

WAS IT SHOWN THAT "CLOSE RELATIONSHIPS AND EMOTIONAL PROCESSING PREDICT DECREASED MORTALITY IN WOMEN WITH BREAST CANCER?" A CRITIQUE OF WEIHS ET AL. (2008)

The title of Weihs et al. (1) declares the finding that "Close relationships and emotional processing predict decreased mortality in women with breast cancer." Yet, upon inspection, the results of their modest study show nothing of the kind. Analyses mustered in support of this conclusion violate well-articulated statistical recommendations, including excellent advice published in this journal for the use and interpretation of regression analyses (2).

The authors cited Brown et al. (3) in hypothesizing that *lower* emotional distress predicts shorter survival. However, that study similarly utilized overfitted regression equations (2) in a sample in which only 80 deaths were predicted among patients with 15 different tumor sites using 14 predictors, including 7 intercorrelated psychological variables. Moreover, these analyses (3) similarly capitalized on chance in eliminating some variables as predictors of mortality on the basis of preliminary inspections of the data. Brown et al.'s purported findings are an anomaly in a literature characterized by mostly null findings, but nonetheless persistent claims that *higher* emotional distress predicts mortality, based on overly small samples, overfitting of preselected predictors, and a strong prejudice against the null hypothesis (4).

In a sample in which 21 women with breast cancer developed recurrences and 18 died over an 8-year period, Weihs et al. found, contrary to their hypotheses, no association between emotional distress or acceptance of emotions (AE) and mortality or recurrence. However, the two predictors

were correlated, .49, and considering them together, Weihs et al. declared a reciprocal suppressor effect, with both related to mortality, but not recurrence. Pearl (5) and others dismiss such suppressor effects, particularly when not anticipated, as illusory. Weihs et al. construct a seemingly compelling display of their purported reciprocal suppressor effect (their Figure 1) with a 2×3 pseudo-orthogonalization (6) of distress and AE: a dichotomized AE is crossed with a trichotomized emotional distress. Skeptical readers may ask why one independent variable was dichotomized and the other trichotomized, rather than both being treated similarly? Scrutinizing the paper carefully, they will notice that the size of the resulting six cells is small in terms of the number of events (deaths) being predicted. Indeed, only one of the six cells has more than three deaths. Not surprisingly, with the data treated in this way, the results are no longer significant.

Weihs et al.'s claims that a composite measure of close relationships was strongly protective against mortality had the benefit of earlier analyses in which multiple measures of close relationships were examined (7). We seriously doubt that the particular variables entered into the composite measure, as well as the ones the authors chose to exclude, would have been selected a priori. Regardless, the entire exercise is based on capitalization on chance and misuse of statistics with a strong confirmatory bias.

Putting aside overwhelming statistical concerns, one can question whether Weihs et al.'s claims pass a common-sense validity check. Namely, they assert that *each* of three psychosocial variables are associated with an adjusted decrease of 78% or greater in recurrence and mortality, a substantially greater amount than can be attributed to an established composite measure of biomedical risk, the Nottingham Risk

Profile. Are we prepared to accept that the effects of any one or more psychosocial "protective factors" will overwhelm risks of poor outcome attributable to disease severity variables?

Unfortunately, the popular press has already alluded to the Weihs et al. study without a critical appraisal of the appropriateness of analyses and interpretations. The implied message is appealing, even if misleading: women can win a reprieve from breast cancer by accepting and expressing their feelings. Yet, despite the persistence of such claims over almost two decades, no intervention trial has ever found that supportive expressive therapy prolongs survival in metastatic breast cancer, (8) and a recent large scale study found an absence of even psychological benefits for early breast cancer (9). Vulnerable patients may be listening and will be misled by Weihs et al.'s claims, quite aside from the paper being a poor model for other researchers seeking to find statistical significance in null findings.

JAMES C. COYNE, PhD
Behavioral Oncology Program
Abramson Cancer Center and
Department of Psychiatry
University of Pennsylvania
Philadelphia, PA

BRETT D. THOMBS, PhD
Department of Psychiatry
McGill University and Sir
Mortimer B. Davis-Jewish
General Hospital
Montreal, Quebec, Canada

REFERENCES

1. Weihs KL, Enright TM, Simmens SJ. Close relationships and emotional processing predict decreased mortality in women with breast cancer: Preliminary evidence. *Psychosom Med* 2008;70:117-24.
2. Babyak MA. What you see may not be what you get: A brief, nontechnical introduction to overfitting in regression-type models. *Psychosom Med* 2004;66:411-21.
3. Brown KW, Levy AR, Rosberger Z, Edgar L. Psychological distress and cancer survival: A follow-up 10 years after diagnosis. *Psychosom Med* 2003;65:636-43.

