

VALUE & OUTCOMES SPOTLIGHT

A magazine for the global HEOR community.



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Improving healthcare decisions

VALUE & OUTCOMES SPOTLIGHT

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The mission of *Value & Outcomes Spotlight* is to foster dialogue within the global health economics and outcomes research (HEOR) community by reviewing the impact of HEOR methodologies on health policy and healthcare delivery to ultimately improve decision making for health globally.

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Mental Health: A Call to Action

Mental health is a crucial determinant of individual and population health, as well as social and economic development. However, mental disorders are among the leading causes of disability and disease burden worldwide, affecting millions of people and their families. Mental disorders can increase the risk of physical health problems, such as heart disease, diabetes, and stroke, as well as impair social and occupational functioning, reduce the quality of life, and increase mortality. Mental disorders also impose a heavy burden on society, causing substantial costs and losses in productivity, welfare, and security.

However, mental health is often neglected and underfunded in many countries, resulting in a large gap between the need for and the availability of quality mental health care. Moreover, mental health is frequently stigmatized and discriminated against, creating barriers to access and recovery. Therefore, there is an urgent need to invest more in mental health promotion, prevention, treatment, and research, as well as to ensure the respect and protection of the rights of people with mental health conditions.

Investing in mental health can benefit individuals and society, such as enhancing well-being, resilience, learning, work performance, social inclusion, and community engagement. Mental health is not only a public health issue but also a development priority that requires multisectoral collaboration and action.

Health economics and outcomes research (HEOR) can be important in informing and supporting mental health policies and practices. Economic evaluation can provide evidence on the costs and benefits of different interventions and strategies for mental health care. It can also help to identify the most efficient and equitable ways of allocating scarce resources for mental health. Lastly, economic evaluation can demonstrate the value for money of investing in mental health, by showing the potential returns on investment in terms of improved health, social, and economic outcomes.

There is a growing body of economic evidence on mental health interventions, covering various settings and populations. For example, economic studies have shown that:

- Screening and treating perinatal depression can improve maternal and child outcomes and save costs in the long-term.
- Preventing or reducing mental health problems in childhood and adolescence can have lasting benefits for individuals and society.
- Scaling up treatment, particularly psychotherapy, for depression can be cost-effective or cost-saving in many contexts.
- Providing community-based early intervention and employment support for psychosis can improve recovery and reduce hospitalization costs.
- Offering cognitive stimulation and multicomponent caregiver interventions for dementia can enhance the quality of life and delay institutionalization.

However, there are still major gaps in knowledge and challenges in translating evidence into policy and practice. Some of the challenges include:

- The lack of high-quality data on the costs and outcomes of mental health interventions in different settings and populations.
- The heterogeneity of mental health conditions, interventions, outcomes, and preferences across individuals and groups.
- The complexity of measuring and valuing outcomes that are not easily captured by monetary or clinical indicators.
- The uncertainty and variability of costs and outcomes over time and across contexts.
- The difficulty of accounting for spillover effects across sectors and stakeholders.
- The barriers to implementation include financial constraints, workforce capacity, organizational culture, stigma, discrimination, etc.

To overcome these challenges, we need to:

- Strengthen the collection and analysis of data on the costs and outcomes of mental health interventions at different levels (individuals, families, communities, society).
- Develop more robust methods and tools for economic evaluation that can capture the complexity and diversity of mental health issues and solutions.
- Engage with stakeholders from different sectors and perspectives to ensure the relevance and applicability of economic evidence for decision making.
- Communicate the findings and implications of economic evaluation in clear and compelling ways to inform and influence policy makers, practitioners, funders, advocates, and users of mental health services.

Mental health is a key component of overall health and well-being that deserves more attention and investment from all sectors and levels of society. HEOR can provide valuable insights and guidance on how to improve mental health care and outcomes in a cost-effective and equitable way. By investing in mental health, we can improve the health outcomes and quality of life of millions of people around the world.

As always, I welcome input from our readers. Please feel free to email me at zeba.m.khan@hotmail.com.



Zeba M. Khan, RPh, PhD
Editor-in-Chief, *Value & Outcomes Spotlight*

FROM THE CEO

Mental Health, HEOR, and the Role ISPOR Can Play in Mapping the Journey Ahead

Rob Abbott, ISPOR CEO and Executive Director

The theme of this issue of *Value and Outcomes Spotlight* is a timely—and important—one. Mental ill health, which includes our emotional, psychological, and social well-being, is on the rise. Prior to the COVID-19 pandemic, mental health challenges were the leading cause of disability and poor life outcomes for young people in the United States. Between 2009 and 2019, the proportion of high school students reporting persistent feelings of sadness or hopelessness increased by 40%; the share seriously considering suicide increased by 36%; and the share creating a suicide plan increased by 44%. The situation is bad enough that the Surgeon General of the United States issued an advisory to protect youth mental health. For adults, the outlook isn't significantly better. As Rachel Werner, Executive Director of the Leonard Davis Institute of Health Economics at the University of Pennsylvania puts it:

The percentage of US adults who receive mental health treatment is increasing. There aren't enough providers to meet existing needs and to ensure equitable access to treatment. Over 75% of US counties don't have a prescriber and wait times for treatment can range from weeks to months.

The net result of the conditions that Werner describes is a reduced quality of life, loss of productivity, and premature mortality. The situation is even worse for those who are homeless living in shelters, transient, or living with the legacy of adverse childhood experiences.

Alongside the very personal cost of poor mental health, there is a rapidly expanding body of empirical and anecdotal evidence demonstrating the huge economic impacts of mental ill-health. In Canada, it is estimated that these impacts are on the order of \$50 billion annually. This is, of course, the thin edge of a much larger wedge when viewed globally.

Alongside the very personal cost of poor mental health, there is a rapidly expanding body of empirical and anecdotal evidence demonstrating the huge economic impacts of mental ill-health.

One of the central questions in strategy—maybe the central question—is understanding what is changing in your operational and competitive environment and how that affects the choices available to you. In the case of mental health, we are facing a perfect storm of systemic challenges that transcend the traditional purview of care providers or patients. I'm

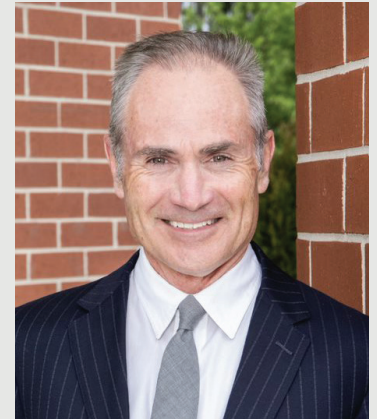
thinking here of poverty, discrimination and systemic racism, health inequities, violence, food insecurity, housing, and the impacts of climate change. If we are to forge strategies and policies that work, we need to firstly understand how these seemingly disparate things come together to “lock” people in a cell of mental ill health.

It should also be acknowledged that enhancing our understanding of how different challenges come together to create a perfect storm for mental health is only the first step. We must also look at gaps in the structures and processes that exist to treat patients. There are, for example, several gaps in the mental health workforce that won't be closed anytime soon.

In the case of mental health, we are facing a perfect storm of systemic challenges that transcend the traditional purview of care providers or patients.

On the one hand, simply training new mental health workers to increase supply takes time. Further, the distribution of those workers is not equal; there are large swaths of the United States (and other countries) where the availability of trained mental health workers is severely lacking—or absent. There is also a problem of how healthcare has historically been viewed and delivered, with inadvertent silos separating primary care from mental health care. The list of structural and process gaps goes on and includes insurer and government payment restrictions that limit access to treatment, and data collection practices that underrepresent certain populations that typically have the highest levels of mental ill health.

So, against the rather grim backdrop I've described so far, what might health economics and outcomes research (HEOR) contribute to inform the development (or renewal) of mental health policy strategies? It is helpful to note that as a discipline, health economics has helped us to better understand a variety of mental health issues across the lifespan. These include perinatal depression identification-plus-treatment; risk-reduction of mental health problems in childhood and adolescence; scaling up treatment (particularly psychotherapy) for depression; community-based early intervention and employment support for psychosis; and cognitive stimulation and multicomponent



care interventions for dementia. These achievements are most properly viewed as a foundation on which new HEOR work can, and should, be done. ISPOR is ready to lead. Health equity, for instance, is something that we take very seriously; it is increasingly woven into the very fabric of all our decisions. I see opportunities for us to help close the gap in our collective understanding of where and how certain vulnerable populations are “left out” or otherwise excluded from data collection practices. I also see ISPOR helping to address payer restrictions that limit access to treatment through our [Payer Summits](#).

Meaningful change is not an event, it’s a process. So, it will take some time to address the mental health challenges here in the United States and elsewhere. Still, I draw inspiration from Maya Angelou, who famously wrote: *Still, I’ll rise*. The journey ahead will

I see opportunities for us to help close the gap in our collective understanding of where and how certain vulnerable populations are “left out” or otherwise excluded from data collection practices.

be a long one, and it will not follow a straight line. There will be challenges and setbacks, but we must summon the courage to keep going, to rise. Mental health is something that affects all of us; we have skin in this particular game. As advocates for better healthcare, as individuals who have lived with mental ill health—or know someone who has—we know it is in our interest to do more and do better.

ISPOR SPEAKS

ISPOR + HEOR: Making an Impact and Transforming Healthcare

Jan Elias Hansen, PhD, Vice President, Genentech, South San Francisco, CA and President (2022-2023), ISPOR, Lawrenceville, NJ, USA

It has been a great privilege and honor to serve as President of ISPOR in 2022-2023. Over the past year, ISPOR and its members have had increased relevance during a time when healthcare decision making around the world is rapidly changing and becoming more complex. I have been fortunate to see this growth and evolution and could not be prouder to be part of our Society!

As my term nears its close, I have reflected on the past year. In 2022, I shared with you the passion I have about making an IMPACT and how I believed (and *still* believe) that ISPOR and the discipline of HEOR can **transform** healthcare by:

- **Engaging** healthcare stakeholders;
- **Applying** HEOR to address challenges and pain points; and
- **Proactively informing** healthcare issues through the use of health economics and outcomes research (HEOR) data and approaches that are scientifically rigorous and sound

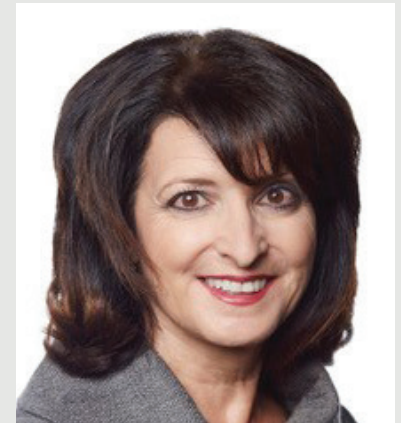
Keep communicating about your work and research and use it to inform the healthcare policy and system debates that are happening in your part of the world each and every day.

In the spirit of “continuous improvement”—where we celebrate what has worked and has been achieved, and are candid about where there is still more work to be done—I want to share with you my own “retrospective” on the past year.

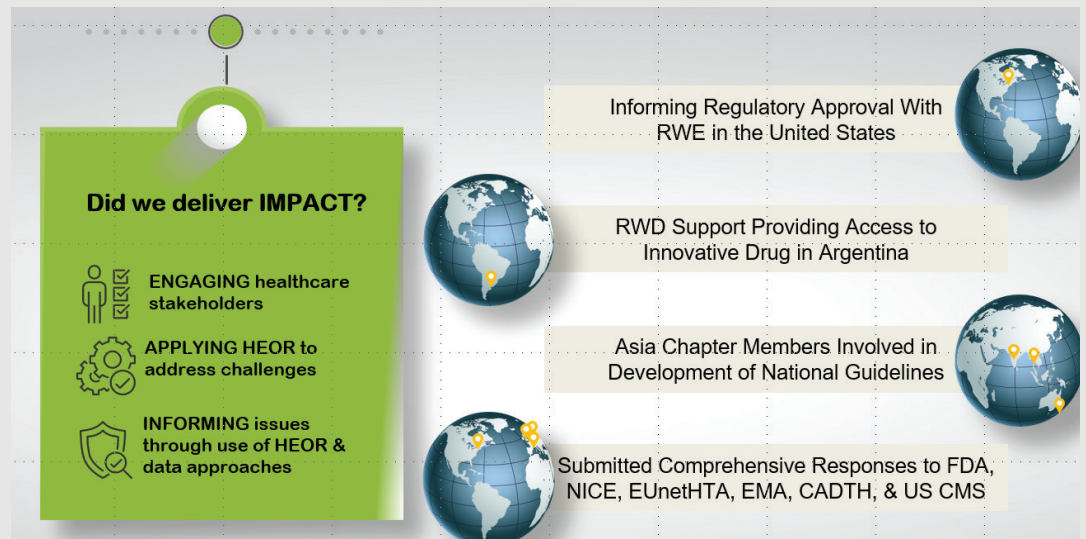
Did we deliver impact by engaging healthcare stakeholders, applying HEOR to address challenges, and informing issues through use of HEOR and data approaches? The resounding answer to this is, “YES, we did!” In terms of IMPACT, here are a few highlights and examples, including:

- **Informing Regulatory Approval With Real-World Evidence in the United States.** We are seeing noninterventional real-world data studies and registries

being used to inform regulatory approvals in the oncology, neuroscience, and infectious disease areas, to name a few.



- **Real-World Evidence (RWE) Supports Providing Access to Innovative Drug in Argentina.** Beyond the United States, real-world data (RWD) were used in developing and implementing a performance-based risk-sharing agreement for patients with HR+ and HER2- advanced or metastatic breast cancer, thereby impacting patients’ access to novel treatments.
- **Asia Chapter Members Involved in the Development of National Guidelines.** ISPOR Chapters in India, New Zealand, and Thailand have been contributing expertise and directly engaging in the development of national guidelines for health technology assessment, pricing, reimbursement, and economic evaluations in their countries in the past year.
- **ISPOR External Responses.** ISPOR’s collective membership is also making an impact via responses to proposed guidelines and healthcare policies in both Europe and the United States. These activities demonstrate ISPOR’s growing influence and reach. Additionally, I’m particularly glad about the opportunity that ISPOR has had in “bringing to light” the HEOR discipline—and all of the scientifically sound and well-studied approaches—in its engagements with the Centers for Medicare & Medicaid Services (CMS) in the United States pertaining to the Inflation Reduction Act of 2022.





These are examples of great IMPACT from across the world from our membership, but we are only starting on our journey to collect and communicate them to all.

AMPLIFY HEOR is a multiyear initiative, unanimously approved and endorsed by the Board last year. I am proud of the critical progress we made on this initiative and am eager to see additional progress made as this initiative takes greater root and matures. It is exciting to share with you all that you will begin to see and be able to reference “The Impact of HEOR” case studies and stories (similar to those mentioned above) on ISPOR.org very soon!

And finally, as I think about the achievement that I was most proud to be part of because of the longstanding IMPACT it will have on ISPOR, it is the process that ISPOR’s Executive Search Committee and Board executed to identify and hire Rob Abbott

as the next CEO and Executive Director of ISPOR. Rob is a highly qualified, innovative, collaborative leader who has the experience and passion to take ISPOR forward during this great time of evolution and rapid change across the healthcare landscape.

amazing job in guiding the Society through and beyond the pandemic. Of course, I offer sincere thanks to Nancy Berg, who expertly led ISPOR for the past 8 years and who is now enjoying a well-deserved retirement. Congratulations to the newly elected Board members, who I know will significantly contribute to the Society.

