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Effect of a community-based medical oncology depression screening program with behavioral health referrals among patients with breast cancer: a randomized clinical trial

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Key Points

Question: Does a depression screening program for patients with breast cancer treated in community oncology practices using tailored implementation science-guided strategies result in a greater proportion of referrals to behavioral health compared to an education-only control?

Findings: In this cluster randomized trial of 1,436 patients with breast cancer at 6 medical centers, a higher proportion of patients at sites randomized to the tailored strategies compared to the educational-only strategy had appropriate referral to behavioral health following screening, 7.9% vs 0.1%, respectively, a difference that was statistically significant.

Meaning: An implementation-strategy guided depression screening program compared to an educational-only control resulted in higher proportion of referrals to behavioral health among patients with breast cancer treated in a community setting.

Abstract

Importance: Implementation of guideline-recommended depression screening in medical oncology remains challenging. Evidence suggests that multicomponent care pathways with algorithm-based referral and management are effective, yet implementation of sustainable programs remains limited and implementation-science guided approaches are understudied.

Objective: To evaluate the effectiveness of an implementation-strategy guided depression screening program for patients with breast cancer in a community setting.

Design, Setting, and Participants: A pragmatic cluster randomized clinical trial conducted within Kaiser Permanente Southern California (KPSC). The trial included 6 medical centers and 1,436 patients diagnosed with new primary breast cancer who had a consultation with medical oncology between 10/1/2017-09/30/2018. Patients were followed up through study end date of 05/31/2019.

Intervention: Six medical centers in southern California participated and were randomized 1:1 to tailored implementation strategies (intervention, 3 sites, N=744) or education-only (control, 3 sites, N=692) groups. The program consisted of screening with the patient health questionnaire-9 (PHQ-9) and algorithm-based scoring and referral to behavioral health services based on low/moderate/high score. Clinical teams at tailored intervention sites received program education,

audit and feedback of performance data, and implementation facilitation, and clinical workflows were adapted to suit local context. Education-only controls sites received program education.

Main Outcome and Measures: The primary outcome was percent of eligible patients screened and referred (based on PHQ score) at intervention versus control groups measured at the patient level. Secondary outcomes included outpatient healthcare utilization for behavioral health, primary care, oncology, urgent care, and emergency department.

Results: All 1,436 eligible patients were randomized at the center level (mean age 61.5 years; 99% women; 18% Asian, 17% Black, 26% Hispanic/Latino, and 37% White) and followed up to study end, insurance membership end, or death. Groups were similar in demographic and tumor characteristics. For the primary outcome, 7.9% of patients at tailored sites were referred compared to 0.1% at education-only sites (difference=7.8%, 95% confidence interval (CI): 5.8%, 9.8%). Three-quarters (N=44) of intervention site patients referred completed a visit with a behavioral health clinician, and the one patient referred at the education-only sites completed a visit. In adjusted models patients at tailored sites had significantly fewer outpatient visits in medical oncology (rate ratio = 0.86, $p=0.001$, 95% CI: 0.86, 0.89), and no significant difference in utilization of primary care, urgent care, and emergency department visits (secondary outcome).

Conclusion and Relevance: Among patients with breast cancer treated in community-based oncology practices, tailored strategies for implementation of routine depression screening compared with an education-only control resulted in a

greater proportion of referrals to behavioral care. Further research is needed to understand the clinical benefit and cost-effectiveness of this program.

Trials identifier: ClinicalTrials.gov #NCT02941614

INTRODUCTION

Background

Implementation of guideline-recommended distress screening in medical oncology remains challenging.¹ In oncology, “distress” is a multidimensional construct encompassing depression, anxiety, and other experiences affecting the ability to cope with cancer.¹ There is a rich literature documenting the associations of depression with negative outcomes in patients with cancer, particularly breast cancer, including associations with decreased physical and social functioning, increased symptom burden, and poor quality of life,²⁻⁴ and the global prevalence of clinical depression in breast cancer is approximately 30%.⁵ Recognizing this, screening for depressive and other symptoms is recommended by the American Society of Clinical Oncology and others.^{6,7} Screening programs for distress are mandated for cancer center accreditation by the American College of Surgeons

Commission on Cancer.⁸ However, depression and depressive symptoms remain under-detected and undertreated in patients with breast cancer.^{2,9}