4. Coyne JC, Pajak TF, Harris J, Konski A, Movsas B, Ang K, Watkins Bruner D. Emotional well-being does not predict survival in head and neck cancer patients: A Radiation Therapy Oncology Group study. *Cancer* 2007;110:2568–75.
5. Pearl J. *Causality: Models, Reasoning and Inference*. Cambridge, England: Cambridge University Press; 2000.
6. Humphrey LG, Fleishman A. Pseudo-orthogonal and other analysis of variance designs involving individual-differences variables. *J Educ Psychol* 1974;66:464–72.
7. Weihs KL, Simmens SJ, Mizahi J, Enright TM, Hunt ME, Siegel RS. Dependable social relationships predict overall survival in stages II and III breast carcinoma patients. *J Psychosom Res* 2005;59:299–306.
8. Coyne JC, Stefanek M, Palmer SC. Psychotherapy and survival in cancer: The conflict between hope and evidence. *Psychol Bull* 2007;133:367–94.
9. Classen CC, Kraemer HC, Blasey C, Giese-Davis J, Koopman C, Palesh OG, Atkinson A, DiMiceli S, Stonisch-Riggs G, Westendorp J, Morrow GR, Spiegel D. Supportive-expressive group therapy for primary breast cancer patients: a randomized prospective multicenter trial. *Psycho-Oncology* 2008;17:438–47.

RESPONSE

Drs. Coyne and Thombs ignored the words “Preliminary Evidence” when referring to the title of our paper: “Close relationships and emotional processing predict decreased mortality in women with breast cancer: Preliminary evidence.” (1) We disagree with their claim that our results show “nothing of the kind.” The study was designed with a priori hypotheses, which were included in the grant application for the project K20 MH00906, as well as in the paper. Thus, even though the sample size is modest, the findings contribute to the literature on the potential influence of emotion expression and social support on breast cancer progression.

Our study design and data analyses to test the hypothesis that acceptance and acknowledgement of distress would have a salutary effect on breast cancer progression, were based on an emotion processing model, informed by basic emotion research, as well as by studies of cancer patients in which suppression of emotion was associated with increased breast cancer mortality (1). Coyne and Thombs objected to our citation of Brown et al. (2) in support of decreased distress being associated with cancer progression. We acknowledge

that the multiple, intercorrelated psychological variables in the Brown et al. study make the results questionable. However, there are several other studies cited in our paper that lend support to our hypothesis (3–6). We agree that the persistent claims that higher emotional distress predicts mortality are not supported by theory or data, and we present our model as an alternative for understanding a possible link between *decreased* emotional processing and breast cancer progression.

We tested the effect of a confiding marital relationship on disease outcomes and found a significant effect on recurrence and mortality, which is illustrated in Figure 2 in our paper (1). At the request of reviewers, we added data from our previous paper on increased dependable non-household supports (7) as predictors of morality in the later manuscript. It was necessary to use a combined variable for the effect of close relationships in the overall model for testing the effects of both emotional processing and close relationships on recurrence and mortality, as our small sample did not allow for more than three predictor variables in one survival analysis.

Regarding Coyne and Thombs’ concern about the illustration of the suppressor effect, our purpose in adding this to the manuscript was to clarify the effects of this phenomenon for readers for whom it may be unfamiliar. It is well accepted that making categories out of continuous data decreases the power and the validity of analyses, and therefore the multiple regression showing the suppressor effect is the main indicator of the significance of this finding in our data. We added the categorical analysis to accompany the figure, for the sake of completeness, and we acknowledge that the model was not statistically significant when analyzed using the categorical rather than the continuous measures for examining the combined effects of distress and emotional acceptance on outcomes.

