Relationships Between Childhood Maltreatment, Adult Health and Psychiatric Outcomes, and Medical Utilization

Bruce A. Arnow, Ph.D.

Childhood maltreatment strongly predicts poor psychiatric and physical health outcomes in adulthood. This overview of the literature shows that individuals who suffer abuse, neglect, or serious family dysfunction as children are more likely to be depressed, to experience other types of psychiatric illness, to have more physical symptoms (both medically explained and unexplained), and to engage in more health-risk behaviors than their nonabused counterparts. The more severe the abuse, the stronger the association with poor outcomes in adulthood. Childhood sexual abuse in particular has been repeatedly associated, in adulthood, with physical complaints such as chronic pain that are likewise associated with depression. Individuals with a history of childhood abuse, particularly sexual abuse, are more likely than individuals with no history of abuse to become high utilizers of medical care and emergency services. Childhood maltreatment is highly prevalent among both men and women, especially in specialty settings such as emergency psychiatric care.

(J Clin Psychiatry 2004;65[suppl 12]:10–15)

hildhood maltreatment is strongly correlated with the later mental and physical health of those who experience it. Child abuse and other forms of maltreatment are significantly associated with a wide range of psychiatric disorders in adulthood including depression, posttraumatic stress disorder, panic disorder, and substance abuse.^{1,2} Numerous studies also show that adults who report suffering maltreatment as children have more physical problems-both medically explained and unexplained-and engage in more high-risk health behaviors than their nonabused counterparts.^{3,4} Childhood sexual abuse (CSA) in particular has been associated with a variety of physical complaints, such as pelvic pain,⁵ headache,6 gastrointestinal symptoms,7 and musculoskeletal pain,8 that are likewise associated with mood disorders, especially depression. Moreover, abused children are likely to become high utilizers of medical care in adulthood.9-11 Inquiry into the sequelae of childhood maltreatment has underlined the high prevalence of this threat to individual and public health.

From the Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, Calif.

Corresponding author and reprints: Bruce A. Arnow, Ph.D. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Rd., Stanford, CA 94305–5722 (e-mail: arnow@stanford.edu).

PREVALENCE OF CHILDHOOD MALTREATMENT

Reported rates of childhood abuse vary depending upon several methodological factors, including the definition of terms (e.g., *childhood* and *abuse*), the survey tactics employed, and the population from which respondents are drawn. Estimates of sexual abuse in retrospective population-based samples range from 8% to 32% for women and 1% to 16% for men. 12 While earlier studies of childhood abuse focused particularly on sexual abuse, research has since expanded to include multiple forms of maltreatment.

In a community sample who responded to mailed questionnaires, 14.2% of men and 32.3% of women reported experiencing sexual abuse (such as unwanted kissing or touching in a sexual way by someone 5 or more years older) before the age of 18 years. ¹³ Physical abuse (such as being hit with a fist, kicked, thrown, burned, or bruised on purpose) was reported by 22.2% of men and 19.5% of women. Approximately 21% of those who had been abused were abused both sexually and physically. Among all respondents, 37% reported either sexual or physical abuse in childhood.

Among a group of male and female primary care patients presenting for treatment and queried about a history of physical, sexual, or emotional abuse, 44% of the sample reported experiencing any abuse and 22% reported multiple types of abuse. As in the findings of Briere and Elliott, significantly more females than males reported a history of sexual abuse, while rates of reported physical

This article is derived from the teleconference "Recognizing the Physical Symptoms of Depression," which was held March 16, 2004, and supported by an unrestricted educational grant from Eli Lilly and Company. Corresponding author and reprints: Bruce A. Arnow, Ph.D.,

abuse were similar for both genders. In a sample comprising women enrolled in a health maintenance organization (HMO), 18% reported sexual abuse, 14% physical abuse, and 24% emotional abuse³; with the definition of abuse expanded to include emotional and physical neglect, 43% of respondents met criteria for childhood maltreatment. The highest rates of abuse, however, are reported in psychiatric settings. When female patients at a psychiatric emergency room were asked whether they had experienced sexual abuse (defined as any sexual contact ranging from fondling to intercourse perpetrated by someone 5 or more years older than the subject) or physical abuse (defined as any intentional act by a parent or caretaker that resulted at a minimum in bruises or bleeding) before the age of 17 years, about 53% reported sexual abuse, 42% reported physical abuse, and 26% reported both.¹⁵ In a study examining female psychiatric inpatients, 55% met criteria for multiple types of abuse.¹⁶

