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## Evaluating the Effectiveness and Implementation of Evidence-Based Treatment: A Multisite Hybrid Design

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### Abstract

The gap between treatment development and efficacy testing to scaled up implementations of evidence base treatment (EBT) is an estimated 20 years, and hybrid research designs aim to reduce the gap. One was used for a multisite study in cancer control, testing co-primary aims: 1)

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determine the feasibility and utility of a flexible EBT implementation strategy, and 2) determine the clinical effectiveness of an EBT as implemented by newly trained providers. Therapists from 15 diverse sites implemented the biobehavioral intervention (BBI) for cancer patients (N=158) as part of standard care. For implementation, therapists determined treatment format, number of sessions, etc. and reported session-by-session fidelity. Patients completed fidelity and outcome assessments. Results showed therapists BBI implementation was done with fidelity, e.g., session “dose” (59%), core content coverage (60–70%), and others. Patient reported fidelity was favorable and comparable to the BBI efficacy trial. Effectiveness data show the primary outcome, patients’ scores on the Profile of Mood States total mood disturbance, significantly improved ( $R^2=0.06$ ,  $\beta=-0.24$ ,  $p < 0.01$ ) as did a secondary outcome, physical activity ( $R^2=0.02$ ,  $\beta=0.13$ ,  $p < 0.05$ ). This first use of a hybrid design in health psychology provided support for a novel strategy that allowed providers implementation flexibility. Still, the EBT was delivered with fidelity and in addition, therapists generated novel procedures to enhance setting-specific usage of BBI and its ultimate effectiveness with patients. This research is an example of translational research spanning theory and efficacy tests to dissemination and implementation.

### Keywords

Hybrid design; evidence based treatment; clinical effectiveness; implementation

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### Introduction

In an Institute of Medicine report, *Crossing the quality chasm: A new health system for the 21st century* (Institute of Medicine, 2001), the lag time in translation between research to health care practice implementation was estimated to be 20 years, due to the failure to move treatment development and testing to scaled up implementations. Bridging the chasm is challenging as an analysis of contributory factors suggests. A key one is separateness of two research traditions. In clinical research, progress is linear, from efficacy to effectiveness studies, with the latter focus on generalizability of the treatment to other patient groups, locales of treatment delivery being in “the real world,” and evidence that the treatment, even with these transitions, can still achieve clinical (patient) and other (quality of life, cost reduction) outcomes. Quite apart is the domain of implementation, which assumes treatment effectiveness and focuses instead on treatment delivery, i.e., its fidelity and the generality of adoption among providers or in systems of care, including the discovery of facilitating and inhibiting factors at each level. “Pure forms” of each differ in the role of randomization, the unit of analysis, the nature of the intervention, and the measured outcomes. The respective contributions are relevant to the other but are mainly nonoverlapping, and notions of adjusting clinical research aims/designs to those of implementation (or vice versa) has been likened to “adapting square pegs to fit in round holes” (Onken, Carroll, Shoham, Cuthbert, & Riddle, 2014, p. 25). However, one pathway across the chasm may be a *blending* of each research tradition, thereby achieving more effective implementations and more rapid translation.

An effectiveness-implementation hybrid design as described by Curran, Bauer, Mittman, Pyne, and Setler (2012) is one with, a priori, a dual focus. Three types have been described,

with the type 1 hybrid testing effects of a clinical intervention on patient outcomes while observing and gathering information on implementation and type 3 testing an implementation strategy in terms of reach, acceptance, implementation, and sustainability (Glasgow, Vogt, & Boles, 1999), for example, while secondarily gathering information on the intervention's patient outcomes. That used here, type 2, is a dual testing of a clinical intervention *and* an implementation strategy to support rapid translation. For a clinical intervention test, at least 1 outcome is measured and at least 1 hypothesis is examined. Regarding the implementation test, it assesses adoption of the clinical treatment and the fidelity of doing so. The test is conducted under a pragmatic set of conditions (rather than under "best" or "worse" case scenarios) to provide more valid estimates of clinical effectiveness.

### Translational Discovery Leading to the Hybrid Design

Science leading to the described study is depicted in Fig. 1. This figure considers models of Khoury et al. (2010) and Onken et al. (2014). Boxes represent empirical efforts and pathways represent theory.

Box A: Scientific discovery (Andersen, Goyal, Westbrook, Bishop, & Carson, 2017).

Studies conducted worldwide have documented the stress and quality of life disruption of cancer. Our work has highlighted an often-unrecognized aspect, i.e., cancer stress promotes a cascade of negative sequelae – some biologic, others behavioral – which, in turn, have their own negative consequences and impact the "whole cancer patient"

Path T1: Biobehavioral model of cancer stress and disease course (Andersen, Kiecolt-Glaser, & Glaser, 1994). A theory (see Fig. 2) conceptualized cancer stress and the accompanying biobehavioral responses leading to their hypothesized relationship to disease progression. Briefly, *stress* and *depressive symptoms* peak at diagnosis, they are accompanied by biologic changes (Andersen et al., 1998), and, if continued, *quality of life* declines (Golden-Kreutz et al., 2005). Negative *health behaviors* (e.g., alcohol use, smoking) may increase with stress (e.g., Armeli, Todd, & Mohr, 2005) and intensify its physiologic effects (e.g., Díaz et al., 2002). Stress is a correlate of poor *treatment compliance* (e.g., Arrieta et al., 2013); patients becoming clinically depressed are more likely to discontinue treatment or die from it (e.g., Loberiza et al., 2002). *Central nervous system (CNS) and neuroendocrine pathways leading to immunity* are hypothesized. Stress and negative affect can contribute to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis (Thornton, Andersen, & Blakely, 2010) and decreased cellular immunity (Thornton, Andersen, Crespín, & Carson, 2007). Innate immune processes play a role in both cancer and depression and are thus also included. Systemic inflammation occurs when cancer cells are identified as foreign and/or when the tumor itself releases proinflammatory cytokines (Coussens & Werb, 2002). Even after the tumor is removed, inflammation can be triggered by adjuvant treatments, and inflammation predicts increased risk of recurrence and cancer death (Molica et al., 2002; Shankar et al., 2006). Regarding depression, several studies have demonstrated that depressed cancer patients show innate immune activation (e.g., Irwin & Miller, 2007). Considering a negative feedback loop (depression ← inflammation), proinflammatory cytokines, including TNF- $\alpha$ , IL-1, and IL-6, interact with CNS pathways to regulate behavior. The latter pathways

may generate “sickness behaviors”(Dantzer, 2009), with neurovegetative signs and affective symptoms (fatigue, pain, sleep problems, cognitive impairment, depression).

