# Randomized Trial of the Effect of Research Design and Publication Characteristics on Physician Change

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**Background:** The primary barrier to translation of research into practice relates to physician use of research. If we are to succeed at translating research into practice, we must understand to which research characteristics and publication formats practitioners attend.

**Objective:** To determine which characteristics of research design (sample characteristics, study design) and publication (type of publication) are most influential on the acquisition of knowledge and change in behavior of family practitioners.

**Method:** This randomized clinical trial was conducted in family practice offices on the 305 family physicians who scored lowest on a survey of knowledge about management of major depressive disorder (MDD), panic disorder, and generalized anxiety disorder (GAD). Subjects were randomly assigned to receive 1 of 3 MDD abstracts differing in study site, 1 of 3 panic disorder abstracts differing in study design, and 1 of 3 GAD communications differing in format. The main outcome measures (knowledge and management strategies) were assessed immediately following the intervention and again 6 months later. Data for the intervention survey were gathered in November 2002.

**Results:** This study found significant increases in knowledge level and use of first-line agents with all interventions; however, knowledge declined again after 6 months for both panic disorder and GAD. The only statistically significant interoption difference was that the POEM (patient-oriented evidence that matters) was associated with better retention of knowledge of the treatment of GAD.

**Conclusion:** In conclusion, all interventions were associated with immediate increases in knowledge and use of first-line treatments. However, such gains were not retained for panic disorder and GAD. Except for better knowledge retention associated with POEM use, no consistent differences between intervention options were noted.

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**E**vidence-based medicine is receiving increasing attention,[1] and efforts for translating research results into practice have received increased funding. Practice-based research networks (PBRNs) are touted as a way to capture practitioners' attention. In addition, the *Journal of Family Practice* and *American Family Physician* have committed themselves to providing research results to practitioners in the form of POEMs (patient-oriented evidence that matters). However, little research has been done to assess the influence of these methods on practitioners. The observation that practice guidelines alone rarely evoke a change in physician behavior[2,3] emphasizes the need to test the ability of these methods to increase physicians' knowledge and change their behavior. Previous work has shown that how statistics are presented to physicians does make a difference in their impact.[4–6]

The primary barrier to translation of research into practice relates to physician use of research. Studies of information use by practitioners have found that they use colleagues and textbooks far more than they use research articles[7,8]; this is especially true of full-time practitioners.[8] Gorman and Helfand[9] found that in only 2 cases out of 88 did family physicians attempt to use a computer search to answer a clinical question. Of all sources of information, family physicians rate research as the least understandable and applicable.[7] In addition, research is rated more credible than only 1 other source—pharmaceutical representatives.[7] As a result, physicians often prefer review articles over research articles—a problematic stance because review articles are frequently out of date[10] and the methodological quality of most reviews published in primary care journals is poor.[11] If we are to succeed at translating research into practice, we

must change these antiresearch attitudes among practitioners and understand to which research characteristics and publication formats practitioners attend.

Do practitioners attend more to randomized controlled trials (RCTs), meta-analyses, or practice guidelines? Although the RCT is generally considered the gold standard and practice guidelines have not been shown to affect physician behavior, direct comparisons among these types of studies have not been done. Prescott et al.[12] found that general practitioners in England rarely used Cochrane reviews, and, in fact, 63% of physicians had never heard of the Cochrane Collaboration and 27% had heard of it but never used it.

By the same token, although study population is cited as a key factor in the applicability of research to primary care,[13,14] we do not know whether it is an important consideration to practitioners. Studies conducted in PBRNs are touted as having the most appropriate setting for family practitioners,[13] but are practitioners more likely to attend to research conducted in PBRNs? Evidence suggests that when family physicians perceive that the answer to a clinical question will be generalizable to their other patients, they are more likely to pursue the question.[9] Perhaps research from practice rather than academic or specialist settings may be perceived as more generalizable.

