# Letters

RESEARCH LETTER

## Effect of Escalating and Deescalating Financial Incentives vs Usual Care to Improve Antidepressant Adherence: A Pilot Randomized Clinical Trial

Although antidepressant medications are efficacious for depression,[1] nonadherence frequently undermines their effectiveness.[2] Antidepressants have a delayed onset and therefore do not offer prompt symptom relief that would support adherence.[3] It is unknown whether financial incentives, which encourage adherence to some[4] but not other[5] health behaviors, improve antidepressant adherence for depression. This randomized clinical trial (ClinicalTrials.gov Identifier: NCT03441399) compared 2 behavioral economics–based financial incentives for daily antidepressant adherence: (1) escalating incentives that leverage loss aversion because patients who initiate treatment face ever-greater lost opportunities if they discontinue medication use and (2) deescalating incentives that leverage a tendency to overweigh present benefits by providing larger rewards to overcome initial inertia concerning treatment initiation.

Supplemental content

**Methods** | Electronic health records identified patients with depression (*International Statistical Classification of Diseases, Tenth Revision, Clinical Modification* [*ICD-10-CM*] codes F33 and F32), aged 21 to 64 years, without antidepressant use in the last 90 days, who had been prescribed an antidepressant in the last 10 days. Five primary care practices in a Philadelphia, Pennsylvania, academic medical center participated. Patients with clinical diagnoses of substance use disorder (*ICD-10-CM* codes F10-F19), schizophrenia and associated disorders (*ICD-10-CM* codes F20 and F25), bipolar disorder (*ICD-10-CM* code F31), or pregnancy (*ICD-10-CM* code Z34) were excluded. Statistical power was based on detection of a moderate to large effect size (Cohen *d*, 0.6; power = 0.80; 2-sided α = .05); 40 participants per arm were assigned in concealed blocks of 6 by random number generation. Patients, who were recruited via telephone by the study team without involvement of clinicians, were invited to give oral informed consent between March 2018 and June 2019 (Trial Protocol in Supplement 2). The University of Pennsylvania institutional review board approved the study.

Patients with depression diagnoses and Patient Health Questionnaire (PHQ)-9 scores of 10 or more (theoretical range, 0-27)[6] who were initiating antidepressant treatment were randomized in equal proportion to receive 6 weeks of (1) usual care, (2) usual care and escalating daily financial incentives ($2/day, increasing by $1/week up to $7/day), or (3) usual care and deescalating financial incentives ($7/day, decreasing to $2/day) for each antidepressant-adherent day. Daily adherence was measured using cellular smart pill bottles and participants in the intervention received weekly credits to a debit card and text notifications.

A mean change in antidepressant adherence was the primary outcome, and adherence of 80% or greater was a post hoc outcome. Depression symptoms were assessed twice with the PHQ-9 by blinded telephone evaluations at screening and 6 weeks postmedication initiation. Analyses compared inter-

Table 1. Background Characteristics of Adult Patients With Depression in Primary Care, by Incentive Group

| Characteristic | Participants, No. (%) | | | Overall *P* value |
|---|---|---|---|---|
| | Escalating group (n = 40) | Deescalating group (n = 40) | Control group (n = 40) | |
| Age, mean (SD), y | 38.9 (12.6) | 41.4 (11.1) | 38.9 (11.2) | .55 |
| Female sex | 36 (90.0) | 31 (77.5) | 33 (82.5) | .32 |
| Black/African-American race[a] | 24 (60.0) | 20 (50.0) | 26 (65.0) | .38 |
| Hispanic ethnicity[a] | 2 (5.0) | 4 (10.0) | 0 (0.0) | .12 |
| Full-time employment | 24 (60.0) | 23 (57.5) | 24 (60.0) | .97 |
| High school education or less | 14 (35.0) | 11 (27.5) | 8 (20.0) | .32 |
| <$40 000 annual household income | 24 (60.0) | 17 (42.5) | 20 (50.0) | .23 |
| Married[b] | 9 (22.5) | 18 (45.0) | 11 (27.5) | .08 |
| Private health insurance | 25 (62.5) | 26 (65.0) | 26 (65.0) | .96 |
| Prior use of antidepressant | 16 (40.0) | 22 (55.0) | 23 (57.5) | .24 |
| Antidepressant type | | | | |
| Selective serotonin reuptake inhibitor | 27 (67.5) | 30 (75.0) | 29 (72.5) | .95 |
| Serotonin-norepinephrine reuptake Inhibitor | 5 (12.5) | 4 (10.0) | 5 (12.5) | |
| Atypical | 8 (20.0) | 6 (15.0) | 6 (15.0) | |
| Patient Health Questionnaire-9 score at screening, mean (SD) | 17.0 (3.8) | 15.6 (3.7) | 16.0 (3.5) | .24 |

[a] Because antidepressant adherence has been reported to vary by race/ethnicity, race/ethnicity data were collected. These data were collected by patient self-report using investigator defined categories.