Box B1: Test of the biobehavioral model and development of the intervention (Andersen et al., 2004, 2007, 2008, 2010). A RCT was designed to answer the following: “Would receipt of a psychological intervention designed to reduce stress and improve behavioral responses reduce the risk for disease progression?” Newly diagnosed patients (N=227) with Stage II/III breast cancer were randomized to Assessment only or Intervention plus Assessment arms. The model guided the design of a multicomponent biobehavioral intervention [(BBI), i.e., understanding and reducing stress, disease/treatment information, problem solving, assertive communication, social support, body image/sexuality, and health behaviors]. It was delivered in a group format of 18 weekly sessions (intensive phase) followed by 8 monthly sessions (maintenance phase). Trial data showed robust, durable gains across secondary outcomes (i.e., reduced negative mood and physical symptoms, increased social support and health behaviors, more favorable chemotherapy dose intensity) for the Intervention arm in contrast to Assessment only; T cell immunity was also enhanced. The maintenance sessions were important for retaining (and accelerating) patient gains through 12 months. Study of the subgroup of patients with moderate to severe depressive symptoms showed the BBI reduced depressive symptoms but also inflammation (Thornton, Andersen, Schuler, & Carson, 2009). Notably, after a mean of 11 years, the BBI arm had a reduced risk of breast cancer recurrence [Hazard Ratio (HR)=0.55 (95% CI 0.32–.96), p=.034] compared to Assessment only patients. Even for those who did recur, BBI arm patients versus Assessment only patients had significantly improved psychological, social, and immune responses in the 12 months following recurrence diagnosis and a lower risk of breast cancer death [HR 0.35 (95% CI 0.17–0.74), p=0.006].

Box B2: BBI generalizability (Brothers, Yang, Strunk, & Andersen, 2011; Thornton et al., 2014). BBI components have been tailored for high-risk groups. BBI components with Cognitive Behavioral Therapy (CBT) treated cancer patients with major depressive disorder and led to depression remission. BBI components were combined with Hope Therapy and mindfulness to successfully reduce anxiety and improve positive affect and QoL for patients with gynecologic or breast cancer with recurrence.

Path T2: STEPS: Conceptualizing EBT dissemination/implementation (DI; Andersen & Dorfman, 2016). A determinant framework specified the levels of action and means to address the DI gap of EBTs in cancer control. STEPS (Setting, Therapist, Education, implementation and Sustainability; see Fig. 3) is multidimensional (setting, therapist, patient) and multilevel, visually suggesting the increasing effort needed to achieve sustained EBT implementation. In health psychology there are dissemination studies (e.g., Jones et al., 2013), though few data on implementations (Kelly et al., 2000). In cancer control there are isolated studies of dissemination (Clark et al., 2012) and none of implementation (Neta et al., 2015).

Box C. Test of STEPS and BBI dissemination (Brothers et al., 2015). Guided by STEPS, multimodal education was offered from 2011 to 2016 in BBI Institutes to oncology mental health providers. For this, BBI was rebranded as Cancer to Health (C2H)

[[www.cancertohealth.osu.edu](http://www.cancertohealth.osu.edu)] and manuals revised for applicability to newly diagnosed male and female patients with any disease site and < 8<sup>th</sup> grade literacy (reading level). BBI was taught by expert trainers using a combination of lectures (40%), role play and group discussions (35%), practice experientials (25%), and therapists' "hands on" familiarity with the therapist manual and patient guide book. The trainee group was large (N=128) and professionally and geographically diverse, representing 33 states in the US, Puerto Rico, and foreign countries (Brazil, Israel, Kenya, and Malaysia), with the majority employed in community settings. Evaluations of the training were very positive, and trainees evidenced demonstrable improvements in BBI knowledge and also facility with using the treatment components clinically in analogue assessments. Training generated positive attitudes toward and high self-efficacy to use BBI, with each predicting their intentions to use BBI post Institute.

Box D1: Test of STEPS and BBI implementation, sustainment (Ryba, Brothers, & Andersen, 2017). Following the Institutes, therapists received six months of support and guidance to achieve setting readiness. Support focused on four areas: a) adaptation planning, i.e., assisting therapists to determine "fit" of BBI with their patients and setting; b) quality monitoring, i.e., monthly (6) conference calls to review BBI principles, problem solve implementation challenges, and encouragement to use patient reported outcome measures to enable therapists to make data-informed clinical decisions; c) marketing materials, e.g., BBI information sheets; and d) financial, i.e., business plan templates to secure resources for implementation, if needed. Unlike the majority of implementation efforts, no support was provided to the setting/organization; therapists alone were responsible for making BBI happen. Over 75% of therapists participated in the support efforts, with their self-efficacy and positive attitudes toward EBTs continuing to increase. Therapists' BBI usage was impressive; the proportion of therapists' patients treated with BBI ranged from 58–68% across 2-, 4-, and 6-month follow-ups, with additional data showing sustained usage at 12-months (71%). As predicted by STEPS, both therapists' positive attitudes toward BBI and setting factors (supervisors' positive attitudes) were associated with usage.

T3: Understanding implementation at the setting level (Williams, Brothers, Ryba, & Andersen, 2015). During conference calls, therapists described challenges to implementation. Qualitative data suggested themes subsequently labeled as *person* (i.e., attitudes, statements, and behaviors of key individuals) and *environment* (e.g., financial resources). Both factors influenced how easily implementation barriers could be addressed, with person support potentially more important. At the environment/setting level, most barriers could be overcome with more resources, but therapists also reported that some administrations were unable to prioritize funds for any new EBT offering (not limited to BBI), in part due to an economic recession. This information was collected across Institutes and incorporated to enhance trainees' understanding of potential facilitators/barriers and, in turn, help in their generation of solutions.

**Translational summary**—The overarching goal is development and testing of psychological treatments for cancer patients, understanding the mechanisms of their efficacy, and promoting dissemination and achieving wide implementation. Basic research and theory grounded the development and testing of the biobehavioral intervention. Designed for the

newly diagnosed, non-metastatic breast cancer patient and offered in a group format, robust psychological, behavioral, biologic, and disease endpoint effects came from the efficacy trial. Later data showed the clinical effectiveness of BBI components for targeted treatments. The DI data demonstrated that therapists could be reliably educated and clinically trained, empowered with positive attitudes and high intentions to implement, and subsequently show high, sustained, BBI usage.

### A Collaborative Study Using a Type 2 Hybrid Design

A multisite translational study was designed to test the “real world” clinical effectiveness of BBI on cancer patient outcomes and to determine the fidelity of BBI as implemented by newly trained oncology mental health providers from diverse settings. Using a Type 2 Hybrid design, the test was under conducted “medium” complexity circumstances. That is, it was not the “worst” because the therapists had been well trained in the content and processes of BBI usage (see C above) and supported in the earliest months of BBI implementation (see D1 above). But, it was not the “best” circumstance either, as unlike some implementation tests (Greenwald, 2000), the period of implementation support had ended, there was no internal or external support for their conduct of a program evaluation, and no added advantage in the settings, such as accrual capitation, to enroll patients.