Finally, does the publication format make a difference? A POEM is a summary of valid research deemed to be relevant to physicians and patients. To be considered as a POEM, a summary must (1) address a question that primary care physicians face frequently, (2) report outcomes that are important to physicians and patients (e.g., symptoms, mortality, quality of life), and (3) have potential to change physician behavior. The brevity of a structured abstract may be equally effective. In light of recommendations that journals should tailor their publications to practitioners,[8] these questions assume greater importance.

The purpose of this study is to determine which characteristics of research design (sample characteristics, study design) and publication (type of publication) are most influential on the acquisition of knowledge and change in behavior of family practitioners. It was hypothesized that physicians would respond most to studies conducted in PBRNs, to meta-analyses, and to POEMs.

## METHOD

### Sample

As described previously,[15] the 3553 members of the Texas Academy of Family Physicians were surveyed concerning their knowledge and use of treatments for major depressive disorder (MDD), panic disorder, and generalized anxiety disorder (GAD), chosen because these disorders are commonly seen and treated in family practice settings, and because the mental health literature has repeatedly reported concern over inappropriate or inadequate treatment by primary care physicians. Respondents were asked to provide their address if they were willing to participate in an interventional study. To maximize our ability to identify an effect of the intervention, we sought to enroll physicians who scored poorest on the baseline assessment of knowledge of these subjects. Because at least 300 physicians were needed for the interventional study, the 305 respondents willing to participate with the lowest total score on the knowledge portion of the survey (scoring less than 242 out of a possible 300) were enrolled in the study. This study was reviewed and approved by the Institutional Review Board at the University of Texas Health Science Center at San Antonio.

### Instruments

Developed for this study, the Mental Health Knowledge and Management Instrument[15] consisted of 2 parts. In part 1, subjects were asked to indicate which treatments from the list provided were effective in the management of MDD, panic disorder, and GAD. In part 2, subjects were asked to indicate how they planned to treat the next patient they saw with each disorder (time 2 [postintervention]) or treated the most recent patient with each disorder (times 1 and 3 [baseline and 6-month follow-up]).

Based on recent practice guidelines and consensus statements,[16–20] each treatment in part 1 was assigned a score (Table 1). A "2" was assigned if the treatment was recommended as a first-line agent, and a "1," if the treatment was not first line but was effective in the disorder. Ineffective treatments were assigned a "0"; the contraindicated neuroleptic treatment of panic disorder was assigned a "–1." One point was also awarded if an ineffective or contraindicated treatment was not selected. Knowledge scores could range from 0 to 15 for MDD, –1 to 12 for panic disorder, and 0 to 14 for GAD. The total knowledge level was computed as the sum across treatments divided by the total score possible times 100 for each disorder. Use of a first-line agent was associated with significantly higher knowledge scores.[15]

Three outcomes were used for each disorder. First, the total knowledge score was used to represent treatment knowledge level. One measure of physician behavior was whether a first-line treatment had been prescribed to the most recently treated patient. The other measure of physician behavior was whether the most recently treated patient had been referred to a mental health provider for treatment other than cognitive-behavioral therapy (CBT). If an intervention was successful, we expected that the knowledge score and the proportion of patients prescribed a first-line treatment would increase, while the proportion of patients referred to mental health providers would decrease.

Table 1. Scoring Key for Physician Knowledge (part 1 of the Mental Health Knowledge and Management Instrument)[a,b]

| Treatment | Major Depressive Disorder | Panic Disorder | Generalized Anxiety Disorder |
|---|---|---|---|
| Antidepressants | | | |
| Tricyclic antidepressants | 2[c–e] | 1[d,f] | 2[d,g] |
| Trazodone | 1[e] | 0[f] | 0 |
| Selective serotonin reuptake inhibitors | 2[c–e] | 2[d,f] | 2[g] |
| Bupropion | 2[c,e] | 0[f] | 0 |
| Venlafaxine | 2[c,e] | 1[f] | 2[g] |
| Anxiolytics | | | |
| Low-potency benzodiazepines | 0[d] | 0[d,f] | 1[d,g] |
| High-potency benzodiazepines | 0[d] | 1[d,f] | 1[d,g] |
| Buspirone | 0[d] | 0[d,f] | 1[d,g] |
| Neuroleptics | 0[c] | –1[f] | 0[g] |
| β-Blockers | 0 | 0[f] | 0 |
| Cognitive-behavioral therapy | 1[c] | 1[f] | 1[g] |