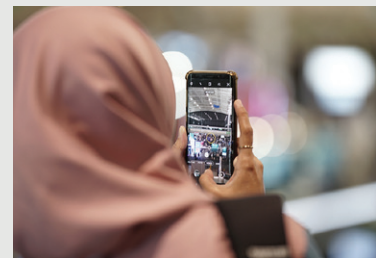
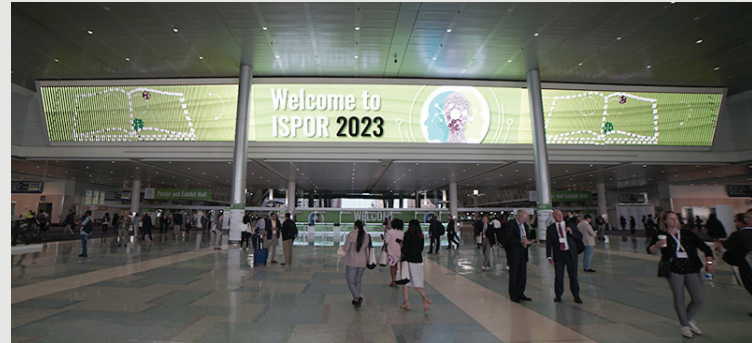
And last, but certainly not least, thanks to *you*—ISPOR’s members. Thank you for your commitment to ISPOR and the discipline of HEOR. Continue to support and engage one another by leveraging each other’s HEOR expertise and the wealth of ISPOR resources available to you! Keep communicating about your work and research and use it to inform the healthcare policy and system debates that are happening in your part of the world each and every day.

Keep making an impact!

ISPOR 2023: BOSTON, MA, USA

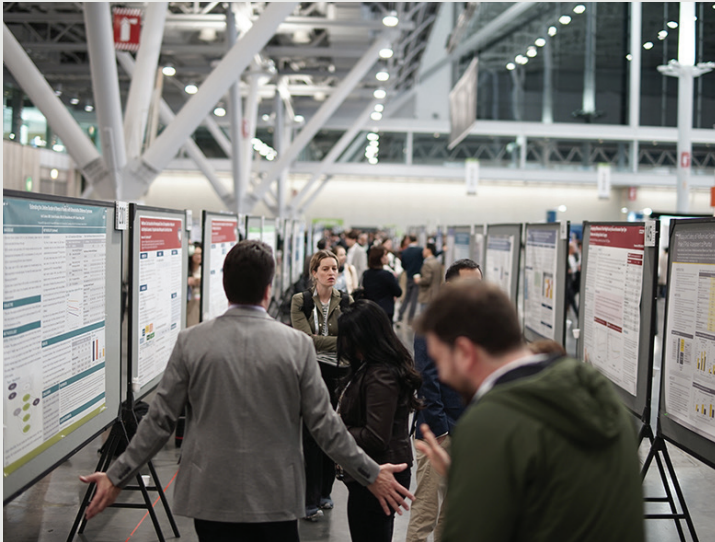
Each year, ISPOR hosts 2 leading conferences that bring together a multistakeholder audience that represents the global health economics and outcomes research community. This year's theme was "Impacting Innovation, Value, and Healthcare Decision Making" and the scientific program included sessions on global policies to manage affordability in healthcare, the integration of artificial intelligence in healthcare research, and research approaches to get the most out of electronic health record data. For more news coverage of the ISPOR 2023 conference, visit our [ISPOR 2023 News Center](#).

Here's a peek into the action from Boston, where more than 4500 people gathered to learn, network, and catch up with good friends.









HEOR NEWS

1 ChatGPT: Not An Author, But A Tool (Health Affairs)

As a tool, ChatGPT does have a place in medical publishing—for example, revising a draft that can be more adherent to reporting guidelines, or by helping investigators not fluent in English prepare manuscripts for publication, possibly increasing the likelihood of acceptance.

[Read more](#)

2 How Is the Cost-of-Living Crisis Affecting Public Health? (Economics Observatory)

With various factors (inflation, post-COVID manufacturer markups, and the Russian war in Ukraine) making food and energy unaffordable in the United Kingdom and in low- and middle-income countries, the outlook for health is worrying and may worsen if the cost-of-living crisis continues.

[Read more](#)

3 PBMs and Pharma Play Blame Game Over Drug Pricing at Hearing (Fierce Pharma)

It was the same story from the heads of 3 pharma companies and 3 PBMs during the Senate Health, Education, Labor and Pensions (HELP) Committee's hearing on legislation on pricing transparency for pharmaceuticals, as each side blamed the other for higher drug costs.

[Read more](#)

4 Economic Effects of Healthy Aging: Functional Limitation, Forgone Wages, and Medical and Long-Term Care Costs (Health Economics Review)

Researchers say health interventions for middle-aged and older people can yield economic benefits by preventing exits from the labor market due to health issues and reducing medical and long-term care costs.

[Read more](#)

5 Hundreds of Children With Type 2 Diabetes to Be Offered Choice of 2 Life-Changing Technologies (NICE)

NICE is recommending the use of real-time continuous glucose monitoring (rtCGM) or intermittently scanned glucose monitoring (isCGM) devices for some children living with type 2 diabetes who are currently using finger prick testing and insulin therapy, giving them less-invasive ways of managing their condition.

[Read more](#)

6 To Eliminate HCV Among Persons Who Use Drugs: Embrace the Complexity (Health Affairs Forefront)

To effectively treat injectable drug users with hepatitis C virus (HCV), it will take more than the White House's plan to treat HCV in the United States by increasing access to direct-acting antiviral agents. Effectively caring for injectable drug users requires an awareness of the internal and external factors (such as unstable housing, incarceration, and shame due to the stigma of drug use) that can influence their willingness to both initiate and complete HCV treatment.

[Read more](#)

7 RWE Shows Efficacy of Nirsevimab for Infant RSV (European Pharmaceutical Review)

The monoclonal antibody nirsevimab may prevent moderate-to-severe respiratory syncytial virus disease in infants after a single dose, according to new real-world data from the phase IIIb trial.

[Read more](#)

8 WHO Advises Not to Use Nonsugar Sweeteners for Weight Control in Newly Released Guideline

The findings of a systematic review of the available evidence suggests that the use of nonsugar sweeteners do not confer any long-term benefit in reducing body fat in adults or children, and the long-term use of nonsugar sweeteners may have potential undesirable effects, such as an increased risk of type 2 diabetes, cardiovascular diseases, and mortality in adults.

[Read more](#)

9 Education and Medication Use Later in Life and the Role of Intelligence (The European Journal of Health Economics)

Researchers found a strong effect of education on prescribed medications for most medications, except for prescribed medication for cardiac diseases and for depression and anxiety.

[Read more](#)

10 Sierra Leone Launches Review to Reinforce Health Emergency Readiness, Response (WHO)

Sierra Leone has become the second African country, and the fifth globally, to launch a review of its health emergency preparedness and response capacity to identify gaps and reinforce measures against health shocks, with priorities in 3 areas of the health response: governance, systems and financing for health emergencies, and universal health coverage.

[Read more](#)

FROM THE JOURNALS

Economic Evaluation of Family-Focused Programs When Parents Have a Mental Health Problem: Methodological Considerations

Zechmeister-Koss I, Strohmaier C, Hölzle L, et al. *Value Health*. 2023;26(5):704-711.

Section Editor: Agnes Benedict; Guest Section Editor: Victoria Molenkamp

Children of parents with mental health problems experience a number of challenges in the long- and short-term, leading to considerable costs for the individual and society. The number of children who are impacted by parents with mental health disorders are estimated to be up to 1 in 4 or 1 in 5 internationally.^{1,2} Not only is the individual child adversely affected but the impact also spreads to the broader society around them. Managing these adverse effects can be costly to individual families and the public healthcare and education sectors that seek to support them.

Interventions aimed at improving the health of children in such households are complex. The impacts can reach beyond the healthcare sector, affecting other public sectors including education, criminal justice, and welfare systems. Traditional outcome measures in economic evaluations may be ill-suited to capture these benefits. The authors of this paper sought to produce evidence-based guidance on which outcomes to include and which designs work best for economic evaluations in this field. By systematically searching the literature, they hoped to gain an understanding of the economic impact of adverse effects experienced by children of parents with mental health problems.

Based on the literature search, the authors created an impact inventory that comprehensively lists the long- and short-

term adverse impacts on children ≥4 years of age who had parents with mental health problems. The adverse impacts were categorized across the following categories: (1) impact on children’s mental and physical health; (2) impact on children’s social functioning; and (3) impact at the socioeconomic level (Figure).

The authors hypothesized the interventions that would be required to counter the adverse effects across all categories, so from that, one could estimate the cost to the economy and society of addressing these impacts. It was clear that costs would be incurred by the children themselves during childhood and into adulthood, and that public sector expenses would also be considerable.

Given these significant estimated costs and long-term impacts, the authors propose that future economic evaluations should consider broad, cross-sector costs when evaluating and estimating the benefits of treatment related to parental mental health problems. Health and nonhealth costs and benefits should be considered, in particular.

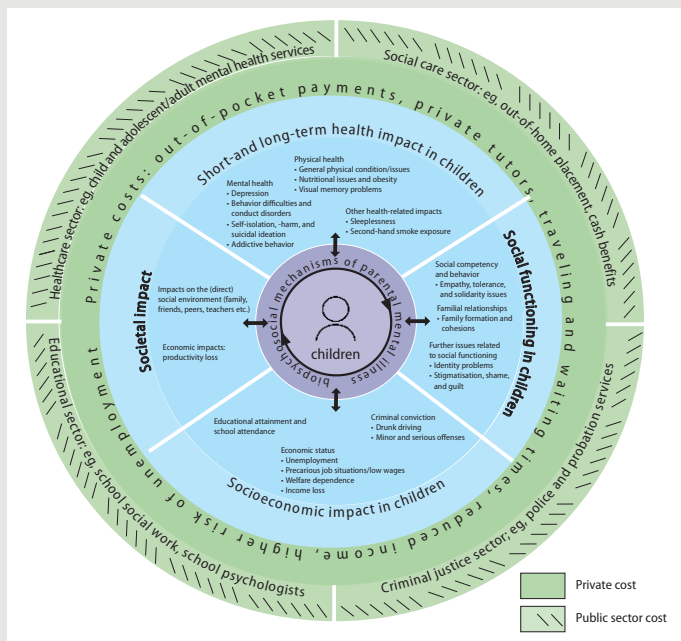
Methodological guidance that the authors suggest includes: (1) incorporating a societal perspective or multiple perspectives to accurately cover costs across multiple sectors; (2) investigating private costs incurred (eg, including the costs of any informal care role children may be fulfilling in their parents’ lives); and (3) employing instruments to measure adverse effect outcomes that go beyond health-related quality of life and are tailored for use in children. In terms of design, they consider using a cost-consequence analysis could be better suited to complex interventions and capturing the long-term impacts but they acknowledge that this depends on data being available.

Although the COVID-19 pandemic highlighted the need to consider broader value elements, it is clear that several other therapy areas need to take into account the broader social implications in an economic evaluation. The impact inventory provides a well-structured framework that may be applicable to the assessment of other programs.

References:

1. Maybery D, Reupert AE. The number of parents who are patients attending adult psychiatric services. *Curr Opin Psychiatry*. 2018;31(4): 358-362.
2. Radicke A, Barkmann C, Adema B, Daubmann A, Wegscheider K, Wiegand Grefe S. Children of parents with a mental illness: predictors of health-related quality of life and determinants of child-parent agreement. *Int J Environ Res Public Health*. 2021;18(2):379.

Figure. Impact inventory



RESEARCH ROUNDUP

Section Editor: **Aakash Bipin Gandhi, BPharm, PhD**, Methodologist Expert, RWD, Sanofi, Cambridge, MA, USA

WHO: pandemic sparked a push for global mental health transformation.

Kuehn BM. *JAMA*. 2022;328(1):5-7.

Summary

The article by Kuehn summarizes key messages from the World Health Organization's (WHO) *World Mental Health Report: Transforming Mental Health for All*. The report discusses the need for transforming the delivery of mental health services that can result in improvement of human rights and foster the implementation of community-based mental health systems aimed at providing preventive care.

Relevance

The WHO report states that nearly 1 in 8 or approximately 1 billion people globally, live with a mental health disorder. Further, it emphasizes the role that the COVID-19 pandemic played in increasing awareness and acceptance surrounding mental health, especially given that the prevalence of conditions such as anxiety and depression increased by around 25% during this period. Despite these alarming numbers, governments around the world spend an average of 2% of their total healthcare budget on mental health care and prevention efforts. Lack of spending on mental health care using existing healthcare budgets is even more pronounced in low- to middle-income countries (~1%). This is concerning given that costs related to mental health are projected to continue rising and reach ~\$6 trillion by 2030 globally. Overall, the report by the WHO aims to be a catalyst for change and improvement in mental health care throughout the world. It emphasizes investing efforts to migrate mental health care from traditional long-term inpatient settings to community-based approaches that are integrated with local primary care centers. Additionally, it highlights the need for preventive measures, information-tracking systems, and investments in mental health research to mitigate any adverse consequences on individuals and society.

Impact of COVID-19 pandemic on mental health in the general population: a systematic review.

Xiong J, Lipsitz O, Nasri F, et al. *J Affect Disord*. 2020;277:55-64.

Summary

Xiong and colleagues present a systematic review that describes the effect of the COVID-19 pandemic on psychological outcomes and associated risk factors among the general population. The study found a high prevalence of symptoms related to anxiety (6.3% to 50.9%), depression (14.6% to 48.3%), posttraumatic stress disorder (7% to 53.8%), psychological distress (34.4% to 38%), and stress (8.1% to 81.9%) in the studied populations. A large degree of heterogeneity was observed across the included studies with prevalence numbers varying by country related to

specific studies that were included in the review. The study also found that the major risk factors associated with mental health symptoms included female sex, age (≤ 40 years), history of chronic or psychiatric conditions, unemployment, and degree of exposure to social media and news.

Relevance

The COVID-19 pandemic drastically impacted mental health of the general population globally. For catastrophic events such as this in the future, government policies that aim to not only mitigate the risk of virus transmission but also take steps to deal with mental health effects on the population are required.

Addressing the mental health crisis.

Creaton J. *Nat Rev Cancer*. 2021;21(1):1-2.

Summary

In this article, Creaton discusses the current state of working environments for researchers. It acknowledges the presence of a mental health crisis in the research community, describes probable causes, and proposes possible steps that can be taken to alleviate adverse consequences in this population. It discusses in detail the factors that may be harmful and damaging to a researcher's mental health. These include daily pressures to progress with publishing research, maintaining a stable income, and working longer than expected hours within a hypercompetitive environment. Potential ways to alleviate these damaging effects would need intervention from both researchers and institutions that they may be affiliated with. Researchers can work on increasing their mental health literacy and discover opportunities to engage with fellow peers and mentors in the community to form a good support network. Institutions can help researchers by setting clear expectations for workload and deliverables to ensure a health work-life balance, as well ensure that any problems arising from systemic discrimination, bullying, and harassment are effectively brought to resolution.

Relevance

There is an increasing need to better manage working environments for researchers given their impacts on an individual's mental health, productivity, and work quality. Both individual and organization-level changes are required to improve mental health outcomes among the research community.

Note from the Section Editor: Views, thoughts, and opinions expressed in this section are my own and not those of any organization, committee, group, or individual that I am affiliated with.

