

**Uncertainties: Does depression screening in primary care improve mental health outcomes?**

Brett D. Thombs, professor<sup>1</sup>; Sarah Markham, visiting researcher;<sup>2</sup> Danielle B. Rice, doctoral student;<sup>1</sup>  
Roy C. Ziegelstein, professor.<sup>3</sup>

<sup>1</sup>Lady Davis Institute for Medical Research, Jewish General Hospital and McGill University, Montréal, Québec, Canada;

<sup>2</sup> King's College London, UK;

<sup>3</sup>Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

**Address for Correspondence:** Brett D. Thombs, PhD; Jewish General Hospital; 4333 Cote Ste Catherine Road; Montréal, Québec, Canada H3T 1E4; Tel (514) 340-8222 ext. 25112; E-mail: [brett.thombs@mcgill.ca](mailto:brett.thombs@mcgill.ca).

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Depression is usually identified when patients report symptoms or when clinicians recognize them through routine assessment of patient well-being. Screening can possibly increase recognition. Depression screening involves administering a symptom questionnaire to all patients not known or suspected of having depression. Unlike other types of screening, which are done to detect early-stage disease before symptoms are apparent, depression screening is intended to identify symptomatic people who may not otherwise be recognized or seek treatment.<sup>1,2</sup> A cut-off threshold is used to classify positive and negative results, with further assessment of those with positive results, and, as appropriate, management. The Patient Health Questionnaire-9 (PHQ-9) is among the most used depression screening tools in primary care.<sup>3</sup>

In the United Kingdom (UK), the National Institute for Health and Care Excellence (NICE) encourages general practitioners to be alert to possible depression but not routinely screen.<sup>4</sup> The National Screening Committee recommends against screening.<sup>5</sup> Depression screening in general practice was financially incentivized by the UK Quality and Outcomes Framework from 2006 to 2013 but was subsequently removed due to disappointing results; almost 1000 patients had to be screened for each new depression diagnosis and almost 700 for each new antidepressant prescription.<sup>6</sup> In North America, the Canadian Task Force on Preventive Health Care (CTFPHC) recommends against screening,<sup>7</sup> whereas the United States Preventive Services Task Force (USPSTF) recommends screening all primary care patients “with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up”.<sup>8</sup> This is described as, at a minimum, dedicated nursing staff to manage the screening process and protocols for referral to evidence-based behavioural treatments. More intensively, it involves components such as dedicated staff training programs, mental health specialists to conduct assessments, trained therapists, and co-payments for medications.<sup>8</sup> Only 3% of US adult ambulatory care visits in 2015, however, included depression screening, even though it has been recommended by the USPSTF since 2009.<sup>9</sup>

In current practice, screening tool cut-offs are typically set to maximize combined sensitivity and specificity, but this does not consider important clinical considerations, such as minimizing false positive screens or identifying patients with high symptom levels and ruling out those who meet diagnostic criteria but have mild symptoms and may be less likely to engage in or benefit from treatment.<sup>10</sup> Assuming 10% prevalence in a general practice setting with half of patients with depression already recognized, screening with the PHQ-9 (standard cut-off  $\geq 10$ ) would result in almost 20% of all patients screening positive with >75% of these false positives (Figure 1).<sup>3</sup>

It is uncertain if depression screening in primary care, alone or combined with other mental health screens (e.g., anxiety), would improve mental health symptoms via better identification and treatment in people with depression who would otherwise go unrecognized.

### **What is the evidence of uncertainty?**

Successful depression screening would require patients without known depression to agree to be screened, identification of a significant number of new cases while limiting false positive screens, and effective treatment of newly identified cases. Thus, trials of screening programs must determine eligibility and randomise prior to screening, exclude patients already known to have depression or in depression treatment, and provide similar depression care options to patients in screened and unscreened trial arms to avoid conflating screening and management effects.<sup>1,11</sup> A 2008 Cochrane review<sup>12</sup> reported that interventions that included depression screening did not reduce depressive symptoms (5 randomised trials; standardized mean difference = -0.02, 95% confidence interval -0.25 to 0.20). However, only 1 included trial<sup>13</sup> randomised participants not known to have depression to be screened or not screened and appropriately separated screening and treatment effects. We identified 4 additional, more recent, trials that have evaluated depression screening in specific patient groups such as postpartum women,<sup>14</sup> patients with osteoarthritis,<sup>15</sup> patients after an acute coronary syndrome,<sup>16</sup> and post-deployment military personnel.<sup>17</sup> These trials reported mixed results or found that mental health symptoms were unimproved among participants randomised to screening; 3 trials found no differences

in mental health symptoms or well-being between screened and unscreened participants,<sup>13,16,17</sup> 1 trial reported both results that showed no difference and results that favoured screening,<sup>14</sup> and 1 trial reported results that showed no difference and results that were worse for screened participants.<sup>15</sup>