To study the clinical effectiveness of BBI, patient reported fidelity and outcome measures previously sensitive to BBI effects were used. These measures, rather than pragmatic ones, enabled direct comparison of findings from the efficacy RCT. The Reliable Change Index (RCI; Jacobson & Truax, 1991) documents the magnitude and reliability of patient improvement. To study implementation, two DI perspectives were considered. The first was Landsverk’s (2013) suggestion that fidelity/integrity be built into the research design by addressing *external validity*. Thus, a multisite design provided diversity of therapists, patients, and economic models of care and geographic locales of settings. To further blend research domains, fidelity as conceived in clinical effectiveness studies was measured: treatment adherence/differentiation and therapist competence and relational. Secondly, Chambers, Glasgow and Srange (2013) suggest the ultimate benefit of an EBT is its ability to “fit” within the setting. Thus, the implementation test used a strategy in which therapists could determine BBI delivery format, sessions conducted, components used, etc. rather than proscribing such as is usually the case.

## METHODS

### Participants

**Sites**—Fifteen facilities in Alabama, California (3), Illinois (2), Indiana, Iowa (2), Kentucky, Maine, Massachusetts, Pennsylvania, and Texas (2) participated. The majority (73%) were in the community [hospitals (n=7, 47%), Cancer Support Community (n=3, 20%), oncology practice (n=1, 7%)], while four (27%) were National Cancer Institute-designated Comprehensive Cancer Centers.

**Therapists**—Therapists (N=15) were mid age ( $M=43.4$  years,  $S.D.=10.3$ , range: 26–62) and included males (n=3) and females (n=12). Professionally, there were doctoral-level

psychologists (n=7, 47%), master's-level social workers (n=6, 40%), a psychology postdoctoral fellow (n=1, 9%), and a master's-level mental health professional (n=1, 9%). They had received their terminal degree 14.3 years previously (*S.D.*=9.2, range: 1–29), had been licensed for 11.8 years (*S.D.*=9.0, range: 1–27), and in their current position an average of 5.6 years (*S.D.*=6.6, range: 0.2–24). All were employed full time and, on average, spent 70% (*S.D.*=22%, range: 30%–100%) of their hours per week in service provision, 18% (*S.D.*=21%, range: 0%–70%) on administrative tasks or meetings, and 7% (*S.D.*=10%, range: 0%–32%) on teaching/supervision.

**Cancer patients**—Across the sites, 158 patients (median=10; range 2–25) were accrued. Patients were middle aged (*M*=53.4 years, *S.D.*=9.9) and primarily Caucasian (85%) and female (87%). They had received a minimum of a high school education (98.7%), and many were employed (47%) with 52% having an annual household income \$75,000, and 87% living in an urban area. Only 51% reported being married. Twelve different cancer sites were represented, with the most common being breast (54%), gynecologic (19%), and colorectal (6%). Extent of disease was local (32%) or regional (46%) rather than distant (13%) or recurrent (13%) and the average time since diagnosis was 2.0 years (*S.D.*=5.7). At baseline, 71% (112) of patients were in treatment or recovering; 28% were post-surgery, 57% receiving chemotherapy, 29% receiving radiation, and 1% received a bone marrow transplant. The remaining 29% (46) had completed treatment longer than 6 months previously; of these, 20% had received chemotherapy, 20% radiation, and 1% bone marrow transplant.

## Procedures

Providers learned of the BBI Institutes via national listserves [e.g., APA's Division 12 (Clinical Psychology) and Division 38 (Health Psychology), Association of Oncology Social Workers], the website (cancertohealth.osu.edu), and word of mouth. During the final afternoon of training for Institutes 1–5, providers (N = 128) learned of the ongoing Cancer to Health Implementation (C2H-I) study. Described as a program evaluation of BBI, therapists learned that a C2H-I Data Coordinating Center (DCC) at The Ohio State University would administer the study and provide the following: 1) A study coordinator to answer questions and provide guidance for accrual, data collection, and related matters. 2) Templates for IRB submission. Settings without a local IRB submitted and had protocols reviewed through the DCC's submission to the Ohio State IRB. 3) BBI marketing materials (e.g. patient brochures). 5) Free patient manuals and relaxation CDs for every patient accrued. 6) A web based (Qualtrics) site for therapist and patient data collection. 7) Within 60 days of completion of data collection, provision of a site-specific summary and de-identified data set.

Therapists were responsible for IRB submission, patient accrual, and providing information to patients to enable completion of study measures. Therapists were required to provide data on BBI components delivered and homework assigned via Qualtrics. Regarding BBI implementation, it was required that BBI be available as part of standard psychosocial offerings in the setting. The BBI therapist manuals detailed delivery of 26 sessions (18 weekly intensive, 8 monthly maintenance) in a closed group format. BBI core content was

stress conceptualization, disease information and MD communication, problem solving, assertive communication, and social support. Sexuality, body image, and health behavior (diet, exercise) were also included. The manual detailed component specific coping strategies (e.g., progressive muscle relaxation for stress conceptualization) and homework assignments (e.g., practice relaxation 3–4 times, 20 min. each, per week). Therapists were to assign, monitor, and engage patients sufficiently to achieve patient usage of the strategies at the recommended level. The patient guidebook summarized session content and had work sheets to be completed during sessions.

During training, it was noted that BBI delivery to individuals was acceptable and was, in fact, recommended as a strategy for therapists to become facile with the content and treatment strategies prior to conducting groups. It was made explicit that BBI might require adaptation to a setting/patient group, with examples provided, such as omitting or shortening content areas, providing fewer sessions, altering the order of sessions. It was, however, recommended that any adaptation retain session 1, Stress Conceptualization, and the teaching of progressive muscle relaxation, with CD provision and app versions available. Inclusion of maintenance sessions was strongly recommended.

IRB documents were uniform in describing procedures of patient accrual and assessment. Eligibility criteria were the following: new (initial) diagnosis of invasive cancer, age  $\geq 21$ , and able to give informed consent. Exclusion criteria were the following: estimated survival  $< 2$  years; non-ambulatory; concurrent significant sensory deficit or diagnosis of organic brain syndrome, dementia, mental retardation, or major mental illness (e.g., schizophrenia); and, non-English speaking. Across sites patients seeking psychosocial services were assigned to any available therapist. If BBI was an appropriate treatment for an assigned patient, the therapist considered the inclusion/exclusion criteria. For those meeting criteria and accepting BBI, patients were informed of the program evaluation study. Across sites, 36 patients approached did not consent to participation. If a group was planned, the non-consenting individual was included with others who did consent and participate in the evaluation. Participating patients completed pre/post psychological measures, either using paper/pencil forms (provided by the therapist but mailed to the DCC) or via Qualtrics administration on a secure server. Following every BBI session, therapists completed fidelity measures on Qualtrics.

## Measures

### **Implementation: Fidelity**

**Adherence/differentiation:** For each session, therapists reported the following: 1) Attendance, 2) Format [group (open, closed), individual], 3) Session duration (in minutes), 4) Delivery of each treatment component (yes/no), 5) Delivery/review of homework (yes/no) by component, and 6) delivery of other interventions.

