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# Preventing the Incidence of New Cases of Mental Disorders

## A Meta-Analytic Review

Pim Cuijpers, PhD,\*† Annemieke Van Straten, PhD,† and Filip Smit, MA†

**Abstract:** To assess the results of studies examining the effects of preventive interventions on the incidence of mental disorders, we conducted a systematic review. A literature search resulted in 13 high-quality randomized trials, six on depressive disorder (including postpartum depression), one on anxiety, one examining both anxiety and depression, three on posttraumatic stress disorders, one on psychosis, and one on any mental disorder. The overall relative risk (RR) was 0.73 (95% CI, 0.56–0.95), indicating a reduction of the risk to become a new case of a mental disorder. The seven studies on prevention of depressive disorder resulted in a RR of 0.72 (95% CI, 0.54–0.96). The risk of posttraumatic stress disorder was somewhat increased after debriefing, but not significantly (RR = 1.33), indicating a possible adverse effect. Prevention of new cases of mental disorders seems to be possible and may be an important way of reducing the enormous burden of these disorders.

**Key Words:** Prevention, meta-analysis, mental disorders, major depressive disorder.

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Although hundreds of controlled studies have examined the effects of mental illness prevention programs in the past few decades (Cuijpers, 2003), few have examined whether prevention programs are actually capable of reducing the incidence of new cases of mental disorders according to diagnostic criteria. Major reasons why this has hardly been examined include the large numbers of research subjects needed to realize sufficient statistical power, the necessity to use elaborate diagnostic interviews, and the resulting high costs of such studies (Cuijpers, 2003). The power problem and the large number of subjects needed are especially

important in studies examining disorders with low incidence rates. This power problem is related to the fact that the exact pathways that lead to mental disorders are not known, and the specificity of most known risk factors is very low. This implies that most subjects who are exposed to the risk factor do not develop the disorder, and that one such risk factor by itself is not sufficient to produce the disorder in most cases (Rothman and Greenland, 1998).

On the other hand, examining the effects of prevention programs on the incidence of mental disorders is one of the most important research questions for mental health prevention. First, effective prevention programs may potentially contribute to the reduction of the enormous burden of mental disorders (Andrews and Wilkinson, 2002). Mental disorders account for 22% of the total burden of disease in established market economies, as measured in disability-adjusted life-years lost (Murray and Lopez, 1997), with the common mental disorders (depression, anxiety, and substance use disorders) accounting for three quarters of the burden of all mental disorders. It is estimated that only half of the burden of the common mental disorders can be averted with existing treatment methods (both psychological and pharmacological) given maximized coverage (the number of people seeking treatment), clinician competence, and patient compliance to treatment (Andrews and Wilkinson, 2002). If we want to reduce the burden of mental disorders further, we can either develop new treatment methods that are considerably better than existing ones, or we can develop preventive interventions that result in reductions of new cases. The option for preventive interventions has not been examined very elaborately, although it can be regarded as a promising way to reduce the burden of psychiatric diseases (Andrews and Wilkinson, 2002).

A second reason why this research is so important is that it may increase our knowledge of the etiology of mental disorders. Until now, most mental disorders have been thought to be caused by multiple factors on different levels (physical, social, psychological), and it is not possible to predict which individual is going to develop the disorder and who is not. If it proves to be possible to prevent new cases of mental disorders, the interventions must somehow change the

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basic mechanisms that lead to the occurrence of the disorder. A third reason is that this research will make it possible for the first time to compare directly the benefits of treatment with those of prevention.

From the second half of the 1990s on, a growing number of researchers has taken up the challenge to conduct studies in this complicated research area, including studies examining the effects of prevention on incidence. With these studies, a new tradition in mental health prevention research is emerging in which psychosocial preventive interventions are linked with the more medically oriented categorizations of mental disorders. In this article, we review the studies that have been conducted in this newly emerging research area, and we perform a statistical meta-analysis to examine the impact the preventive interventions can have on the incidence of mental disorders.

## METHODS

### Literature Search

We conducted a systematic literature search. First, we conducted a search in major bibliographical databases (Medline, Psycinfo, and ERIC), in which we combined key words of *prevention* and major categories of mental disorders (all mood disorders, all anxiety disorders including posttraumatic stress disorder (PTSD), schizophrenia, eating disorders, conduct disorders, oppositional defiant disorder, and ADHD), limiting the results to randomized controlled trials. We also searched for combined randomized trials of subclinical forms of the major categories of mental disorders (with key words such as *subthreshold*, *minor*, and *subclinical*).

