enrollment in the future. We made similar observations of limited accrual to the National Clinical Trials Network Molecular Analysis for Therapy Choice trial after treating physicians were provided with detailed enrollment information following identification of a qualifying sequence variation through the molecular testing platform at the University of Chicago Medical Center. These findings raise the hypothesis that the biggest barrier to enrollment, as in other settings, is motivation of treating physicians and that algorithms for identifying potential participants need to be aligned with patients' treatment trajectory.[5,6]

This study was limited by not addressing other relevant factors associated with patient enrollment, including financial barriers, availability of standard-of-care options, and socioeconomic factors such as travel barriers. Larger-than-anticipated target populations, better coordination between outreach efforts and enrollment status, and directed patient outreach may be necessary.

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Acquisition, analysis, or interpretation of data: Paydary, DeLuca, Wall, Stadler.
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Assessment of Psilocybin Therapy for Patients With Cancer and Major Depression Disorder

About 15% of patients with cancer experience major depression, which is associated with lower treatment adherence and reduced quality of life.[1,2] Yet, oncologists often feel inadequate to address mental health issues, and many treatments have limited success in treating depression.[3]

Psilocybin is a 5-HT_{2A} receptor agonist with success in reducing a variety of psychiatric symptoms while using 2 therapists per patient.[4] To create a scalable, rapidly effective depression treatment, this nonrandomized controlled trial administered psilocybin in a 1-to-1 therapist-to-patient ratio to groups of patients with cancer who were diagnosed with major depression disorder in a community cancer center.

Supplemental content

Methods | Thirty participants were recruited at Aquilino Cancer Center and through referrals from specialized psychiatric and oncology services. They were grouped into cohorts of 3 to 4 by timing of recruitment. Participants were adults with a diagnosis of cancer (*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes C00-C97) and major depression disorder. The study protocol (Supplement 1) was approved by the Advarra Institutional Review Board, and written consent was obtained from each participant.

This was a phase 2, single-center, fixed-dose, open-label study. Cohorts of 3 to 4 patients were simultaneously treated with a 25-mg dose of COMP360 (COMPASS Pathways) in adjacent rooms open to a common space, in a 1-to-1 therapist-to-patient ratio. The cohorts received group therapy in 1 preparation and 2 integration sessions, supplemented by individual therapy. Outcome measures included safety and improvement in depression, which was primarily measured with the Montgomery-Asberg Depression Rating Scale (MADRS), with higher scores denoting greater severity. Sustained response to treatment was defined as a decrease in MADRS score of 50% or more from baseline to week 3 and week 8, and remission as a MADRS score lower than 10 posttreatment. Other measures of depression included the Quick Inventory of Depressive

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Table. Demographic and Clinical Characteristics of Study Participants (N = 30)

Characteristic	No. (%)[a]
Age, mean (range), y	56 (30-78)
Gender	
Female	21 (70)
Male	9 (30)
Race and ethnicity	
Asian, Asian American, or Pacific Islander	2 (7)
Black	3 (10)
Hispanic or Latin	1 (3)
Non-Hispanic White	24 (80)
Marital status	
Married	20 (67)
Divorced/separated	5 (17)
Never married	5 (17)
Employment status	
Employed	25 (83)
Retired	4 (13)
Unemployed	1 (3)
Cancer prognosis	
Noncurable	16 (53)
Curable	14 (47)
Lines of cancer therapy	
≤1	9 (30)
>1	21 (70)
No. of depressive episodes	
≤3	9 (30)
>3	12 (40)
Unknown	9 (30)
No prior antidepressant use	
Yes	15 (50)
No	11 (37)
Unknown	4 (13)
Baseline depression via MADRS score, mean (range)	25.9 (14-40)

Abbreviation: MADRS, Montgomery-Asberg Depression Rating Scale.

[a] Percentages may not add to 100% due to rounding.

Symptomatology-Self-Report[5] and the Maudsley Visual Analogue Scale.[6]

Results | A total of 30 participants were enrolled and completed the study per protocol; the attrition rate was 0%. The mean (SD) age was 56 (12) years with 9 (30%) men and 21 (70%) women (**Table**). Fourteen (47%) participants had curable cancers, while 16 (53%) had noncurable cancers. Half of the sample reported previous antidepressant drug therapy (n = 15).

No treatment-related serious adverse events occurred, and there was no suicidality based on the Columbia Suicide Severity Rating Scale. Adverse events were mild or expected and included headache (n = 24), nausea (n = 12), altered mood (n = 8), anxiety (n = 7), and hallucinations (n = 1).

Efficacy was suggested with a robust reduction in MADRS scores from baseline to posttreatment of 19.1 points (95% CI, −22.3 to −16.0 points; $P < .001$) by week 8. A sustained response was observed in 24 (80%) patients, with 15 (50%) patients showing full remission of depressive symptoms.

These findings were supported by self-reported measures of depressive symptoms. Quick Inventory of Depressive Symptomatology-Self-Report scores declined by an average of 5.9 (95% CI, −7.2 to −4.6) points, a 48% reduction from baseline to week 8. The Maudsley Visual Analogue Scale showed a change of −46.2 (95% CI, −61.6 to −30.7) points, a 53% decrease in self-rated depression severity.

Discussion | To our knowledge, this is the first psilocybin therapy trial conducted in a community cancer setting rather than a psychiatric hospital or academic center. With an innovative study design of treating cohorts simultaneously, using 1 therapist per patient, and providing group therapy support, participants experienced clinically meaningful, rapid, and sustained improvement in symptoms of depression over 8 weeks following a single treatment of psilocybin therapy. This occurred in patients with both curable and metastatic cancer.