ISPOR Conferences and Events

ISPOR 2023 | 12-15 November
Bella Center Copenhagen, Copenhagen, Denmark



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ISPOR Education

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July 13 |

10:00AM – 11:00AM EDT

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- Explain potential approaches to estimating causal treatment effect during treatment sequencing in oncology

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Economic Evaluation of Digital Health Technologies

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- Provide an overview of the frameworks and models for economic evaluation of digital health technologies
- Learn about the impact of digital health technologies in healthcare today, including examples of real impact on health outcomes

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COMMENTARY

Improving Access to Care and Support for Mental Health Conditions: A Call to Action

Lucinda S. Orsini, DPM, MPH, Vice President, Value and Outcomes Research, COMPASS Pathways, Skillman, NJ, USA

The occurrence of mental health disorders is growing at an increasing rate with pervasive consequences at both the personal and population levels. Brain health is a key component of our overall health. As Director-General of the World Health Organization (WHO) Tedros Adhanom Ghebreyesus, MSc, PhD said, “Ultimately, there is no health without mental health.” The WHO defines brain health as “a state in which every individual can learn, realize their potential, and optimize their cognitive, psychological, neurophysiological, and behavioral responses, while adapting to changing environments”.¹ The WHO has included mental health in its sustainable development goals, recognizing that global [health and economic] development targets cannot be achieved without attending to mental health issues introducing global objectives as part of a comprehensive mental health action plan.² There is also an ongoing special initiative (2019–2023) for mental health, calling for universal coverage for mental health services with the goal of ensuring access to quality and affordable care for mental health conditions in 12 priority countries.³

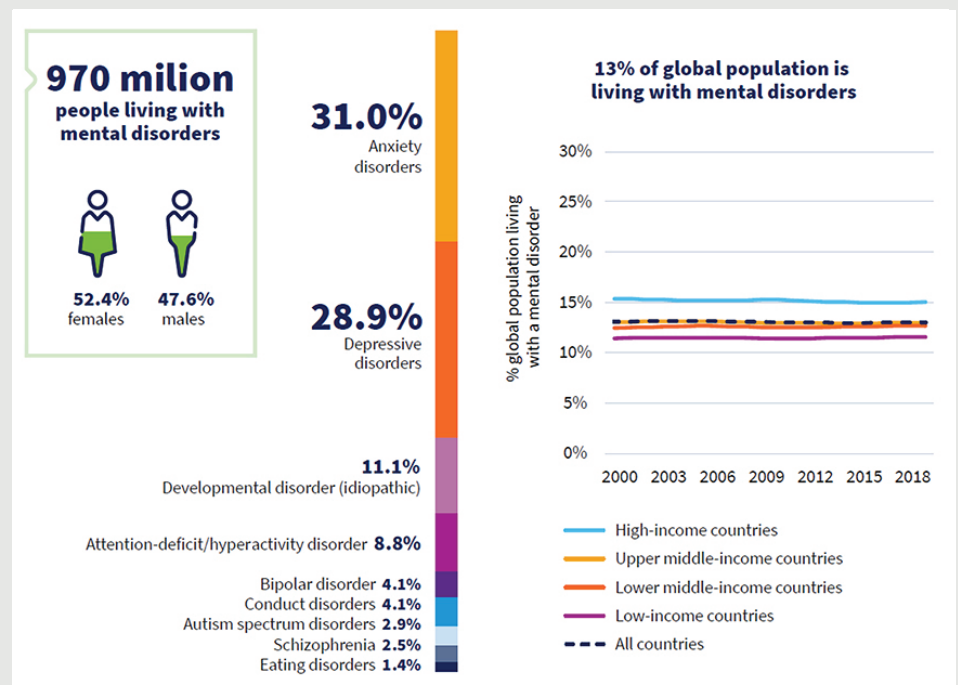
These advocacy efforts were already in play prior to the COVID-19 outbreak. The pandemic has only intensified the mental healthcare crisis and increased the urgency to recognize and address the widening gaps between our behavioral and mental healthcare needs and the available coverage and treatment. To provide services, we need to understand the magnitude of the problem and appropriate the correct resources toward rectification. However, the data that we have regarding the size and demographics of mental health disorders need to be interpreted with caution. While long-standing global studies offer the best available evidence, they remain uncertain due to a lack of evidence in many countries. Estimates are often based on incomplete input data that do not cover all parameters or all countries, as well as information that is outdated or poor quality. According to the WHO’s report on mental health, “it is important to acknowledge that mental disorders can be conceptualized in different ways across cultures, which raises challenges for measuring them from a particular reference point, such as in the global burden of disease studies.”⁴

Figure 1, replicated from the [World Mental Health Report: Transforming Mental Health for All](#),⁴ shows that 970 million people are living with mental health disorders worldwide and anxiety and depressive

disorders are the most common issues from which people suffer. Rates of depression rise worldwide as the population ages—among adults, depression is the most prevalent of all mental disorders.⁴ The COVID-19 pandemic has also had an impact with estimates of increases of 28% in the prevalence of depression and 26% increase in the prevalence of anxiety between 2019 and 2020.⁴ Mental health disorders are a leading cause of disability worldwide with depression being the major contributor to the burden of disability-adjusted life years (DALYs) (Figure 2).⁵ Depressive disorders alone are the second-leading cause of years lived with a disability among all causes of disabilities globally, followed by back and neck pain.⁵ Major depressive disorder (MDD) is also the leading cause of disability in the United States.⁶

MDD is challenging to treat due to the episodic nature of occurrence and the varied set of symptoms that people experience. A combination of factors—including genetic, biological, environmental, and psychological factors—contributes to the risk for developing depression. MDD is often a chronic disease in which the episodes vary in severity and duration. Symptoms can be severe enough that they impact daily life and individual function; in its most severe form, depression can become life-threatening.^{7,8} In some cases, people with MDD do not respond adequately to treatment, leaving them with

Figure 1. The global prevalence of mental disorders in 2019



Reproduced from *World Mental Health Report: Transforming Mental Health for All*.⁴

persistent symptoms and higher risk of relapse.⁹ MDD that isn't helped after 2 or more adequate antidepressive treatments of adequate dose and duration is referred to as treatment-resistant depression (TRD). There is a 20% to 30% prevalence of TRD among people with MDD.^{10,11} People with TRD are more likely to exhibit suicidal ideation, intent, and attempts.

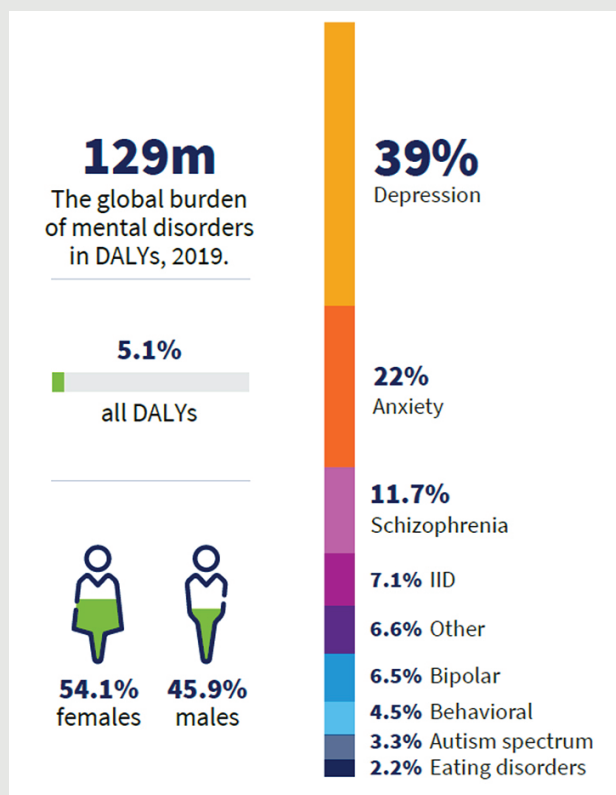
Worldwide 1 person dies from suicide every 40 seconds with 20 attempts for every death.¹² While globally the suicide rate has decreased since 2000, the suicide rates in the Americas have increased 17% over the past 20 years, ranking as a top 10 leading cause of death in the United States and is the leading cause of death in young adults.⁴ Risk of suicide increases with severe and persistent mental disorders.¹³ Approximately 90% of individuals who die from suicide in the United States have an underlying mental illness, and about half of those suffer from MDD.^{14,15} People exhibiting suicidal ideation, intent, and attempts account for a majority of emergency room and hospital admissions for reasons related to mental health.

In terms of economic consequences, a systematic review of cost of illness studies from many countries showed that the average annual cost of mental health conditions per person ranged between \$1180 and \$18,313 depending on which condition they experienced.¹⁶ This number accounts for direct and indirect costs. Annual spending on mental healthcare in the United States accounts for approximately 5% of total healthcare spending, with governmental payers (eg, Medicare and Medicaid) picking up ~75% of the costs.¹⁷ While schizophrenia tends to be the costliest mental health condition, depressive and anxiety disorders which are often comorbid, are much more prevalent and account for the majority of overall national mental health spend.¹⁶ People with TRD tend to incur higher levels of healthcare utilization compared to people with non-TRD MDD, including higher nonmental health-related healthcare costs which actually form the larger proportion of overall spending.¹⁸ Inpatient and outpatient costs are the highest drivers of healthcare spend for both TRD and MDD.

In summary, mental health conditions are ubiquitous, costly, and often severely underserved. The WHO has highlighted 4 main gaps in our ability to address this crisis in its world mental health report.⁴ The first is the information gap that consists of incomplete or lacking data on the scope of the issue as well as insufficient research into these issues. The second is a governance gap that includes inadequate policies, plans, and laws, along with misplaced priorities on interventional care versus prevention. The third is a resources gap consisting of scant spending, lack of essential medicines, scarce workforce, and the digital divide which means telehealth and digital solutions remain out of reach of many. The fourth gap is in access to services—both poor treatment coverage and limited range and quality of services.

Health economics and outcomes researchers have an opportunity to help inform or fill many of the gaps that are mentioned here. Focus on the information/data gaps are what we do best in terms of applying evidence to scoping the issue both in terms of size and costs. This evidence can then be applied to inform the governance gap to show how reprioritizing resources could impact outcomes and the overall healthcare

Figure 2. The global burden of mental disorders in disability-adjusted life years (DALYs), 2019



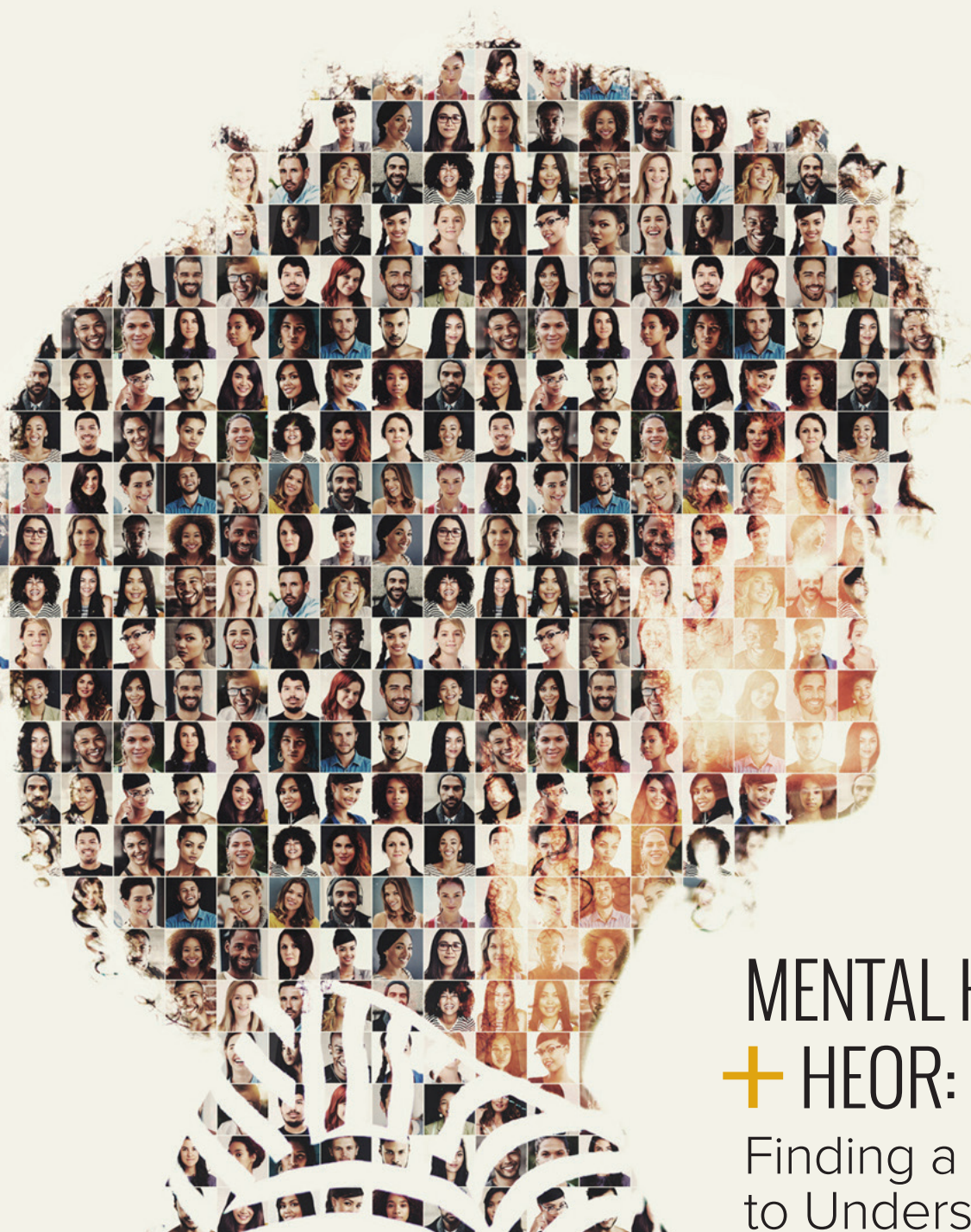
Reproduced from *Global Health Estimates 2019: Disease Burden by Cause, Age, Sex, by Country and by Region*.⁵

spend. Changes in governance can influence incentives for coverage of medications/services and perhaps incentivize innovation in this space which is sorely needed. Incentives can also influence workforce development and infrastructure to ensure more people have access to the care they need. This can begin to shift access to services and eventually improve the quality of services offered. However, we need to prioritize mental health and serious mental illness in our research programs. Most everyone either has lived experience, knows, or is caring for someone with a mental health condition at this moment. This is a call to action to put a spotlight on this highly prevalent and growing issue. We need to come together to work on these challenges to improve access to care and support for mental health conditions. We ignore these issues at our own peril.

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MENTAL HEALTH + HEOR: Finding a Clear Path to Understanding

As the danger of the COVID-19 pandemic continues to fade, healthcare systems around the world find themselves grappling with a new crisis—that of mental health, as conditions such as depression, anxiety, and mental health-related substance abuse skyrocket. According to [Mental Health America's 2023 State of Mental Health](#) survey, 21% of adults in the United States—50 million people—are experiencing at least 1 mental illness and 55% of adults with a mental illness have not received any treatment. Of the adults with mental illness, 5.44% are experiencing severe mental illness. Additionally, more than 12.1 million adults (4.8%) have reported serious thoughts of suicide—and this figure more than doubled among adults who identify as 2 or more races.

And with more people reporting mental health concerns, only 28% say they were able to find the care they needed. Some of the most common barriers to finding and getting mental health care include a lack of affordable options, reported by 42% of respondents and lack of awareness about where to go for services, according to 27% of respondents; 19% of the respondents reported that they had no time to get treatment.

The World Health Organization (WHO) reports that in 2021, more than 150 million people in the WHO European Region lived with a mental health condition, and only 1 in 3 people living with depression received the care they needed. In response, WHO/Europe launched the [Pan-European Mental Health Coalition](#), with the goal of transforming mental health services by integrating mental health into emergency response and recovery efforts, as well as promoting mental health and preventing mental ill health across the life course.