Thus, a history of childhood maltreatment is highly prevalent among both men and women. Some evidence suggests that reported rates of sexual abuse are higher among women than men, while reported rates of physical abuse are similar. Given evidence that childhood maltreatment is strongly associated with psychiatric and physical illness, 3-8 as well as with high utilization of medical services, 9-11 it is not surprising that victimization is more prevalent among respondents seeking care in primary, specialty, or emergency care than among those gathered in random community samples.

CHILDHOOD MALTREATMENT AND ADULT PSYCHIATRIC OUTCOMES

Research indicates that childhood abuse or maltreatment, including certain forms of dysfunction within the child's household, are significant risk factors for later psychological symptoms and disorders.

Data from the National Comorbidity Survey,² a nationally representative general population study, indicated a relationship between CSA and the subsequent onset of psychiatric disorders including major depressive disorder (MDD), posttraumatic stress disorder, social phobia, and substance abuse or dependence. Findings revealed that 78% of women and 82% of men who reported sexual abuse in childhood met criteria for at least 1 lifetime psychiatric disorder versus 49% and 51%, respectively, among those who did not report CSA. The odds ratio for lifetime history of depression was 1.8 among both men and women who reported a history of CSA (versus those who did not). Overall, after controlling for other childhood adversities, CSA was found to be significantly associated with 14 mood, substance use, and anxiety disorders in women and with 5 such disorders in men.

In another community study, the Ontario Health Supplement, ¹⁷ a reported history of childhood physical abuse

was significantly associated with lifetime MDD and substance abuse/dependence among women. A history of CSA among women was associated with significantly higher rates of all disorders examined including MDD, any anxiety disorder, alcohol abuse/dependence, illicit drug abuse/dependence, and antisocial behavior. Among males, childhood physical abuse was associated with significantly higher rates of all of these except MDD and illicit drug abuse/dependence, while CSA was associated with significantly higher lifetime rates of alcohol abuse/dependence.

Adversities such as sexual abuse frequently occur in the context of other types of childhood maltreatment. Co-twin studies, which permit comparisons of twin pairs who may be discordant for specific types of abuse, provide an opportunity to estimate associations between abuse while controlling for other adverse family factors. If twin members who are positive for abuse have higher risk of dysfunction compared with their counterparts who are negative, the increased risk may be attributable to the abuse itself as opposed to shared family background factors. In a community study¹⁸ of young adult Australian twins, a history of CSA was associated among female respondents with adverse outcomes including MDD, conduct disorder, alcohol dependence, and social anxiety. The findings for male respondents were similar. Among CSA-discordant twin pairs, those who were positive for CSA including intercourse had significantly greater risk for all adverse outcomes assessed compared with their CSA-negative cotwins, suggesting unique risk associated with CSA beyond other adverse family factors. CSA-positive individuals who did not report intercourse had higher risks than their CSA-negative co-twins only for MDD and social anxiety. In separate analyses, controlling for other adverse family factors such as parental alcohol abuse, conflict, neglect, and physical abuse, the results were similar, indicating again that CSA contributes uniquely to adverse psychiatric outcomes beyond other family factors. In another co-twin study, Kendler and colleagues¹ found that among twins discordant for CSA in which the abuse involved intercourse, the risks for depression, alcohol dependence, and comorbidity of 2 or more psychiatric disorders were significantly higher in the twin positive for CSA.