Only studies published later than 1980 were included, because most modern diagnostic definitions of mental disorders (such as the Research Diagnostic Criteria and the DSM-III) were not broadly used before this date. The end date of the searches was August 1, 2002. The resulting abstracts were studied by two researchers independently. Studies that possibly met inclusion criteria, studies with no abstract, and studies that could not clearly be excluded were retrieved and examined more extensively. All disagreements between the two researchers were discussed elaborately, and when some doubt remained, the complete articles were retrieved, studied, and discussed again until agreement was reached.

In the second part of the literature search, we collected major meta-analyses and reviews of prevention studies. We examined the same bibliographical databases for reviews and meta-analyses (combining key words and text words of mental disorders and *prevention* with *meta-analysis* or *review*). In this way, we identified major reviews and meta-analyses of prevention studies of depression (Compas et al., 1997; Gillham et al., 2000; Katz et al., 1994; Munoz, 1993), anxiety disorders (Donovan and Spence, 2000; Rose et al., 2002), conduct disorders (Prinz and Connell, 1997; Tremblay et al.,

1999), and eating disorders (Franko and Orosan-Weine, 1998; Stewart, 1998). We also examined major reviews and meta-analyses of school-based mental health prevention programs (Durlak and Wells, 1997, 1998; Hudley and Graham, 1995; Wilson et al., 2001) and general systematic reviews of the field (Greenberg et al., 2001; Mrazek and Haggerty, 1994). We collected the abstracts of the studies included in these reviews and examined them using the same procedure as in the first part of the literature search.

The third part of the literature search consisted of the examination of the reference lists of included studies. Studies that possibly met inclusion criteria were retrieved and examined for possible inclusion.

### Inclusion Criteria

We included only studies that used a pretest-posttest randomized controlled design, and that examined the effects of a preventive intervention on the incidence of new cases of mental disorders compared with a control group that did not receive the intervention. Studies had to use a standardized diagnostic interview (such as the DISC, CIDI, or SCAN) to exclude to presence of the full-blown mental disorder at pretest and to examine the incidence of the mental disorder at follow-up. We also included studies that examined interventions aimed at reducing the consequences of specific life events (traumatic events, children of divorced parents, death of the spouse, postnatal depression) and did not measure the presence of mental disorder at pretest (but did examine the presence of mental disorders at posttest).

### Resulting Studies

Thirteen studies met inclusion criteria. In these 13 studies, 16 comparisons between a preventive intervention and a control group were made. In one of the studies (McGorry et al., 2002), we were not sure about its inclusion, because the control group received a "needs based" intervention, which could be regarded as an active treatment condition instead of a control condition. To examine a possibly disturbing effect of this study on the overall meta-analyses, we conducted all meta-analyses with and without this study, but found no major differences between the analyses with and without this study. Therefore, we decided to include this study.

Overall, 1,570 subjects were included in these studies, 860 in the experimental conditions and 710 in the control conditions. Selected characteristics of the studies are presented in Table 1. Six studies examined prevention of depressive disorder (including two studies on postpartum depression), one examined prevention of anxiety, and one prevention of both anxiety (generalized anxiety disorder) and depression (two comparisons). Three examined prevention of PTSDs (four comparisons), one psychosis, and one any mental disorder (two comparisons). Five studies (six comparisons) examined indicated prevention programs (aimed at

**TABLE 1.** Selected Characteristics of Studies Examining the Effects of Interventions on the Incidence of New Cases of Mental Disorders