Table 1 shows trial details.

We did not identify adequately powered, well-conducted trials on the benefits and harms of depression screening in general practice patient populations. The diverse populations and screening approaches used in the trials we identified, along with small sample sizes and methodological limitations in some, result in uncertainty whether routine screening would reduce depression in general practice.

### **Is ongoing research likely to provide relevant evidence?**

We searched Clinicaltrials.gov, WHO International Clinical Trials Registry Platform, and ISRCTN for ongoing trials. We did not identify any ongoing depression screening trials in any setting that planned to randomise people not known to have depression to screening or no-screening conditions and that appropriately separated screening and management.

Research on screening tool accuracy and methods is underway. We are part of an international collaboration (<https://www.depressd.ca/>) that is aggregating large databases from primary studies on depression screening tool accuracy. One goal of the collaboration is to determine how clinicians might move away from a crude dichotomous screening approach and instead use individualized risk estimates based on actual screening tool scores and individual risk factors (e.g., sex, age, medical comorbidities). Such an approach could increase precision for individual patients. It could be also be used to engage patients in shared decision making and to better identify appropriate care options, as recommended by NICE.<sup>19</sup>

### **What should we do in light of the uncertainty?**

Instead of screening with symptom questionnaires, we encourage clinicians to engage patients in discussions about their overall well-being, including mental health.<sup>19</sup> Recognizing depression may be a process that takes more than a single consultation. Be alert to clinical cues that could suggest depression, particularly among patients at risk due to factors such as family or personal history of mental health concerns, including problematic substance use; unexplained medical symptoms; or overly frequent use of medical services.<sup>4</sup> These include both somatic cues, such as insomnia, anhedonia, or fatigue, and psychological cues, such as low mood or overly negative thinking. If mental health concerns are reported by a patient or are otherwise identified, provide education about depression and other common mental health conditions, including the different ways that symptoms may be experienced and, when appropriate, discuss different management options.<sup>4</sup>

As national guidelines differ, clinicians are expected to be aware of and adhere to local guidance regarding screening. Until further evidence becomes available, it will be important to make an informed decision regarding screening in primary care after considering the benefits and harms. Depression screening would require substantial resources. Busy general practitioners must evaluate or refer all patients who have positive screens.<sup>1,7,11</sup> Like other types of screening, it can also lead to overdiagnosis or misdiagnosis. Overdiagnosis occurs in depression when people with mild, transient symptoms are diagnosed and treated, but will not benefit, since symptoms will subside without intervention. Misdiagnosis can occur if screening leads to some people being diagnosed and treated even though they do not meet diagnostic criteria, including people with symptoms due to another health condition.<sup>10</sup>

Outside of the context of screening, depression symptom questionnaires are often used in general practice settings for other purposes. They can be useful for assessing and discussing symptoms among patients who may be unsure if they have depression and for monitoring treatment response among patients with a diagnosis of depression.<sup>20</sup>

## **FIGURE LEGEND**

Screening results assuming 10% prevalence with half of depressed patients already recognized prior to screening, using a cut-off of 10 or greater on the Patient Health Questionnaire-9. Original calculator is based on Levis et al.,<sup>3</sup> and can be accessed at <http://www.depressionscreening100.com/phq/>.