[a]Reprinted with permission from Katerndahl and Ferrer.[15]
[b]Scoring was as follows: 2 = first-line agent, 1 = effective, 0 = not effective, –1 = contraindicated.
[c]Data from the American Psychiatric Association.[17]
[d]Data from the Institute for Clinical Systems Improvement.[19]
[e]Data from Snow et al.[20]
[f]Data from the American Psychiatric Association.[16]
[g]Data from Ballenger et al.[18]

## Intervention

For each disorder, 3 instructional interventions were prepared. Each intervention contained the same information and treatment recommendations for that disorder. For MDD, the intervention consisted of a structured abstract purportedly for a blinded randomized clinical trial; the 3 options differed only in the study site—a mental health setting, a family practice residency, and a PBRN. For panic disorder, the intervention consisted of a structured abstract reporting research purportedly conducted in a family practice setting but differing in the study design—a randomized clinical trial, a meta-analysis, and a practice guideline. Finally, the intervention for GAD differed in the communication format. One option consisted of the full article[21] with its abstract deleted; the other 2 options were developed from the article[21] and consisted of a structured abstract and a POEM created for this study.

Once enrolled in the study, each subject was randomly assigned using a random number generator to receive 1 of the 3 options for each disorder, with twice as many subjects receiving the option anticipated to have the greatest impact (i.e., PBRN, meta-analysis, POEM). Subjects were asked to read all 3 interventions that they received and then complete the survey instrument concerning their knowledge about treatment of the 3 disorders and indicate how they intended to treat the next patient they diagnosed with each disorder. To assess retention of effect, subjects were asked to complete the survey again 6 months later, indicating how they treated their most recent patients. Data collection and entry were done blinded to which intervention was received.

## Analysis

Because each mailing resulted in a markedly diminished response, analysis was separated into 2 phases; one phase focused on immediate response to the intervention, and the second phase dealt with retention of change. Approximately 6 months elapsed between the baseline assessment and the intervention, and another 6 months elapsed between the intervention and the follow-up. All respondents were used in analyses. To assess knowledge level, analyses of variance with repeated measures were conducted for each diagnosis comparing baseline and postintervention knowledge levels and comparing postintervention and 6-month follow-up results. Similarly, to assess use of first-line treatment and non-CBT mental health referral, CATMOD (SAS Institute, Inc.; Cary, N.C.) analyses with repeated measures were conducted for each diagnosis comparing baseline and postintervention results and comparing postintervention and 6-month follow-up results. CATMOD is a method of categorical data modeling that fits linear models to functions of response frequencies and can be used for repeated measurement analysis.[22] A p value ≤ .05 was considered significant. Post hoc testing used the Ryan-Einot-Gabriel-Welsch F (REGWF) method to assess interoption differences for each intervention. REGWF identifies homogeneous subsets of means and is based on an F test.[23] Intention-to-treat analyses were not performed. Power analyses show that the study had statistical powers of 97% for improvement with intervention and of 82% for retention of effect when seeking a large effect size and a p value ≤ .05.[24]

## RESULTS

Of the 387 initial survey respondents who agreed to participate (surveyed in June 2002), 305 were enrolled (Figure 1). Only 108 (35%) responded to the interventional survey in November 2002, and, of these, only 66 (61%) returned the 6-month follow-up survey in May 2003. The 108 subjects responding to the interventional survey were similar demographically to the 305 subjects enrolled (Table 2). Similarly, the 66 subjects returning the follow-up survey were demographically similar to the postintervention survey respondents. Although the baseline knowledge levels increased across these groups, the differences in mean scores from baseline were less than 2 points. Overall, use of first-line treatments was not associated with significant differences in knowledge level.