[b] Includes being married and living with someone as though married.

Table 2. Outcomes at 6 Weeks of Adult Patients With Depression in Primary Care, by Incentive Group

| Outcome | No. (%) | | | *P* value | | |
|---|---|---|---|---|---|---|
| | Escalating group | Deescalating group | Control group | Escalating vs deescalating[a] | Escalating vs control | Deescalating vs control |
| Antidepressant adherence at 6 wk[b] | | | | | | |
| Antidepressant adherence percentage, mean (SD), % | 90.7 (14.6) | 83.4 (22.8) | 74.9 (23.6) | .09 | <.001 | .12 |
| Antidepressant adherence (≥80%) | 35 (87.5) | 26 (68.4) | 18 (47.4) | .04 | <.001 | .06 |
| PHQ-9 score at 6 wk[c] | | | | | | |
| Depression symptom response[d] | 26 (65.0) | 24 (63.2) | 14 (40.0) | .87 | .03 | .048 |
| Depression symptom remission[e] | 14 (35.0) | 10 (26.3) | 3 (8.6) | .41 | .01 | .048 |
| Financial incentives provided, mean (SD), $ | 163 (5.3) | 168 (5.3) | NA | .53 | NA | NA |

Abbreviations: NA, not applicable; PHQ-9, Patient Health Questionnaire–9.

[a] Post hoc comparison.

[b] The escalating group had 40 participants in this analysis; the deescalating group, 38; the control group, 38.

[c] The escalating group had 40 participants in this analysis; the deescalating group, 38; the control group, 35.

[d] Symptom response denotes 50% or greater decrease in score from screening.

[e] Symptom remission denotes PHQ-9 score of 0 to 4 at 6 weeks.

vention groups and the control group on changes in PHQ-9 scores from screening to 6-week follow-up, with standard cutoffs for depression response (≥50% decrease in score) and remission (score, <5) as secondary outcomes. Group differences are tested with $\chi^2$ for categorical variables and analysis of variance for continuous variables. Stata version 15 (StataCorp) generated $\chi^2$ and *t* test *P* values (2-sided tests, α = .05) and the csi command generated 95% CIs.

**Results** | Background characteristics (N = 120; female sex: control group, 33 of 40 [82.5%]; escalating group, 36 of 40 [90.0%]; deescalating group, 31 of 40 [77.5%]; mean [SD] ages: escalating group, 38.9 [12.6] years; deescalating group, 41.4 [11.1] years; control group, 38.9 [11.2] years) and mean (SD) PHQ-9 scores (escalating group, 17.0 [3.8]; deescalating group, 15.6 [3.7]; control group, 16.0 [3.5]) of the 3 patient groups are presented in **Table 1** and the eFigure in Supplement 1. During the 6 week follow-up, the escalating group was significantly more likely to be adherent than control participants (mean [SD] adherence, 90.7% [14.6%] vs 74.9% [23.6%]; difference, 15.8%; 95% CI, 7.0%-24.6%), although the deescalating and control groups did not differ. Compared with control participants, the escalating group was significantly more likely to achieve symptom response (25 [65.0%] vs 14 [40.0%]; *P* = .04), remission (14 [35.0%] vs 3 [8.6%]; *P* = .01), and adherence of 80% or more (35 [87.5%] vs 18 [47.4%]; *P* < .001) (**Table 2**). Compared with control participants, the deescalating group was also more likely to achieve symptom response (24 [63.2%] vs 14 [40.0%]; *P* = .048) and remission (10 [26.3%] vs 3 [8.6%]; *P* = .048) but not adherence of 80% or more. In post hoc analyses, the escalating group compared with the deescalating group was more likely to be have adherence of 80% of more (35 [87.5%] vs 26 [68.4%]; *P* = .04) but was not significantly more likely to achieve symptom response or remission.