**Competence and relational:** Two measures of therapist competence were used (Andersen, Shelby, et al., 2007). The *Component Usage* asks a patient to report usage of 11 strategies (e.g., progressive muscle relaxation practice) during the last month on a nine-point frequency scale (e.g., 0= *not at all*, 1=*once a month*, 2=*2–3 times per month*, 3=*once per*

week; 4=2–3 times a week, 5=4 per week; 6=5–6 per week; 7=once a day; 8=2 or more times a day). The *Component Evaluation* uses 14-items to assess the helpfulness of BBI components/strategies (e.g., “relaxation practice with tapes”), each rated on a 4-point Likert scale of helpfulness (1=*not at all helpful*, 2=*a little bit*, 3=*moderately*, 4=*very helpful*). The patient/therapist relationship was assessed (Andersen, Shelby, et al., 2007). *Relational/Cohesion* had 2 items for patients to rate a) felt support during treatment and, b) involvement in treatment, each on a 10-point scale ranging from 0=*not at all supported/involved* to 9=*extremely supported/involved*.

**Clinical effectiveness: Patient reported**—Measures sensitive to BBI effects were used. They are reliable, valid, and common to cancer intervention studies (e.g., Antoni et al., 2001).

**Individual difference: Cancer stress:** Interventions may be differentially effective depending on initial distress levels. As previously (Andersen et al., 2004), cancer-specific stress was tested as a covariate of treatment outcome with the Impact of Events Scale (IES; Horowitz, Wilner, & Alvarez, 1979). Using 15 items, patients rate the frequency of intrusive thoughts and avoidant thoughts and behaviors in the previous week on a 5-point Likert scale (0=*not at all* to 4=*often*). Items are summed for a score ranging from 0 to 75. Cronbach’s alpha was 0.86.

**Primary: Emotional distress:** The Profile of Mood States (POMS; McNair, Lorr, & Droppelman, 1971) has 65 items assessing negative mood (e.g., happy, sad) experienced in the last week, rated on a 5-point Likert scale (0=*not at all* to 4=*extremely*). A Total Mood Disturbance Score (TMD) score, ranging from –32 to 200, is calculated by summing the tension-anxiety, depression-dejection, anger-hostility, fatigue-inertia, and confusion-bewilderment subscales and subtracting the vigor-activity subscale. Cronbach’s alpha was 0.92.

**Secondary:** BBI component specific measures were used. 1) *Social support.* The Perceived Social Support from Family (Procidano & Heller, 1983) scale has 20 items assessing support needs fulfilled by one’s family. Items are summed and scores range from 0 to 20. Cronbach’s alpha was 0.70. 2) *Sexual functioning.* The Sexual Experience Scale (Derogatis & Melisaratos, 1979) (one item) assesses global sexual satisfaction on 9-point Likert scale (0=*could not be worse* to 8=*could not be better*). 3) *Physical activity.* The Godin-Shepard Leisure-Time Physical Activity Questionnaire (PAQ; Godin & Shephard, 1985) is a seven-day retrospective measure of leisure-time physical activity. Responses are transformed to metabolic equivalent task (MET) values, i.e., the rate of energy consumption during a specific physical activity. Then, the following health-related categories are used: 2=*active* (< 24 METS), 1=*moderately active* (14–23 METS), 0=*insufficiently active* (<14 METS). 4) *Dietary habits.* The Food Habits Questionnaire (Kristal, Bowen, Curry, Shattuck, & Henry, 1990) has 19 items assessing dietary behaviors, e.g., avoiding fat. Items are scored on a 5-point Likert scale (0=*usually/always* to 3=*rarely* and 4=*not applicable*) and then averaged to provide a total score ranging from 0 to 4, with higher scores indicating greater adherence to a diet lower in fat and higher in fruits and fiber.

## Analytic Strategy

The representativeness of the C2H-I settings, therapists, and patients were compared to BBI Institute data (N=99 sites, N=128 therapists) for contextual analysis. For the primary analyses, data from all sites were merged and checked for anomalies. Descriptive statistics are reported for implementation fidelity. When relevant, data are compared with those from the BBI efficacy RCT. Clinical effectiveness is tested with pre-treatment (baseline) to post-treatment change on patient outcome measures using hierarchical multiple linear (HLM) regression analyses. Assumptions underlying the analyses were checked. The primary outcome was the POMS total mood disturbance, with the Impact of Events scale (IES) tested as a moderator. In hierarchical linear model (HLM) regressions, variables were entered in the following order: (1) baseline IES score; (2) time; and (3) interaction of IES and time in prediction of POMS. The same procedure, excluding the IES, was used for the secondary outcomes. Significance was specified at the 0.05 level. All statistical analyses were conducted using IBM SPSS 22. Additionally, the Reliable Change Index (RCI; Jacobson & Truax, 1991) was used to determine the magnitude and reliability of patient improvement. For it,  $RCI = (x_2 - x_1) / (\sqrt{2(S_E)^2})$ , where  $x_1$  is a patient's pre-treatment score,  $x_2$  is the post-treatment score, and  $S_E$  represents the standard error of measurement of the measure. A significant change is indicated by an improvement of  $RCI \geq 1.96$  on the measure. Finally, for significant clinical outcomes, analyses explored the relationship between change and treatment fidelity.

## RESULTS

### Contextual analysis

**Setting level**—Trainees from five BBI Institutes (N=128) came from 99 different settings. Of them, therapists from 38 sites (38%) expressed interest in participating in C2H-I and 16 (16%) joined. IRB applications were completed an average of 13 months ( $S.D.=9.1$ ) post-Institute; the Data Coordinating Center (DCC) was the IRB of record for 5 sites. Accrual began approximately 3 months ( $S.D.=2.8$ ) later, roughly 1.5 years after completion of training. Of the 16 sites, 15 sites accrued patients and collected data as of March 2017.

**Therapist level**—Of the 128 BBI trainees, 15 became investigators; 5 of the 15 also had BBI trained co-therapists. The 15 represent 12% of the eligible sample. The 15 therapists and 5 co-therapists represented 38% of the full-time oncology therapists (52) employed at these sites. Compared to the trainee group, the C2H-I therapists did not differ in age, years since terminal degree, licensure, duration of current position, discipline, or time spent in clinical work or teaching (all  $p$ 's  $> 0.25$ ). The only significant difference was weekly time spent on administrative tasks ( $t=-2.45$ ,  $df=127$ ,  $p < 0.02$ ), with C2H-I therapists reporting a greater percentage of time per week, 18% ( $S.D.=21\%$ ) versus 9% ( $S.D.=13\%$ ).

**Patient level**—Across sites, 158 patients were enrolled ( $M=10.53$ ). N's by site were as follows: Alabama=15; California A=23; California B=11; California C=8; Illinois A=13; Illinois B=10; Indiana=9; Iowa A=12; Iowa B=11; Kentucky=6; Maine=3; Massachusetts=7; Pennsylvania=3; Texas A=25; Texas B=2). Of the 158, 1 patient was later found ineligible

and 24 left treatment, resulting in 133 (84%) patients completing pre- and post-intervention assessments.