In a community study specifically focused on the relationship between childhood abuse and risk of adult depression, Wise and colleagues¹⁹ reported that the relative risk of depression, compared with the risk among nonabused individuals, was 2.4 for those with a history of physical abuse, 1.8 for those with a history of sexual abuse, and 3.3 for those with a history of both types of abuse. In a community study using a semistructured interview to assess a variety of abusive experiences in childhood²⁰ as well as present and previous depressive illness, psychological abuse, physical abuse, sexual abuse, neglect, and other forms of childhood maltreatment were strongly associated with lifetime chronic or recurrent depression.²¹

Typically, *abuse* is defined broadly. For example, CSA is frequently defined as unwanted sexual contact of any kind between a child younger than 15 years of age and someone 5 or more years older, but the cutoff age defining *child* has ranged in the research from 12 to 18 years. ^{22,23} In addition to fondling and intercourse, some definitions of sexual abuse have included indecent exposure and sexual threats (e.g., MacMillan et al.¹⁷ and Drossman et al.²⁴); such incidents may have occurred once or scores of times. It therefore makes sense to inquire about dose-response relationships—that is, whether greater severity (e.g., intrusiveness, higher frequency) of abuse or exposure to a greater number of different categories of maltreatment are associated with greater risk of psychiatric or other sequelae in adulthood.

Wise et al.19 reported a linear dose-response relationship between abuse severity (i.e., none, mild, moderate, severe) and lifetime MDD. Additionally, the risk of MDD was highest among women reporting histories of both physical and sexual abuse. Bifulco and colleagues²¹ reported dose-response relationships between abuse severity and chronic or recurrent MDD that were expressed in several ways. Among those reporting psychological abuse in childhood, rates of chronic or recurrent MDD were 83% for those who suffered "marked" abuse, 70% for those who experienced "moderate" abuse, 55% for those who experienced "mild" abuse, and 37% for those who reported little or no abuse. A similar pattern was observed when examining exposures to different types of childhood maltreatment; the greater the number of categories of maltreatment the individual reported, the higher the probability of lifetime chronic or recurrent depression. Further, in a large primary care sample, a dose-response relationship was observed in which the number of different types of maltreatment reported was associated with progressive decrements in mental health scores using a continuous measure.²⁵ In an investigation by Kendler et al., incidents of sexual abuse were separated into types: nongenital (e.g., sexual invitation), genital (e.g., fondling), intercourse, and any sexual abuse. Rates of psychiatric illness tended to increase with the severity of the type of abuse. Intercourse was more strongly associated with each of the psychiatric conditions examined than was any other category of abuse.

The experience of childhood maltreatment is also associated with increased risk of suicide attempts. In a study²⁶ involving more than 1900 women in primary care, sexual or physical abuse in childhood was associated with a significantly higher frequency of attempted suicide in adulthood. Evidence of a significant association between childhood abuse and attempted suicide has also been reported in another primary care sample.¹⁴ In the co-twin study conducted by Nelson and colleagues,¹⁸ the risk of suicide attempt was significantly higher among those with reported CSA history than among those without such his-

tory. Additionally, among discordant twin pairs, CSA-positive twins had significantly higher risk of suicide attempt than did CSA-negative co-twins. Bifulco and colleagues²¹ found significantly higher frequency of suicide attempts among those who reported physical, sexual, or psychological abuse. Additionally, the more categories of such experience reported, the higher the likelihood of suicidal behavior.

Among psychiatric disorders, MDD is most frequently associated with attempted and completed suicide.²⁷ However, the majority of depressed patients do not make suicide attempts. In a study investigating relationships between abuse history and suicide attempts in a sample of adults meeting DSM-III-R criteria for MDD, those reporting a history of childhood sexual or physical abuse were significantly more likely to have attempted suicide than those with no such history.²⁸

Several studies have examined relationships between self-reported abuse history and particular features of depression such as onset and course. Childhood history of abuse is associated with early onset of depression^{29,30} as well as chronic depression.^{31–33} Bernet and Stein³⁴ found that self-reported history of childhood maltreatment was associated with earlier onset of depression, greater number of depressive episodes, and more extensive comorbidity.