While the need for large-scale screening seems intuitive, screening programs incur costs and there is inadequate knowledge regarding key outcomes.¹⁰ While *efficacy* has been demonstrated in randomized trials at academic centers, typically showing increased number of referrals to psychosocial services,¹¹ there is a paucity of evidence supporting the *effectiveness* of depression screening programs under routine practice conditions.¹² Oncology clinicians have expressed concerns regarding program acceptability, usefulness, and sustainability, and pilot programs have not been uniformly successful.¹⁰ The reduction in benefit in less tightly controlled settings may be due to lack of thorough consideration of local context and resources relevant to program implementation.¹³ Implementation science-guided studies have been largely overlooked.^{14,15} Implementation strategies that are feasible and responsive to local context may be critical elements of program adoption and sustainment.^{3,13,16} The purpose of this study was to evaluate if a depression screening program for patients with breast cancer in community medical oncology practices using tailored implementation science-guided strategies resulted in a greater proportion of appropriate referrals to behavioral health compared to an education-only strategy.

METHODS

Setting and Participants

We conducted the trial at 6 medical centers within Kaiser Permanente Southern California (KPSC), an integrated healthcare system providing comprehensive care to

over 4.5 million members. KPSC membership broadly reflects the socioeconomic and racial/ethnic diversity of southern California.¹⁷ This study received approval from the KPSC Institutional Review Board (IRB #11103). All patients with a new diagnosis of breast cancer and a consultation in medical oncology between 10/1/2017-09/30/2018 were included, with no exclusions by stage of disease, histology, gender, race and ethnicity, co-morbidities, or other clinical or demographic characteristics. The study received a waiver for individual patient consent (passive enrollment). We followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for cluster randomized trials. The trial protocol and statistical analysis plan is available in Supplement 1.

Randomization

The principal statistician used SAS 9.3 (SAS Institute Inc., Cary, NC) to generate the randomization scheme for the 6 sites. Clusters were at the medical center-level. While cluster randomization may be less statistically efficient than individual randomization, it allowed evaluating the effectiveness of the program while avoiding contamination. Additionally, it balanced medical center-level factors that were otherwise unable to be reliably measured. Outcomes were analyzed at the individual patient level.

Study Design

We used an effectiveness-implementation hybrid study design.¹⁸ Hybrid designs have *a priori* focus on simultaneously assessing outcomes relevant to clinical effectiveness and implementation. The Consolidated Framework for Implementation Research (CFIR), which consists of five domains (intervention characteristics, inner

setting, outer setting, individual characteristics, and implementation processes) was used to guide critical elements of the design. This included selection of the screening instrument and workflow adaptability (*intervention characteristics*), engagement of key clinical and administrative stakeholders during study development and planning (*inner setting, process*), and building on clinician self-efficacy and knowledge regarding the program (*individual characteristics*).^{19,20} The CFIR was also used for planning, coding, and analysis of qualitative data collected on implementation, not reported in this article. We used the Expert Recommendations for Implementing Change (ERIC)²¹ to identify and select implementation strategies during study planning. With input from clinical and administrative staff, we selected ERIC strategies considered appropriate for the scientific question, feasible to use and familiar to staff, and replicable at scale using health system resources beyond the study timeframe.

This trial used a pragmatic approach, guided by the Pragmatic-Explanatory Continuum Indicator Summary-2 (PRECIS-2). Our research question, design, and methods aligned with pragmatic trial methodological standards.^{22,23} The trial had several design elements to maximize both the utility of our findings and generalizability as described below.

Intervention

The depression screening program followed guideline recommendations,²⁴ offering screening with the Patient Health Questionnaire-9 item (PHQ-9) to all newly diagnosed patients with breast cancer, with repeated screening encouraged at follow-up visits. We used the PHQ-9 scoring rubric of 0-9 (mild), 10-19 (moderate), and 20+ (severe).²⁵ Patients with mild scores received general information about KPSC and community behavioral health resources. Patients with moderate scores

were referred to either the oncology licensed clinical social worker (LCSW), depression care management (staffed with LCSWs and nurse practitioners), or both. Patients with severe scores were directly referred to behavioral health (psychiatry/psychology), provided with an immediate telephone crisis consultation, or both, as appropriate. Program education consisted of up to 4 education sessions: 1 in-person site visit and 2-3 teleconference calls.