With the urgent need for new and better ways to treat mental health conditions, the field of health economics and outcomes research (HEOR) needs to turn its attention to studies that validate (or disprove) the value of new and current treatment paradigms. The information can help policy makers determine what is effective and what should be funded—and it will take concerted efforts from all stakeholders, including HEOR scientists, patient advocates, and manufacturers, to come up with solutions that policy makers can use. But there are several challenges yet to overcome.

The Gap Between HEOR Studies and Policy Making

“One of the things to recognize is that policy works in a different rhythm than research and is much less tractable,” says Sherry Glied, PhD, MA, Dean of New York University’s Robert F. Wagner Graduate School of Public Service. “So, policy makers are understandably reluctant and appropriately reluctant to change what they’re doing based on one study. One study is one study. And especially in an area like mental health, where there are so many variations in how things work out, I don’t think it is realistic to imagine that policy makers are going to turn on a dime because somebody shows that some program has been cost-effective.”

“One of the things to recognize is that policy works in a different rhythm than research and is much less tractable.”

– Sherry Glied, PhD, MA

According to Glied, this is a reasonable attitude to have because there are “real differences” between programs—and even medications—when they’re administered in the context of a study versus when they’re administered in real life. “The first thing we need to do as researchers is to temper our expectations a little bit and to recognize that making a change in Medicaid policy is a big effort; it’s a big lift. It’s going to take not just one study. One study does not constitute evidence for policy making no matter how wonderful that study is.”

One thing health services researchers need to consider when designing studies to examine mental health programs is how

to translate their research into the kind of evidence that policy makers can understand and implement. “Policy makers want to be able to answer the question, ‘If I do X—where X is a policy like a payment change or authorization for something—what’s going to happen?’ And that’s often not what we produce,” Glied says. “As researchers, we need to think about how we assemble studies in a way that actually gives that kind of evidence to policy makers so that they can sensibly act upon it.”

But a significant stumbling block in making evidence-based policy making for mental health “is that our measures of mental health are terrible,” Glied says. “We have a huge problem of defining what is wrong with somebody or if there’s something wrong with what the condition is, how much it has improved. We don’t have measures of severity or anything that comes close to the kind of measures that many physical health conditions do. I think that creates the concern among policy makers that funding things will be gamed, as we’ve seen with risk adjustment.”

“As researchers, we need to think about how we assemble studies in a way that actually gives that kind of evidence to policy makers so that they can sensibly act upon it.”

– Sherry Glied, PhD, MA

One of the inherent limitations in doing HEOR in mental health is that the nature of the conditions makes it harder to draw conclusive findings and to argue that they are universal, Glied points out. “In fact, we have a very complicated relationship with the idea of universal and mental health. We’re not absolutely persuaded that the same program or medication is going to work for everybody with a particular set of symptoms because our measures are so lousy. So that, again, is an ill fit with policy making.”

The lack of good measures for the effectiveness of mental health treatments is also coupled with a dearth of studies of these treatments in general. “From my own perspective, another thing that we’ve done poorly in mental health services research is that we rarely focus on some of the costliest interventions that we don’t understand very well,” Glied says.

For example, even though a majority of mental health spending goes to inpatient hospital care, “no one’s ever done a study on what constitutes appropriate inpatient hospital care,” Glied says. “How long should an inpatient stay be? Does it matter if hospital stays are shorter or longer? This is not a thing we study. We probably could not do it as a randomized trial, but we probably could study it somehow.”

Coordinating With Patient Advocates and Industry

As HEOR experts figure out how to viably measure mental health advancements and translate them in ways that policy makers can actually use them, patient advocacy groups can offer an important resource.

Phyllis Foxworth, BS spent 10 years working in Peer and Policy Advancement for the Depression and Bipolar Support Alliance, a peer-focused organization for people living with mood disorders. As part of her work there, she started an initiative called Transforming the Definition of Wellness for People Living With Mood Disorders. The initiative was designed to address the fact that while patients understood the purpose of the scales of symptom-based skills used in clinical trials, they were concerned that what was being measured was not the treatment outcomes that they were seeking.

"At the end of the day, what we ended up with was a patient-focused drug development meeting with the FDA [US Food and Drug Administration] to share the insights that we were learning," Foxworth says.

Another goal of the initiative was creating a new clinical outcome assessment for depression and wellness. The group had identified 3 domains for the clinical outcome assessment: **resiliency** (eg, being able to adapt to changes, identify how to stay or become well); **self-awareness** (eg, recognizing having a chronic condition and understanding the impact it has on life); and **positive focus** (eg, having goals and a purpose). "Getting a clinical outcome assessment that focuses on depression wellness that can be used by health economists is really a step forward," Foxworth says.

"Getting a clinical outcome assessment that focuses on depression wellness that can be used by health economists is really a step forward."

– Phyllis Foxworth, BS

Patient advocates and health economists may not have the same goals, but Foxworth believes both need to work together. "I will always say upfront, 'I recognize the tension between the two groups—we don't need to be adversaries.'" "In some ways, there is an adversarial relationship going on here. But we are respectful of each other and we try to understand each other's points," Foxworth says.

Foxworth does see a problem in the common measure—the quality-adjusted life year (QALY)—used in HEOR when it comes to mental health outcomes research. While the QALY focuses on what lengthens or improves patient lives, Foxworth has heard repeatedly from patients with mood disorders that they

would rather have a smaller number of years of *quality life* rather than living for a much longer time, "because living with a mental health condition is so debilitating and so painful."

"We all want the same thing. Let's find a way that we can work together so that we're measuring the outcomes that are important to patients and that we're applying sound health economics to measuring those outcomes that are important to patients."

– Phyllis Foxworth, BS

And in some cases, the medication a patient treated for mental health is taking can interact quite badly with medications taken for other chronic issues. "Many people living with PCOS [polycystic ovary syndrome] also live with bipolar disorder—there's a connection, but the research isn't being done," Foxworth says. "But the problem for these women is that often the treatment for PCOS interferes with the treatment for the bipolar disorder." One patient flatly told Foxworth that she was stopping her PCOS treatment because she could not live with the pain of the mental health condition.

HEOR scientists would call this woman "noncompliant," but Foxworth says, "she's not noncompliant. It's the medical healthcare system that's noncompliant because it hasn't given her a treatment option."

Foxworth points out that the average individual with a mood disorder dies 25 years sooner than the average population. "That's not because of suicide, but because of comorbidities," she says, adding that when HEOR studies look at the cost-effectiveness of a treatment based on the QALY, these comorbidities are not taken into consideration.

"We all want the same thing. Let's find a way that we can work together so that we're measuring the outcomes that are important to patients and that we're applying sound health economics to measuring those outcomes that are important to patients," Foxworth says.

At the same time, throwing the entire task of determining new measurement guidelines at the feet of patient advocacy organizations does not work either because that's not their core competency.

For companies that are trying to bring new mental health treatments to market, the challenge will be showing that these treatments work and should be funded. Compass Pathways is a 7-year-old company focused on finding new treatments that bring better outcomes for patients living with serious mental

illness. The company is testing psilocybin, the active chemical in magic mushrooms, for the treatment of severe treatment-resistant depression—typically for patients who have failed to respond to 2 or more treatments.

According to Kabir Nath, MBA, MA, CEO of Compass Pathways, in the populations the company has studied, nearly 70% had at some point experienced suicidal ideation or thoughts of suicide in the past. “This is a very large, chronically ill population that doesn’t just suffer from depression, but possibly also from the inability to work, anhedonia, and all sorts of other personal issues,” he says.

“A lot of the data and the insights generated around the costs and burdens of serious mental illness—to individuals, to caregivers, to society—have to be used to transform some of our approaches to dealing with people living with serious mental illness”

– Kabir Nath, MBA, MA

Bringing this treatment to market and getting it accepted by payers poses many challenges, Nath points out. “Many systems, both in the United States and Europe, tend to evaluate the effectiveness of treatments on a very narrow basis, just around an economic cost basis and so on.”

But in mental illness, which comes with the burden of so many comorbidities, looking at the whole patient is important. “We need to look at some of these patient-reported outcomes. We need to look beyond just the economic cost of the system,” Nath says. “That said, even the economic costs of patients living with chronic severe depression are very substantial, especially when you consider the cost of the healthcare system, the costs on the family and the caregivers, and so on.”

Nath says Compass is using its outcomes research disciplines to understand what happens to a patient over the course of their illness because many patients cycle in and out of treatments like selective serotonin reuptake inhibitors, cognitive behavioral therapy, and other forms of therapies.

“We’re using our ability to look at big data sources to understand the patient journey much better and why the outcomes are poor.”

Nath also realizes that mental health outcomes are poor not just because of the failure of therapies, “it’s the fact that the entire system of care for people living with serious mental illness does not operate effectively. If somebody breaks their leg, you know what to do: You know to go to the ER and what happens next. If somebody has a psychotic break, you have no idea what to do. Do you go to the ER? Do you call the police? Do you call some other first responder?”

“So again, a lot of the data and the insights generated around the costs and burdens of serious mental illness—to individuals, to caregivers, to society—have to be used to transform some of our approaches to dealing with people living with serious mental illness.”

Compass is not only testing psilocybin, but also testing the way the drug is administered, which entails a 3-part process. First, a patient receives counseling from a therapist to know what to expect. Then, the patient is given a 25-milligram dose and is observed in a 6- to 8-hour session, where they receive “psychologic support” from a therapist. A week or so later is the “integration” session, where the patient talks with a therapist about what they experienced.

The company has already taken steps to ensure that providers can administer the therapy and payers are able to account for it, Nath says. “We’ve already done the work to obtain a specific CPT [Current Procedural Terminology] tracking code that will enable physicians and healthcare to prepare primary care physicians to start tracking the work put into the administration session because no such code existed. Demonstrating that the whole cost—including the 6 to 8 hours—is actually economically viable is going to be fundamental.”

The Future of Mental Health Care

As the economic burden of mental illness grows, HEOR will have a crucial role to play in determining the effectiveness and value of treatments. This will take revamping the models used to evaluate mental health interventions, designing studies with outcomes that can be understood and implemented by policy makers, and working with patient advocates and industry.

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By the Numbers: Mental Health: A Silent Pandemic

Section Editor: The ISPOR Student Network

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Estimated costs of mental health in different high-income countries prior to COVID-19

Estimated costs of mental health in high-income countries

| Country and year of data | Estimated annual costs of mental health |
|--------------------------|--|
| European Union (2011) | €798 billion (indirect and direct costs) |
| United Kingdom (2013) | £79.5–113.6 billion |
| Germany (2015) | €147 billion |
| France (2018) | €163 billion |
| Australia (2019) | €7 billion |

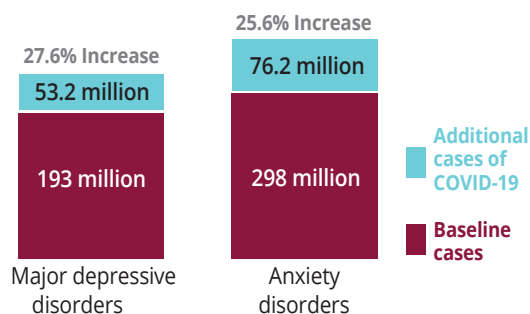
Costs of mental health in France

| Type of cost | Cost (2018) | Percentage difference of costs 2007*-2018 |
|---|--|--|
| Direct healthcare | €23.4 billion | 74.7% ↑ |
| Indirect costs (medical-social, loss of productivity, loss of DALY) | Total: €139.2 billion • Medical social: €13.0 billion • Loss of productivity: €43.2 billion • Loss of DALY/QoL: €83.0 billion | Medical social: 106.8% ↑ Loss of productivity: 77.1% ↑ Loss of DALY/QoL: 26.1% ↑ |
| Estimate individual | €2430 per individual with mental disorder each year | ~ 50% ↑ |

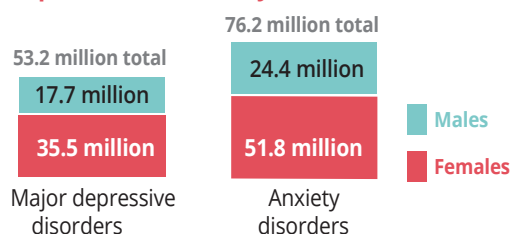
*The values in 2007 reflect €13.4 billion direct healthcare, €6.3 billion medico social, €24.4 billion loss of productivity, €65.1 billion loss of DALY/QoL.
DALY indicates, disability-adjusted life year, QoL, quality of life.

Impact of the COVID-19 pandemic on health cost burden across 204 countries in 2020

Impact of the COVID-19 pandemic on depression and anxiety disorders



Gender differences among individuals with depression and anxiety disorders



Mental health impacts on caregivers

Time spent providing care between caregiver and patient

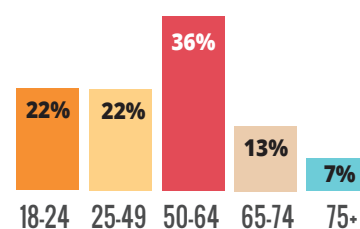
| Relative Caregiver (living together) | Nonrelative (living apart) |
|--------------------------------------|----------------------------|
| 37.4 hours/week | 23.7 hours/week |

- A caregiver, on average, spends about 4.3 years caring for their patient.
- 4 out of 10 caregivers spend 5+ years providing care.
- 2 out of 10 caregivers spend a decade or more of their lives caring for family members.
- 1 out of 5 family member caregivers spend 40+ hours per week providing care.



Average age of unpaid family caregivers

44 million individuals (1 out of 5 adults) over the age of 18 are caregivers in the United States



Understanding Value: US Payers' Perspectives

Editor's note: This is part 6 of a series exploring what value means to the stakeholders in healthcare. Part 1, "Expanding the Value Conversation," appeared in the May/June 2021 issue, part 2, "Understanding Value in Cancer Care," appeared in the July/August 2021 issue, part 3, "Understanding Value: The Providers' Perspective," appeared in the November/December 2021 issue, part 4, "Understanding Value: Patients' Perspectives," appeared in the March/April 2022 issue, and part 5, "Understanding Value: Manufacturers' Perspectives," appeared in the July/August 2022 issue.



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The concluding article in this series ends with the stakeholders that pay the bills. Central governments perform this function in much of the world, and multiple payers exist in some other countries,¹ but the US system, with its mixture of large and small private insurers, self-insured employers, and federal and state government programs is unique. Regardless of type, payers perform similar functions that provide coverage, promote value, and work to maintain affordability.

Understanding payers requires historical perspective. Health insurance was a product of the contemporaneous arrivals of modern medicine and the industrial revolution. "Sickness funds" offered by employers or labor unions began to appear. The Progressive movement and unions pressured employers to provide medical coverage. Blue plans and health maintenance organizations (HMOs) arose during the 1930s and 1940s. In 1965, Medicare and Medicaid were created to cover the elderly and the poor. The federal government shaped the health insurance market through the HMO Act (1973), Employee Retirement Income Security Act (ERISA, 1974), Medicare Modernization Act (MMA, 2003), and Affordable Care Act (ACA, 2010). With electronic billing, pharmacy benefit managers (PBMs) became intermediaries connecting payers, pharmacies, medical providers, pharmaceutical manufacturers, and patients.²

"The simplest way of describing value would be outcomes over cost."

– Ryan Pistorosi, PharmD, MS

Healthcare evolved beyond the independent practices and hospitals of 1900, when most people could afford the cost. Insurance, originally intended to cover catastrophic expenses, expanded to cover all care. Because it spreads risk across a large pool of members, insurance works when only a few individuals incur catastrophic costs. Over time, this original purpose was forgotten by the public, and health insurers became health plans that paid for routine care.