Although substantial evidence indicates that abuse history is a risk factor for psychiatric illness, we know little about whether such history affects treatment response. To date, only one study has investigated this question. In a large sample of chronically depressed patients, Keller and colleagues³⁵ reported that combined antidepressant medication and psychotherapy were significantly more effective than either treatment alone. Consistent with the results of many other studies, ^{36–39} the 2 monotherapies were equally effective. However, Nemeroff and colleagues⁴⁰ reanalyzed data from the Keller et al.35 trial and examined whether childhood trauma including parental loss, physical abuse, sexual abuse, and neglect prior to 15 years of age moderated treatment response. They found that those who met criteria for early childhood trauma responded significantly better to psychotherapy than to medication. Moreover, the significant advantage for combined therapy reported by Keller et al.35 was not present among those reporting early childhood trauma. While the inclusion of those with parental loss deviates from other studies in the abuse literature, the finding suggests that this area requires further study.

Overall, the evidence is substantial that childhood maltreatment is a risk factor for a wide range of adult psychiatric sequelae. The more severe the abuse, the stronger the association with psychiatric symptoms in adulthood. Abuse is also associated with more malignant forms of psychiatric illness including suicide attempts, early onset of depressive illness, chronic forms of depression, and increased number of depressive episodes. Prospective

studies are required to determine whether child maltreatment is a risk factor that affects response to standard treatment for those psychiatric disorders, such as MDD, with which it is associated.

CHILDHOOD MALTREATMENT AND ADULT HEALTH OUTCOMES

Physical symptoms, especially chronic and/or diffuse physical pain unrelated to known organic physical illness, are frequent signs of underlying depression. It has been theorized that some physical symptoms are neurochemically linked with depression via the serotonergic and noradrenergic systems⁴¹ and that a history of abuse in child-hood may render the individual less able to control pain or more vulnerable to pain owing to stress-induced pathophysiologic states like hypocortisolism.

Walker and colleagues⁵ studied women with chronic pelvic pain who were undergoing laparoscopy and women with specific but painless gynecological problems (such as infertility) undergoing the same procedure. Both groups were questioned regarding psychiatric diagnoses and history of CSA. The psychiatric interviewers and the gynecologists who examined the results of the laparoscopy were blinded to one another's findings. Laparoscopy revealed organic pathology in an equivalent number of women in each group. However, the women with chronic pelvic pain had statistically significantly higher rates of CSA and current and lifetime MDD. Histories of depression and sexual abuse were roughly 4 and 3 times more common, respectively, in subjects with chronic pain versus those with a specific gynecological condition. Current depression was about 9 times more common among patients with chronic pelvic pain than among those with a specific disorder. Although only 1 pelvic pain patient met the full diagnosis for somatization disorder, pelvic pain patients as a group reported a significantly higher number of somatic symptoms in interview than did comparison subjects. These complaints included gastrointestinal problems, backaches, headaches, weakness, dizziness, and general ill health. These findings led the authors to hypothesize that chronic pelvic pain may be an expression of chronic psychological pain.

Another study⁸ elicited sexual and physical abuse histories from women with fibromyalgia, a condition without known medical explanation, and women with rheumatoid arthritis, which has known medical etiology. Compared to those with rheumatoid arthritis, participants with fibromyalgia reported higher rates of childhood emotional abuse, physical abuse, sexual abuse, and emotional neglect. Data have indicated positive associations between abuse suffered in childhood and other types of functional, as opposed to organic, physical symptoms as well. Talley et al.⁷ concluded that childhood victimization is linked to irritable bowel syndrome and increased health care-

seeking behavior in a general population sample. Golding⁶ found childhood sexual assault to be strongly associated with headache across 5 general population studies.

Childhood maltreatment has also been correlated with behaviors that place the individual's health in jeopardy. In a random sample of women enrolled in an HMO, subjects who had been abused or neglected as children (\leq 17 years of age) were more likely than their peers to report that as adults they frequently drove while intoxicated, frequently had sex without knowing their partner's sexual history, irregularly wore a seatbelt, did not engage in regular exercise, and had a lifetime body mass index above the obesity threshold.³

