-7 IT HAS BEEN INCREASINGLY RECOGNIZED THAT INDIVIDUALS WITH SUBTHRESHOLD DEPRESSION DO NOT HAVE A SIMILAR PROGNOSIS TO THOSE WHO ARE ASYMPTOMATIC. HOWEVER, THERE IS LITTLE AGREEMENT ON HOW TO ADDRESS THE DIAGNOSIS OF SUBTHRESHOLD DEPRESSION.3,8 MODERN CLASSIFICATION SYSTEMS SUCH AS THE DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS, FOURTH EDITION (DSM-IV) HAVE ESTABLISHED DIAGNOSTIC CATEGORIES FOR SUBSYNDROMAL DEPRESSIVE SYMPTOMS, INCLUDING “DYSTHYMIA,” “BRIEF RECURRENT DEPRESSION,” AND “MINOR DEPRESSIVE DISORDER.”9 ALTERNATIVELY, EVIDENCE SUGGESTS THAT THERE IS A CONTINUUM OF DEPRESSIVE DISORDERS THAT DO NOT EXIST WITHIN DISCRETE CATEGORIES.10,11 INCREASING EVIDENCE SUGGESTS THAT INDIVIDUALS WITH SUBTHRESHOLD DEPRESSION HAVE AN INCREASED RISK OF SUBSEQUENT MD AND OTHER ADVERSE OUTCOMES.11-14 FOR EXAMPLE, LEWINSOHN ET AL10 FOUND THAT INCREASING LEVELS OF SUBTHRESHOLD DEPRESSIVE SYMPTOMS PREDICTED LATER MD AND SUBSTANCE ABUSE OR DEPENDENCE. HOWEVER, THERE ARE A NUMBER OF LIMITATIONS TO THE RESEARCH EVIDENCE IN THIS AREA. FIRST, IN MOST STUDIES, THE LENGTH OF FOLLOW-UP FROM THE INITIAL DIAGNOSIS WAS RELATIVELY SHORT (TYPICALLY 1 YEAR; SEE CUIJPERS AND...
Smit\(^6\), which raises issues about the extent to which subthreshold depression is prognostic of later outcomes. Second, most studies focused on the extent to which subthreshold depression predicts later MD but did not address the extent to which individuals with subthreshold depression are at risk for other mental disorders. Finally, little attention was given to the issue of confounding. In particular, the higher risks experienced by individuals with subthreshold depression might not be due to the sequelae of subthreshold depression per se but might reflect social, contextual, and related factors that are associated with the reporting of subthreshold depression and related to later MD and other mental disorders.

Against this background, we report the results of a 7-year prospective study of the linkages between subthreshold depression in adolescence (17-18 years) and subsequent mental health in young adulthood (18-25 years) using data on a birth cohort of more than 1000 New Zealand young people studied to the age of 25 years. The aims of this study were (1) to document the prevalence of subthreshold depression, (2) to examine the linkages between subthreshold depression and subsequent mental health outcomes, and (3) to adjust the associations between subthreshold depression and later mental health outcomes for potentially confounding factors.

METHODS

PARTICIPANTS

Data were gathered as part of the Christchurch Health and Development Study—a longitudinal study of a birth cohort of 1265 children (635 males, 630 females) who were born in the Christchurch (New Zealand) urban region in mid 1977. This cohort was studied at birth, at 4 months, at 1 year, and at annual intervals to age 16 years and again at ages 18, 21, and 25 years using information from a combination of sources, including parental interviews, teacher reports, psychometric testing, self-reports, and medical and police records.\(^{16}\) All study information was collected on the basis of signed and informed consent from study participants. The analyses reported in this article were based on the sample of 1006 young people who were assessed on measures of depression at age 18 and on mental health outcomes at age 21 or 25 years. This sample represented 80% of the initial cohort of 1265 sample members.

EXTENT OF DEPRESSION

At age 18 years, sample members had a comprehensive mental health interview designed to assess aspects of psychosocial adjustment. Part of this interview used items from the Composite International Diagnostic Interview (CIDI)\(^17\) to assess depression. For the present analysis, this information was used to construct 2 measures of suicidal behavior for each interval (18-21 years, 21-25 years): (a) whether the individual met DSM-IV diagnostic criteria for a major depressive episode at any time during the interval, (b) a count of the number of DSM-IV symptom criteria for MD reported at any time during the interval, and (c) whether the respondent sought treatment for depression from a mental health professional (general practitioner, psychiatrist, psychologist, counselor) during the interval.