Payers fund access to providers. As stewards of the money entrusted to them, they try to purchase best value, which involves population management, quality improvement, and contracting with providers, pharmacies, manufacturers, PBMs, and other vendors. Payer pharmacists come from a variety of backgrounds and focus their skills on different aspects of value.

The interviewees in this article work in different plans, large and small, HMO, commercial group, employer self-funded, health insurance exchange, Medicare, and Medicaid. Collectively, they describe payers' vision of value.

Managing care requires both population-level and individual patient perspectives. Ryan Pistorosi, PharmD, MS, is assistant chief pharmacy officer at the Washington State Health Care Authority, which manages the state's Medicaid plan and the plan that covers state government employees. "When we think of policy, we are looking at the population level," he explains. "But we also want to make sure that we have opportunities for individuals who may not meet those criteria but have clinical justification. Our clinicians review and approve medications in those unique circumstances." Those exceptions reflect value to individual patients that may not be evident from the trials on which coverage policy is based.

Omar Daoud, PharmD, senior director of pharmacy at Community Health Plan of Washington, agrees. "To me, value is based on member-focused care. It starts with what we do to bring value to our members, and secondary to that is the value from a financial perspective to healthcare overall. Were there savings? Were there any optimizations? The value is what can be provided to the member in terms of outcome, healthcare—all of that."

This vision extends beyond the traditional economist's definition of value to a more person-centered approach. According to an HMO clinical pharmacist, "In healthcare, the simplest way of describing value would be outcomes over cost. It's challenging to define value because it can vary widely based on individual patients' circumstances. Sometimes value is determined by patient-reported outcomes. Sometimes it's defined by a validated marker like overall survival or progression-free survival. It's trickiest to define for diseases and situations for which there aren't a lot of options and in rare diseases. Products can appear to be low value because of their very high cost, but there's a total lack of other therapeutic options." This is true of newer cancer treatments as well as ultrarare diseases. Some cost millions of dollars—amounts most people couldn't repay in a lifetime. The value to these patients depends on life circumstances, goals, and the needs of people around them. Payers can add value when they help each member achieve their personal goals.

Managed care pharmacists use sophisticated methods to analyze medical and pharmacy claims. Patrick Gleason, PharmD, BCPS, assistant vice president, Health Outcomes at Prime

Therapeutics, a Blues-owned PBM, explains how this works. “Value in healthcare is assessing medications and what impact the medication can have on clinical outcomes, event rates, effectiveness, and safety. I think in terms of numbers needed to treat or harm and the financial impact those events carry from direct medical cost offsets. I wish I could expand that to societal benefits, caregiver benefits, work productivity benefits—I just don’t have the means to do that. So, for those, I rely on other entities like the Institute for Clinical and Economic Research (ICER).³

“We know actual paid amounts with network and other discounts, including market access rebates and volume discounts from the manufacturer. Then we receive medical claims from our Blues plans. For example, I’m looking at the real-world impact of glucagon-like peptide-1 agonists (GLP-1a, eg, Wegovy [semaglutide injection], Ozempic [semaglutide injection]) for weight loss. I’m going back to 2022 and 2021, finding individuals that initiated a GLP1a and excluding those with an ICD-10 code or drug therapy for diabetes. I think these people are using it for weight loss. I’m creating a temporally controlled, propensity score-matched comparison group, who have at least one pharmacy claim for anything, don’t have the criteria for diabetes, and do have an obesity ICD-10 code or obesity BMI Z code. Then I will do a 1-year difference-in-difference analysis of total medical costs of the 2 groups pre- and post-index date, as well as events like bariatric surgery, onset of diabetes, cardiovascular events, and hip or knee replacements. We try to do very in-depth real-world analytics to assess the value of therapies.”

Quality is closely connected to value in the minds of managed care clinicians. We believe that optimal clinical management applied at the right time to the right patient will save cost in the long run. We may not save with every patient, but across the right population over time, we expect this to hold true. Thus, clinical quality management programs are an integral part of a payer’s tool set. The Centers for Medicare & Medicaid Services (CMS) recognizes this and uses Healthcare Effectiveness Data and Information Set (HEDIS) and Consumer Assessment of Healthcare Providers and Systems (CAHPS) scores in determining reimbursement rates for managed Medicare plans.

“Value in healthcare focuses on the overall improvement of health outcomes and the value it contributes to whatever we do,” says Saira Jan, MS, PharmD, vice president & chief pharmacy officer at Horizon Blue Cross Blue Shield of New Jersey. “We need to focus on improving outcomes. Health systems look at hospitalizations and emergency room visits. We look at quality measures like HEDIS, so constant improvement is a reflection of what you’re putting in and what you’re getting out. If you look at it internationally, an obvious question is who determines whether outcomes are actually improved and how? “The Dartmouth Atlas international comparisons show healthcare spend and mortality rate comparing different countries; that’s the standard.⁴ For a long time, we just compared ourselves within the United States and not to other countries. You need to understand which geography has prevalence of what medical conditions. You have your baseline programs and then measurements every year. We measure ourselves.”

Managed care pharmacists have an ongoing conversation about value and affordability with their providers. The dynamics vary from plan to plan. “Being a staff model takes profit or revenue out of the equation for our physicians,” the HMO pharmacist notes. “We saw this played out with the infused biosimilars. When provider groups or health systems make revenue on medication, anything that lowers the cost of care for patients can lower their revenue as well. Since our physicians are salaried, they’re not paid based on the quantity of care they provide. With the launch of biosimilars, it was tremendously valuable from the health plan standpoint to have cheaper versions of medications that were just as safe and effective. In the internal model, we made that flip on a dime, no problem. It was all savings and value. But in the external contracted network, those conversations were more complicated because when those medications became cheaper it reduced revenue for those provider groups.”

“Value in healthcare is assessing medications and what impact the medication can have on clinical outcomes, event rates, effectiveness, and safety.”
– Patrick Gleason, PharmD, BCPS

Aligning incentives with providers in a network plan like CHPW is more complex. “It’s a cultural thing in terms of identifying and understanding value,” says Daoud. “Once you have that established, I think it’s an approach and a vision and mission that drives value across all lines of business. I don’t see us making decisions around value that are line-of-business specific. I think sometimes we overcomplicate what the provider’s goal is. I don’t think they see value differently. The provider is in many instances payer agnostic. If they get reimbursed, things must be OK, let me treat the patient and not think about other things. They’re trying to take care of whatever that member needs, from a physical, mental, or behavioral perspective. I don’t think that a provider looks up a patient’s health plan before they see them to decide how they’re going to treat or how to manage the patient.

Payment systems can create perverse incentives for providers, as Jan describes. “All these years we reimbursed providers for activities. You see a patient, you get reimbursed for the visit, but not for making sure that the patient is at goals or doing the things that reduce hospitalization and emergency room visits. We are moving toward that, but I think it needs to be a more conscious and intensified approach. So, it’s not the access issue that we have here. We have other issues that are really catering to bad outcomes.

“In New Jersey, we have value-based contracting with a lot of health systems, where I have embedded pharmacists,” she explains. “Even where the pharmacists are not embedded, we work very closely with them to determine value, close gaps, and measure return on investment, translating that into reduction in hospitalization and emergency room visits, using data to do predictive modeling for targeted interventions that drive value. Our pharmacists do case management for high-cost members.”

Case managers can create value, helping patients navigate the system, bridging gaps, and ensuring that patients receive all the services they need to achieve the best possible outcomes. These goals are important to payers and providers alike, and payers' real-world data can play a critical role when they work together with providers.

The health plan may have embedded pharmacists in partner provider groups, but a payer is always dependent on the individual provider's view. The HMO pharmacist reminds us that, "What our providers have in front of them is a patient. In a lot of ways, they're much better at bringing the patient perspective. They're thinking about individual patient care and what could be a good outcome for that member. I believe that having an integrated system allows for a more bidirectional conversation between provider and payer." A robust primary care system is critical to success because population management always comes down to the individual patient level.

"In a manufacturing setting, you know that the ultimate customer defines value. What makes defining value complex from a payer perspective is that it isn't always clear who is the ultimate customer."

— Megan McIntyre, PharmD, MHA

In HEOR terms, value is a ratio of cost to net clinical benefit. Provider and payer each have part of that picture and it takes a partnership to put the pieces together. "I think when the providers are looking at value, they really see the patient in front of them and they look at those circumstances," Pistoiresi explains. "They may not know the value from our perspective because they don't necessarily know the cost. When we think about value, it's cost divided by outcome. We may have a shared understanding of that outcome but we don't have shared visibility of cost. It's our duty to help guide providers to the most cost-effective option that has the appropriate health outcome."

"That's where I think value in healthcare gets complicated," adds Daoud. "We are trying to solve the complex puzzle of cost management, while driving quality improvement and figuring out how to contract with the provider using value-based payment models. The health plan has a goal of improving its quality outcomes. The provider has a goal of taking care of their members but also staying financially sound so they can continue to take care of those members. That's where integration between health plan and care delivery is so crucial."

Employers pay for over half the insured members in the United States. In 2021, they covered 179 million lives (54.7%).⁵ Their knowledge of healthcare and attitudes toward coverage are very diverse. Some, particularly in industries with tight margins, seek low plan cost. Others use rich benefits to recruit and retain top talent. A few have in-house medical directors, pharmacists, and staff and may operate their own plans, bypassing traditional payers and hiring a PBM to assist with the pharmacy benefit.

All are feeling the pinch of rising costs and finding their options limited by looming unaffordability.

COVID has brought a new attention to benefits. Companies want to make sure their employees are taken care of and that benefits are equitable. Along with traditional health benefits, there is more attention on wellness, prevention, emotional health, and other factors that impact health. Employers are looking for ways to reduce cost and improve quality without negatively impacting the employee experience. Care coordination and navigation can create a seamless experience that guides members to providers and services that will optimize their care.

Advised by consultants, employers may carve out separate benefits, selecting a different vendor for each piece. While this may appear logical, it works against holistic population management. Fragmentation is already a serious problem in healthcare; more integration, not separation, is needed. Payers can address this by offering integrated benefit packages that include these specialized vendors in a seamless whole. Employers that want to do the right thing urgently need value explanations that a layperson can understand. Many want to see employer perspective analyses that include productivity, absenteeism, and presenteeism. Early loss from the workforce due to disability takes away skilled mid-level associates. In addition to recruitment and replacement costs, retiring employees take valuable institutional knowledge with them.

Megan McIntyre, PharmD, MHA, vice-president, Pharmacy and Strategic Programs at Premera Blue Cross, brings a different perspective, having assumed her present role after many years of experience in a large health system. "In a health system, the patient was at the top of our strategic plan and that focus was always so visible," she remembers. "You knew who they were. You could see them. You were one or two hand touches away, so there was a lot closer connection. That showed up in the way we made decisions. You think about value as defined by the patient." That aligns with the perspectives of pharmacists that have been in the payer world much longer, including my own. We share a common member-centric vision, supported by the Affordable Care Act, which was designed to align payer and provider incentives. In the environment it created, we need each other more than ever.

McIntyre uses her Lean (Kaizen) training to analyze the problem. "you know that the ultimate customer defines value. What makes defining value complex from a payer perspective is that it isn't always clear who is the ultimate customer. It could be the purchaser, which in some cases is the patient or an enrollee purchasing coverage for the patient. It could be an employer, and the way they define value is going to be different. An employer might think about value as stretching scarce resources or as opportunity cost trade-off—what they pay for health benefits taking funds away from an IT upgrade or some other business opportunity. Tradeoffs exist at many different levels. An employer might also view value in recruitment or retention strategies for skilled employees. Employers may be thinking about value through different frameworks. 'What benefits do we cover?'"

Quality is an important emphasis in managed Medicare programs, where the regulatory environment is structured to emphasize it. “It’s weighted differently,” McIntyre notes. “There’s a lot more of the clinical quality outcomes tied to CMS incentives. It brings in more of the managed care whole patient total cost of care perspective, because the incentives are aligned around that.” Medicare’s use of CAHPS scores gives weight to the patient experience, a very important part of healthcare, balancing service versus efficiency and economic value.

An important goal of the multistakeholder conversation is to define common interests and goals. To achieve that, stakeholders must broaden their perspectives. Providers tend to focus on the patient level, whereas payers’ perspectives are usually more aggregate. “I certainly had that sort of framework at times,” McIntyre recalls, “I think that’s one of the differences that exist.” Since moving to Premera, she has diversified her reading list. “I think the ISPOR value ‘flower’ is really interesting.⁶ It starts to go a different way. What I liked about it is that it tried to make other dimensions of value more objective. As payers, we have a more objective mathematical view of value. We look at health benefits, costs, and outcomes. Other things matter to patients, like the value of hope.” Hope is an important element of the provider-patient relationship, one traditionally overlooked by payers.

As the healthcare affordability problem increases, value-based prioritization decisions become more critical. Like their provider colleagues, payers recognize the importance of patients’ perspectives and experience. Robust dialogues with these stakeholders are critical, but payers do not usually have the resources to do much of this. Organizations such as ICER are helping fill the gap, and payers should ask manufacturers to share data from qualitative patient research. Over the next

several years, artificial intelligence-based research methods will likely enrich our understanding of what patients are thinking and experiencing. ISPOR is also engaging in robust dialogue with patient representatives, and patient centricity will be the focus of *Value & Outcomes Spotlight’s* November/December issue.

Regardless of payer type and line of business, quality and value—not cost-cutting—are top of mind for payers. Although they must manage tight budgets, they are well aware that choosing the lowest cost option in the short run does not necessarily return the best value. To be successful, payers, providers, and other stakeholders must work together with focus on long-term results.

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Comparison of Depression Trends in the Japanese and US Populations Before and During the COVID-19 Pandemic: A Retrospective Observational Study Using Real-World Data

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Claims data from Japan and the United States were used to investigate the prevalence of major depressive disorder (MDD) and the incidence of newly treated MDD during the COVID-19 pandemic compared to pre-COVID-19 conditions.

The overall trends of prevalence in both countries increased during the pandemic.

The proportion of teenagers with newly treated MDD substantially increased and psychological disorders were the most common comorbidities across countries.

Claims-based real-world data studies can inform broad insights on patients with MDD.

Introduction

Since the declaration of the COVID-19 pandemic by the World Health Organization (WHO) in March of 2020,¹ there have been thousands of mental health-related surveys and reviews reported globally. Despite the abundance of mental health research, studies based on the analysis of real-world databases on the prevalence of major depressive disorder (MDD) are lacking. Compared

Understanding disease trends during the pandemic in a time- and cost-efficient manner would have been far more difficult without the support of large-scale real-world databases. Real-world studies such as this one can estimate the impact of government measures on trends in diseases such as major depressive disorder.

to surveys and reviews, analyses on real-world databases can efficiently and quickly provide broad insights from outcomes data. This study used claims data from the United States and Japan to investigate the prevalence counts of MDD, and incidence of newly treated MDD were evaluated and compared for both countries.

Databases and Cohort Definitions

This retrospective, noninterventional cohort study used the Japan IQVIA claims database and the US IQVIA PharMetrics® Plus claims database to compare the prevalence counts of MDD and the incidence of newly treated MDD patients in both countries.

The IQVIA claims database consists of payer claims data from the health

insurance union for Japanese workers that were used to represent the Japanese population, while the IQVIA PharMetrics® Plus data, which captures fully adjudicated medical and pharmacy claims data from national and subnational health plans and self-insured employer groups, were used for the United States. All datasets were anonymized to protect patient privacy.