Tailored Implementation Strategies

We selected three implementation strategies for the intervention sites: tailored audit and feedback, facilitation, and adaptable workflow. Audit and feedback is often a necessary element for implementing practice change but may not be sufficient to sustain practice change alone.²⁶ Sites received weekly emails with tailored anonymized audit and feedback reports of progress compared to the other intervention sites: proportion eligible, proportion screened, proportion appropriately referred graphed over time. Facilitation is a guided interactional process to aid implementation and sustainment of practice change.²⁷ A nurse researcher led the facilitation activities, consisting of monthly teleconference check-ins and quarterly in-person site visits to address issues (e.g., staff turnover, technical problems) with each tailored intervention site individually. The nurse received training materials and mentoring in facilitation from the study principal investigator (Hahn). Clinical workflows at each site were adapted to address unique local context and resources. The critical *functions* of the program—offering screening and using the scoring rubric for appropriate referral—were mandated; the *forms* that the screening took were adaptable. For example, the screening could be given on paper or entered

directly into the EMR by a nurse, or the timing of the screening could be before or after vital signs.

Screening instrument

The screening instrument was the PHQ-9, a widely used instrument which has been validated for cancer distress screening,^{28,29} and was available within the electronic medical record (EMR). The PHQ-9 was in use in other KPSC departments (behavioral health, obstetrics, primary care).

Education-Only Control

Education-only controls sites were provided with general education about the screening program at study initiation; the PHQ-9 questionnaire and scoring/referral algorithm were available to control sites to use at their discretion. This is comparable to the approach often used for program implementation outside of research studies, which typically feature initial education for knowledge building but lack ongoing support.¹⁵

Outcomes and Data Collection

The primary outcome was percent of eligible patients screened and referred (based on PHQ score) at tailored intervention versus education-only sites. Secondary outcomes included proportion with complete referral, defined as receiving any type of visit (telephone, video, in-person) with a behavioral health clinician; and outpatient utilization for oncology, primary care, urgent care, and emergency department (ED). There is little known about the effect of a depression screening program on utilization for outpatient and ED clinical visits, and there was not an a

priori hypothesis for the findings. It is possible that a program designed to identify and refer patients with symptoms of depression could decrease utilization for these services, but utilization could increase due to from patients seeking mental health care from their oncologist, primary care physician, or the urgent care/ED setting. We measured utilization using rates of outpatient visits to medical oncology, primary care, and urgent and ED care, measured from time of initial medical oncology consultation through May 31, 2019 or death/disenrollment. Patient-reported outcomes were also measured but are not presented in this article.

Post Hoc Analysis

The prespecified primary outcome was limited to measuring referrals to and visits with behavioral health services only in patients screened with the PHQ-9, which may have biased the study towards a positive finding. To address this, a post-hoc analysis was included to measure all referrals and visits to behavioral health in all participants regardless of screening status. Referring department (oncology or primary care/other specialty care) was also examined.

Covariates

In accordance with the pragmatic nature of the trial, all covariates were based on data available within the EMR: patient age, gender, partner status, race and ethnicity, preferred language, insurance type, census-track education and income (linked geo-coded data), cancer stage, and Charlson Comorbidity Index categorized into 3 groups: 0 (low); 1-3 (medium); and ≥ 4 (high). Race and ethnicity were prespecified to be included in the adjusted models for outpatient utilization to account for confounding due to sociodemographic characteristics and self-reported

by the patient in the EMR via fixed categories. Cancer stage was obtained through the KPSC pathology database and verified via chart review as needed.

Sample Size Calculation

Sample size for the primary outcome was calculated based on estimates of annual incident breast cancer cases within participating KPSC centers. Because this was an effectiveness study, we assumed relatively small standardized effect sizes z-scores ranging from 0.2-0.4 for all patient-reported outcomes. Power analysis was conducted using methods described by Donner and Klar³⁰ and implemented in PASS.³¹ To achieve 80% power with a significance level of 0.05 for a score test, our per-center sample size requirement ranged from as few as 20 for large effect size (0.4) and zero intraclass correlation (ICC), to about 400 for small effect size and large ICC (0.2 and 0.01, respectively), and assumed equal cluster sizes.³⁰ Given an expectation of a total of 1,200 patients across the 6 centers, the study was adequately powered to detect effect sizes as small as 0.2, given ICCs no greater than 0.007.

Statistical Analysis

For the primary analyses, patients were analyzed according to their randomization group and all patients at intervention and control sites were included regardless of participation in screening. Follow-up time was 12 months from the date of the initial oncology consultation for the primary outcome and up to 18 months for secondary outcomes. For patients who died or disenrolled from the health plan, data before disenrollment were used, and the shorter duration of follow-up was incorporated into the analysis. All patients had data on primary outcomes. Patients with unknown

race or ethnicity were grouped with the “Other/Missing” category. An “Unknown” category was created for those with missing cancer stage. Patients with missing information on partner status were categorized as “Un-partnered.” Patient characteristics were compared between intervention and control sites using means, standard deviations, frequencies, and percentages. Comparisons were made using t-tests or Wilcoxon rank-sum tests for continuous variables or chi-squared or Fisher’s exact tests for discrete variables, along with reporting of confidence limits. The prespecified primary analysis compared rates of PHQ-9 screening completion and referral to and completion of visits with behavioral health between the intervention and control sites at the patient level using risk differences and Wald asymptotic confidence limits.