MENTAL HEALTH OUTCOMES

At ages 21 and 25 years, sample members again had a comprehensive mental health interview that examined aspects of psychosocial adjustment since the preceding assessment. Items from the CIDI were used to assess DSM-IV symptom criteria for MD. Sample members were questioned about depressive symptoms occurring over the past month, the past 12 months, and the period since the previous assessment, as well as any associated impairment. In addition, any participant who reported either of the core major depressive symptoms (depressed mood, loss of interest) was also questioned about seeking treatment for depression. We used this information to construct the following measures of depression for each interval (18-21 years, 21-25 years): (a) whether the individual met DSM-IV diagnostic criteria for a major depressive episode at any time during the interval, (b) a count of the number of DSM-IV symptom criteria for MD reported at any time during the interval, and (c) whether the respondent sought treatment for depression from a mental health professional (general practitioner, psychiatrist, psychologist, counselor) during the interval.

We questioned sample members on the frequency of suicidal thoughts or suicide attempts occurring since the previous assessment. This questioning was conducted separately from the questioning about depressive symptoms and was used to construct 2 measures of suicidal behavior for each interval (18-21 years, 21-25 years): (a) whether the sample member reported any suicidal ideation during the interval and (b) a count of the number of suicide attempts (if any) reported in each interval.

CONFOUNDING FACTORS

Data gathered during the course of the study provided information on a wealth of factors that might confound the associations between the extent of depression at ages 17 to 18 years and later mental health. The following factors were selected as potential confounders on the basis of previous analyses on the cohort.\(^{19,20}\)

Maternal education at the time of the survey child’s birth was classified in 3 levels according to the mother’s highest level of educational attainment (no formal qualifications, high-school qualifications, tertiary qualifications). Maternal age was coded in whole years at the time of the survey child’s birth. Family socioeconomic status was assessed at the point of birth using the Elley-Irving\(^11\) scale of socioeconomic status for New Zea-
land. This index classifies families into 6 levels on the basis of paternal occupation. The quality of family living standards was assessed at annual intervals from ages 1 to 10 years on the basis of interviewer ratings made on a 5-point scale from very good to very poor.

As part of the study, detailed information was obtained at annual intervals from birth to age 15 years on any changes in family composition. An index of family instability during childhood used a count of the total number of changes of parents experienced by the child up to age 15 years. The quality of parental attachments during adolescence was assessed at age 15 years using the Armsden and Greenberg22 Parental Attachment Scale. The reliability of this scale, assessed using coefficient α, was 0.87. When sample members were aged 13 years, parents were questioned about their history of alcoholism or problems with alcohol; 11.9% of the sample had at least 1 parent who reported alcohol problems. When sample members were aged 11 years, parents were questioned about their use of cannabis or other illicit drugs; 24.4% of the sample had at least 1 parent with a history of illicit drug use.

At ages 18 and 21 years, sample members were questioned concerning their experience of childhood sexual abuse prior to age 16 years and the nature and context of any episodes of abuse. Using these data, we constructed a 4-level classification of the severity of any abuse reported at either age23: parents never used physical punishment (78.2%), at least 1 parent regularly used physical punishment (4.5% of the sample), noncontact sexual abuse only (2.7%), contact sexual abuse not involving attempted or completed intercourse (5.1%), or attempted or completed intercourse (6.2%). The extent of childhood physical abuse was assessed on the basis of the young people’s reports of the extent of parental use of physical punishment during their childhoods (prior to age 16 years), also obtained when sample members were aged 18 years and 21 years. The extent of physical punishment was coded on a 4-point scale based on the highest level of physical punishment reported at either age23: parents never used physical punishment (4.5% of the sample), parents rarely used physical punishment (78.2%), at least 1 parent regularly used physical punishment (11.3%), or at least 1 parent used physical punishment too often or too severely (6.0%).