The study population consisted of patients with an MDD diagnosis (*International Classification of Diseases, 10th Revision, ICD-10 codes: F32, F33*) between October 2018 and September 2021. The pre-COVID-19 cohort (cohort 1) comprised patients who received their first antidepressive treatment between April 2019 and September 2019. The baseline demographic characteristics for the Japanese cohorts can be found in **Table 1**. The COVID-19 cohort (cohort 2), investigated following the declaration of the COVID-19 pandemic by the WHO, comprised patients who received their first antidepressive treatment between April 2020 and September 2020. The

Table 1. Baseline demographics of cohorts 1 and 2

| Age Group | Cohort 1 | | Cohort 2 | |
|-----------|----------|------|----------|------|
| | Female | Male | Female | Male |
| 05 - 09 | 2 | 5 | 2 | 6 |
| 10 - 14 | 22 | 25 | 40 | 33 |
| 15 - 19 | 192 | 123 | 245 | 123 |
| 20 - 24 | 463 | 346 | 552 | 346 |
| 25 - 29 | 623 | 538 | 606 | 518 |
| 30 - 34 | 497 | 453 | 515 | 462 |
| 35 - 39 | 570 | 511 | 566 | 524 |
| 40 - 44 | 609 | 508 | 542 | 528 |
| 45 - 49 | 618 | 607 | 569 | 524 |
| 50 - 54 | 583 | 550 | 565 | 480 |
| 55 - 59 | 465 | 462 | 398 | 393 |
| 60 - 64 | 310 | 310 | 264 | 277 |
| 65 - 69 | 165 | 107 | 131 | 123 |
| 70 - 74 | 105 | 56 | 88 | 65 |
| 75 - 79 | 27 | 18 | 16 | 14 |

study design can be found in **Figure 1**. All analyses were performed using the IQVIA Evidence 360 Software-as-a-Service Platform containing global real-world datasets from more than 1 billion anonymized patient records.

The Impact of COVID-19 on Patients With MDD

The prevalence counts remained steady until a significant drop in April 2020 in both countries. The prevalence counts increased gradually since then (**Figure 2**). Real-world data have been used to estimate the rate of transmission of the COVID-19, population-level vaccination status, and deaths in many countries.^{2,3} Understanding disease trends during the pandemic in a time- and cost-efficient manner would have been far more difficult without the support of large-scale real-world databases. The WHO declared the COVID-19 pandemic in March of 2020. Since then, there was a significant drop in the diagnosis of MDD in Japan and the United States, likely due to a decrease in hospital visits due to social distancing measures and fears of COVID-19 transmission from hospital visits.⁴ MDD diagnoses increased steadily in the months that followed. Real-world studies such as this one can estimate the impact of government measures on trends in diseases such as MDD.

The top comorbidity for patients with newly treated major depressive disorder in Japan was insomnia, while the top disorders for the United States were related to anxiety.

Additionally, the results from this study are generally in agreement with a global systematic review from 2021 on the prevalence of depression and anxiety during COVID-19.⁵ Our study has thus shown the importance of using real-world data in the mental health field.

In Japan, the overall incidence of newly treated MDD patients increased from 2.0% to 2.3% from pre-COVID-19 (April 2019 to September 2019) to the time during COVID-19 (April 2020 to

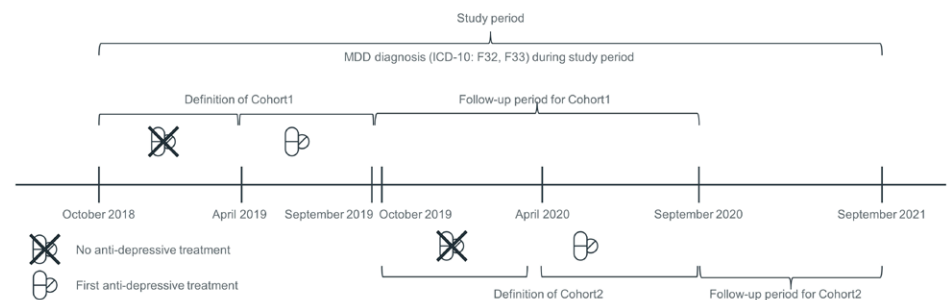
September 2020) (**Table 2**). The United States, on the other hand, saw no change in incidence during the same period (5.0% during both periods) (**Table 2**). Patients in neither country demonstrated a significant change in the duration of treatment. The discrepancy in overall incidence may result from a variety of

factors such as cultural, economic, and policy in the patients between the 2 countries. Further investigation of the context surrounding these data may reveal why incidence increased in Japan but remained steady in the United States during the pandemic.

Table 2. Incidence of newly treated patients with MDD.

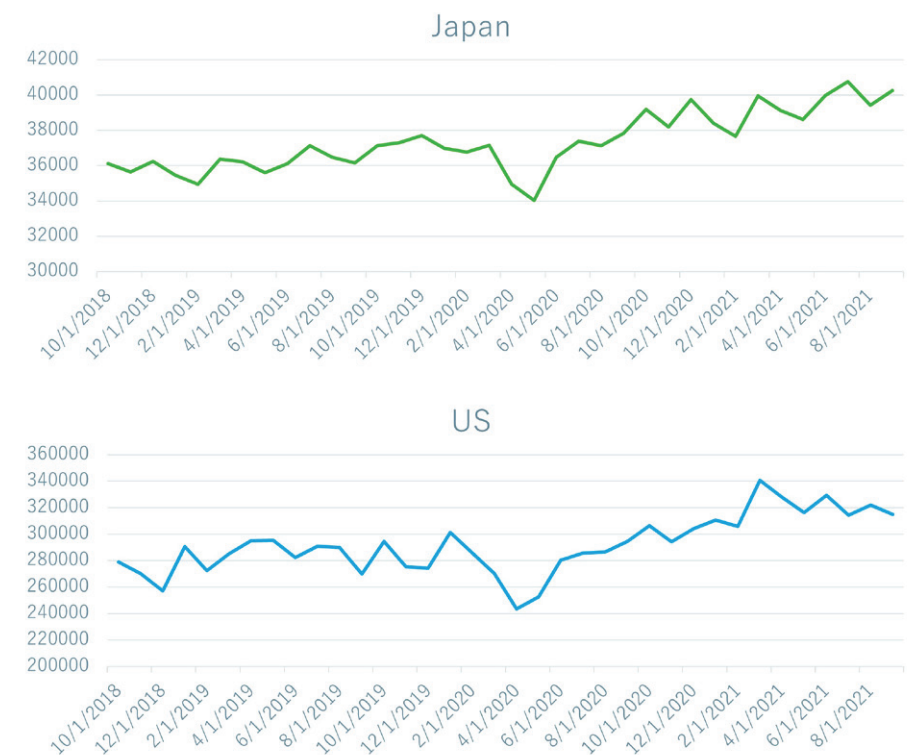
| | Japan | United States |
|---|-------|---------------|
| Pre-COVID-19 (April 2019 - September 2019) | 2.0% | 5.0% |
| During COVID-19 (April 2020 - September 2020) | 2.3% | 5.0% |

Figure 1: Study design.



ICD-10 indicates International Classification of Diseases, 10th Revision; MDD, major depressive disorder.

Figure 2: Prevalence counts of MDD in Japan and the United States during 2018-2021.



MDD indicates major depressive disorder; US, United States.

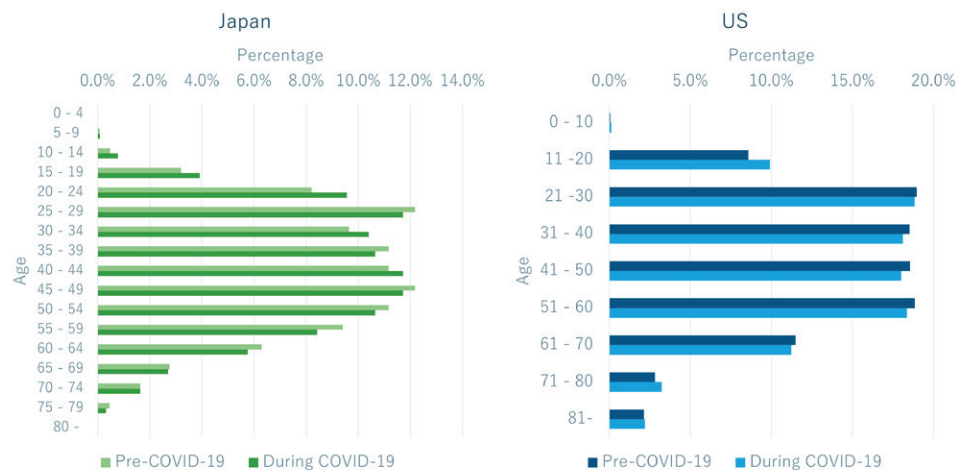
Before the pandemic, 3.7% of patients with newly treated MDD in Japan were below the age of 20 as opposed to 4.8% during the same period the following year (Figure 3). Interestingly, a similar increase was also observed in the United States with 8.6% and 9.9% of the patients being under 20 before and during the pandemic, respectively. Both countries implemented distance learning to various degrees during the pandemic, which may partially explain the increases in newly treated MDD. These trends are also seen in a survey study performed in the United Kingdom, indicating that similar trends may exist globally.⁶ There is ample research indicating the psychological burdens placed on children and adolescents from being barred from face-to-face interactions with their friends and peers during the pandemic.^{7,8} Future investigations of MDD for each country stratified by the timing of when children and adolescents returned to school may provide insights on the impact of distance learning on mental health.

The top comorbidity for patients with newly treated MDD in Japan was insomnia, while the top disorders for the

United States were related to anxiety (Figure 4). Other common comorbidities included respiratory diseases, lower back pain, and headache. These results are in line with other studies that indicate a rise in the mental health issues throughout the pandemic.^{9,10} Remote learning and work have been implemented in both countries to varying degrees and are

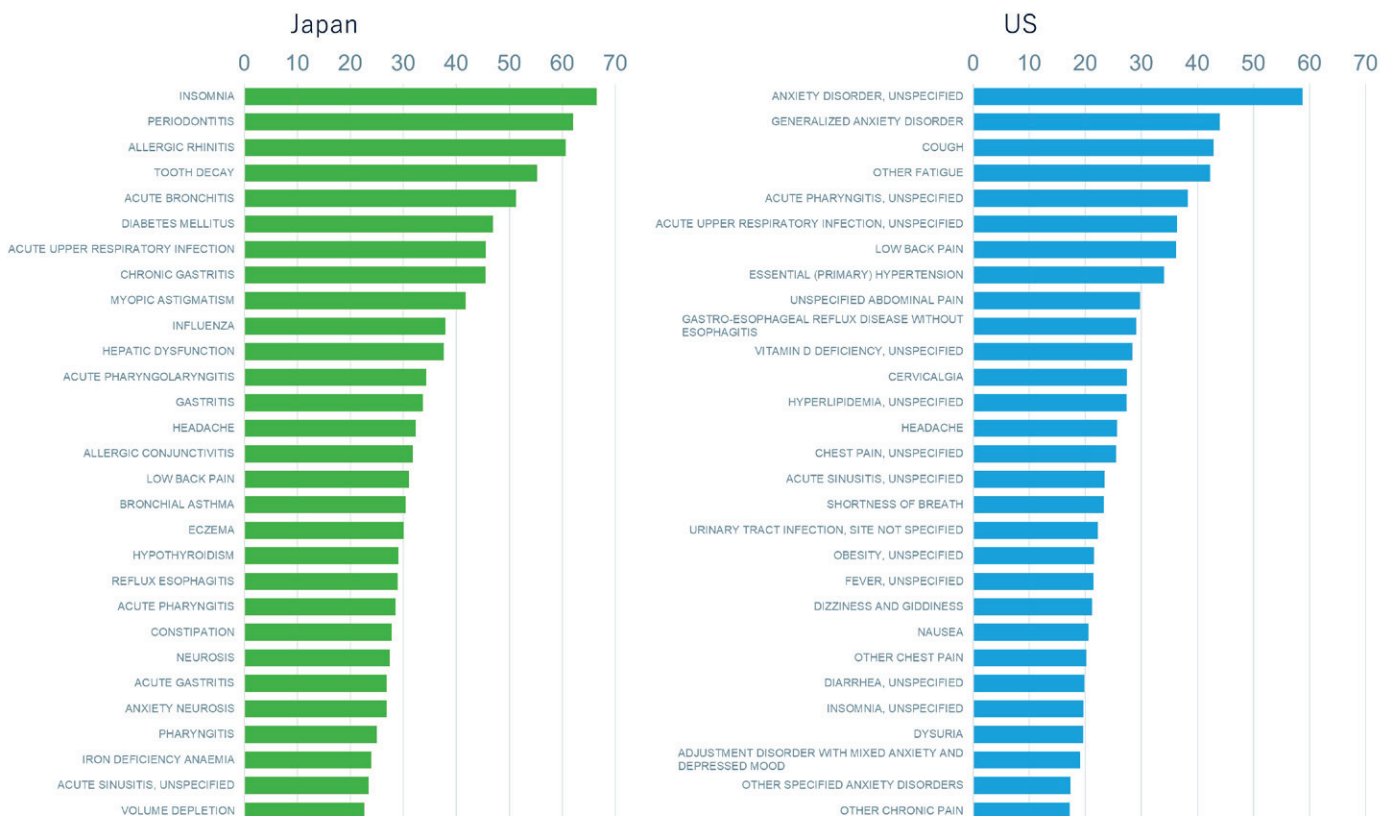
expected to remain remote and to some extent continue even after the pandemic. Future database studies such as this one can be used to understand how these comorbidities may change over time as adjustments are made to the conditions brought about by events such as a pandemic.

Figure 3: Proportion, categorized by age, of newly treated MDD patients in Japan and the United States.



MDD indicates major depressive disorder; US, United States.

Figure 4: Top 30 comorbidities of patients with newly treated MDD in Japan and the United States during COVID-19.



Limitations

Although database studies are a crucial component to gaining broad insights from real-world evidence studies, there are also several limitations. In this study, the number of elderly patients aged 60 and above is lower in the claims database than that according to actual Japanese and US demographics. Additionally, accurate denominators are required to determine prevalence, but are not available in the study data which may introduce bias during sample extraction. Finally, database studies in general do not necessarily reflect the overall population and the results may not be fully generalizable.

Conclusion

The prevalence count trends of MDD increased during COVID-19 in both Japan and the United States. However, the incidence of newly treated MDD was slightly increased during COVID-19 compared to pre-COVID-19 in Japan whereas there was no change in the United States. Among these, children and teenagers tended to have a higher proportion of newly treated MDD during the COVID-19 outbreak in both countries. Our study suggests the

importance of using real-world data in the mental health field.

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Combining Social Determinants With Real-World Clinical Data for Better Mental Health Research

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Real-world data sources can play an important role in mental health research by capturing data on large, heterogeneous patient populations, including patients from diverse racial, ethnic, and socioeconomic backgrounds.

Real-world clinical and administrative claims data can be linked to social determinants of health data to describe disparities in treatment patterns and outcomes by factors such as race, income, and credit risk.

Real-world evidence suggests that low income, high credit risk scores, and Black race combine as important and persistent social determinants of mental health in terms of access to care and overall disease burden.

Recent research has highlighted the extraordinary influence of social determinants of health (SDoH) on mental health, with many studies finding increased prevalence and severity of depression, anxiety, and other mental health conditions in populations that experience chronic stress and discrimination.¹⁻³ Studies have also described the relationship between SDoH and access to care, showing that reduced access to treatment linked to SDoH results in poorer outcomes.⁴ The COVID-19 pandemic further heightened attention to this growing area of research, as unemployment, chronic stress, and social isolation led to increases in mental health diagnoses.⁵ The relationship between SDoH and mental health diagnosis, treatment, and outcomes is now an area of intense focus for both research and health policy experts.