### Response to Intervention

*Knowledge level.* Table 3 shows that all interventions produced significant increases in knowledge level. Looking at specific treatments, knowledge of CBT in MDD improved the most, while for GAD the largest changes

Figure 1. Diagram of Participant Flow
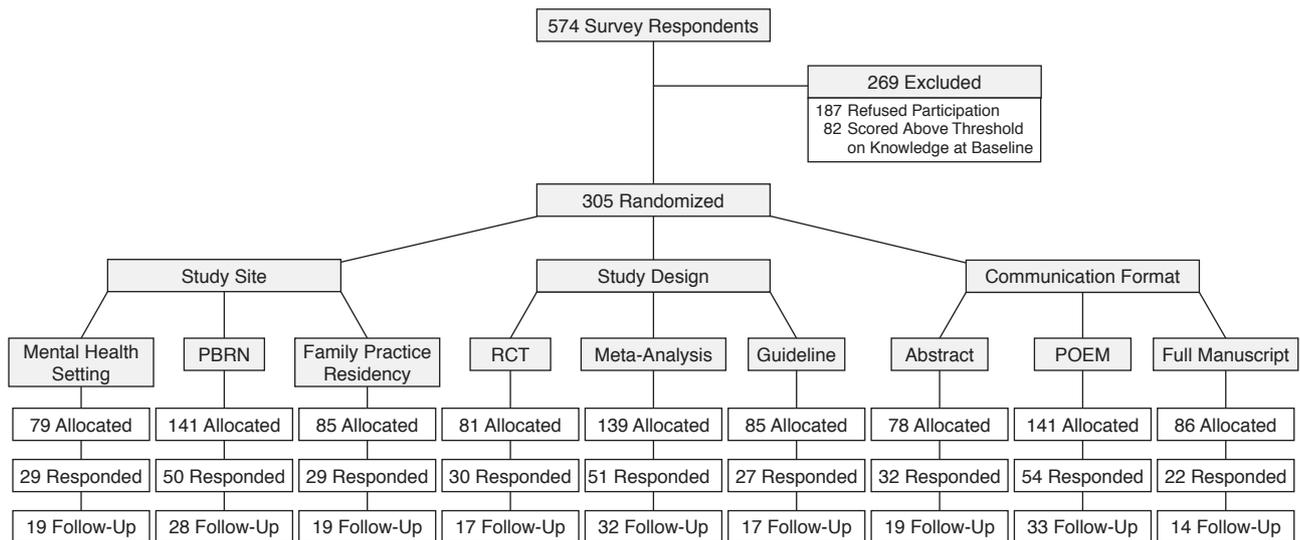


Abbreviations: PBRN = practice-based research network, POEM = patient-oriented evidence that matters, RCT = randomized controlled trial.

were for TCAs and β-blocker. For panic disorder, interventions were associated with increases in knowledge of TCAs and venlafaxine and decreases in belief of effectiveness of low-potency benzodiazepines and β-blocker.

*Treatment use.* Table 3 also demonstrates that all interventions were associated with increased use of first-line treatments, and in MDD and GAD, all interventions were associated with decreased non-CBT referrals. For MDD, interventions resulted in increased use or planned use of bupropion, venlafaxine, and CBT. For both panic disorder and GAD, interventions were associated with increased use of venlafaxine and CBT. Paradoxically, intervention was associated with an increase in non-CBT referral.

**Retention of Effect**

*Knowledge level.* Although knowledge level of MDD did not significantly decline (Table 4), knowledge levels decreased for both panic disorder and GAD. For panic disorder, subjects failed to retain knowledge of effectiveness of TCAs and venlafaxine, but forgot the lack of effectiveness of β-blocker. For GAD, subjects failed to retain knowledge of effectiveness of TCAs and CBT.

*Treatment use.* Table 4 demonstrates that subjects continued to use first-line treatments for MDD and continued to minimize non-CBT referrals for GAD. However, improvements in use of first-line treatments for panic disorder and GAD and changes in non-CBT referrals in MDD and panic disorder were not retained. Improvements in the use of bupropion, venlafaxine, and CBT declined the most for MDD. Use of CBT in both panic disorder and GAD also declined, as did use of venlafaxine in panic disorder.