The first individual characteristic recorded was gender. We assessed child neuroticism using a short-form version of the neuroticism scale of the Eysenck Personality Inventory,24 which was administered when sample members were aged 14 years. The reliability of this scale, assessed using coefficient α, was 0.80. Novelty seeking was assessed using the novelty-seeking subscale of the Tridimensional Personality Inventory,25 administered when sample members were aged 16 years. The reliability of this scale, assessed using coefficient α, was 0.76. We obtained a measure of self-esteem at age 15 years using the Coopersmith Self-Esteem Inventory.26 The full-scale score was used in the present analysis, and this measure had a reliability (α) of 0.76.

At ages 15 and 16 years, sample members were questioned using components of the Diagnostic Interview Schedule for Children27 to assess DSM-III-R28 criteria for MD and anxiety disorders, including overanxious disorder, generalized anxiety disorder, social phobia, and simple phobia, over the previous 12 months. In addition, we questioned sample members about suicidal thoughts and suicide attempts over this period. This information was combined over the 2 assessment periods to provide measures reflecting the history of MD, anxiety disorder, and suicidal behaviors prior to age 17 years.

When the sample members were 18 years old, we obtained information on a range of other mental health problems that were comorbid with depressive symptoms. CIDI items were used to assess DSM-IV diagnostic criteria for a range of anxiety disorders, including generalized anxiety disorder, social phobia, specific phobia, panic disorder, and agoraphobia. We also used CIDI items to assess DSM-IV diagnostic criteria for a range of substance-use disorders, including alcohol abuse, alcohol dependence, illicit drug abuse, and illicit drug dependence. Sample members were also questioned about suicidal thoughts and suicide attempts occurring since the previous assessment.

### STATISTICAL METHODS

The statistical significance of the bivariate associations between the extent of depression at ages 17 to 18 years and subsequent mental health outcomes at 18 to 21 years and 21 to 25 years (Table 1) was tested using the χ² test for dichotomous outcomes and negative binomial regression for count data. Tests of the linearity of the observed associations were conducted using the Mantel-Haenszel χ² test of linear trend for dichotomous outcomes and negative binomial regression for count data.

To adjust the observed associations for confounding by childhood and family factors and comorbid disorders, we fitted generalized estimating equation models29,30 to the data. These models pooled the repeated measures on each outcome at ages 18 to 21 years and 21 to 25 years to produce an estimate of the population-averaged effect of the level of depression at ages 17 to 18 years on the outcome after adjustment for covariates. For dichotomous outcomes, we fitted logistic regression models, whereas for count outcomes, we used negative binomial models. The general form of the fitted model was

\[
g (Y_{it}) = B_0 + B_1 X_{i1} + B_2 X_{i2} + \sum B_j Z_{ij} + U_{it}
\]

where \(Y_{it}\) represented the outcome \(Y\) for subject \(i\) in interval \(t\); \(g (Y_{it})\) represented the log odds of \(Y\) for dichotomous outcomes or the logarithm of \(Y_{it}\) for count data; \(X_{i1}\) and \(X_{i2}\) were design variables representing membership of the subthreshold or MD groups respectively for each subject; \(Z_{ij}\) was the set of confounding factors for subject \(i\); and \(U_{it}\) represented the disturbance terms for the model. The disturbance terms \(U_{it}\) were assumed to be correlated over time. From the fitted model, estimates of the covariate adjusted rate ratios were obtained. The generalized estimating equation model in the equation yields an estimate of these ratios averaged over the 2 measurement periods (18-21 years, 21-25 years). (These estimates were given by \(e^{B_1}\) and \(e^{B_2}\).) The fitted model parameters were also used to conduct multiple tests of significance between pairs of model parameters. We fitted all generalized estimating equation models using Stata 6.0.31 To test for gender × depression interactions, we extended the model in the equation to include gender × depression interaction terms.

To examine the implications of loss to follow-up, missing data, and possible sample selection bias on the results, we used the data weighting methods described by Carlin et al.32 These methods involved a 2-stage analysis process. In the first stage, we constructed a sample selection model by using data gathered at birth to predict participation at each time point. This analysis showed that there were statistically significant (\(P<.05\)) tendencies for the attained sample at each age to underrepresent children from socially disadvantaged backgrounds (low parental education, low socioeconomic status, single-parent family). The sample was then poststratified into a series of groups and the probability of study participation estimated for each group at each age. In the second stage of the analysis, we reanalyzed the data with the observations for each individual weighted by the inverse of the probability of study participation at each age. This analysis produced essentially identical conclusions to the analysis reported here, suggesting that the effects of sample selection bias on the results were likely to be minimal.
ASSOCIATIONS BETWEEN EXTENT OF DEPRESSION AND LATER MENTAL HEALTH

Table 1 shows the cohort classified into 3 groups (asymptomatic, subthreshold, MD) on the basis of measures of MD at ages 17 to 18 years. For each group, the table reports on mental disorders and treatment-seeking at ages 18 to 21 years and 21 to 25 years. Each comparison was tested for statistical significance using the $\chi^2$ test for dichotomous outcomes and negative binomial regression for count data.