Coyne and Thombs’ letter is wrong in stating that we claim our results show an adjusted decreased risk of 78% or greater in recurrence and mortality in

relation to each psychosocial variable. The relative risk reduction for each change in one standard deviation (SD) of the psychosocial variables ranged from $RR = 0.31$ to $RR = 0.46$. This reflects a reduced risk of $1 - RR$, yielding a reduction in risk of 54% to 69% associated with one SD increase in the psychosocial variable. It is important to note the confidence interval for each relative risk reported in our results, within which we can be 95% confident to find the *actual* risk associated with a given predictor variable for the entire population of subjects from whom the sample was drawn. The confidence intervals are wide (with risk reduction of 1% to 90% for the range of individual psychosocial variables tested) since our sample was relatively small, hence our claim that this evidence is preliminary. Coyne and Thombs compare the risk associated with the disease severity indicator to that associated with the psychosocial variables. A one standard deviation increase in the disease severity variable was associated with a 60% increased risk of mortality, with a confidence interval of 5% and 141% increase in risk. Therefore, our data do not show a greater change in risk associated with the psychosocial variables than with the disease severity variable.

Coyne and Thombs’ critique of our report repeats an error from another of their publications, (8) which was pointed out by Spiegel and Kraemer (9) who wrote “They confound hypotheses regarding whether psychotherapeutic interventions promote survival, and the idea that baseline emotion processing and close relationships predict survival.” The data for our study were collected from 90 breast cancer patients, who contributed their time with the understanding that the knowledge gained might improve the well being of other women with breast cancer. Despite the risk that scientific data can be misinterpreted, we stand by our conviction that these results make a worthwhile contribution to the overall goal of understanding potential psychosocial influences on breast cancer progression.

LETTERS TO THE EDITOR

KAREN L. WEIHS, MD
Department of Psychiatry
University of Arizona
Tucson, AZ

TIMOTHY M. ENRIGHT, PhD
Psychiatry and Behavioral Sciences
The George Washington University
Washington, DC

SAMUEL J. SIMMENS, PhD
Epidemiology and Biostatistics
The George Washington University
Washington, DC

REFERENCES

1. Weihs KL, Enright TM, Simmens SJ. Close relationships and emotional processing predict decreased mortality in women with breast cancer: Preliminary evidence. *Psychosom Med* 2008;70:117–24.
2. Brown KW, Levy AR, Rosberger Z, Edgar L. Psychological distress and cancer survival: A follow-up 10 years after diagnosis. *Psychosom Med* 2003;65:636–43.
3. Dean C, Surtees PG. Do psychological factors predict survival in breast cancer? *J Psychosom Res* 1989;33:561–9.
4. Cassileth BR, Walsh WP, Lusk EJ. Psychosocial correlates of cancer survival: a subsequent report 3 to 8 years after cancer diagnosis. [See comment]. *J Clin Oncol* 1988;6:1753–9.
5. Jensen MR. Psychobiological factors predicting the course of breast cancer. *J Pers* 1987;55:317–42.
6. Reynolds P, Hurley S, Torres M, Jackson J, Boyd P, Chen VW. Use of coping strategies and breast cancer survival: results from the Black/White Cancer Survival Study. *Am J Epidemiol* 2000;152:940–9.
7. Weihs KL, Simmens SJ, Mizrahi J, Enright TM, Hunt ME, Siegel RS. Dependable social relationships predict overall survival in stages II and III breast carcinoma patients. *J Psychosom Res* 2005;59:299–306.
8. Coyne JC, Pajak TF, Harris J, et al. Emotional well-being does not predict survival in head and neck cancer patients: A Radiation Therapy Oncology Group study. *Cancer*. 2007;110:2568–75.
9. Spiegel D, Kraemer HC. Correspondence: Emotional well-being does not predict survival in head and neck cancer patients: A Radiation Therapy Oncology Group study. *Cancer*. 2008;112:2326–7.

SELECTIVE SOUND INTOLERANCE AND EMOTIONAL DISTRESS: WHAT EVERY CLINICIAN SHOULD HEAR

We report two cases of selective sound intolerance associated with intense emotional distress and functional impairment. To our knowledge, there have not been any previous cases of this

nature documented in the psychiatric literature.

Case 1 – Over the course of 4 to 5 months, a 13-year-old girl became increasingly unable to tolerate the sounds of people licking their lips, eating, and speaking. This decreased sound tolerance was accompanied by intense feelings of anxiety and avoidant behavior. She experienced intrusive images of mouths, and urges to mimic the distressing sounds resulting in repetitive lip movements and mouth-smacking noises. As a consequence, she experienced a rapid decline in social function, and was no longer able to attend school or participate in family and social activities. She had no previous psychiatric history and was otherwise healthy. She reported some additional mild obsessive-compulsive symptoms such as checking. There were no inciting stressors or illnesses identified. Medical work-up, including hearing assessment and computed tomography scan of the head, was normal. Relaxation techniques and a trial of fluoxetine provided some symptomatic improvement and decrease in distress, although she currently remains out of school. Exposure therapy to stereotyped distressing sounds was limited by noncompliance.