**Interoption Comparisons**

No statistically significant interoption differences in interventions were found in either knowledge or treatment use for baseline versus postintervention. For MDD, the study option conducted in PBRNs tended to show the poorest effect, while that conducted in family practice residencies showed the best treatment usage. In terms of retention of effect, the RCT option tended to show the poorest retention of treatment usage and non-CBT referral in panic disorder, while the full paper option showed the poorest retention of treatment use and non-CBT referrals in GAD. The only statistically significant interoption difference found was that the POEM was significantly associated with retention of knowledge in GAD.

**DISCUSSION**

This study found significant increases in knowledge level with all interventions; however, knowledge declined again after 6 months for both panic disorder and GAD. Similarly, all interventions were associated with increases in the use of first-line treatments, but these declined after 6 months in panic disorder and GAD. Finally, all interventions were associated with decreases in the non-CBT referral rate in MDD and GAD, but changes were not retained after 6 months for MDD or panic disorder. No consistent differences between intervention options were noted.

There are several limitations to this study. First, the results are limited by the poor response rate. The initial response rate of 35% in our study is lower than the rates of 70% and 50% found by Bucher et al.[4] and Barry et al.,[25]

## Table 2. Sample Demographics[a]

| Characteristic | Respondents (N = 574) | Volunteers (N = 387) | Enrolled (N = 305) | Postintervention (N = 108) | Follow-Up (N = 66) |
|---|---|---|---|---|---|
| Gender | | | | | |
| Female | 160 (28) | 105 (27) | 79 (26) | 26 (24) | 14 (21) |
| Male | 413 (72) | 282 (73) | 226 (74) | 82 (76) | 52 (79) |
| Race | | | | | |
| Caucasian | 474 (83) | 327 (85) | 260 (85) | 93 (86) | 58 (88) |
| Black | 11 (2) | 8 (2) | 6 (2) | 2 (2) | 1 (2) |
| Asian | 41 (7) | 25 (7) | 19 (6) | 9 (8) | 3 (5) |
| Other | 43 (8) | 24 (6) | 18 (6) | 4 (4) | 4 (6) |
| Ethnicity | | | | | |
| Hispanic | 67 (12) | 42 (11) | 31 (10) | 8 (7) | 5 (8) |
| Non-Hispanic | 389 (68) | 272 (70) | 241 (70) | 84 (78) | 51 (77) |
| Age | | | | | |
| < 45 y | 253 (44) | 177 (46) | 133 (44) | 51 (47) | 32 (49) |
| 45–64 y | 280 (49) | 182 (47) | 145 (48) | 50 (46) | 30 (45) |
| ≥ 65 y | 34 (6) | 25 (7) | 24 (8) | 7 (7) | 4 (6) |
| Site | | | | | |
| Rural | 184 (32) | 126 (33) | 101 (33) | 39 (36) | 19 (29) |
| Urban | 380 (66) | 256 (66) | 200 (66) | 68 (63) | 47 (71) |
| Years in practice, mean ± SD | 15.6 ± 11.1 | 15.6 ± 11.4 | 16.5 ± 11.6 | 15.8 ± 10.9 | 16.3 ± 10.6 |
| Practice setting | | | | | |
| Private practice | 472 (82) | 312 (81) | 247 (81) | 84 (78) | 50 (76) |
| University department | 40 (7) | 30 (8) | 22 (7) | 8 (7) | 6 (9) |
| Residency program | 45 (8) | 32 (8) | 26 (9) | 12 (11) | 8 (12) |
| Baseline knowledge, mean ± SD[b] | | | | | |
| Major depressive disorder | | | 89.3 ± 13.1 | 90.4 ± 12.8 | 91.1 ± 11.7 |
| Panic disorder | | | 64.1 ± 12.8 | 64.7 ± 12.7 | 64.8 ± 12.2 |
| Generalized anxiety disorder | | | 62.0 ± 11.2 | 63.4 ± 10.0 | 63.9 ± 9.6 |