Other childhood adversities, especially when multiple, can have a deleterious impact on later health and health risk behaviors. In a study by Felitti et al., 4 adult patients who had recently presented for a standard yearly physical by a primary care provider were mailed surveys that probed not only sexual, physical, and emotional abuse but also adverse childhood experiences involving family members within the household: mental illness, imprisonment, substance abuse, or violent treatment of the respondent's mother. Fifty-two percent of respondents reported experiencing at least one of these categories of abuse or household dysfunction in childhood. These data were then compared with measures of health-risk behavior, illness, and other outcomes. Findings suggested a strong and cumulative association between exposure to household dysfunction and later health risks and disease states, including heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease. Compared with subjects who had experienced none, subjects who had experienced 4 or more of the types of adverse childhood experiences queried were 4 to 12 times more likely to report alcoholism, drug abuse, depression, or a suicide attempt in adulthood; 2 to 4 times more likely to be smokers, to have poor self-rated health, to have had sexual intercourse with 50 or more partners, and to have contracted a sexually transmitted disease; and 1.4 to 1.6 times more likely to be physically sedentary and severely obese.

Clearly, childhood maltreatment is associated with later health problems involving both medically explained and unexplained physical symptoms. Additionally, childhood maltreatment is associated with such health risks in adulthood as alcoholism and obesity. Evidence suggests that greater exposure to abuse—or, according to some research, adverse circumstances within the household such as criminality or substance abuse—is associated with a higher frequency of health problems in adulthood.

CHILDHOOD MALTREATMENT, DEPRESSION, AND MEDICAL UTILIZATION

As many as 20% to 30% of patients presenting in primary care settings for treatment have been shown to

suffer from depression and other psychiatric illnesses. 40-46 Moreover, such patients are more likely to present with somatic, as opposed to psychological, symptoms. 47 This may result in unnecessary medical tests and procedures, as well as in delayed or missed diagnosis of psychiatric conditions.

A number of studies focusing on depressed patients have found that they use significantly more medical services than those who are not depressed. In 3 well-done studies, all of which controlled for medical morbidity and used computerized records to assess health care utilization, 48-50 depressed patients were shown to use approximately 1.5 times as many medical services as nondepressed patients. A parallel literature has revealed a relationship between child maltreatment and high utilization of medical services. Walker et al.⁵¹ found that women who reported CSA had higher primary care and total outpatient costs as well as more emergency room visits than women who did not report CSA. Other research10 revealed an interaction whereby those with both a history of CSA and symptoms of depression used significantly more emergency room services than those reporting a history of CSA without depression. Another study found that those with both psychological distress and a history of CSA had significantly more emergency room visits than those with distress only (i.e., no reported history of CSA) or CSA only (i.e., no evidence of psychological distress).¹¹ Finally, those with psychological distress and both sexual and physical abuse in childhood made significantly more visits to the emergency room than those with both distress and CSA, CSA without distress, or distress without CSA.¹¹ This group also had a significantly higher frequency of pain complaints in both emergency and primary care settings. Moreover, among those with distress and CSA, those who also met criteria for physical abuse were found to have significantly higher distress scores, to have suffered more severe forms of sexual abuse per measures like frequency of completed intercourse, and to have suffered more severely on other indices of childhood maltreatment including emotional abuse and emotional neglect. These data suggest a graded relationship between severity of childhood maltreatment, poor psychological outcomes in adulthood, pain complaints, and medical utilization.

CONCLUSION

Childhood maltreatment is a major risk factor for psychiatric conditions and numerous physical symptoms in adulthood. As the severity of childhood maltreatment increases, so does the likelihood of serious dysfunction in adulthood, which can lead to high utilization of medical and emergency care. Adverse childhood experiences are also associated with future health risk behaviors that further complicate adult outcome.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

REFERENCES

- Kendler KS, Bulik CM, Silberg J, et al. Childhood sexual abuse and adult psychiatric and substance use disorders in women: an epidemiological and cotwin control analysis. Arch Gen Psychiatry 2000;57:953–959
- Molnar BE, Buka SL, Kessler RC. Child sexual abuse and subsequent psychopathology: results from the National Comorbidity Survey. Am J Public Health 2001;91:753