**Discussion** | In this pilot study, escalating incentives for daily antidepressant adherence significantly improved adherence compared with a control group during the critical first 6 weeks of treatment. The outcomes of deescalating and control groups did not significantly differ.

Limitations include small sample sizes, a possible Hawthorne effect associated with the smart pill bottles, a brief period of follow-up, heterogeneity of antidepressant prescribing, and generalizability limited to nonelderly adult patients without common psychiatric comorbidities. Future research should include evaluations of financial incentives powered to ascertain sustainability of antidepressant adherence and symptom improvement.

**Steven C. Marcus, PhD**
**Megan E. Reilly, MPH**
**Kelly Zentgraf, MS**
**Kevin G. Volpp, MD, PhD**
**Mark Olfson, MD, MPH**

**Author Affiliations:** University of Pennsylvania School of Social Policy and Practice, Philadelphia (Marcus); Perelman School of Medicine, University of Pennsylvania, Philadelphia (Reilly, Zentgraf, Volpp); Department of Psychiatry, Columbia University, New York, New York (Olfson).

**Accepted for Publication:** July 27, 2020.

**Corresponding Author:** Steven C. Marcus, PhD, University of Pennsylvania School of Social Policy and Practice, 3701 Locust Walk, Philadelphia, PA 19104 (marcuss@upenn.edu).

**Published Online:** September 23, 2020. doi:10.1001/jamapsychiatry.2020.3000

**Author Contributions:** Dr Marcus had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
*Concept and design:* Marcus, Zentgraf, Olfson.
*Acquisition, analysis, or interpretation of data:* All authors.
*Drafting of the manuscript:* Marcus, Reilly, Zentgraf, Olfson.
*Critical revision of the manuscript for important intellectual content:* All authors.
*Statistical analysis:* Marcus, Reilly.
*Obtained funding:* Marcus, Olfson.
*Administrative, technical, or material support:* Reilly, Zentgraf, Volpp.
*Supervision:* Marcus, Volpp.

**Conflict of Interest Disclosures:** Dr Volpp reported grants from National Institute of Mental Health during the conduct of the study; grants from Hawaii Medical Services Association, Vitality/Discovery, Humana, WW, and Oscar; personal fees from Center for Corporate Innovation, Lehigh Valley Medical Center, Vizient, Greater Philadelphia Business Coalition on Health, American

Gastroenterological Association Tech Conference, Bridges to Population Health Meeting, and Irish Medtech Summit outside the submitted work; and being a part owner and consultant at VAL Health, a behavioral economics consulting firm. Dr Marcus reported grants from National Institute of Mental Health during the conduct of the study and personal fees from Allergan and Sage Therapeutics outside the submitted work. Dr Olfson reported grants from National Institute of Mental Health during the conduct of the study. No other disclosures were reported.

**Funding/Support:** This study was funded through National Institute of Mental Health (grant P50 MH113840).

**Role of the Funder/Sponsor:** The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Data Sharing Statement:** See Supplement 3.

**1**. Park LT, Zarate CA Jr. Depression in the primary care setting. *N Engl J Med*. 2019;380(6):559-568. doi:10.1056/NEJMcp1712493

**2**. Silhan P, Urinovska R, Kacirova I, Hyza M, Grundmann M, Ceskova E. What does antidepressant drug level monitoring reveal about outpatient treatment and patient adherence? *Pharmacopsychiatry*. 2019;52(2):78-83. doi:10.1055/s-0044-101838

**3**. Gudayol-Ferré E, Guàrdia-Olmos J, Peró-Cebollero M, et al. Prediction of the time-course pattern of remission in depression by using clinical, neuropsychological, and genetic variables. *J Affect Disord*. 2013;150(3):1082-1090. doi:10.1016/j.jad.2013.04.024

**4**. Volpp KG, John LK, Troxel AB, Norton L, Fassbender J, Loewenstein G. Financial incentive-based approaches for weight loss: a randomized trial. *JAMA*. 2008;300(22):2631-2637. doi:10.1001/jama.2008.804

**5**. Gopalan A, Shaw PA, Lim R, et al. Use of financial incentives and text message feedback to increase healthy food purchases in a grocery store cash back program: a randomized controlled trial. *BMC Public Health*. 2019;19(1):674. doi:10.1186/s12889-019-6936-5

**6**. Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. *CMAJ*. 2012;184(3):E191-E196. doi:10.1503/cmaj.110829