Study	Type	Disorder	Target Population	Procedure	Intervention	Follow-up	Conditions	N
Allart-Van Dam, 2003	IND	MDD	Subjects with depressive symptoms (BDI $\geq$ 10), no MDD	Recruitment of subjects through local media	12 group sessions CBT (2 h)	1 y	1. Intervention	68
							2. Care as usual	42
Bisson et al., 1997	SEL	PTSD	Adult burn trauma victims (16–65 y)	40 consecutive admissions to a regional burns unit	30–20 min debriefing	13 mo	1. Intervention	57
							2. No intervention	46
Brugha et al., 2000	SEL	PPD	Primiparous women at risk for depression	1300 women were screened at antenatal clinics	6 sessions psychoeducation + coping skills	1/4 y	1. Intervention	94
							2. Routine care	96
Clarke et al., 2001	IND	MDD	Adolescents (13–18 y) with subclinical depression + parent treated for MDD in past year	3935 parents + adolescents were recruited through HMO	15 group sessions CBT (of 1 h)	1 y	1. Intervention	45
							2. Care as usual	49
Clarke et al., 1995	IND	MDD	Adolescents (15–16 y) with subclinical depression	1652 adolescents were screened at school with the CES-D	15 group sessions CBT (3/4 h)	1 y	1. Intervention	76
							2. Care as usual	74
Conlon et al., 1998	SEL	PTSD	Victims of minor road traffic accidents (16–65 y)	40 consecutive trauma clinic attenders	1 session of counseling (1/2 hour)	99 d	1. Intervention	18
							2. No intervention	22
Dadds et al., 1997	IND	Anx	Primary school children (7–14 y) with subclinical anxiety	1786 children were screened with several measures	10 weekly 1–2 h CBT sessions	1/2 y	1. Intervention	19
							2. Treatment as usual	14
McCorry et al., 2002	IND	PSY	Patients at incipient risk of progression to first-episode psychosis	Referrals to early psychosis prevention and intervention center	Protooled CBT (number of sessions not reported)	1 y	1. CBT + medication	28
							2. Needs-based supportive psychotherapy	31
Muñoz et al., 1995	SEL	MDD	GP patients (minority and chronically ill) without MDD	GP patients with clinic appointments in past 3 mo	8 weekly CBT group sessions	2 y	1. Intervention	62
							2. Treatment as usual	72
Rose et al., 1999	SEL	PTSD	Victims of violent crimes	2161 victims were asked to participate within 1 mo	Debriefing (1 h)	1/2 y	1. Debriefing + info	54
							2. Information only	52
							3. Assessment only	51
Seligman et al., 1999	SEL	MDD GAD	University students scoring high on the ASQ	ASQ was sent by mail to all new students	8 weekly CBT group sessions (2 h)	3 y	1. Intervention	106
							2. Care as usual	119
Wolchick et al., 2002	SEL	ANY	Children of divorced parents	Recruitment through court records (letters + calls) + media	Parent training + conflict reduction; coping + CBT (11 group sessions)	6 y	1. Mother + child program	83
							2. Mother program	81
							3. Control	76
Zlotnick et al., 2001	SEL	PPD	Pregnant women at risk for depression	122 women were screened for participation	4 weekly group sessions of interpersonal therapy	1/4 y	1. Intervention	17
							2. Care as usual	18

Abbreviations :*ANY* = Any mental disorder according to the DISC; *ASQ* = Attributional Style Questionnaire; *CBT* = cognitive behavior therapy; *IND* = indicated; *MDD* = major depressive disorder; *SEL* = selective prevention.

subjects with subclinical symptoms of the disorder without meeting full-blown diagnostic criteria), eight selective prevention (aimed at high-risk groups; 11 comparisons). Seven

studies used cognitive behavioral interventions (aimed at prevention of depression and anxiety; eight comparisons); three (four comparisons) used debriefing (PTSDs).

The quality of all studies was high. All used randomized controlled designs, well-validated measurement instruments, well-described and theoretically well-founded interventions, and adequate statistical analyses.

## Analyses

### Follow-Up Period

Because the follow-up period of the studies differed considerably, we based the calculation of the incidence rates on person-years. That is, we divided the number of new cases of mental disorder that occurred in the period (the numerator) by the total amount of person-time units (person-years) of the group at risk (the denominator). Technically, this is known as the *person-time incidence rate* or the *incidence density rate*. The person-time incidence rate is an appropriate measure of incidence when follow-up times are unequal (Rothman, 1988). In two studies, this method could not be used directly because the number of subjects was larger than the number of person-years as a result of the short follow-up period and the relatively large number of new cases during this period. For example, when 12 persons are studied for 3 months, the observation period is 4 person-years. If more than four persons develop a disorder during the follow up, the person-years incidence rate cannot be calculated. To solve this problem, we first calculated the person-months instead of the person-years for all studies. Next, we recalculated the person-months into person-years for combined sets of studies. For each study, we calculated the relative risk (RR) of developing a mental disorder in experimental subjects compared with the risk in control subjects.

### Meta-Analyses

In the meta-analyses, we first calculated overall RRs with the method of DerSimonian and Laird (1986). We conducted all meta-analyses both with the fixed effects model and with the random effects model (Clarke and Oxman, 1999). The resulting RRs were comparable, and because the random effects model results in more conservative 95% CIs, we present only the results of the latter analyses. For the analyses, we used the computer program from the Cochrane Collaboration, RevMan (version 4.0.4; Clarke and Oxman, 1999). We calculated the  $\chi^2$  statistic to estimate heterogeneity between study outcomes.