[a]Values shown as N (%) unless otherwise noted. Percentages sum less than 100% for some variables due to missing data.
[b]The total knowledge level was computed as the sum across treatments divided by the total score possible times 100 for each disorder. (Scoring for each treatment was as follows: 2 = first-line agent, 1 = effective, 0 = not effective, −1 = contraindicated.) Knowledge scores could range from 0 to 15 for major depressive disorder, −1 to 12 for panic disorder, and 0 to 14 for generalized anxiety disorder.

respectively. In addition, the response rate progressively declined over the course of the study, although respondents were generally similar to all subjects enrolled. However, the proportion of physicians reporting use of a first-line treatment at baseline is higher than we would expect based on the low rates (32%–35%) of guideline-concordant care provided for MDD, panic disorder, and GAD reported by Wing et al.[26] Second, the wording of assessment of treatment changed from period to period. Whereas at baseline and 6-month follow-up treatment focused on the last patient seen, postintervention treatment focused on the next patient seen. Finally, the high knowledge level for depression at baseline may have reduced our ability to detect differences among the options.

Compared with the previous literature, this study agrees with findings that providing clinicians with information can increase knowledge level[27] and produce behavior change. Such change, however, is usually slow.[28] Little work has been done on the retention of change in knowledge or behavior. Whereas this study found significant immediate effects of all interventions on both knowledge and behavior, only in MDD did changes last 6 months. This may reflect more interest in depression among these physicians at baseline as evidenced by their high baseline knowledge levels.

Previous literature has not looked at the possible differential effect of research based on sample site. Despite the enthusiasm for PBRNs in academic family medicine, practitioners may be unfamiliar with or skeptical about their use and results, feeling more comfortable that researchers in residency programs know what they are doing.

Similarly, no quantitative differences were found among the study design options. This may seem counterintuitive because physicians are indoctrinated in medical school about the validity of the RCT design and previous work has shown that physicians generally do not respond to practice guidelines.[2,3] However, our findings suggest that physicians may recognize that, although RCTs yield valid results, they are more limited than meta-analyses and practice guidelines in their generalizability.

Finally, although none of the communication formats were associated with differences in immediate effect, the study presented as a POEM led to significantly better knowledge retention. Previous work comparing immediate effect of abstracts versus POEMs found no difference.[25] Although our study agrees in terms of immediate effect, our POEM was associated with better knowledge retention. Similarly, previous work found that no difference in comprehension was observed when compar-

Table 3. Change in Physician Knowledge and Behavior With Intervention (N = 108)

| Intervention | Treatment Knowledge Score, Mean[a] | | | First-Line Treatment Use, % | | | Non-CBT Referral, % | | |
|---|---|---|---|---|---|---|---|---|---|
| | Baseline | Postintervention | p[b] | Baseline | Postintervention | p[b] | Baseline | Postintervention | p[b] |
| Major depressive disorder | | | ≤ .001 | | | ≤ .001 | | | ≤ .001 |
| Study site | | | | | | | | | |
| Mental health setting | 86.9 | 94.0 | | 44.8 | 100 | | 34.5 | 6.9 | |
| Family practice residency | 91.7 | 95.7 | | 40.0 | 98.0 | | 44.0 | 12.0 | |
| Practice-based research network | 91.7 | 93.8 | | 51.7 | 100 | | 24.1 | 13.8 | |
| Panic disorder | | | ≤ .001 | | | ≤ .01 | | | ≤ .001 |
| Study design | | | | | | | | | |
| Randomized clinical trial | 66.7 | 73.3 | | 66.7 | 86.7 | | 16.7 | 36.7 | |
| Meta-analysis | 64.2 | 75.0 | | 74.5 | 84.3 | | 19.6 | 35.3 | |
| Practice guideline | 63.3 | 77.4 | | 81.5 | 88.9 | | 18.5 | 37.0 | |
| Generalized anxiety disorder | | | ≤ .001 | | | ≤ .001 | | | ≤ .005 |
| Communication format | | | | | | | | | |
| Research abstract | 61.6 | 73.9 | | 50.0 | 78.1 | | 28.1 | 6.3 | |
| POEM | 65.1 | 74.5 | | 53.7 | 87.0 | | 14.8 | 3.7 | |
| Research paper | 62.0 | 71.4 | | 40.9 | 95.5 | | 22.7 | 9.1 | |