Limitations include a lack of control arm. Comparison with placebo and other antidepressant treatments for patients with cancer is needed. Nonetheless, this study demonstrates the safety and preliminary efficacy of psilocybin treatment for patients with cancer and depression using a scalable model with a 1-to-1 therapist-to-participant ratio and simultaneous administration, justifying a randomized clinical trial.

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Correction: This article was corrected on July 11, 2024, to fix errors in the Table.

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Concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Agrawal, Emanuel, B. Richards, Roddy, Thambi.
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College; serving as an uncompensated speaker, panelist, or moderator for Center for Global Development, American Academy of Arts and Sciences, University of California, San Francisco, World Affairs, Unite Us, University of Pennsylvania Engaging Minds, Vagelos College of Physicians and Surgeons, United Nations Educational, Scientific and Cultural Organization Global Conference, School of Pharmaceutical and Biotech Business, National Institutes of Health Demystifying Medicine Series, American Society of Preventive Oncology 45th Annual Meeting, Blue Cross Blue Shield National Customer Advisory Council, University of Pennsylvania Cellicon Valley 2021, Independent Health and Aged Care Pricing Authority Activity Based Funding Conference, University of Pennsylvania Leonard Davis Institute of Health Economics, Penn Medicine Alumni Weekend, National Health Equity Summit, Galien Foundation, Temple Sholom of Chicago, Perry World House Graduate Association, the Italian Medicine Agency, Penn Rising Scholar Success Academy, Syllable and Oak Portico, Rainbow PUSH Coalition, Infectious Diseases Society of America, VinFuture, Leonard David Institute, Brown University, Organisation for Economic Co-operation and Development, 21st Population Health Colloquium, VillageMD, University of Pennsylvania College of Liberal and Professional Studies, University of Sydney, Tel Aviv University, American Philosophical Society, Health Action Alliance, Yale University, Association of Bioethics Program Directors Spring Meeting, Icahn School of Medicine at Mount Sinai, Abramson Cancer Center, University of Minnesota, Institute for Peace and Security Studies Addis Conference, Faith Health Alliance, The Wharton School at the University of Pennsylvania, Oak CEO Summit, Centers for Disease Control and Prevention, American Academy of Political and Social Science, Primary Care Transformation, 16th World Congress of Bioethics, Blue Cross Blue Shield Alliance for Health Research, White House Cancer Moonshot, BC Philadelphia, American Society of Clinical Oncology Quality Care Symposium, and Brookings Institution; serving on the board of advisors of Notable, external advisory board of VillageMD, advisory board of Health Innovation Exchange, internal advisory board of Colton Center for Autoimmunity, advisory board of JSL Health Fund, expert advisory board of the World Health Organization COVID-19 Ethics & Governance Working Group, and advisory board of President Biden's Transition COVID-19 Committee; and serving as special advisor to the World Health Organization director general, member of the advisory board of the Peterson Foundation, advisor for Clarify Health, unpaid board member for Oncology Analytics, founding member of COVID-19 Recovery LLC, founding partner of Embedded LLC, venture partner of Oak HC/FT, and a member of the board of advisors for Cellares. Dr W. Richards reported grants from COMPASS Pathways during the conduct of the study and stock in COMPASS Pathways outside the submitted work. Dr Thambi reported nonfinancial support from COMPASS Pathways and grants from Shady Grove Medical Center Foundation during the conduct of the study, as well as stock in Sunstone Therapies outside the submitted work. No other disclosures were reported.

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COMMENT & RESPONSE

Association of Polycystic Ovary Syndrome With Pancreatic Cancer

To the Editor We read with much interest the Research Letter by Peeri et al[1] on the association of polycystic ovary syndrome (PCOS) with an increased risk of pancreatic cancer and would like to commend the authors for taking the initiative to address this underreported issue. While stating novelty just second to the Swedish registry-based study[2] and with a claim of being the first to be adequately powered, there are some points that demand further clarification.

First, being a case-control study,[1] it is perhaps optimal to have 4 controls for each case,[3] or maybe a 1:1 ratio; however, composing a cohort of which two-thirds are cases of pancreatic cancer is indeed questionable. It is therefore interesting to see how well matched the controls were to the cases or how they differed, but no such statistical analysis was presented, unfortunately. Furthermore, diagnosis of PCOS was self-reported by participants,[1] although diagnosis of PCOS is not without limitations even for experienced practitioners, let alone for the public.[4] However, much more enigmatic are the numbers. While as per the authors[1] the study was adequately powered, notwithstanding that such calculation was not presented, it is obvious that 11% vs 9% is far from being statistically significant in this study ($P = .43$), and it is not surprising that the odds ratio was not presented (1.3 [95% CI, 0.74-2.30]). Importantly, it is not understandable why such a nonsignificant variable was entered into the logistic regression, and why other variables were entered as well, as they seem similar in the table presented. An explanation of how missing data were entered into the regression analysis is also lacking, and performing a logistic regression for an outcome that is present in two-thirds of the cohort should also be explained. Lastly, discussing pancreatic cancer risk without mentioning genetic susceptibility, such as *BRCA* gene carrier status, should be avoided. Summarizing, we would avoid statements indicating a strong association when the confidence interval is 1.02 to 3.46 in light of the abovementioned. We believe it is too early to conclude that PCOS is associated with pancreatic cancer based on this research letter. Hopefully, a thorough statistical analysis will provide more data.

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