 –760
- Walker EA, Gelfand A, Katon WJ, et al. Adult health status of women with histories of childhood abuse and neglect. Am J Med 1999;107: 332–339
- Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. Am J Prev Med 1998:14:245–258
- Walker E, Katon W, Harrop-Griffiths J, et al. Relationship of chronic pelvic pain to psychiatric diagnoses and childhood sexual abuse. Am J Psychiatry 1988;145:75–80
- Golding JM. Sexual assault history and headache: 5 general population studies. J Nerv Ment Dis 1999;187:624

 –629
- Talley NJ, Fett SL, Zinsmeister AR, et al. Gastrointestinal tract symptoms and self-reported abuse: a population-based study. Gastroenterology 1994;107:1040–1049
- Walker EA, Keegan D, Gardner G, et al. Psychosocial factors in fibromyalgia compared with rheumatoid arthritis, 2: sexual, physical, and emotional abuse and neglect. Psychosom Med 1997;59:572–577
- Felitti VJ. Long-term medical consequences of incest, rape, and molestation. South Med J 1991;84:328–331
- Newman MG, Clayton L, Zuellig A, et al. The relationship of childhood sexual abuse and depression with somatic symptoms and medical utilization. Psychol Med 2000;30:1063–1077
- Arnow BA, Hart S, Scott C, et al. Childhood sexual abuse, psychological distress, and medical use among women. Psychosom Med 1999;61: 762–770
- 12. Finkelhor D. Current information on the scope and nature of child sexual abuse. Future Child 1994;4:31–53
- Briere J, Elliott DM. Prevalence and psychological sequelae of selfreported childhood physical and sexual abuse in a general population sample of men and women. Child Abuse Negl 2003;27:1205–1222
- Gould DA, Stevens NG, Ward A, et al. Self-reported childhood abuse in an adult population in a primary care setting: prevalence, correlates, and associated suicide attempts. Arch Fam Med 1994;3:252–256
- Briere J, Woo R, McRae B, et al. Lifetime victimization history, demographics, and clinical status in female psychiatric emergency room patients. J Nerv Ment Dis 1997;185:95–101
- Swett C, Alpert M. Reported history of physical and sexual abuse in relation to dissociation and other symptomatology in women psychiatric inpatients. J Interpers Violence 1993;8:545–555
- MacMillan HL, Flemming JE, Streiner DL, et al. Child abuse and lifetime psychopathology in a community sample. Am J Psychiatry 2001;158:1878–1883
- Nelson EC, Heath AC, Madden PA, et al. Associations between selfreported childhood sexual abuse and adverse psychosocial outcomes. Arch Gen Psychiatry 2002;59:139–145
- Wise L, Zierler S, Krieger N, et al. Adult onset of major depressive disorder in relation to childhood and adolescent violence victimization: a case-control study. Lancet 2001;358:881–887
- Moran P, Bifulco A, Ball C, et al. Exploring psychological abuse in childhood, 1: developing a new interview scale. Bull Menninger Clin 2002;66:213–240
- Bifulco A, Moran P, Baines R, et al. Exploring psychological abuse in childhood, 2: association with other abuse and adult clinical depression. Bull Menninger Clin 2002;66:241–258
- Briere J. Methodological issues in the study of sexual abuse effects.
 J Consult Clin Psychol 1992;60:196–203
- Wyatt GE, Peters SD. Issues in the definition of child abuse in prevalence research. Child Abuse Negl 1986;10:231–240
- 24. Drossman DA, Leserman J, Nachman G, et al. Sexual and physical abuse