[a]The total knowledge level was computed as the sum across treatments divided by the total score possible times 100 for each disorder. (Scoring for each treatment was as follows: 2 = first-line agent, 1 = effective, 0 = not effective, –1 = contraindicated.) Knowledge scores could range from 0 to 15 for major depressive disorder, –1 to 12 for panic disorder, and 0 to 14 for generalized anxiety disorder.
[b]p Values represent comparisons of baseline and postintervention scores for each disorder.
Abbreviations: CBT = cognitive-behavioral therapy, POEM = patient-oriented evidence that matters.

Table 4. Retention of Effect of Intervention on Physician Knowledge and Behavior (N = 66)

| Intervention | Treatment Knowledge Score, Mean[a] | | | First-Line Treatment Use, % | | | Non-CBT Referral, % | | |
|---|---|---|---|---|---|---|---|---|---|
| | Postintervention | 6-month | p[b] | Postintervention | 6-month | p[b] | Postintervention | 6-month | p[b] |
| Major depressive disorder | | | NS | | | NS | | | ≤ .005 |
| Study site | | | | | | | | | |
| Mental health setting | 93.7 | 92.3 | | 100 | 100 | | 5.3 | 26.3 | |
| Family practice residency | 95.2 | 91.9 | | 96.4 | 100 | | 10.7 | 32.1 | |
| Practice-based research network | 94.0 | 94.0 | | 100 | 94.7 | | 21.1 | 42.1 | |
| Panic disorder | | | ≤ .001 | | | ≤ .005 | | | ≤ .001 |
| Study design | | | | | | | | | |
| Randomized clinical trial | 69.0 | 64.7 | | 88.2 | 64.7 | | 29.4 | 11.8 | |
| Meta-analysis | 75.0 | 64.5 | | 87.5 | 71.9 | | 37.5 | 18.8 | |
| Practice guideline | 78.1 | 67.4 | | 88.2 | 70.6 | | 47.1 | 11.8 | |
| Generalized anxiety disorder | | | ≤ .01 | | | ≤ .01 | | | NS |
| Communication format | | | | | | | | | |
| Research abstract | 72.9 | 59.4 | | 84.2 | 73.7 | | 10.5 | 10.5 | |
| POEM | 71.6 | 70.6[c] | | 81.8 | 72.7 | | 3.0 | 6.1 | |
| Research paper | 69.9 | 63.3 | | 92.9 | 64.3 | | 14.3 | 28.6 | |

[a]The total knowledge level was computed as the sum across treatments divided by the total score possible times 100 for each disorder. (Scoring for each treatment was as follows: 2 = first-line agent, 1 = effective, 0 = not effective, –1 = contraindicated.) Knowledge scores could range from 0 to 15 for major depressive disorder, –1 to 12 for panic disorder, and 0 to 14 for generalized anxiety disorder.
[b]p Values represent comparisons of baseline and postintervention scores for each disorder.
[c]p ≤ .05 for POEM vs. research abstract and research paper.
Abbreviations: CBT = cognitive-behavioral therapy, NS = nonsignificant, POEM = patient-oriented evidence that matters.

ing a summary versus a full review manuscript.[29] However, previous work has focused on immediate effects, while the differences we found were in retention of effect.

The results of this study imply that we can affect change using the best evidence available from whatever site and design, communicating such results via the simplest format. However, there is a clear need for more research in this area using larger samples, better follow-up, and diverse clinical problems.

In conclusion, all interventions were associated with immediate increases in knowledge and use of first-line treatments. However, such gains were not retained for panic disorder and GAD. The only statistically significant interoption difference was that the POEM was associated with better retention of knowledge of the treatment of GAD.

*Drug names:* bupropion (Wellbutrin and others), venlafaxine (Effexor).

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