When applying to the BBI Institutes, therapists reported the general characteristics of patients typically treated (Brothers et al., 2015). Comparison of the C2H-I therapists' application data with the C2H-I patients showed no differences in ethnicity or income. However, C2H-I patients were more likely to be female ( $t=2.27$ ,  $df=157$ ,  $p=0.03$ ), Caucasian ( $t=2.02$ ,  $df=157$ ,  $p=0.05$ ), live in an urban area ( $t=-10.21$ ,  $df=155$ ,  $p < 0.01$ ), and have a breast cancer diagnosis ( $t=8.69$ ,  $df=157$ ,  $p < 0.01$ ) than the “average” patient treated by all institute therapists.

### Implementation: Fidelity

**Format**—In the efficacy RCT BBI was delivered in closed groups, i.e., patient entry at session 1 and exit at the end of Maintenance (session 26). In C2H-I, eight sites (53%) conducted closed groups, 5 sites (33%) conducted ‘managed’ open groups, one site (7%) conducted both open and closed groups, and one site conducted individual treatment only (7%). Patients in managed open groups completed 26 sessions as follows: 1) Session 1 was conducted individually. 2) A patient then joined a group as a module was begun (see Table 1 for designation of modules a–d). 3) When a patient completed a–c (regardless of the order), s/he would begin Maintenance (d). At the patient level, 15% received individual treatment, 50% received treatment in “managed” open groups, and 35% received treatment in closed groups.

**Duration**—For the efficacy RCT, BBI was delivered in 18 weekly sessions (intensive) and 8 monthly sessions (maintenance), with each being 90 minutes. As expected, C2H-I individual sessions were <60 minutes whereas group sessions were > 60 minutes. The total number of sessions delivered across sites was 597 ( $Md=35$ , range 2–196; see Table 1). Per site intensive sessions ranged from 3 to 14, with a mean of 10.6 ( $S.D.=2.91$ ;  $Md=11.1$ ). The duration of individual sessions (196 delivered) averaged 39 minutes ( $S.D.=14$ ,  $Md=40$ , range 10–60), open group sessions (279 delivered) averaged 86 minutes ( $S.D.=12$ ,  $Md=90$ , range 19–105), and closed group sessions (122 delivered) averaged 92 minutes ( $S.D.=14$ ,  $Md=90$ , range 15–120). Ten sites (67%) included maintenance, with a mean of 2.8 sessions ( $S.D.=1.78$ ) and a median of 2.75. In comparison to the BBI RCT, C2H-I BBI was implemented with 59% and 23% of the number of intensive and maintenance sessions, respectively.

**Content delivery**—For the BBI RCT, BBI Session 1 provided a conceptualization for the stresses of cancer and introduced progressive muscle relaxation, and it was recommended that C2H-I implementations begin with this key session. The remaining core components are information and communication, problem solving, assertive communication, and social support. In C2H-I, core topics were delivered to roughly 60–70% of the patients treated with BBI (see Table 1). Fewer patients, 50–56%, were provided coverage of sexuality and health behaviors.

For the BBI RCT, patients were assigned homework at the end of sessions and it was reviewed at the beginning of the following session. In C2H-I, therapists reported delivering

homework in the majority of sessions (67%), an average of 6.24 sessions ( $S.D.=2.73$ , range: 0.00–10.00) of the 10.69 conducted. Eighty nine percent (89%) of patients had at least 1 session in which homework was reviewed. Homework was most frequently included in the core component sessions.

**Therapist competence and relational**—Therapists were responsible for directing patients to use the BBI coping strategies and communicating a level of compliance (see “Component usage – BBI Recommended” column in Table 2). Excepting social support (3.5 vs. 4), patients’ reported usage of core strategies *exceeded the rate* recommended (see Table 2, “Component usage – Reported”). Levels lower than recommended were reported for non-core components: sexuality ( $M=1.91$  vs. 3), indicating that patients used sexuality strategies (2–3 times per month versus the recommended once per week) and dietary strategies to reduce fat ( $M=5.66$  vs. 7) and increase fiber ( $M=5.93$  vs. 7).

Regarding component helpfulness evaluation (rated 0–4; see Table 2), patients found BBI to be very helpful, with a grand mean across components of  $M=3.48$  ( $S.D.=0.71$ ). Components with the highest helpfulness ratings were social support ( $M=3.70$ ,  $S.D.=0.60$ ), stress conceptualization ( $M=3.65$ ,  $S.D.=0.58$ ), and assertive communication ( $M=3.61$ ,  $S.D.=0.61$ ). Even sexuality, with the lowest rating ( $M=3.03$ ,  $S.D.=0.85$ ), was still regarded as moderately helpful. Regarding the therapeutic relationship, patients reported high levels of perceived support ( $M=7.97$ ,  $S.D.=1.47$ ) and high involvement in BBI treatment ( $M=7.52$ ,  $S.D.=1.60$ ).

### Clinical Effectiveness

Time between pre- and post-intervention assessments averaged 17 weeks ( $S.D.=5.5$  weeks). The moderator test revealed baseline IES to independently predict pre-to-post change in the POMS above and beyond the effect of time ( $\beta=0.56$ ,  $p < 0.01$ ), but the interaction of IES and time was not significant ( $R^2 < 0.001$ ,  $\beta=0.01$ ,  $p=0.96$ ). The latter indicates that regardless of initial IES magnitude, patients improved. Previously greater POMS improvements were found for those with initially higher IES scores (Andersen, Farrar, et al., 2007); here, BBI was effective across patients. As predicted, patients reported significant pre- ( $M=39.7$ ) to post-intervention ( $M=22.7$ ) decreases on the POMS ( $R^2=0.06$ ,  $\beta= -0.24$ ,  $p < 0.01$ ). Also, the Reliable Change Index indicated POMS improvement was reliable and significant for 26% of the patients.

For secondary outcomes, there was a significant pre- ( $M=1.39$ ) to post-intervention ( $M=1.52$ ) increase in PAQ physical activity scores ( $R^2=0.02$ ,  $\beta=0.13$ ,  $p < 0.05$ ) with patients reporting being “moderately active” at pre-and “active” at post. No significant pre/post changes ( $ps > 0.06$ ) were found for the remaining secondary measures.

As in the BBI RCT, moderation analyses tested the relationship between component-specific outcomes and strategy usage. Change in POMS was tested with stress conceptualization use and progressive muscle relaxation use, and change in the PAQ was tested with physical activity strategy use. The moderation effects were not significant ( $ps > 0.05$ ).

## Relationship of Clinical Effectiveness and Fidelity

Correlational analyses related POMS change to all fidelity variables and of them, treatment format covaried. POMS scores were correlated with BBI format ( $r=0.25$ ,  $p < 0.05$ ), such that patients in groups reported larger POMS decreases than patients treated individually,  $-16.1$  versus  $-0.1$ , respectively. Further, POMS scores were correlated with group type ( $r=0.22$ ,  $p < 0.05$ ), such that participants from open groups evidenced larger decreases than patients in other treatment formats,  $-18.8$  versus  $-7.7$ , respectively. Similar analyses examined fidelity and physical activity (PAQ) scores, finding that PAQ scores were also correlated with BBI format ( $r=0.24$ ,  $p < 0.05$ ), such that patients in groups reported PAQ increases ( $M=0.15$ ) while patients treated individually reported PAQ decreases ( $M=-0.21$ ). PAQ scores were also correlated with session length ( $r=0.30$ ,  $p < 0.01$ ), such that patients whose BBI sessions lasted longer (i.e., in group treatments) reported greater improvements in PAQ physical activity scores.