The prespecified secondary analysis compared healthcare utilization between the groups. For utilization, we restricted to participants with ≥ 100 days of KPSC insurance membership following their initial visit to medical oncology. We used multivariable Poisson regression to assess the association between the intervention and outcomes, accounting for variable length of follow-up with an offset parameter and using robust standard errors to correct for potential variance misspecification. All statistical tests were two-tailed and considered statistically significant if $p \leq 0.05$. Because of the potential for type 1 error due to multiple comparisons, findings for analyses of secondary endpoints should be interpreted as exploratory. Analyses were conducted using SAS 9.3.

RESULTS

Participants

We enrolled a total of 1,436 patients with 744 patients in the intervention group and 692 in control. Figure 1 shows the participant flow. The mean age was 61.5 years (SD: 12.9), 99% were women, the mean Charlson Comorbidity Index was 2.2 (SD: 2.7), 87% spoke English as their primary language followed by 9% Spanish and 4% other. Eighteen percent self-reported being Asian/Pacific Islander, 17% Black, 26% Hispanic, and 37% White. Eighty-two percent had stage 0-II breast cancer. Groups were balanced on all characteristics (Table 1).

During the study period, 28 participants died: 19 intervention, 9 control (difference, 1.3%; 95% CI, -0.2% to 2.7%); 93 disenrolled from the health plan: 51 intervention, 42 control (difference, 0.8%; 95% CI, -1.8% to 3.3%). Deaths were due to metastatic cancer or other advanced comorbid conditions. Within the intervention group, there was no significant difference in PHQ-9 score between those who died and those who did not: difference, 0.7 (95% CI, -1.5 to 2.9).

Primary Outcome

Over the study period, 59 out of 744 patients (7.9%) eligible for screening received a referral to behavioral health services at tailored intervention sites; 1 out of 692 patients (0.1%) was referred at education-only sites (difference, 7.8%, 95% CI, 5.8% to 9.8%) (Table 2).

Secondary Outcomes

Behavioral Health Referrals and Utilization

Five hundred ninety-six patients (80%) at tailored sites had PHQ-9 screening offered at the consultation appointment versus 3 (<1%) at control sites (difference =

79.7%, 95% CI: 76.8%, 82.6%). Of the tailored site screenings, 63 patients (11%) scored in the moderate or high range indicating need for immediate referral; 94% received an appropriate referral (moderate scores referred to oncology LCSW or depression care management; high scores referred to psychology/psychiatry) and 6% either declined or were not offered a referral. Of those referred, 75% completed a visit with a behavioral health clinician and 25% either declined to schedule, cancelled, or did not show. Of the 3 screened patients at education-only sites, 2 scored in the low and 1 in the moderate range; the moderate scoring patient was referred to and completed a visit with a LCSW.

Utilization

Within the utilization cohort, mean follow up time in the 730 participants in the tailored group compared to the 683 education-only controls was 1.15 years versus 1.14 years (difference, 0.003; 95% CI, -0.028 to 0.034). Participant characteristics for the utilization cohort did not differ significantly between the groups (eTable 1, Supplement 2).

In unadjusted comparisons, the rate difference per person-year of outpatient oncology visits at tailored intervention sites vs. education-only sites was -1.81 (95% CI: -2.11, -1.51); for outpatient primary care, 0.04 (95% CI: -0.17, 0.24); for urgent care, -0.18 (95% CI: -0.27, -0.09); and for ED visits, 0.04 (95% CI: -0.04, 0.12). In models adjusted for age, race/ethnicity, cancer stage, partner status, and Charlson comorbidity index, patients at tailored intervention sites had statistically significantly fewer outpatient visits in medical oncology (adjusted rate ratio (aRR) = 0.86, $p=0.001$, 95% CI: 0.86, 0.89) (Figure 2). There was no statistically significant

difference in primary care (aRR = 1.07, 95% CI: 0.93, 1.24), urgent care (aRR = 0.84, 95% CI: 0.51, 1.38) or ED visits (aRR = 1.16, 95% CI: 0.84, 1.62).