The relationship between SDoH and mental health diagnosis, treatment, and outcomes is now an area of intense focus for both research and health policy experts.

The increased interest in SDoH has raised new questions about how to capture and use these data in research studies for additional insights and to advance the field. Real-world data (RWD) sources are a valuable tool for facilitating mental health research, as these sources offer an efficient means of assembling large, heterogeneous patient populations and observing real-world treatment patterns and outcomes across different practice settings.⁶ While clinical trials typically enroll a narrow patient population, RWD sources capture information about routine clinical care from broader patient populations, including racially and ethnically diverse patients from different socioeconomic backgrounds.

Determining how to incorporate SDoH data into RWD sources is an important challenge for stakeholders interested in advancing mental health research and informing mental health policy. This article describes 2 analytic approaches to using multiple data sources linked to real-world clinical notes, outcome measures, and administrative claims to better understand the role of SDoH in mental health.

Examining Outcomes by Income and Race

One approach to understanding the impact of SDoH on mental health is to incorporate data on income and race in outcomes research. This approach was used in a retrospective, observational cohort study that described the associations between race and household income and measures of major depressive disorder (MDD) burden in a real-world cohort of Black and White patients with MDD in the United States.⁶

Data were drawn from the OM1 PremiOM™ MDD Dataset and linked to a SDoH dataset. The MDD dataset includes linked electronic medical records and administrative claims data from OM1's Mental Health Network of over 3 million patients seen in more than 2000 community-based practices across all 50 states. The SDoH dataset is a patient-level data source that includes sociodemographic and behavioral attributes of adults (age ≥18) in the United States. Data elements include race, ethnicity, occupation, credit risk score, educational attainment, household income, and homeownership. The SDoH data source is considered generalizable to the broader United States population as it includes information on over 250 million people.

The analysis looked at age, race, sex, insurance type, education, household income, and Patient Health Questionnaire-9 (PHQ-9) scores (an outcome measure of depression symptom severity), as well as mental

healthcare-related visits and antidepressant prescriptions. More than 123,000 Black patients and 1 million White patients were included in the analysis.

The study found that median PHQ-9 scores for Black patients were higher than for White patients at baseline (10.8 vs 8.8; $P < .0001$). In addition, patients with annual incomes at or below the federal poverty level of \$25,000 had higher mean PHQ-9 scores than patients with incomes of at least \$25,000 (9.7 vs 8.9; $P < .01$). In terms of access to treatment, emergency and inpatient mental healthcare use was significantly higher in Black patients, and Black patients had fewer outpatient mental health visits than White patients. Prescription fills for antidepressant therapy in the 12 months after baseline were also lower for Black patients suggesting a lack of adequate treatment. Importantly, these disparities by race and income persisted over the course of the study's 18-month follow-up period.

Examining Outcomes by Credit Risk Score

Although similar to income, credit risk scores offer a different lens into the financial health of patients and are another important variable to help assess the impact of SDoH on mental health treatment, and outcomes. In this example, credit risk was analyzed in a retrospective, observational cohort study that described the disease burden in patients with clinical depression. Data were also drawn from the OM1 PremiOM™ MDD dataset and included information on age, race, sex, insurance type, and PHQ-9 scores as a measure of disease burden.

This real-world study included more than 3.4 million patients with MDD. Patients with high credit risk scores had a median household income of ~\$47,000, while patients with low credit risk scores had a median income of ~\$80,000. Black patients made up 16% of the high credit risk group and 5% of the low credit risk group. In terms of symptom severity, patients with high credit risk had higher PHQ-9 scores than patients with low credit risk (13.3 vs. 12.4; $P < .001$). Similar to the previous study, patients in the high credit risk group also had more emergency and inpatient mental

healthcare use, lower outpatient mental healthcare visits, and fewer prescription fills for antidepressant therapy. As in the income and race analysis, the credit risk score disparities persisted through the study follow-up period.

Implications for Real-World Research

These examples highlight the substantial independent impact of racial and financial SDoH variables on treatment patterns and outcomes in depression and emphasize the importance of incorporating these data into mental health studies. Researchers seeking to use RWD for mental health research should consider leveraging SDoH variables to better characterize their patient population and understand the complex factors that influence outcomes.

Researchers should also keep in mind the limitations and complexities of SDoH data. For example, many RWD sources are missing data on race and ethnicity. The source of the data, including whether it is patient-reported or clinician-reported, should also be considered, as should the recency of the data.

As the crisis in mental health in the United States continues, improving outcomes will require further research and understanding of the complex interplay between social determinants and mental health variables.

Inclusion of SDoH data in mental health research may also help to identify potential policy initiatives for improving outcomes. The studies described above point to areas such as improving access to outpatient mental healthcare and identifying and addressing reasons for medication discontinuation as options for further research. When reviewing studies that focus on mental health, policy makers should consider whether SDoH variables were included, as studies that incorporate these data may provide greater insights into disparities in disease burden and offer opportunities for improving care.

Research has shown that an individual's physical health is strongly linked to social and environmental factors both at the individual and broader community levels. There is growing evidence that this is true for mental health as well. As the crisis in mental health in the United States continues, improving outcomes will require further research and understanding of the complex interplay between social determinants and mental health variables. RWD sources can play an important role by capturing data on diverse patient populations and linking those data to SDoH datasets to further describe disparities, guide future research, and identify areas for policy-based initiatives with the goal of improving outcomes for all.

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Unlocking the Potential of Electronic Health Records in Neuroscience for Health Economics and Outcomes Research

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There is a need for further understanding of the underlying neurobiology, environmental factors, psychological mechanisms, and social determinants involved in psychiatric disorders to inform the development of new treatments, that have the potential to improve the quality of life of those living with mental illness and to be of great benefit to wider society.

To lay the groundwork for successful development of novel therapeutics, a deeper characterization of these disorders is necessary to ensure the right patient receives the right treatment at the right time.

Leveraging psychiatric electronic health record data to deeply characterize the clinical trajectories of patients can provide a data source that explores how EHR data can be realized in the context of the United Kingdom's National Health Service.

Psychiatric disorders are a leading cause of disability globally,¹ representing a huge unmet need for people living with these conditions. Despite increased healthcare spending and the use of psychotropic medications, this burden has remained stable over the past 30 years,¹ with suboptimal clinical practice and lack of primary prevention identified as likely explanations.² This lack of progress in the treatment of psychiatric disorders also manifests in poor success rates for clinical trials in psychiatry; only 7.3% of drugs advance from phase I to approval.^{3,4} The complexity and heterogeneity of psychiatric disorders compared to other disease areas is one factor that has hindered progress so far, presenting a unique challenge for the research community. To bring about progress, there is a need for further understanding of the underlying neurobiology, environmental factors,

EHRs represent a rich source of data from real-world clinical practice; despite their richness, EHR data have been challenging to analyze in their raw form, and difficult or impossible to access outside the NHS.

psychological mechanisms, and social determinants involved in psychiatric disorders to inform the development of new treatments, which have the potential to improve the quality of life of those living with mental illness and to be of great benefit to wider society. This understanding will also be of great relevance to the health economics and outcomes research (HEOR) community, given the increasing demand from payers for evidence of the disease and economic burden associated with conditions during treatment appraisal processes.

Psychiatric disorders cross the boundaries of diagnoses, both in terms of clinical

presentation and disease biology.⁵ To lay the groundwork for successful development of novel therapeutics, a deeper characterization of these disorders is necessary to ensure the right patient receives the right treatment at the right time. This characterization requires a longitudinal and biopsychosocial approach to understand the synergistic interplay between these factors over a patient's lifetime. Bringing together data sources that cover the entire landscape of psychiatric disorders—from genes to socioeconomic factors—is necessary for an integrated approach, together with large sample sizes for meaningful analyses. Moreover, a data source that captures diverse, hard-to-reach patient populations is essential for the comprehensive characterization of psychiatric disorders. In this article, we outline how leveraging psychiatric electronic health record (EHR) data to deeply characterize the clinical trajectories of patients can provide just such a data source and explore how the potential of EHR data can be realized in the context of the United Kingdom's National Health Service (NHS).

EHRs represent a rich source of data from real-world clinical practice. Because they capture patients' experience over a lifetime, EHRs have the power to inform analyses of disease burden and resource utilization, in addition to capturing clinical outcomes following care and treatment interventions. In the NHS, psychiatric EHRs record not only diagnoses and treatment, but also rich, narrative detail on disease severity/progression, symptoms, treatment pathways, and potentially the social context of the patient in question. NHS psychiatric EHRs contain some key structured data, including demographics, some coded diagnostic data, and patient-reported outcomes. However, most clinically relevant information is recorded as unstructured data, including free text clinical notes, referral letters, and discharge summaries. Such documents represent a large part of the clinically actionable information

contained within EHR systems. There is immense research value in these rich, transdiagnostic descriptions of patient states, but utilizing them for research poses significant challenges. Unstructured data are difficult to analyze, particularly at scale, and the sensitivity of clinical text documents (even when personally identifiable information like names and addresses have been masked) is too great to permit access outside of the controlling healthcare organization. Therefore historically, despite their richness, EHR data have been challenging to analyze in their raw form and difficult or impossible to access outside the NHS.

When levered against clinical documents in EHRs, NLP can unlock this rich data source for research at scale, providing billions of data points related to patient care.

To improve the accessibility of psychiatric EHRs, a data-structuring solution is required. Specifically, this solution needs to allow clinical free-text

data to be translated into a structured format, preserving the richness and contextual nuance of the source, while rendering the data more tractable for quantitative analysis. Crucially, data structuring would also allow EHRs to be anonymized or aggregated, preserving patient privacy, and so enabling access from outside the NHS.

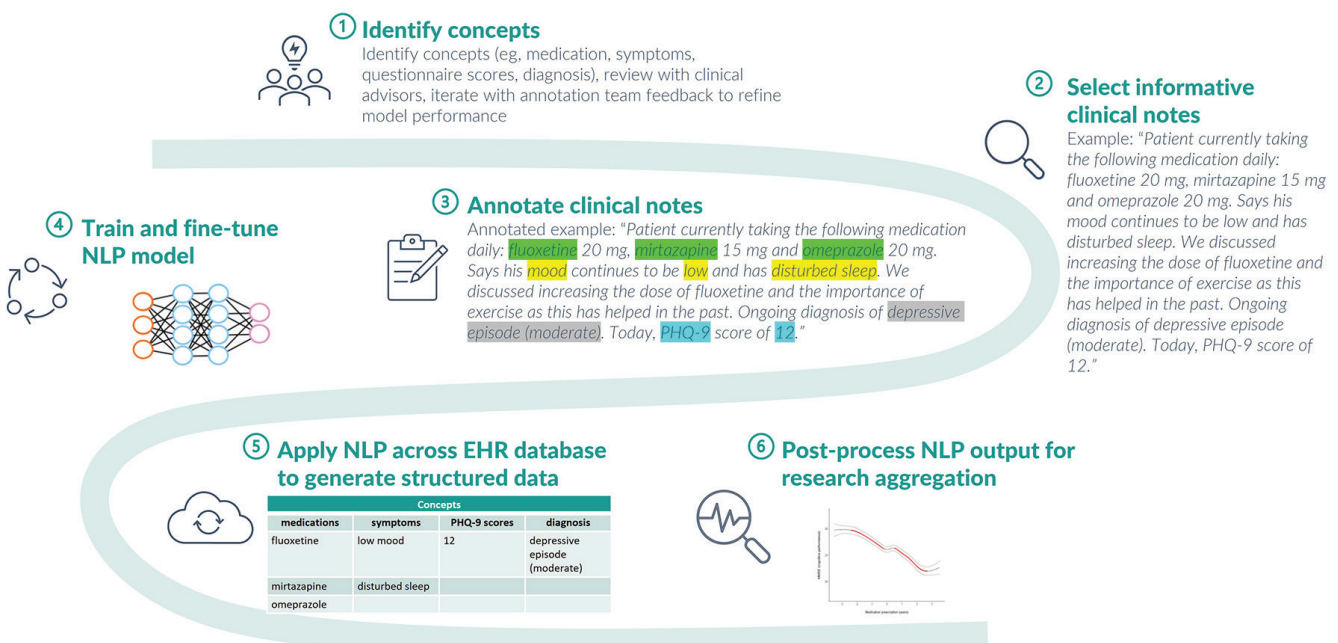
Natural language processing (NLP) methods can provide this kind of data structuring solution. NLP describes a broad range of methods for automatically processing natural language data and includes a variety of techniques for structuring free text. When levered against clinical documents in EHRs, NLP can unlock this rich data source for research at scale, providing billions of data points related to patient care. These data points provide a source of information for retrospective analyses in psychiatric conditions, from assessing clinical outcomes to quantifying healthcare resource utilization.

When developing NLP data structuring models for use on clinical text data, it is critical to retain the contextual nuance of the original document. This is achieved by taking a clinically orientated approach to NLP concept design (Figure 1).

Extensive qualitative analysis of how concepts (eg, medications, diagnosis, and symptoms) are described in source EHR data and direct involvement of practicing clinicians in the concept design process are vital to the development of a thorough NLP approach. For example, developing an NLP concept for medication requires knowledge of how this is usually described by clinicians—what medication information is relevant to clinical care, what gets recorded, and often more importantly, what does not. Medication descriptions in NHS psychiatry usually refer to current usage, past usage, or discussions of potential usage, but rarely ever include explicit “negation” (describing medications a patient is not taking). Hence, the medication concept includes categories of “is on,” “was on,” and “other”, but no “not on” category. Inclusion of clinically redundant fields (regardless of their potential research utility) can lead to poor model performance, so data exploration and direct clinical involvement are vital to match concept design to the reality of source data (Figure 2).

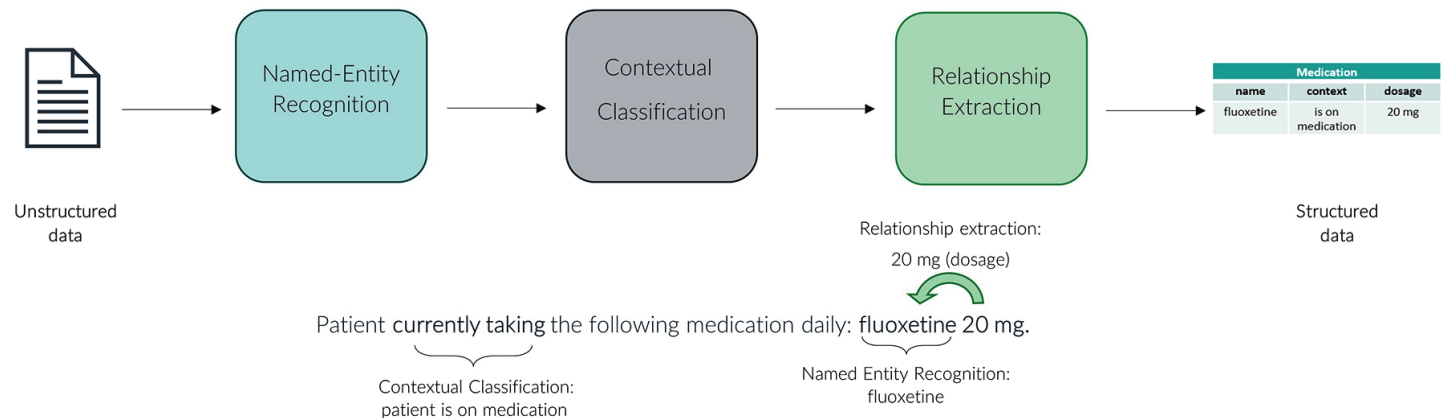
In the context of health economics, structuring medication data in this way allows it to be factored into, for example,

Figure 1: Using NLP to capture a broad range of clinical concepts from unstructured clinical notes



EHR indicates electronic health record; mg, milligram; NLP, natural language processing; PHQ, patient health questionnaire.