## RESULTS

### All Studies

The overall RR across all studies was found to be 0.73 (95% CI, 0.56–0.95), which indicates a statistically significant and clinically substantial risk reduction. Although this was not expected, the test of homogeneity was not significant ( $\chi^2 = 20.30$ ;  $df = 15$ ;  $p = .16$ ; Table 2), indicating that the

**TABLE 2.** Meta-Analyses of Studies Examining the Effects of Preventive Interventions on New Cases of Mental Disorders

	$N_{comp}$	RR (95% CI)	$\chi^2$
All studies	16	0.73 (0.56–0.95)	20.30 NS
Disorder			
Depression	7	0.72 (0.54–0.96)	5.86, NS
PTSD	4	1.33 (0.75–2.37)	3.89, NS
Type of intervention			
Cognitive behavior therapy	8	0.69 (0.53–0.89)	5.73, NS
Debriefing (PTSD)	4	1.33 (0.75–2.37)	3.89, NS
Level of prevention			
Selective	11	0.81 (0.59–1.11)	13.76, NS
Indicated	5	0.58 (0.37–0.92)	4.92, NS

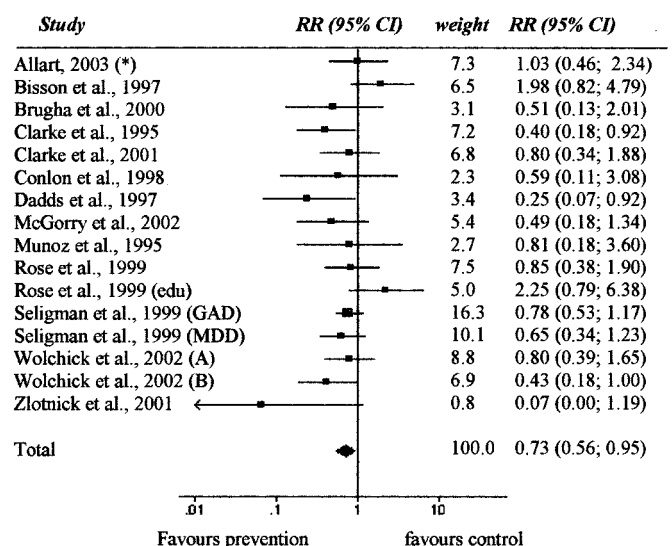
$N_{comp}$  = Number of comparisons.

set of comparisons was homogeneous. The RR of each of the studies and the pooled RR are presented in Figure 1.

### Subcategories of Studies

Next, we conducted several meta-analyses within subsets of studies. In all of these subsets, the Q-statistic was not significant, indicating that all subsets were homogeneous.

First, we analyzed subsets of studies examining the prevention of specific disorders. Only two disorders were examined in more than two studies (depressive disorder and PTSD; Table 2). The RR of getting a depressive disorder (including postpartum depression) was statistically significant



**FIGURE 1.** RRs and 95% CIs of studies examining the effects of preventive interventions on the incidence of new cases of mental disorders.

(RR = 0.72; 95% CI, 0.54–0.96) in favor of the preventive interventions. The RR of getting PTSD appeared somewhat increased in experimental subjects compared with control subjects (RR = 1.33; 95% CI, 0.75–2.37), but this was not significantly different from 1.

Next, we examined the effects of two types of interventions, cognitive behavioral interventions and debriefing. The seven studies (eight comparisons) examining the effects of cognitive behavioral interventions on depression or anxiety were found to have an RR of 0.69 (95% CI, 0.53–0.89), which was significant. The four studies examining debriefing were the same as the studies examining the effects of prevention of PTSD.

Finally, we examined the effects of two levels of prevention: selective prevention (aimed at high-risk groups) and indicated prevention (aimed at subjects with subclinical symptoms of a mental disorder, without meeting diagnostic criteria for the full-blown disorder). We found that selective prevention resulted in a risk reduction which did not reach significance levels (RR = 0.81; 95% CI, 0.59–1.11). Indicated prevention did result in a significant risk reduction (RR = 0.58; 95% CI, 0.37–0.92).

### Fail-Safe Analyses

We conducted several fail-safe analyses. First, we examined how many studies with no effect (RR = 1) had to be added to the analyses to result in a nonsignificant effect. For all studies together, we had to include 13 studies with an RR of 1 and an average sample size to make the overall effect nonsignificant. For the eight comparisons of cognitive behavioral interventions, another eight studies with an RR of 1 had to be included to result in an overall nonsignificant effect. To make the effects of the five indicated interventions no longer significant, only two studies with no effect had to be added to make the overall RR nonsignificant.