**Table 1. Randomised Controlled Trials of Depression Screening Interventions**

First Author Year Country	Setting and Eligible Participants  Participant Characteristics	Trial Design  Depression Screening Tool  Follow-up for Outcomes	Screening Intervention  Comparator	Number Randomised (Number Assessed for Primary Trial Outcomes)  Intervention  Comparator:	Depression or General Mental Health Symptoms for Intervention versus Comparator: SMD or RR of Depression with 95% CI (Negative Numbers and Ratios < 1 Reflect Better Outcomes for Intervention unless noted)	Clinical Considerations in Evaluating Applicability for Depression Screening in General Practice	Important Limitations in Evidence that Could Reduce Confidence in Effect Estimates for Depression Screening in General Practice
Williams <sup>13</sup> 1999 United States	Adult family medicine or general internal medicine patients.  Mean age 58 years, 71% female, 60% Hispanic, 26% Spanish- speaking, generally low income.	Multi-site RCT with individual randomisation, stratified by clinic.  Single item or CES-D  3 months post- screen. <sup>a</sup>	Two screening arms received either single screening question or 20-item CES-D (cutoff $\geq$ 16) with results combined across arms. Results reported to physicians on bright orange report form.  Usual care with no screening.	653 (153) <sup>b</sup>  316 (65) <sup>b</sup>	<u>Major or minor DSM-III-R depression:</u> RR 0.79 (0.57 to 1.11)	<u>Limitations:</u> Study included patients already known by clinicians to have depression, and only 11 of 41 (27%) depression diagnoses made in screening and non- screening conditions were new diagnoses. <sup>c</sup>	Follow-up for depression outcome occurred in only 3 of 4 clinics with follow-up attempted for all patients with depression at baseline (N = 101) and a random sample of patients without depression at baseline (N = 129).
Leung <sup>14</sup> 2011 Hong Kong	Chinese- language proficient mothers of 2- month-old babies attending maternal and child health centers for routine child health services.  Generally low- income and low- education (30% secondary education or higher).	Multi-site RCT with individual randomisation.  EDPS  4 months post- screen.	Intervention: Clinical assessment for depression + depression screening with EPDS (cutoff $\geq$ 10) or suicide ideation (EPDS item 10).  Usual care with clinical assessment for depression.	231 (215)  231 (215)	<u>General mental health (GHQ-12):</u> SMD -0.17 (-0.36 to 0.02)  <u>Depression symptoms (EPDS):</u> SMD -0.35 (-0.54 to -0.16) RR (EPDS $\geq$ 10) 0.64 (0.43 to 0.97)  <u>Parental stress (PSI):<sup>d</sup></u> SMD -0.18 (-0.37 to 0.01)  <u>Marital satisfaction (CKMSS):</u> SMD 0.16 (-0.03 to 0.35) <sup>e</sup>	<u>Strengths:</u> Compared addition of screening to standard unstructured clinical assessment, to assessment alone, which is encouraged as good standard care.  Appropriately excluded women already receiving mental health care.  <u>Limitations:</u> Included only post- partum women with unknown applicability to other patients.  Did not describe counselling offered to participants with depression in screening and non-screening trial arms.	GHQ-12 (not statistically significant) was registered primary outcome, and EPDS (statistically significant) was registered secondary outcome, but these were reversed in publication, which raises concern, generally, about the fidelity of trial conduct and reporting. <sup>16</sup>  Effect size per additional women who received counselling in screening arm compared to usual care arm equivalent to 6-7 times what would be expected based on meta-analyses of similar counselling interventions, raising concern about whether these results represent what would occur in actual clinical practice. <sup>18</sup>