Figure 2: Three NLP models to capture the depth of information within a clinical concept



mg indicates milligram; NLP, natural language processing.

healthcare resource utilization analyses and estimations of medical costs for psychiatric disorders. Without NLP, these analyses would not be possible at scale, given that most/all medication data are within unstructured free-text clinical notes in psychiatric EHRs. Additionally, these data allow for the clinical benefit of medications to be monitored over time. For novel therapeutics, this allows for further generation of evidence for clinical benefit beyond the short time frame of randomized controlled trials, which is particularly pertinent to medications assessed under value-based agreements where drug pricing is linked to clinical outcomes. Patient outcomes in terms of changes in rates of hospitalization, service use, and disease-relevant symptoms can be monitored following prescription of the medication in question.

Linking these datasets, along with other national datasets/registries, allows mental health outcomes to be mapped over a lifetime.

A use case of these structured medication data is the identification of patient groups defined by treatment patterns. Treatment-resistant depression (TRD), also conceptualized as difficult-to-treat depression (DTD),⁶ is defined as patients who fail to respond to 2 or more antidepressant drugs of adequate

dosing and treatment duration.⁷ With medication data structured using NLP, the parameters within this definition can be operationalized to identify TRD. The contextual classification of medication mentioned in the free text

Real-world data within psychiatric EHRs provide a unique opportunity to gain insights into the complex and heterogeneous nature of psychiatric disorders.

allows the sequence of medications taken to be mapped. A study using this approach in a secondary care dataset found patients with TRD were more likely to be hospitalized and have more comorbidities than patients with depression that is not resistant to treatment.⁶ In the future, further use of NLP to structure information related to socioeconomic factors (eg, employment and accommodation information) from the free text will help capture a more holistic set of resource utilization indicators for TRD and other psychiatric disorders.

While the insight from a large secondary care dataset described the disease burden associated with TRD,⁶ it is known that many patients with TRD are managed in primary care⁸ and therefore linking primary and secondary care datasets would provide a fuller picture

of treatment pathways and health outcomes. Linking these datasets, along with other national datasets/registries, allows mental health outcomes to be mapped over a lifetime.^{9,10} As we emphasized at the beginning of this article, a biopsychosocial approach is required to understand the influence of multiple factors on mental health outcomes. Linkage of datasets from across healthcare services, social care, and biomedicine is crucial to this integrated approach and will provide exciting research opportunities.

Real-world data within psychiatric EHRs provide a unique opportunity to gain insights into the complex and heterogeneous nature of psychiatric disorders. EHRs are a valuable source of information related to a patient's experience of care, and there is a growing need to develop innovative approaches to effectively leverage these data to inform the development of future treatment strategies and to improve care practices. Well-designed methods that can effectively integrate and analyze data from multiple sources will be critical in fully realizing the potential of EHRs in mental health research. This will involve developing sophisticated algorithms and tools for NLP and data harmonization. The implementation of innovative approaches can enhance accessibility of EHR data for mental health research, improve our understanding of factors influencing patient outcomes, and inform evidence-based interventions in real-world settings.

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Humanistic Burden of Postpartum Depression in the United States

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Postpartum depression is a common obstetric complication with significant morbidity and mortality implications.

Results of this study indicate that, compared to their counterparts, women with postpartum depression have significant and clinically meaningful impairment of mental health status and health-related quality of life.

Findings from this study highlight the need for effective screening measures and disease management using targeted therapies.

Overview

Approximately 3.6 million live births were recorded in the United States in 2021.¹ According to the Centers for Disease Control and Prevention (CDC), 1 in 8 women reported severe and long-lasting symptoms of depression after giving birth,² representing 450,000 women in 2021. This form of depression after childbirth is a common obstetric complication, termed as postpartum depression (PPD). Current evidence suggests that many biological, social, and psychological factors are responsible for the development of PPD,³ which reportedly occurs in 13% to 20% of new mothers.⁴ However, there often exists a stigma around appropriate screening measures and missed opportunities by healthcare providers to enquire about depression during prenatal and postpartum visits. Therefore, the actual incidence of PPD is likely to be higher in the United States than the reported estimates.^{2,5}

Due to similar symptoms, PPD is often considered synonymous with another common manifestation of depression following childbirth called “postpartum blues” or “baby blues.” While the latter

starts within 1 to 3 days after birth without significantly inhibiting maternal functioning, symptoms of PPD can occur and persist up to a year following childbirth and even result in functional

There were no specific drugs or pharmacotherapies approved by the US Food and Drug Administration for treating postpartum depression until the approval of brexanolone in 2019.

impairment.⁴ Moreover, in contrast to symptoms of postpartum blues, which resolve with emotional support and reassurance, PPD usually requires interventions such as interpersonal psychotherapy, cognitive behavioral therapy, psychodynamic psychotherapy, medications, or a combination of these.⁴ The commonly occurring symptoms of PPD are summarized in **Figure 1**.

The severity of this condition is reflected in the fact that suicide accounted for approximately 20% of postpartum deaths

Figure 1: Common symptoms of postpartum depression among new mothers



PPD indicates postpartum depression.

among new mothers.⁵ Besides affecting the mothers, PPD also has spillover effects on the welfare of newborns and may adversely affect their behavioral, emotional, and cerebral development in the long-term.⁵ Therefore, there is substantial morbidity and mortality associated with PPD and a considerable burden from societal and economic perspectives. The treatments for PPD mainly consisted of strategies and therapies similar to the treatment of major depressive disorders,⁶ and there were no specific drugs or pharmacotherapies approved by the US Food and Drug Administration for treating PPD until the approval of brexanolone in 2019.⁶ Brexanolone has a multipronged mechanism of action with neuroprotective, anxiolytic, and antidepressant properties. This approval, a transformative breakthrough in the treatment landscape of PPD, has also opened opportunities for further development of more targeted drugs.⁵

Based on the diagnoses of mental health conditions or prescription of medications for PPD, 550,268 women (~11%) annually had evidence of PPD.

Few prior studies have examined the quality of life among women with PPD and assessed the effects of this condition on maternal health-related quality of life (HRQoL).⁷ Moreover, such data for the United States are limited. In this study, the authors have examined the impact of PPD on HRQoL of adult women with childbirth in the United States using a generic quality-of-life instrument for mental and physical health status. The findings of this study can help in understanding the impairment of HRQoL due to PPD and the need to improve the quality of care using targeted treatments.

Study Details

This study used the Medical Expenditure Panel Survey (MEPS) data for the years 2016 to 2019. We identified women aged 18 to 50 years with a childbirth event (ie, diagnosis of pregnancy or delivery or encounter of postpartum examination/lactating women) and no evidence of prior mental health

Table 1: Study cohort characteristics

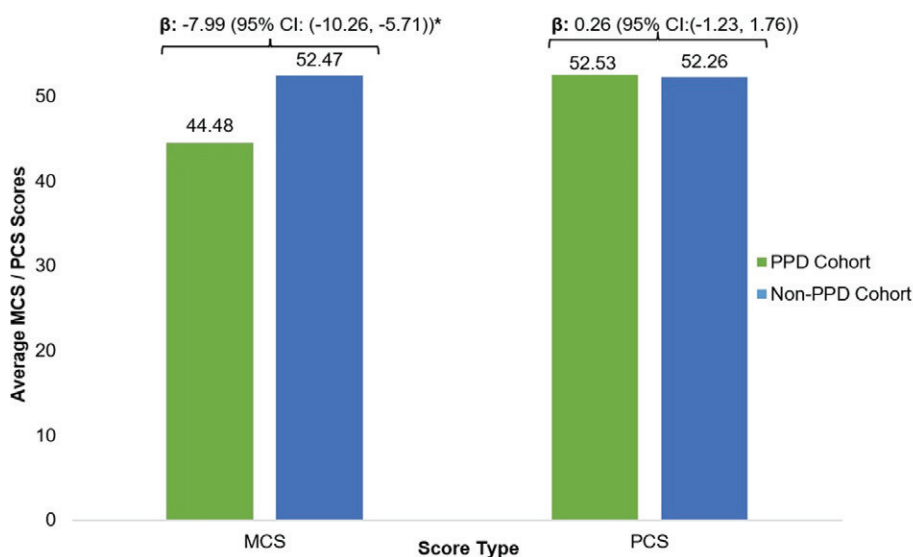
| Characteristics | PPD cohort (N=550,268) | Non-PPD cohort (N=4,299,893) | Standardized Difference in Percent |
|--|------------------------|------------------------------|------------------------------------|
| Age, Mean (SD) | 29.59 (5.15) | 29.55 (5.52) | 0.01 |
| Family size, Mean (SD) | 3.54 (1.32) | 3.48 (1.54) | 0.05 |
| Number of concurrent conditions, Mean (SD) | 0.98 (1.21) | 0.95 (1.53) | 0.03 |
| Bachelor's Degree or Higher, % | | | |
| Yes | 47.5% | 46.0% | 3.11 |
| No | 52.5% | 54.0% | -3.11 |
| Marital Status, % | | | |
| Married | 61.9% | 61.2% | 1.49 |
| Widowed | 0.6% | 1.0% | -3.86 |
| Divorced | 4.0% | 4.6% | -2.92 |
| Separated | 0.8% | 1.2% | -4.69 |
| Never married | 32.7% | 32.0% | 1.42 |
| Region, % | | | |
| Northeast | 21.6% | 20.4% | 2.90 |
| Midwest | 26.0% | 25.8% | 0.48 |
| South | 30.5% | 30.9% | -0.89 |
| West | 21.9% | 22.9% | -2.35 |
| Smoker, % | | | |
| Yes | 17.2% | 20.6% | -8.74 |
| No | 82.8% | 79.4% | 8.74 |
| Family Income Status, % | | | |
| Near poor | 22.9% | 25.0% | -5.08 |
| Poor | 7.3% | 6.1% | 4.91 |
| Low income | 11.5% | 8.4% | 10.48 |
| Middle income | 20.6% | 22.4% | -4.45 |
| High income | 37.7% | 38.1% | -0.75 |
| Race/Ethnicity, % | | | |
| Hispanic | 16.4% | 15.8% | 1.82 |
| Non-Hispanic White only | 70.8% | 71.0% | -0.62 |
| Non-Hispanic Black only | 8.6% | 9.4% | -2.79 |
| Non-Hispanic Asian only | 2.7% | 2.0% | 4.39 |
| Non-Hispanic other or multiple races | 1.5% | 1.8% | -2.03 |
| Survey Year, % | | | |
| 2016 | 38.3% | 35.5% | 5.67 |
| 2017 | 22.0% | 22.3% | -0.81 |
| 2018 | 20.6% | 19.4% | 3.12 |
| 2019 | 19.1% | 22.8% | -8.98 |

N represents the weighted annual sample size.
PPD indicates postpartum depression; SD, standard deviation.

conditions. PPD cases in the study were identified using diagnosis codes associated with depression, mood, or anxiety disorders or drug codes for prescription medications concerning PPD. Two mutually exclusive cohorts, ie, PPD and non-PPD, were created after classifying women with either diagnosis codes or drug codes pertaining to PPD in the former cohort.

Furthermore, the HRQoL of women was examined using short form-12 version 2 (SF-12v2) mental component summary (MCS) and physical component summary (PCS) scores. These scores are components of the SF-12v2 HRQoL instrument and include 12 items capturing information regarding mental and physical health status. The MCS score includes social functioning and mental or psychological health, whereas

Figure 2: Comparison of MCS and PCS scores



β coefficient indicates the average incremental effect of PPD on MCS and PCS scores.

* Indicates statistical significance at 5%.

CI indicates confidence interval; MCS: Mental Component Summary; PCS: Physical Component Summary; PPD: postpartum depression.

the PCS score captures limitations in physical activities and pain. The higher the MCS and PCS scores, the better the mental and physical health status.

This study assessed the effect of PPD on HRQoL while controlling for other characteristics such as age, family size, number of concurrent priority health conditions, education status, marital status, region, smoking status, family income status, race/ethnicity, and survey year. The study cohorts, PPD and non-PPD, were balanced on the characteristics mentioned previously by using propensity score-based inverse probability of treatment weighting (IPTW). Separate linear regression models were used to assess the effect of PPD on MCS and PCS scores. The analysis used appropriate weighting and the complex survey design considerations of the MEPS data to evaluate the relationships and to generate nationally representative estimates.

Findings

The study cohort for this analysis included an unweighted sample of 1873 women aged 18 to 50 years with a childbirth event and no evidence of prior mental health conditions in the United States, representing a weighted sample

of approximately 4.3 million women annually. Based on the diagnoses of mental health conditions or prescription of medications for PPD, 550,268 women (~11%) annually had evidence of PPD. These national estimates appear to be consistent with those estimated by CDC.²

The inverse probability of treatment weights were calculated for the study population using age, family size, number of concurrent conditions, education status, marital status, region, smoking status, family income status, race/ethnicity, and survey year. Furthermore, to adjust for potential confounders, these characteristics were balanced in PPD and non-PPD cohorts using IPTW. Most women with PPD were non-Hispanic White, without bachelor's degrees, with high family incomes, and nonsmokers. **Table 1** depicts summary statistics for study cohorts.

The mean MCS score for women with PPD was 44.48, in contrast to 52.47 for women without PPD. Moreover, the IPTW-adjusted linear regression model indicated that, on average, women with PPD had 7.99 points lower MCS scores than women without PPD. However, there was no significant impact of PPD on physical health status based on the PCS scores (**Figure 2**). When we

converted the MCS and PCS scores to SF-6D utility score⁸ (data not shown), this translated into a utility difference of 0.07 (0.76 and 0.83 for PPD and non-PPD, respectively), which is higher than the minimal clinically meaningful difference.

Closing Remarks

This study found that women with postpartum depression experience significant and clinically meaningful impairment in their mental health status compared to their counterparts. While women with PPD are also believed to experience changes in physical health status through loss of appetite,⁴ our study did not find a significant impact of PPD on physical health status using PCS scores. This may be attributed to the lack of sensitivity of the SF-12v2 PCS scale in measuring the impact of PPD symptoms, such as eating habits and weight changes, on physical well-being.

While other studies have assessed the economic burden of PPD on affected households,^{3,9} our findings present a unique contribution to quantify the humanistic burden of PPD in terms of HRQoL in the US civilian population. Additionally, prior studies have collectively assessed the impact on new mothers and their families,¹⁰ but the present study assessed the burden of PPD for the primary affected

The availability of PPD-specific effective treatment approaches may improve not only the quality of life of mothers but also their newborns and families.

group (ie, new mothers). However, a few limitations of this study should be noted. First, MEPS is survey data, which comes with inherent biases such as missing data and recall bias. Second, less severe cases of PPD, which may not have required a visit to the healthcare provider, might not have been captured through either diagnosis of mental health conditions or prescription of medications concerning PPD. This indicates that the actual impact of PPD on HRQoL is likely to be underestimated, and further research is needed to assess the impact of PPD based on disease severity.

However, despite the above limitations, our study found that PPD has a significantly adverse impact on the mental health status of new mothers. The availability of PPD-specific effective treatment approaches may improve not only the quality of life of mothers but also their newborns and families.

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