## DISCUSSION

The overarching goal to add substantively to both the implementation and clinical effectiveness literatures was achieved. While there are examples of treatment implementations “going to scale” (Kilbourne et al., 2012; Solberg et al., 2015), to our knowledge, this is the first use of a hybrid design in the health psychology DI literature and more generally, it is one of the few studies of adaptation in the context of implementation (Chambers, 2018). A type 2 hybrid design studied co primary aims to determine 1) the feasibility and utility of a flexible EBT implementation strategy, and 2) the clinical effectiveness of an EBT as implemented by newly trained providers. In this study, adaptation was anticipated and planned but not regimented (Bell, Marcus, & Goodlad, 2013). Data detailed the adaptations and showed the BBI to be implemented with fidelity. Sixty to seventy percent of the core content was provided and homework included, with minimal additions of other content or strategies by the therapists. Moreover, data suggest the therapists were competent, with their reports of treatment delivery consistent with patient reports of treatment receipt/usage, which was high. Patients’ satisfaction with BBI was high and they viewed their therapists as competent and supportive. Finally, effectiveness data show significant reductions in patients’ negative moods and for 26% of the sample, the magnitude being significant and reliable.

Conditions under which the type 2 design is best used have been described (Curran et al., 2012). One is having a strong base of indirect evidence for the clinical intervention to be tested. For BBI, efficacy tests showed it to yield robust positive effects which were conceptually replicated with studies of tailored versions. All of the latter, however, came from the same research group with no effectiveness tests by others. Overall, we were aware of the high uptake of BBI (Ryba, et al., 2017), but neither the fidelity of therapists’ implementations nor impact of BBI on patient outcomes was known. Another condition of the type 2 design is conduct when there is “implementation momentum.” Specifically, C2H-I therapists began accrual ten months after their training, consultation for BBI adaptation and addressing barriers, and implementation support (Williams et al., 2015). More broadly, new standards and cancer patient guidelines specified the use of EBTs (e.g., “cognitive change,

biobehavioral strategies... treatments using stress reduction, problem solving, assertive communication”) (Andersen et al., 2014, p. 1610, 1615). Thus, conditions for a Type II study were timely.

The breadth of the fidelity data clarifies the nature of BBI provided, and they show an adapted BBI (i.e., planned or purposeful changes to the design or delivery of the intervention to retain fidelity to fundamental elements) rather than a modified one (i.e., planned or unplanned changes to improve treatment fit, engagement, or effectiveness) (Wiltsey Stirman, Gutner, Crits-Cristoph, Edmonds, Evans, & Beidas, 2015). We use Wiltsey Stirman et al.’s (2017) definition of types of content level modifications. Considering them, the data suggest there was little tailoring (minor alterations), addition or diffusion of non BBI treatments or components, no shortening of session time, no lengthening of number of sessions or time, or no repeating of content not proscribed for such. Instead, what occurred was removal or shortening coverage of non-core components (e.g. health behaviors, maintenance). A novel “real time” adaptation by some therapists occurred, a reordering of BBI components after the foundational session. These data shed light on how the BBI was adapted into routine care, aligning with the growing interest to precisely capture the nature of adaptations of implemented EBTs (Chambers & Norton, 2016).

NIH recommendations to achieve treatment fidelity in implementations (Bellg et al., 2004) were incorporated into the design and conduct of BBI dissemination, support to providers for implementation, and the type 2 study. This included several elements: a) rigorous BBI training, also resulting in therapists having high motivation and intent to implement BBI; b) feedback to therapists on their anticipated adaptations, making clear that drift to non BBI content or strategies would change an empirically supported treatment to one without support; c) problem solving implementation barriers; d) providing manuals and supporting materials for therapists and patients; and, e) implementation support.

A multicomponent assessment of fidelity was used (Schoenwald, et al., 2011), but there is currently no standard metric as to what constitutes implementation with fidelity versus not. Regarding differentiation, the low frequency of “other treatments offered” entries suggested addition of non-BBI content was negligible. Regarding adherence, the modular/component structure of BBI facilitated the fidelity analysis. Importantly, the evidence suggests that the fidelity of BBI implementation was at the least acceptable in overall level, and when compared to BBI RCT data, implemented met or exceeded several benchmarks. Regarding adherence, the core components (specific factors) of BBI had the highest levels of delivery, ranging from 60 to 100% of patients receiving the content. For the non-core content adherence was lower, in the range of 50–56, perhaps driven by specific circumstances. For sexuality/body image, therapists were trained, but for the majority this was unfamiliar content and one that requires considerable practice to achieve facility and comfort with delivery. For health behaviors, it was suggested that dietary and/or exercise personnel could be integrated into the sessions as was done in the RCT. Some delivered the content and others used resource persons and or made referrals. An important element of BBI is in- and out of session activities/homework, but latter are often removed in routine care (Cook, Dinnen, Thompson, Siminola & Schnurr, 2014). Yet, therapists reported delivering homework and reviewing homework in the large majority of sessions. Maintenance is a

novel aspect of BBI and was important to sustaining change; its inclusion was strongly recommended to therapists. While two thirds of the sites offered maintenance, the median number of sessions was one third of the recommended dose. Admittedly, BBI is a lengthy treatment, comparable to some offerings, such as CBT, though not others. Anecdotally suggested, historical circumstances may have also been relevant to the discrepancy between the number of sessions offered (11 intensive) versus sessions manualized (18). Much of the data collection occurred during an economic recession when personnel budgets for psychosocial services became even tighter with some organizations not replacing therapists or pressuring remaining ones to limit session numbers to see more patients.

The therapist fidelity data are very positive and reflect the competence of the therapists and patients' satisfaction with BBI. Importantly, therapists' reports of component delivery (Table 1) and patients' reported usage (Table 2) are consistent. Moreover, patients' reported usage of core strategies typically exceeded the rate recommended for the RTC. Patients viewed the therapists as very supportive and BBI as a very helpful treatment, with the rating virtually identical with those from the RCT (Andersen, Shelby, et al., 2007). Collectively, the fidelity data show BBI is "implementable," but contextually, it is a treatment showing high acceptability, engagement, and satisfaction by therapists and patients. Metrics such as these provide the rationale and data for managers to advocate for service expansion and for settings to expand market share.