Mallen <sup>15</sup> 2017 United Kingdom	<p>Patients aged 45 or older with osteoarthritis attending GP clinic.</p> <p>Mean age 65 years, 57% female, 98% White race/ethnicity.</p>	<p>Pragmatic cluster RCT with randomisation by GP practices</p> <p>PHQ-2</p> <p>3, 6, and 12 months post-screen.</p>	<p>Point-of-care screen for anxiety (GAD-2) and depression with PHQ-2 items and yes/no response format (yes to either = positive). Electronic template signposted and encouraged management per NICE guidelines.</p> <p>Usual care with no screening.</p>	<p>24 practices with 3473 eligible patients (646 to 911 per outcome time point)<sup>f</sup></p> <p>20 practices with 2439 eligible patients (371 to 501 per outcome time point)<sup>g</sup></p>	<p><b><u>Depression symptoms (PHQ-8):<sup>h</sup></u></b> 3 months: SMD 0.14 (0.01 to 0.26) 6 months: SMD 0.22 (0.09 to 0.35) 12 months: SMD 0.10 (0.03 to 0.23)</p> <p><b><u>General mental health (SF-12 MCS):<sup>h</sup></u></b> 3 months: SMD 0.10 (-0.02 to 0.23) 6 months: SMD 0.05 (-0.08 to 0.17) 12 months: SMD 0.04 (-0.09 to 0.16)</p>	<p><b><u>Strengths:</u></b> Pragmatic trial designed to replicate screening by GPs as in normal practice with standard mental health care based on NICE guidelines.</p> <p>Appropriately excluded patients with mental health diagnosis or treatment in last 12 months.</p> <p><b><u>Limitations:</u></b> Included screening for anxiety in addition to depression.</p> <p>Included only patients with osteoarthritis with unknown applicability to other patients.</p>	<p>Although conducted in general practice, only patients with osteoarthritis were included.</p> <p>&lt; 25% of eligible participants were mailed and returned initial study questionnaires and included in trial.</p> <p>Among included participants, follow-up of 71% to 78% across time points.</p>
Kronish <sup>16</sup> 2020 United States	<p>Patients aged 21 or older with acute coronary syndrome 2 to 12 months prior to enrolment identified via health system record review.</p> <p>Mean age 66 years, 28% female, 72% White race-ethnicity, 64% at least some college education.</p>	<p>Multi-site RCT with individual randomisation</p> <p>PHQ-8</p> <p>6, 12, and 18 months post-screen</p>	<p>Screen for depression with PHQ-8 (cutoff <math>\geq 10</math>) by centralized study personnel with positive screens reported to patients' cardiologists and/or GPs with treatment.<sup>i</sup></p> <p>Usual care with no screening.</p>	<p>501 (437)</p> <p>500 (439)</p>	<p><b><u>Depression symptoms (PHQ-8):<sup>j</sup></u></b> 18 months: SMD -0.03 (-0.15 to 0.10)</p> <p><b><u>Depression symptoms (10-item CES-D):<sup>j</sup></u></b> 6 months: SMD 0.02 (-0.10 to 0.14) 12 months: SMD -0.10 (-0.23 to 0.02) 18 months: SMD -0.06 (-0.18 to 0.07)</p>	<p><b><u>Strengths:</u></b> Appropriately excluded patients with current depression treatment or known history of depression.</p> <p><b><u>Limitations:</u></b> Participants identified via centralized health system records and screening carried out via contact by study personnel and not in clinics.</p> <p>Included only patients post-acute coronary syndrome with unknown applicability to other patients.</p>	<p>Participants were limited to patients post-acute coronary syndrome, and screening was done centrally rather than in clinics by health care providers.</p>
Rona <sup>17</sup> 2017 United Kingdom	<p>Royal Marines and Army personnel who had recently returned from deployment in</p>	<p>Pragmatic cluster RCT with randomisation by platoons.</p> <p>PHQ-9</p>	<p>Screen in person, via email, or via mail for posttraumatic stress disorder (PCL-C), anxiety (GAD-7), alcohol misuse (AUDIT), and</p>	<p>274 platoons with 6350 randomised and 5577 baseline responders (3996)</p> <p>160 platoons with</p>	<p><b><u>Depression or anxiety symptoms (PHQ-9 and GAD-7):</u></b> aOR (PHQ-9 <math>\geq 6</math> or GAD-7 <math>\geq 15</math>) 0.91 (0.71 to 1.16)</p> <p><b><u>Any mental disorder (PCL-C, PHQ-9,</u></b></p>	<p><b><u>Strengths:</u></b> Zelen design allowed all eligible participants to be included.</p> <p><b><u>Limitations:</u></b></p>	<p>Approximately 86% of eligible participants returned baseline screening questionnaires, but only 63% in follow-up.</p>