For measures of depression, anxiety, and suicidal behaviors, the table shows clear and significant trends for the extent of depression at ages 17 to 18 years to be related to subsequent mental health outcomes at ages 18 to 21 years. In most instances, the results suggested a dimensional model in which rates of subsequent outcomes varied with the extent of depression at ages 17 to 18 years. To test this dimensional model, we applied tests of linearity to the data, and all cases showed evidence of significant linear trends between the extent of depression at ages 17 to 18 years and later outcomes.

COVARIATE ADJUSTED RESULTS

The findings in Table 1 fail to take into account potential confounding factors that might have been related to depression at ages 17 to 18 years and also to later outcomes. As explained in the Methods section, a number of potentially confounding factors were identified on the basis of previous analyses of this cohort. These confounding factors included child, family, social, and related life history measures; comorbid mental disorder at age 18; and MD, anxiety disorders, and suicidal behaviors prior to age 17.

To take these factors into account, we fitted generalized estimating equation models to the data at ages 18 to 21 years and 21 to 25 years. For dichotomous outcomes, we fitted logistic regression models, whereas for the count variables, we used negative binomial regression models. From these models, we computed estimates of covariate-adjusted, population-averaged rate ratios (see Methods), comparing the rate of disorder in the subthreshold and MD groups relative to the asymptomatic group for each outcome (Table 2). In all analyses, we made planned comparisons between the rate ratios for various groups, and the table also gives the overall statistical significance of the association with each outcome after adjustment for confounding. The table shows the following:

1. Following control for confounding, significant associations remained between the extent of depression at ages 17 to 18 years and subsequent depression (MD, depressive symptoms, treatment-seeking). In all comparisons, the results show that those individuals in the subthreshold and MD groups had significantly higher rates of subsequent outcomes compared to the asymptomatic group.
of subsequent depression and treatment-seeking than those in the asymptomatic group. However, the adjusted rates of disorder and treatment-seeking in the subthreshold and MD groups were not significantly different.

2. For measures of subsequent anxiety disorder, the adjusted associations with prior depression were generally modest and not statistically significant. The adjusted rates of anxiety disorder in the subthreshold group were no different from those in the asymptomatic group, whereas those in the MD group had mildly elevated rates of anxiety disorder in comparison with the other groups. However, treatment-seeking for anxiety-related problems remained significantly associated with the extent of prior depression after adjustment. In addition, the adjusted rate ratios of treatment-seeking in the subthreshold and MD groups were similar and significantly higher than those in the asymptomatic group.

3. The results for measures of suicidal behavior were similar to those for the depression outcomes. For suicidal ideation, the association with extent of depression at ages 17 to 18 years remained significant after adjustment for confounding. Further, the adjusted rates of suicidal ideation in the subthreshold and MD groups were significantly higher than for the asymptomatic group but were not significantly different from each other. For suicide attempts, the pattern of adjusted rate ratios was suggestive of increasing risk with increasing severity of depression at ages 17 to 18 years. However, the adjusted association with extent of depression at ages 17 to 18 years was only marginally significant, perhaps reflecting the reduced precision of this analysis as a result of the low base rate of suicide attempts.

SUPPLEMENTARY ANALYSES

To examine the extent to which the associations between early depression and later outcomes varied with gender, the models in Table 2 were extended to include gender by extent of depression interaction terms. No significant interactions were found, suggesting that the associations between the extent of depression at ages 17 to 18 years and subsequent mental health were generally similar for males and females.

We also extended the analysis to examine the extent to which depressive symptoms were related to later substance dependence (alcohol, illicit drugs) at ages 18 to 21 years and 21 to 25 years. The analysis suggested that early depression was unrelated to later substance dependence when due allowance was made for covariate factors.