- in women with functional or organic gastrointestinal disorders. Ann Intern Med 1990;113:828–833 $\,$
- Edwards VJ, Holden GW, Felitti VJ, et al. Relationship between multiple forms of childhood maltreatment and adult mental health in community respondents: results from the adverse childhood experiences study. Am J Psychiatry 2003;277:1453–1460
- McCauley J, Kern DE, Kolodner K, et al. Clinical characteristics of women with a history of childhood abuse: unhealed wounds. JAMA 1997;277:1362–1368
- Henrikkson MM, Aro HM, Marttunen MJ, et al. Mental disorders and comorbidity in suicide. Am J Psychiatry 1993;150:935–940
- Brodsky BS, Oquendo M, Ellis SP, et al. The relationship of childhood abuse to impulsivity and suicidal behavior in adults with major depression. Am J Psychiatry 2001;158:1871–1877
- Bifulco A, Brown GW, Moran P, et al. Predicting depression in women: the role of past and present vulnerability. Psychol Med 1998;28:39–50
- Young EA, Abelson JL, Curtis GC, et al. Childhood adversity and vulnerability to mood and anxiety disorders. Depress Anxiety 1997;5: 66–72
- Brown GW, Moran P. Clinical and psychosocial origins of chronic depressive episodes, 1: a community survey. Br J Psychiatry 1994;165: 447–452
- Brown GW, Harris TO, Hepworth C, et al. Clinical and psychosocial origins of chronic depressive episodes, 2: a patient enquiry. Br J Psychiatry 1994;165:457–465
- Zlotnick C, Ryan CE, Miller IW, et al. Childhood abuse and recovery from major depression. Child Abuse Negl 1195;19:1513–1516
- Bernet CZ, Stein MB. Relationship of childhood maltreatment to the onset and course of major depression in adulthood. Depress Anxiety 1999;9:169–174
- Keller MB, McCullough JP, Klein DN, et al. Comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. N Engl J Med 2000;342:1462–1470
- Rush AJ, Beck AT, Kovacs M, et al. Comparative efficacy of cognitive therapy and pharmacotherapy in the treatment of depressed outpatients. Cognit Ther Res 1977;1:7–37
- Murphy G, Simons AD, Wetzel RD, et al. Cognitive therapy and pharmacotherapy: singly and together in the treatment of depression. Arch Gen Psychiatry 1984;441:33–41

- Hollon SD, DeRubeis RJ, Evans MD, et al. Cognitive therapy and pharmacotherapy for depression: singly and in combination. Arch Gen Psychiatry 1992;49:774

 –781
- DeRubeis RJ, Gelfand LA, Tang TZ, et al. Medication versus cognitive behavior therapy for severely depressed outpatients: meta-analysis of 4 randomized comparisons. Am J Psychiatry 1999;156:1007–1013
- Nemeroff C, Heim C, Thase M, et al. Differential responses to psychotherapy versus pharmacotherapy in patients with chronic forms of major depression and childhood trauma. Proc Natl Acad Sci U S A 2003;100:14293–14296
- Greden JF. Physical symptoms of depression: unmet needs. J Clin Psychiatry 2003;64(suppl 7):5–11
- Barrett JE, Barrett JA, Oxman TE, et al. The prevalence of psychiatric disorders in a primary care practice. Arch Gen Psychiatry 1988;45: 1100–1106
- Goldberg D. Detection and assessment of emotional disorders in a primary care setting. Int J Ment Health 1979;8:30–48
- Olfson M, Fireman B, Weissman M, et al. Mental disorders and disability among patients in a primary care group practice. Am J Psychiatry 1997;154:1734–1740
- Schulberg HC, Burn BJ. Mental disorders in primary care: epidemiologic, diagnostic, and treatment research directions. Gen Hosp Psychiatry 1988; 10:79–87
- Spitzer RL, Williams JB, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care: the PRIME-MD 1000 study. JAMA 1994:272:1749–1756
- Bridges KW, Goldberg DP. Somatic presentation of DSM-III psychiatric disorders in primary care. J Psychosom Res 1985;29:563–569
- Simon GE, VonKorff M, Barlow W. Health care costs of primary care patients with recognized depression. Arch Gen Psychiatry 1995;52: 850–856
- Henk H, Katzelnick DJ, Kobak KA, et al. Medical costs attributed to depression among patients with a history of high medical expenses in a health maintenance organization. Arch Gen Psychiatry 1996;53:899–904
- Untitzer J, Patrick DL, Simon G, et al. Depressive symptoms and the cost of health services in HMO patients aged 65 and older: a 4-year prospective study. JAMA 1997;277:1618–1623
- Walker EA, Unutzer J, Rutter C, et al. Costs of health care use by women HMO members with a history of childhood abuse and neglect. Arch Gen Psychiatry 1999;56:609–613