Afghanistan	10-24 months post-screen	depression with PHQ-9 (cutoff $\geq 6$ ) with tailored advice for getting help with positive screens via letter.  General mental health advice without consideration to screening results via letter.	3840 randomised and 3149 baseline responders (2369)	<b>GAD-7):</b> aOR (PCL-C $\geq 50$ , PHQ-9 $\geq 6$ , or GAD-7 $\geq 15$ ) = 0.95 (0.79 to 1.16)	Screening carried out by study personnel not in health clinic.  Screening results provided by mail rather than in person by a health care provider.  Included screening for posttraumatic stress disorder, anxiety, and alcohol misuse in addition to depression.  Included only recently deployed military personnel with unknown applicability to GP patients or to mixed-gender populations.
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**Abbreviations:** AUDIT = Alcohol Use Disorder Identification Test; CI = confidence interval; CES-D = Center for Epidemiologic Studies Depression Scale; CKMSS = Chinese version of Kansas Marital Satisfaction Scale; DSM = Diagnostic and Statistical Manual; EPDS = Edinburgh Postnatal Depression Scale; GAD-2 = General Anxiety Disorder-2; GAD-7 = General Anxiety Disorder-7; GHQ-12 = General Health Questionnaire-12; GP = general practice; NICE = National Institute for Health and Care Excellence; PHQ-2 = Patient Health Questionnaire-2; PCL-C = PTSD Checklist – Civilian Version; PSI = Parental Stress Index; RCT = randomised controlled trial; RR = relative risk; SF-12 MCS = Short-Form 12 Health Survey Mental Component Summary; SMD = standardized mean difference.

<sup>a</sup>Some patients were assessed up to 6 to 12 months post-screening with retrospective report of onset to 3 months post-screening.

<sup>b</sup>Eligibility was determined and randomisation occurred pre-screening. However, only 218 of 969 total participants randomised (22%) were assessed for depression outcomes. Authors reported that they followed-up all participants who met criteria for current depression at baseline (N=101) and a random sample of non-depressed participants (N=129). Follow-up was reported to have been completed for 216 of these participants; however, authors reported results based on 218 participants.

<sup>c</sup>Numbers based on published article. Corresponding author clarified that patients were classified as new diagnoses if there was no evidence of a depression diagnosis in the chart and the patient reported that not diagnosed or treated in last 2 years.

<sup>d</sup>Total score only reported here. Leung et al. also reported results from 3 subscales with none statistically significant.

<sup>e</sup>Positive score reflects better outcome for intervention.

<sup>f</sup>4238 potentially eligible – 765 found to be ineligible = 3473 (includes 1339 mailed post-consultation questionnaire, 1177 where physician escaped from electronic health record protocol, 50 declined to take part, and 907 not mailed questionnaire for reasons not known).

<sup>g</sup>21 practices randomised, but one withdrew pre-initiation of study protocol; numbers included for 20 practices only. 3041 potentially eligible – 602 found to be ineligible = 2439 (includes 703 mailed post-consultation questionnaire, 1021 where physician escaped from electronic health record protocol, 40 declined to take part, and 675 not mailed questionnaire for reasons not known).

<sup>h</sup>Based on values not adjusted for clustering. This resulted in confidence intervals that do not cross zero, but these outcomes were not significant when presented with raw scores and adjusted for clustering in the trial results.

<sup>i</sup>Trial was a 3-arm trial with (1) screening alone; (2) screening + provision of patient-preference stepped depression care free to patients; and (3) usual care (no screening). Only screening alone and usual care are included here, since the screening + stepped depression care arm did not have a screening comparator with similar depression care resources. Results for screening alone and screening + stepped depression care did not differ.

<sup>j</sup>From supplemental tables and assuming intent-to-treat with total N.

<sup>k</sup>Based on numbers reported at follow-up.

**BOX: What you need to know**

- International guidelines and practice differ regarding screening for depression; it is not currently recommended in the UK.
- There is a lack of high-quality evidence from primary care settings on the benefits of depression screening in improving mental health outcomes for patients.
- Instead of routinely screening all patients in primary care, engage patients in discussions about their overall well-being, including mental health and be alert to clinical cues that could suggest depression.