The analyses show significant change on the POMS, with large magnitude, reliable mood improvement for 26%. Physical activity changed significantly with time as it did in the BBI RCT. Regarding the latter, 71% of the patients were still receiving cancer treatment at baseline, and maintaining, resuming or beginning physical activity anew during this period is difficult. We do not know, but the gains might have been greater if more maintenance sessions had been included as the RCT showed acceleration of gains during maintenance (Andersen, Shelby, et al., 2007). With the dual aims, we were able to examine the relationship of fidelity and patient outcome data. Multiple aspects of BBI dose [e.g., number of sessions (-.033), minutes attended (-.137), receipt of components (<.001 to .135)] and POMS change showed no relationship, whereas BBI offered in groups was associated with greater gains. In general, research suggests that when compared to the original, adapted protocols show small, if any, differences in effects (e.g., Stirman et al., 2017). We do know, however, if the passage of time accounted any patient improvements.

The study's strengths and weakness are considered. The multiple-dimension heterogeneity of the locales, models of care provision, therapists, and patients are key to the generalizability and implications of the findings. Comparison amongst the latter was not intended nor was it possible because of the variable rates of accrual. Unlike the RCT, therapists came from multiple disciplines, heterogeneous experience levels, included males, and a range of care circumstances. The therapists spent more time per week on administrative tasks than the other Institute attendees, perhaps providing the time to manage study tasks. Unlike the RCT, the patient sample included males, many disease sites, and was geographically diverse. However, these individuals *received* treatment, which few cancer patients do (Owen, Goldstein, Lee, Breen, & Rowland, 2007). While cancer patients with less economic, educational, and other resources were present, they were under represented.

Type 2 hybrid designs test clinical and implementation aims, but a “test” need not be a RCT, and here, two conditions supported the use of a non-randomized Type 2 design. For one, prior efficacy studies showed robust gains with BBI and prior data showed BBI delivery to the majority (60–70%) of providers’ patients, suggesting they would be reluctant to offer a treatment *other than* BBI. Secondly, the implementation strategy—flexible rather than proscribed BBI delivery—was neither complex nor taxing for therapists or settings and was, in fact, an advantageous one to study. Regarding the dual aims, trials can be described in terms of their original intent using the PRECIS-2 metric (PRagmatic Explanatory Continuum Indicator Summary; Loudon et al., 2015). By design, this study was pragmatic in terms of eligibility, recruitment, setting, primary outcome, and primary analysis, but reflected a stronger efficacy orientation in its organization, flexibility in EBT adherence and delivery, and follow-up [See Supplementary Materials]. Regarding clinical effectiveness measures, those from BBI trials were used for explicit comparison. In studies with other purposes, pragmatic measures, such as those recommended in guidelines for the assessment of anxiety and depressive symptoms in cancer patients or those included in the Patient-Reported Outcomes Measurement Information System (PROMIS; see <http://www.healthmeasures.net/explore-measurement-systems/promis>) can be chosen. The fidelity measures reflected current conceptualizations (e.g. Schoenwald et al, 2011). Obtaining additional specifics of the component delivery (e.g., “Was social support from employers, friends, family, partner, and children discussed, as is manualized?”) added burden. However, detail on the nature of EBT adaptations is increasingly important in implementation science (Chambers & Norton, 2016).

In conclusion, models describe stages of intervention development, dissemination, and implementation. The BBI provides one example, moving from theory, RCT and companion studies, inclusion in treatment guidelines, dissemination, implementation, to this study of implementation fidelity and patient outcomes. C2H-I was a partnership with front line providers, which is sorely needed (Cook, 2018), and as such the data sheds light on the implementation adaptations that occur in routine care. These data show that a strategy of therapist/setting-directed implementation can still achieve treatment fidelity, and further, clinically important outcomes for patients in the community. The simultaneous study of the two challenges of disseminating and implementing mental health treatments—training and supporting providers and achieving fidelity and documenting patient outcomes—might lead to the greatest scientific gains in implementation science and clinical effectiveness knowledge, with this study providing one example toward the ultimate goal of impacting the health and well-being of cancer patients at the population level.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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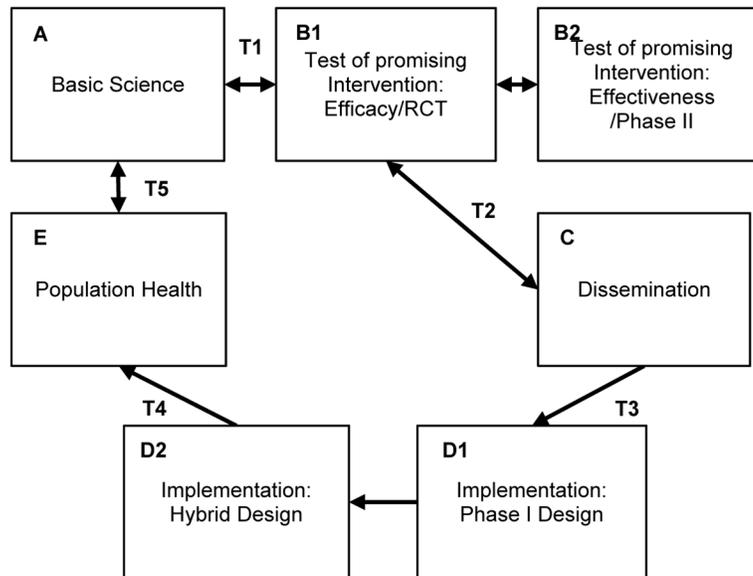
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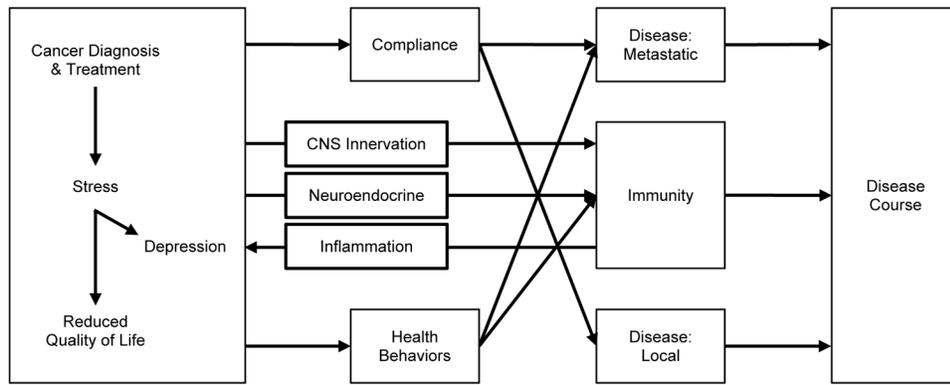
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**Fig. 1.** Translational science discoveries (A–E) and theoretical linkages (T1–T5) leading to improved population health. Discoveries impact (and interact with) other discoveries (e.g., D1 leading to B1) in addition to those specified.