Case 2 – A 25-year-old woman presented with intense emotional distress precipitated by the sounds of people eating, speaking, or picking their nails. This began when she was 12 years old and has persisted without remission over the past 13 years. Triggering stimuli have increased over time to include visual images (e.g., lips moving). Although she endorsed some mild premorbid obsessive-compulsive behaviors, there was otherwise no clear evidence of mental illness prior to the onset of decreased sound tolerance. She was subsequently diagnosed with panic disorder, social phobia, body dysmorphic disorder, mixed personality disorder, and marijuana abuse, although her primary complaint remained sound sensitivity. Medical workup, including hearing assessment, was normal. During two hospitalizations of several months she showed

minimal response to trials of antidepressants, typical and atypical antipsychotics, anxiolytics, stimulants, and mood stabilizers. Exposure therapy was limited by noncompliance and perceived lack of benefit. Treatment with sound generators also showed no therapeutic effect.

The etiology of the selective sound intolerance in these young women is unclear. One potential model to understand this is found in the audiology and otolaryngology literature where the term “misophonia” has been used to describe a condition of decreased sound tolerance(1). Misophonia is said to arise in individuals with normal hearing or, more commonly, in the context of hyperacusis or tinnitus, with one center reporting misophonia in 60% of its tinnitus patients(2). Both misophonia and tinnitus are postulated to result from similar mechanisms by which abnormal activation of limbic and autonomic systems occurs with benign sounds. This sets up a conditioned negative response cycle with hypervigilance and increasing emotional distress, similar to a number of the functional somatic syndromes in other systems of the body. Recommended treatment includes tinnitus retraining therapy, which involves a systematic conditioning paradigm that shares aspects of cognitive behavioral therapy(1).

Another potential model for understanding these two cases is as an obsessive-compulsive disorder spectrum illness. In both cases, the egodystonic repetitive preoccupation with sounds as well as the associated intrusive images of lips and mouths appear phenomenologically similar to obsessions. The younger patient also had urges to mimic the sounds resulting in repetitive lip smacking, which could be seen as a compulsion. In support of this model, both patients also disclosed obsessive-compulsive symptoms unrelated to their sound sensitivity.

Although we could find no mention of selective sound intolerance in the psychiatric literature, search of the World Wide Web revealed an online support group of over 600 members

for people with selective sound sensitivities suggesting this condition is more common than previously recognized (<http://health.groups.yahoo.com/group/Soundsensitivity/>).

Clinicians not familiar with this poorly understood condition may misdiagnose such patients, or worse, be unwittingly dismissive of their complaints. For instance, the patient in the second case described having her complaints of sound sensitivity attributed by multiple physicians to personality-related behaviors. However, it is worth highlighting that neither of these two patients experienced any functional impairment prior to the onset of their decreased sound tolerance.

Our two cases reported herein are intended to alert clinicians to selective

sound intolerance and its associated emotional distress and functional impairment. Research clarifying the phenomenology, pathophysiology, prevalence, and treatment of this putative condition is in order.

GEORGE HADJIPAVLOU, MD, MA
Department of Psychiatry
University of British Columbia
Vancouver, BC, Canada

SUSAN BAER, MD, PhD
Department of Psychiatry
British Columbia Children's
Hospital and University of
British Columbia
Vancouver, British Columbia,
Canada

AMANDA LAU
Department of Medicine
University of British Columbia
Vancouver, British Columbia,
Canada

ANDREW HOWARD, MD
British Columbia Neuropsychiatry
Program and University of
British Columbia
Vancouver, British Columbia,
Canada

REFERENCES

1. Jastreboff PJ, Jastreboff MM. Tinnitus retraining therapy for patients with tinnitus and decreased sound tolerance. *Otolaryngol Clin N Am* 2003;26:321-36.
2. Jastreboff PJ, Jastreboff MM. Tinnitus retraining therapy: a different view on tinnitus. *Otolaryngology* 2006;68:23-30.