**Box: Data Sources and selection strategy**

We reviewed systematic reviews done to support depression screening guidelines for adults in general practice or in other populations (women during pregnancy or postpartum, children and youth) by the United Kingdom National Screening Committee, the CTFPHC, and the USPSTF for randomised controlled trials (RCTs) that investigated the effects of depression screening interventions on health outcomes. We then searched for more recent trials via Medline, Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, PsycInfo, Embase, CINAHL, and the Cochrane Registry of Controlled Trials through March 12, 2021. Search terms, which included depression, depressive disorder, mass screening, and screen\* are available online (<https://osf.io/ptqdk/>). We searched for RCTs that compared outcomes among participants randomised to screening versus no screening. To avoid conflating effects of screening and different treatment options, we limited to RCTs in which participants in both arms had access to similar depression management options.<sup>1,11</sup> We excluded trials that compared communication or management strategies among patients with positive depression screens or an established diagnosis of depression, because, in practice, decisions about screening need to occur before screening results are known.

**Box: Recommendations for further research**

**Objectives:** Test whether different depression screening approaches, with standard or enhanced management options, improve mental health compared to

(1) not screening but providing access to the same management options;

(2) health care provider education programs which would seek to improve depression identification and management. Additionally, education programs would ideally be tested against no-screening usual care.

**Design:** Clustered pragmatic trials with general practices randomised to screening, non-screening usual care, or health care provider and patient education trial arms.

**Population:** All adults in general practice setting without a current diagnosis of depression and not receiving treatment for depression. In addition, screening that targets patients with risk factors (e.g., social disadvantage, long-term unemployment) may be considered.

**Interventions:** Option 1 (Dichotomous Screening): Positive and negative results determined using an a priori defined cut-off. Participants with positive screens are assessed for depression and, if appropriate, receive depression treatment. Treatment may be limited to treatments available in usual care or may include enhanced depression care with staff assistance to ensure accurate diagnosis, guideline-consistent treatment, and follow-up. Option 2 (Risk-based screening): Risk levels are determined by a model using actual screening tool scores and patient characteristics with several intervention options available (e.g., watchful waiting, low-intensity management option, high-intensity management option) based on risk and shared decision-making. Option 3 (Education): Depression identification and management education is provided to health care providers to attempt to improve identification, communication with patients, and management.

**Comparison:** Option 1 (Screening or education compared to no-screening usual care): Participants in comparison trial arm are not screened for depression. Participants identified as possibly depressed via self-report or unassisted recognition by a health care professional are assessed for depression, and, if appropriate, receive depression treatment. Management options should be the same as in the intervention arm. Option 2 (Screening compared to education): Head-to-head comparison of screening (dichotomous or risk-based) and education.

**Outcome:** The effect of depression screening on the severity of depressive symptoms, number of depression cases, suicidal thinking and attempts, and quality of life.

**Box: What patients need to know**

- As many as 1 in 10 patients in general practice settings may have depression, and this may be as high as 1 in 5 for patients with some chronic medical conditions.
- Most mild depression symptoms go away quickly without medical attention, but this is not always the case; symptoms that are ongoing and serious enough to affect your ability to enjoy social interactions or take care of home or work responsibilities usually require treatment.
- Using a questionnaire to screen for depression may not improve mental health outcomes compared to clinicians talking to patients about their experiences and concerns to determine if they may be depressed.
- There are effective treatments for depression. If you are experiencing symptoms that might be related to depression, such as sad mood, difficulty enjoying activities that you normally like, feelings of worthlessness or guilt, fatigue or lack of energy, or changes in your sleep patterns, it is important to discuss with your health care provider.
- Your health care provider can discuss your symptoms with you; help you to decide if you would like to undergo treatment, which usually involves taking medication or engaging in psychological therapy; discuss advantages and disadvantages of options; and help you to determine your preferences.

**Box: Education into practice**

- What do you do to ensure that patients know that you are able to help them if they are depressed and want to communicate their mental health concerns with you?
- How would you discuss patients' well-being with them and integrate questions about their mood and experiences that will allow you to evaluate if you should further assess for depression?

- What local referral resources do you have for patients who would benefit from additional assessment or mental health treatment, and are they accessible to patients with limited resources?

**Box: How patients were involved in the creation of this article**

One of our authors, Dr. Sarah Markham, is a patient advisor and a member of BMJ's International Patient Panel. She provided input on the article content, including on the need to ensure that patients are informed about the purpose of and evidence on depression screening; possible harms from screening; and the need for education of patients and health care providers on depression diagnosis and management. In addition, a patient reviewer kindly reviewed this paper for The BMJ and made similar recommendations regarding the importance of patient education and physician training. We are grateful for their input.

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