Post-Hoc Outcomes

Regardless of PHQ-9 screening, a significantly greater number of patients in the tailored intervention group received a referral for any behavioral health service compared to the education-only group during the study period: 135 patients (18%) versus 74 (11%), difference, 7.5% (95% CI: 3.7%,11.2%) (Table 3; referral-level data is included in eTable 2, Supplement 2). Broken out by referral to psychiatry, depression care management, social services (services provided by licensed clinical social workers), and external (non-Kaiser Permanente) behavioral health referral, a greater number of intervention group patients received all referral types with the exception of external referrals: zero patients in the tailored group versus 13 patients in education-only received external referral, difference, -1.9% (95% CI: -3.0%, -0.7%). A significantly greater number of patients in the tailored intervention group received referrals to behavioral health generated from the oncology department: 97 (59%) versus 23 (26%), difference, 32.7% (95% CI: 19.9%, 45.4%) (eTable 3, Supplement 2).

Missing Data

For the primary and utilization outcomes, there were no missing data. For covariates used in the Poisson models, 3 patients were missing information on race and ethnicity, 59 on cancer stage, 15 on partner status.

DISCUSSION

Among patients with breast cancer treated in community-based medical oncology practices, a tailored implementation strategy-guided depression screening program compared with education-only resulted in a greater proportion of referral to appropriate behavioral care.

The proportion of eligible patients screened at the tailored intervention sites was high (80%); in Commission on Cancer-accredited institutions, rates of adherence to distress screening protocols varied from 47% to 73% of eligible participants.³² Internationally, similar rates have been documented: approximately 62% of clinicians reported engaging in any distress screening in Australia, and 40% to 60% of eligible patients in Cancer Care Ontario Regional Cancer Centers.^{1,33} Given the high burden of depression in patients with breast cancer, effective screening and referral programs are needed.³⁴ In the current era of heightened health-related concerns due to SARS-CoV-2, which may disproportionately affect patients with cancer and survivors, systematic depression screening and referral for patients with cancer may be even more important.^{35,36}

The strategies for the tailored implementation group (facilitation, audit and feedback, adaptability) were selected for feasibility of use during the trial and sustainability using health systems resources. The strategy of facilitation is likely to be replicable and scalable within the KPSC system. However, other studies have noted multiple implementation challenges including intervention complexity, unrealistic workload/workflow, lack of guidance for assessment or management of

high scores, and lack of staff engagement.^{13,16,32,37} It is possible that these issues could be addressed by engaging local stakeholders to co-design a feasible and sustainable workflow adaptive to available resources and context.³⁸ The United States Preventive Services Task Force recommends depression screening in adult primary care settings, and a 2016 evidence review that includes multiple randomized trials concluded that the evidence supports the benefits of primary care-based screening in the general adult population.³⁹ However, these programs can have from the same implementation-related barriers as seen in the oncology setting.³⁹ Other types of implementation strategies (e.g., financial, policy, restructuring) may provide benefit in different settings.²¹

Analysis of secondary outcomes found significantly less outpatient oncology utilization in the intervention group and no significant difference between the groups for primary care, urgent care, or ED visits. These results suggest that this type of screening program may not lead to increased healthcare utilization, although the study would need replication in other settings. Few studies have examined utilization in this context; a 2017 study found that cancer centers with high adherence to an oncology distress screening protocol had significantly less ED utilization and hospitalizations (risk ratios 0.82 and 0.81, respectively).⁴⁰

Limitations

This study has several limitations. First, the analysis did not include mental health clinical outcomes for patients referred to behavioral health services. Thus, it is unknown if patients referred had an improved clinical outcome compared to those who were not referred. Not all patients who are referred will have a clinically

important benefit, so the magnitude of the benefit of screening cannot be inferred from these findings. Second, restricting the primary analysis of behavioral health referrals and visits to patients screened with the PHQ-9 biased the study to have a positive result. However, a post-hoc analysis that included all behavioral health referrals and visits regardless of screening status had consistent findings. Third, the focus on patients with breast cancer may limit generalizability to other cancer types. Fourth, the integrated nature of KPSC may limit generalizability to other clinical settings, such as academic centers or stand-alone oncology centers. Fifth, the study did not screen for financial distress, which is increasingly recognized as an important dimension of cancer-related distress. Sixth, fewer patients had high levels of depressive symptoms than reported in other studies (e.g., studies using the National Comprehensive Cancer Center Distress Thermometer have found 37-64% of patients with cancer with high distress^{32,41}); this could be due to variability in the screening instrument (e.g., depression screening versus anxiety/distress screening), cancer type, cancer stage, or clinical setting (e.g., academic center vs. community).