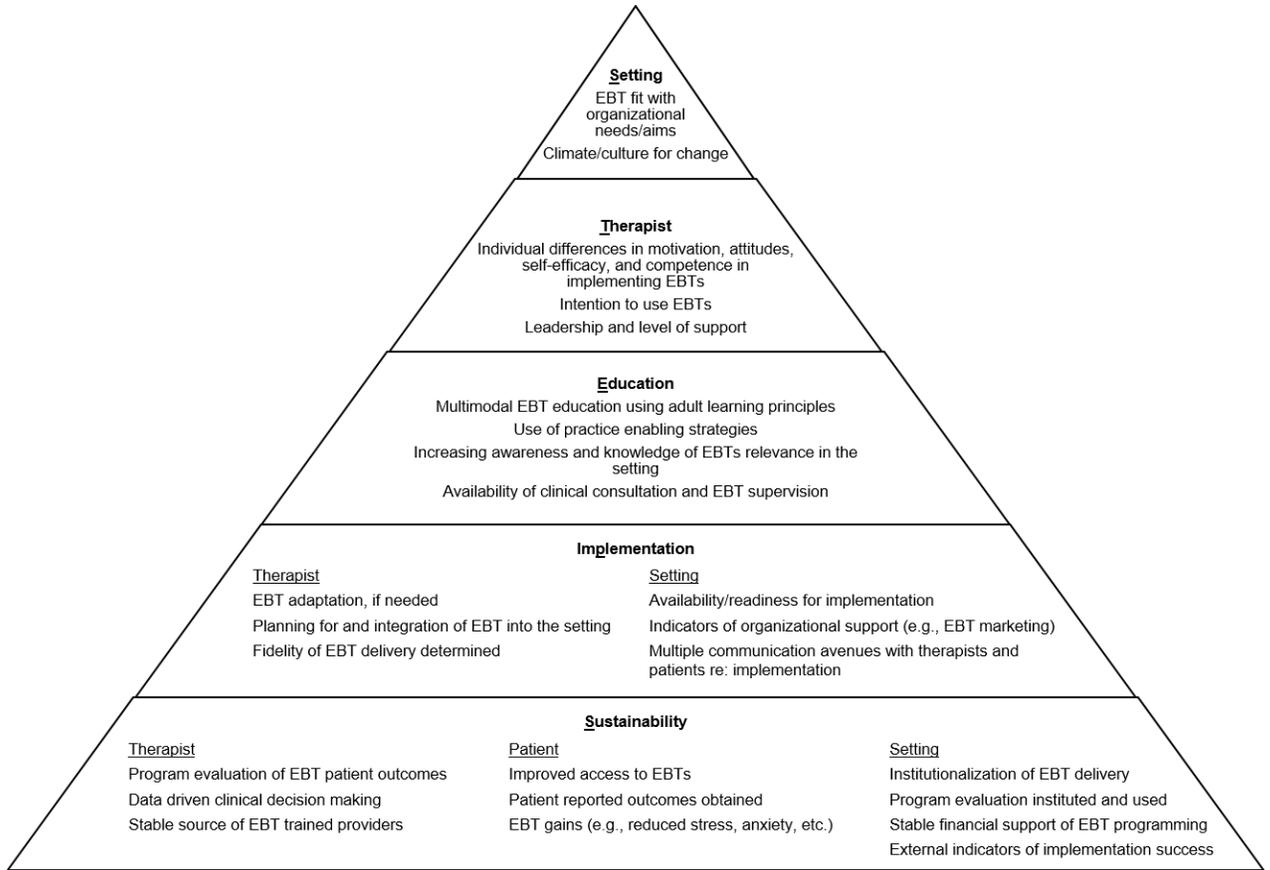
**Fig. 2.** Biobehavioral Model of cancer stress and disease course with inclusion of depression and inflammation pathways.

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**Fig 3.** Multidimensional framework of Setting, Therapist, Education, Implementation and Sustainability (STEPS) factors and illustration of increasing activity and engagement required of therapists and settings to achieved sustained provision of evidence based mental health treatment to patients.

C2H-I therapists' (N=15) reports of fidelity of BBI delivery as measured by number of sessions delivered for each component, with comparison to session numbers in BBI efficacy RCT (Andersen et al., 2004), and as measured by the percentage of C2H-I patients (n=158) receiving the component.

**Table 1**

Treatment Phase (Module) Component	BBI RCT			C2H-I		
	Number of Sessions	Number of Sessions Delivered (Median, Range)	Patients Receiving 1 Session (Mean %, Range)	Number of Sessions	Number of Sessions Delivered (Median, Range)	Patients Receiving 1 Session (Mean %, Range)
Intensive	18	11.10 (3.00–14.00)				
(a) Stress Conceptualization	1	1.00 (1.00 – 1.00)	100.0% (100%–100%)			
(a) Comm./Seeking Info.	2	1.00 (0.00 – 2.00)	67.5% (0% – 90%)			
(a) Problem Solving	2	1.02 (0.00 – 1.75)	66.3% (0%–100%)			
(b) Assertive Comm.	1	1.00 (0.00 – 2.00)	60.6% (0% – 86%)			
(b) Social Support	4	1.55 (0.00 – 5.00)	70.0% (0%–100%)			
(b) Body Image	1	0.72 (0.00 – 1.13)	55.0% (0%–100%)			
(b) Sexuality	1	0.61 (0.00 – 1.00)	50.6% (0% – 83%)			
(c) Physical Activity	1	0.52 (0.00 – 1.50)	51.2% (0% – 83%)			
(c) Diet and Nutrition	3	0.86 (0.00 – 1.75)	56.3% (0% – 85%)			
(d) Intro. to Maintenance	1	0.65 (0.00 – 1.00)	41.9% (0% – 82%)			
Other (transition)	1	NA	NA			
Maintenance*	8	2.75 (0.23 – 5.00)	47.2% (23% – 73%)			
Homework Review	25	6.00 (0.00–10.00)	91.8% (0%–100%)			

\* Numbers from the 10 of 15 sites that included a maintenance phase.

**Table 2**

Patients (N=158) reported fidelity as measured by their self-reported frequency of strategy use for each component, with comparison of recommended usage in BBI efficacy RCT (Andersen et al., 2004). Fidelity was also measured by patients' evaluation of the helpfulness of the component and its strategies.

Treatment Component	Component/strategy Usage		Evaluation (Helpfulness)	
	BBI Recommended	C2H-I Reported*	C2H-I Reported**	Mean SD
Stress Conceptualization	4	5.09	2.05	3.65 0.58
Progressive Muscle Relax.	4	4.21	1.86	3.46 0.77
MD Comm./Seeking Info.	2	3.03	2.23	3.34 0.70
Problem Solving	3	3.62	2.25	3.50 0.67
Assertive Communication	3	4.36	2.35	3.61 0.61
Social Support	4	3.54	2.43	3.70 0.60
Body Image	3	4.09	2.41	3.35 0.67
Sexuality	3	1.91	1.96	3.03 0.85
Physical Activity	4	4.67	1.89	3.53 0.73
Diet and Nutrition				3.55 0.70
Dietary Fat	7	5.66	2.25	
Dietary Fiber	7	5.93	1.83	

\* Patient reported usage of the component strategies in the last month on the following scale: 0= not at all, 1=once a month; 2=2-3 times per month; 3=once per week; 4= 2-3 times a week, 5=4 per week; 6=5-6 per week; 7=once a day; 8= 2 or more times a day.

\*\* Evaluation is a 4-point scale ranging from 1=not at all helpful to 4=very helpful.