In this study, we used data gathered over the course of a 25-year longitudinal study to examine the longer-term consequences of depressive symptoms in adolescence. The study showed that at the age of 18 years, more than a quarter of the cohort reported at least 1 core DSM-IV symptom of MD, with 18.4% meeting criteria for MD. The rate of MD in our cohort at age 18 years was comparable with the rate reported for the Dunedin Multidisciplinary Study (17.2%) at age 18 years. Overall, 7.3% of the sample met criteria for subthreshold depression. This rate is somewhat lower than that reported in other studies, and it might reflect specific features of this study, including the age of the cohort and the methods used to define MD.

Two major findings emerged from this analysis. First, in comparison with those who were asymptomatic, young people with subthreshold depression had elevated risks of later depression and suicidal behaviors. Second, the risks of future adverse outcomes for those with subthreshold depression were similar to the risks experienced by those meeting criteria for MD. Collectively, these findings make a strong case for the view that those with subthreshold depression should not be classified as "non-cases" and treated as though they have a similar prognosis to those who are asymptomatic. Rather, the results suggest that the future mental health risks faced by those with subthreshold depression are similar to the risks experienced by those with MD.

These findings confirm and extend previous research in this area in at least 3 ways. First, the findings show that the increased risks associated with subthresh-
old depression are not transitory and might be evident up to 7 years following an index episode. These findings are consistent with other studies using similar follow-up periods. Second, the results show that the associations between subthreshold depression and later outcomes hold, even following control for confounding factors. Third, the results suggest that subthreshold depression might be associated with increased risks of other mental health problems, such as suicidal ideation and attempts, in addition to increased risks of future depressive symptoms and MD. To our knowledge, no current study has examined all of these factors in combination, using a prospectively assessed representative population sample.

The findings clearly support the view that measures of MD are best described by a dimensional model in which the severity of symptoms ranges from none to severe. Under this model, those meeting diagnostic criteria for MD represent the extreme of a continuum rather than a distinct group of individuals suffering from a specific disorder. In turn, these conclusions raise important issues about the classification of depression. The traditional method of classifying depression in current diagnostic systems, including the DSM-IV36 and International Classification of Diseases, 10th Revision,34 has been to distinguish those with clinically significant symptoms from others. As shown in this article, such an approach leads to a neglect of those with symptoms that fall below threshold and might also obscure the dimensional features of depressive disorder.

An alternative approach to current methods of classification is to base the classification of disorders on the distinction between individuals with and without symptoms. Those with symptoms may then be classified further into those with various levels of symptoms, ranging from mild to severe. Under this approach, the population is classified into a series of ordered sets that describe the extent of depressive symptoms on a continuum from none to severe. This continuum subsumes those meeting diagnostic criteria but also recognizes the distinction between those who are asymptomatic and those who have a subthreshold disorder. This issue has been addressed to some degree by the addition of further diagnostic categories to the DSM-III9,18,36 The inclusion of “dysthymic disorder” as a diagnosis of subthreshold depressive symptoms dates back to the DSM-III, but “recurrent brief depression” and “minor depressive disorder” were appended to the DSM-IV. However, a potential difficulty with these extensions is that they lead to the classification of an increasing number of “disorders,” which might simply reflect the fact that measures of depressive symptoms are dimensional and range from none to severe. It might be parsimonious and accurate to classify individuals on the basis of the extent of their depressive symptoms rather than create a complex vocabulary to describe different “types” of depression.

A number of limitations apply to the present study. First, the results apply to a specific cohort that was studied at a specific time and in a specific context. The extent to which these findings can be replicated in other populations and contexts requires verification. Second, despite the relatively large sample size, statistical power might have been too small to detect significant differences, such as between the subthreshold group and the asymptomatic group in suicide attempts.

The present findings have clinical implications to the extent that individuals with subthreshold disorders clearly form a population who is at a significantly increased risk for further depression and suicidal behaviors. There is a clear case for suggesting a need for increased clinical attention and surveillance for those with symptoms of depression who fail to meet current criteria for MD. The recognition of early symptoms of depression then raises the question as to whether the onset of MD can be prevented by treating subthreshold symptoms and how to do so. Future research can be directed toward answering these questions.

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