Conclusions

Among patients with breast cancer treated in community-based medical oncology practices, tailored strategies for implementation of routine depression screening compared with an education-only control resulted in a greater proportion of referrals to behavioral care. Further research is needed to understand the clinical benefit and cost-effectiveness of this program.

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Author contributions

Dr. Hahn had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Hahn, Shen, Gould.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Hahn, Munoz-Plaza, Shen, Lee, Hong, Gould.

Critical revision of the manuscript for important intellectual content: All authors.

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Conflicts of interest

The authors declare no conflicts of interest.

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Role of funder

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Data Sharing Statement: See Supplement 3

REFERENCES

1. Dudgeon D, King S, Howell D, et al. Cancer Care Ontario's experience with implementation of routine physical and psychological symptom distress screening. *Psycho-oncology*. 2012;21(4):357-364.
2. Adler N, Page A. *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs*. Washington, DC: National Academies Press; 2008.
3. Ehlers SL, Davis K, Bluethmann SM, et al. Screening for psychosocial distress among patients with cancer: implications for clinical practice, healthcare policy, and dissemination to enhance cancer survivorship. *Transl Behav Med*. 2019;9(2):282-291.
4. Suppli NP, Johansen C, Christensen J, Kessing LV, Kroman N, Dalton SO. Increased risk for depression after breast cancer: a nationwide population-based cohort study of associated factors in denmark, 1998-2011. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2014;32(34):3831-3839.
5. Pilevarzadeh M AM, Afsargharehbagh R, Rafiemanesh H, Hashemi SM, Balouchi A. . Global prevalence of depression among breast cancer patients: a systematic review and meta-analysis. *Breast cancer research and treatment*. 2019;Aug;176(3):519-33.

6. Andersen BL, DeRubeis RJ, Berman BS, et al. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. *J Clin Oncol*. 2014;32(15):1605-1619.
7. Riba MB, Donovan KA, Andersen B, et al. Distress Management, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network : JNCCN*. 2019;17(10):1229-1249.
8. American College of Surgeons Commission on Cancer. Cancer Program Standards: Ensuring Patient-Centered Care Manual (2016 Edition). Standard 3.2 - Psychosocial Distress Screening, pp. 56-57 Available from: <https://www.facs.org/quality-programs/cancer/coc/standards>.
9. Stanton AL. Psychosocial concerns and interventions for cancer survivors. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2006;24(32):5132-5137.
10. Mitchell AJ, Lord K, Slattery J, Grainger L, Symonds P. How feasible is implementation of distress screening by cancer clinicians in routine clinical care? *Cancer*. 2012;118(24):6260-6269.
11. McCarter K, Britton B, Baker AL, et al. Interventions to improve screening and appropriate referral of patients with cancer for psychosocial distress: systematic review. *BMJ Open*. 2018;8(1):e017959.
12. Carlson LE, Waller A, Mitchell AJ. Screening for distress and unmet needs in patients with cancer: review and recommendations. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2012;30(11):1160-1177.
13. Jacobsen PB, Norton WE. The role of implementation science in improving distress assessment and management in oncology: a commentary on "Screening for psychosocial distress among patients with cancer: implications for clinical practice, healthcare policy, and dissemination to enhance cancer survivorship". *Transl Behav Med*. 2019;9(2):292-295.
14. Lazenby M, Ercolano E, Grant M, Holland JC, Jacobsen PB, McCorkle R. Supporting commission on cancer-mandated psychosocial distress screening with implementation strategies. *Journal of oncology practice / American Society of Clinical Oncology*. 2015;11(3):e413-420.
15. McCarter K, Fradgley EA, Britton B, Tait J, Paul C. Not seeing the forest for the trees: a systematic review of comprehensive distress management programs and implementation strategies. *Curr Opin Support Palliat Care*. 2020;14(3):220-231.
16. Smith SK, Loscalzo M, Mayer C, Rosenstein DL. Best Practices in Oncology Distress Management: Beyond the Screen. *Am Soc Clin Oncol Educ Book*. 2018;38:813-821.
17. Koebnick C, Langer-Gould AM, Gould MK, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *The Permanente journal*. 2012;16(3):37-41.
18. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Medical care*. 2012;50(3):217.
19. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a