Because the weight of two studies was high (Seligman et al., 1999; Wolchick et al., 2002), we conducted several analyses without these two studies to make sure that the results did not depend too much on these studies. We conducted a meta-analysis of all studies, but excluding one of the studies (Wolchick et al., 2002), and then conducted another meta-analysis, excluding the other study (Seligman et al., 1999). The resulting RRs did not differ very much from the overall RR in which the two studies were included but did not reach significance levels. The overall RR was 0.73; the RR excluding the study by Wolchick et al. (2002) was 0.75 (95% CI, 0.56–1.01), the RR excluding the study by Seligman et al. (1999) was 0.72 (95% CI, 0.52–1.02), and the RR excluding both studies was 0.75 (95% CI, 0.50–1.12).

## DISCUSSION

This study has several limitations. First, the number of studies examining the effects of preventive interventions on

the incidence of mental disorders is relatively small. Also, the studies that were found examined several different interventions and were aimed at several distinct mental disorders. However, surprisingly, the studies that we identified were found to be a homogeneous set of studies with regard to their outcomes (the RRs). These were found to be of approximately the same magnitude. Furthermore, because of the differences in follow-up periods, we calculated the number of new cases over the total follow-up period, assuming that the new cases were evenly distributed over the follow-up period. This is not necessarily the case, of course, and this could have distorted the outcomes. Because of these limitations, the results of this study should be considered with caution.

On the other hand, we did find clear indications that preventive interventions are capable of reducing the incidence of mental disorders. This effect seems to be especially clear in cognitive behavioral interventions aimed at depressive and anxiety disorders. In the examined populations, approximately 12% to 19% of the new cases are prevented. However, these results must be interpreted with caution, because our fail-safe analyses showed that the weight of some studies is large and that the results are no longer significant when these studies are removed. Further studies with sufficient statistical power in this area are certainly warranted.

In our analyses, we found that debriefing did not prevent the onset of PTSDs. Debriefing may even increase the risk of getting PTSS, because the RR we found was larger than 1. Earlier reviews in this field already pointed at this problem (Rose et al., 2002).

Critics may have argued that indicated prevention may not be actual prevention at all, because these symptoms could be part of the prodromal phase of the disorder, and prevention is in fact early intervention in such cases. In this study, we found that the RR of selective prevention was comparable with the RR of indicated prevention. However, the RR of selective prevention did not reach significance levels, whereas the RR of indicated prevention did. This could be related to insufficient statistical power. More research in this area is clearly needed. The question of whether selective prevention is effective is important from an etiological point of view, because this indicates that the process in which a mental disorder is developed can be identified and changed through interventions before the disorder actually develops. From a clinical point of view, there is of course no difference between selective and indicated prevention: any prevented case is important.

An important point is whether the studies in this meta-analysis are representative for the intervention research in the mental illness prevention field. If this is the case, then it could be assumed that the interventions from the broader prevention field could have important effects on the incidence of psychiatric disorders, although this is examined in few randomized trials. However, we think that most of the studies

included in this meta-analysis are not representative of the interventions in the mental health prevention field. What differentiates the indicated prevention studies from other prevention research is the focus on subjects with subthreshold disorders without meeting diagnostic criteria. In our literature searches, we found no other studies aimed at subjects with subthreshold disorders in which subjects with psychiatric disorders were excluded on the basis of a diagnostic interview. The studies on indicated prevention that were included in this meta-analysis can easily be regarded as representatives of a new tradition in prevention research. This is also true for the study by McGorry et al. (2002) on the prevention of first-episode psychosis, which is the first of its kind. However, the studies on PTSD can be considered to represent a larger research tradition on debriefing after traumatic events (Rose et al., 2002), just as the study on children of divorce can be regarded as a typical preventive intervention for children and youths at risk (Durlak and Wells, 1998).

More research in this area is clearly warranted, especially in the promising new tradition of indicated prevention research in which subjects meeting diagnostic criteria for a mental disorders are actually excluded. One area where the results seem most promising is indicated prevention for depressive and anxiety disorders.

In an earlier study, we showed that one of the major problems in this type of prevention research is statistical power, with the huge number of subjects that have to be included and the resulting high costs (Cuijpers, 2003), especially in mental disorders with low incidence rates. Therefore, it is advisable to focus future randomized trials on indicated prevention of common mental disorders in target groups with high incidence rates. These high incidence rates can probably be found among high-risk groups with multiple risk factors. A good example is the study by Clarke et al. (2001), who focused their intervention on adolescent children of depressed parents who had high levels of depressive symptoms themselves.

Undoubtedly, it is encouraging that prevention of new cases of mental disorders seems to be possible. In addition to treatment, prevention may be an important way to reduce the enormous burden of mental disorders in the next decades.

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