- consolidated framework for advancing implementation science. *Implement Sci.* 2009;4:50.
20. Damschroder LJ, Hagedorn HJ. A guiding framework and approach for implementation research in substance use disorders treatment. *Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors.* 2011;25(2):194-205.
 21. Powell BJ WT, Chinman MJ, Damschroder LJ, Smith JL, Matthieu MM, Proctor EK, Kirchner JE. A refined compilation of implementation strategies: results from the Expert Recommendations for Implementing Change (ERIC) project. . *Implementation Science.* 2015;10(21).
 22. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ (Clinical research ed).* 2015;350:h2147.
 23. Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *Journal of clinical epidemiology.* 2009;62(5):464-475.
 24. Pirl WF, Fann JR, Greer JA, et al. Recommendations for the implementation of distress screening programs in cancer centers: report from the American Psychosocial Oncology Society (APOS), Association of Oncology Social Work (AOSW), and Oncology Nursing Society (ONS) joint task force. *Cancer.* 2014;120(19):2946-2954.
 25. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine.* 2001;16(9):606-613.
 26. Ivers NM, Grimshaw JM, Jamtvedt G, et al. Growing literature, stagnant science? Systematic review, meta-regression and cumulative analysis of audit and feedback interventions in health care. *Journal of general internal medicine.* 2014;29(11):1534-1541.
 27. Berta W, Cranley L, Dearing JW, Doherty EJ, Squires JE, Estabrooks CA. Why (we think) facilitation works: insights from organizational learning theory. *Implementation Science.* 2015;10(1):141.
 28. Smith AB, Rush R, Wright P, Stark D, Velikova G, Sharpe M. Validation of an item bank for detecting and assessing psychological distress in cancer patients. *Psycho-oncology.* 2009;18(2):195-199.
 29. Mitchell AJ. Short Screening Tools for Cancer-Related Distress: A Review and Diagnostic Validity Meta-Analysis. *Journal of the National Comprehensive Cancer Network.* 2010;8(4):487-494.
 30. Donner A, Klar N. Statistical considerations in the design and analysis of community intervention trials. *Journal of clinical epidemiology.* 1996;49(4):435-439.
 31. Hintze J. PASS 13. 2014; available at www.ncss.com.
 32. Zebrack B, Kayser K, Sundstrom L, et al. Psychosocial Distress Screening Implementation in Cancer Care: An Analysis of Adherence, Responsiveness, and Acceptability. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2015;33(10):1165-1170.
 33. Fradgley EA, Byrnes E, McCarter K, et al. A cross-sectional audit of current practices and areas for improvement of distress screening and management in Australian cancer services: is there a will and a way to improve? *Supportive Care in Cancer.* 2020;28(1):249-259.

34. Burgess C, Cornelius V, Love S, Graham J, Richards M, Ramirez A. Depression and anxiety in women with early breast cancer: five year observational cohort study. *BMJ (Clinical research ed)*. 2005;330(7493):702.
35. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *The Lancet Oncology*. 2020;21(3):335-337.
36. Nekhlyudov L, Duijts S, Hudson SV, et al. Addressing the needs of cancer survivors during the COVID-19 pandemic. *J Cancer Surviv*. 2020.
37. Donovan KA, Grassi L, Deshields TL, Corbett C, Riba MB. Advancing the science of distress screening and management in cancer care. *Epidemiology and Psychiatric Sciences*. 2020;29:e85.
38. Fitch MI, Ashbury F, Nicoll I. Reflections on the implementation of screening for distress (sixth vital sign) in Canada: key lessons learned. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2018;26(12):4011-4020.
39. O'Connor E RR, Henninger M, Groom HC, Burda BU, Henderson JT, Bigler KD, Whitlock EP. . *Screening for Depression in Adults: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force*. Vol Evidence Synthesis No. 128. AHRQ Publication No. 14-05208-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2016.
40. Zebrack B, Kayser K, Bybee D, et al. A practice-based evaluation of distress screening protocol adherence and medical service utilization. *Journal of the National Comprehensive Cancer Network*. 2017;15(7):903-912.
41. Mehnert A, Hartung TJ, Friedrich M, et al. One in two cancer patients is significantly distressed: Prevalence and indicators of distress. 2018;27(1):75-82.

TABLES AND FIGURES

Figure 1. CONSORT cohort diagram for cluster randomized trial

Table 1. Demographics and cancer characteristics of participants

	Tailored intervention (N=744)	Education only (N=692)
Age, mean (SD), y	61.1 (12.4)	62.0 (13.3)
Sex		
Female	740 (99%)	689 (99%)
Male	4 (<1%)	3 (<1%)
Stable Partner Status ^a	428/740 (58%)	382/681 (56%)
Race and ethnicity ^b	N=743	N=691
Asian/Pacific Islander	149 (19%)	117 (17%)
Black	98 (13%)	139 (20%)
Hispanic	204 (27%)	172 (25%)
Multiple	2 (<1%)	2 (<1%)
White	278 (37%)	255 (37%)
Other	12 (2%)	6 (1%)
Preferred Language		
English	639 (86%)	607 (88%)
Spanish	75 (10%)	58 (8%)
Other	30 (4%)	27 (4%)
Insurance Type		
Commercial/Private Pay	440 (59%)	383 (55%)
Medicare	273 (37%)	265 (38%)
Medicaid	20 (3%)	25 (4%)
Dual Medicare/Medicaid	10 (1%)	15 (2%)
Non-Kaiser Permanente Insurance	1 (<1%)	4 (1%)
Census Tract Education	N=723	N=676
High school or less	271 (37%)	251 (37%)
Some college	210 (29%)	196 (29%)
College+	242 (33%)	229 (34%)
Census Tract Family Income >=\$50,000	450/723 (62%)	420/676 (62%)
Charlson Comorbidity Index Score ^c	N=743	N=690
Median (IQR)	1.0 (0.0, 4.0)	1.0 (0.0, 3.0)
Breast Cancer Stage, early/late	N=744	N=692
Early Stage (0-IIb)	617 (87%)	559 (84%)
Late Stage (III-IV)	95 (13%)	106 (16%)

Unknown	32 (4%)	27 (4%)
<p>^aMarried or living together as committed partners</p> <p>^bMultiple race and Other were self-reporting options in the electronic health record</p> <p>^cThe weighted Charlson Comorbidity Index is a method of mortality prediction based on comorbidities captured in electronic health record or administrative data using International Classification of Disease (ICD) codes. In this study the score is based on ICD codes for the year prior to the initial consult and ranges from 0-29; the variable has been categorized into 0 (low) 1 to 3 (moderate) and 4 or greater (high)</p>		

Table 2. Primary outcome: percent of eligible patients screened and referred (based on Patient Health Questionnaire-9 score) at tailored intervention versus education-only sites

	Tailored intervention sites (n=744)	Education-only sites(n=692)	Risk Difference (95% Confidence Interval)
Received a referral to behavioral health services based on PHQ-9 score	59 (0.079)	1 (0.001)	0.078 (0.058, 0.097)
PHQ-9 score distribution (percent based on number screened) ^a	Low: 89% (533)	Low: 67% (2)	
	Moderate: 10% (57)	Moderate: 33% (1)	
	High: 1% (6)	High: 0	

^a The PHQ-9 scores were calculated based on participant responses to each of the nine items. Each item of PHQ-9 was scored on a scale of 0-3 (0 = not at all; 1 = several days; 2 = more than a week; 3 = nearly every day). The PHQ-9 total score ranges from 0 to 27: 0-9 Low, 10-19 Moderate, and ≥ 20 High

Figure 2. Adjusted rate ratios for outpatient utilization of primary care, medical oncology, urgent care, and emergency department visits

Figure 2 Legend: Visits are compared between intervention and control group, restricted to those with ≥ 100 days of Kaiser Permanente insurance membership from date of cancer diagnosis; models adjusted for age, race/ethnicity, marital status, Charlson comorbidity index score, and cancer stage; the median (IQR) follow-up time per patient in the tailored intervention group is 1.14 (0.89, 1.39) years vs. 1.12 (0.89, 1.40) years in the education-only control group.

Table 3. Total number of referrals and visits made to Behavior Health, Depression Care Management, Psychiatry, and Social Services (services provided by Licensed Clinical Social Worker) from initial consult to May 2019 by group; percent is out of group total and row counts are patient-level (post-hoc analysis)

	Referrals			Visits		
	Tailored intervention (n=744)	Education only (n=692)	% Difference (95% CI)	Tailored intervention (n=744)	Education only (n=692)	% Difference (95% CI)
Any Behavioral Health ^a	135 (18%)	74 (11%)	7.5 (3.7, 11.2)	75 (10%)	36 (5%)	4.9 (2.0, 7.7)
Depression Care Management	70 (9%)	18 (3%)	6.8 (4.3, 9.4)	24 (3%)	1 (0%)	3.1 (1.6, 4.5)
Psychiatry	29 (4%)	23 (3%)	0.6 (-1.5, 2.6)	16 (2%)	10 (1%)	0.7 (-0.8, 2.2)
Social Services	61 (8%)	33 (5%)	3.4 (0.8, 6.1)	44 (6%)	27 (4%)	2.0 (-0.4, 4.4)
Behavioral Health, External Referral ^b	0 (0%)	13 (2%)	-1.9 (-3.0, -0.7)	-	-	

^a Patients may have referrals and visits to more than one behavioral health resource

^b External referrals to non-Kaiser Permanente clinicians