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Study Title: Impact of High Deductible Health Plans on Patients With Bipolar Disorder

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BACKGROUND [*Relevant PCORI Methodology Standard RQ-1*]

A.1. Bipolar Disorder is a Major Cause of Disability, Morbidity and Mortality [*RQ-3*]: Bipolar disorder is a severe mental illness characterized by early onset, high risk of recurrent mania or hypomania and depressive episodes, persistent risk of suicide, and low rate of fully sustained recovery. It is the sixth leading cause of adult disability in industrialized countries.² In the US, the 12-month prevalence of bipolar spectrum disorders is 2.8% and the lifetime prevalence is 4.4%.³ These estimates include bipolar-I and –II disorder as well as subthreshold bipolar disorders. Subthreshold cases account for half of bipolar spectrum disorders,³ although less intense, they cause significant morbidity and functional disability.⁴ Patients with bipolar disorder have a ~10-15% lifetime suicide risk,⁵ and, compared to the general public, greater risk of substance abuse,³ cardiovascular disease, diabetes, and obesity.⁶ Further, bipolar disorder causes poor social and psychological functioning, work impairment and absenteeism, and a low health-related quality of life.⁷

A.2. Efficacious Treatments Exist for Bipolar Disorder: Although specific psychotherapies have demonstrated efficacy in improving bipolar disorder outcomes,⁸⁻¹³ pharmacotherapy remains the foundation of acute and long-term management.^{14,15} Acute treatment aims to stabilize mood and relieve mania or depression symptoms. Maintenance treatment is required to decrease mortality, and prevent relapse and recurrence.¹⁴ Effective medications for bipolar disorder include lithium, anticonvulsants, and antipsychotics.^{14,16,17} While patients with bipolar disorder can have asymptomatic periods, episodes of clinical instability are common,^{18,19} thus office visits to general practitioners and mental health specialists are also a fundamental component of high quality pharmacological and interpersonal care.¹⁴

A.3. High-Deductible Health Plans in the US are Expanding at Unprecedented Rates [*RQ-5*]: The US has been grappling for decades with rising health spending, which outpaces inflation and is often cited as a threat to the economic sustainability of governments, employers, and families.²⁰ In response, payers²¹ and employers²² have increasingly turned to high-deductible health plans (HDHPs) with high levels of patient cost-sharing. Compared with traditional plans, HDHPs have lower monthly premiums, but they subject most services to annual deductibles of \$2,600 to \$12,900 per family.²³ Families might therefore pay the entire deductible amount out-of-pocket before more generous coverage, such as full coverage or coinsurance, begins.

Two types of HDHPs predominate in the US: Health Savings Accounts (HSA) eligible and HSA-ineligible HDHPs. The 2003 Medicare Modernization Act created HSAs that allow employers and employees to contribute tax-free funds into accounts for medical services payments.²⁴ Such accounts must be connected to HDHPs that have a regulated structure including minimum deductible amounts, maximum annual account contributions, and defined coverage requirements. HSA-eligible HDHPs with "value-based" out-of-pocket exclusions often fully cover a limited number of preventive services (e.g., cancer screening), have a moderate copayment (e.g., \$20) for annual primary care physician preventive visits, but require full cost-sharing up to the annual deductible for all other services (e.g., mental health visits, medications, tests, hospitalizations). In contrast, HSA-ineligible HDHPs (i.e., Health Reimbursement Arrangement plans or those without an associated account) are also designed to be "value-based," but generally include more generous drug coverage (i.e., relatively low medication copayments as in traditional plans) and specialist visits might be exempt from the deductible; most other services including mental health visits and hospitalizations are subject to the deductible.

"Value-based" HDHPs can be defined as those with low or no out-of-pocket costs for certain preventive services or medications with evidence of effectiveness.²⁵ Proponents theorize that these financial incentives will steer patients toward testing and treatments that have a high benefit-to-cost ratio, ultimately driving down healthcare costs. However, this definition of "value" is generally a top-down conception from policymakers, payers, and insurers hoping to reduce long-term healthcare spending. The voice of patients in articulating what care is "valuable" to them is largely excluded. In addition, evidence that value-based HDHPs improve outcomes and lower costs is limited at best.^{26,27} HDHP critics are concerned that patients facing higher out-of-pocket cost burdens, especially vulnerable populations such as those with chronic mental illness, might defer or avoid needed care.^{28,29}

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Both HSA-eligible and -ineligible HDHPs have shown unprecedented growth;²¹ national enrollment quadrupled between 2006 and 2014 and 41% of workers now have HDHPs (Figure 1).^{1,30} The Affordable Care Act, which went into full effect in 2014 is likely to cause an “explosion”^{31,32} in HDHPs because of their lower premiums, coverage mandates, and an imminent “Cadillac tax” on more generous plans.

A.4. Insurance Coverage Affects Treatment and Outcomes for Patients with Serious Mental Illness:

Although most prior studies

of medication coverage among the severely mentally ill have not included commercially-insured individuals, their results are nonetheless illuminating. Patients with mental illness are particularly vulnerable to restrictions in coverage, especially medication coverage, due to either financial barriers (e.g., cost-sharing, caps on reimbursable prescriptions) or administrative barriers (e.g., prior authorization requirements). Financial barriers are commonly used in private health plans to manage psychotropic medication utilization.³³ Increased patient cost-sharing could worsen already high rates of non-adherence among the mentally ill.^{34,35} In previous studies, we found that imposing caps on the number of reimbursable prescriptions or increasing drug copayments reduced adherence to psychotropic medications and increased rates of emergency services, nursing home admissions, and partial hospitalizations.³⁶⁻³⁸ Even a modest increase in copayments from \$2 to \$7 caused a 25% decrease in psychiatric medication refills among patients with schizophrenia.³⁹ Higher patient cost-sharing is also a barrier to antipsychotic medication adherence in commercially insured patients.⁴⁰

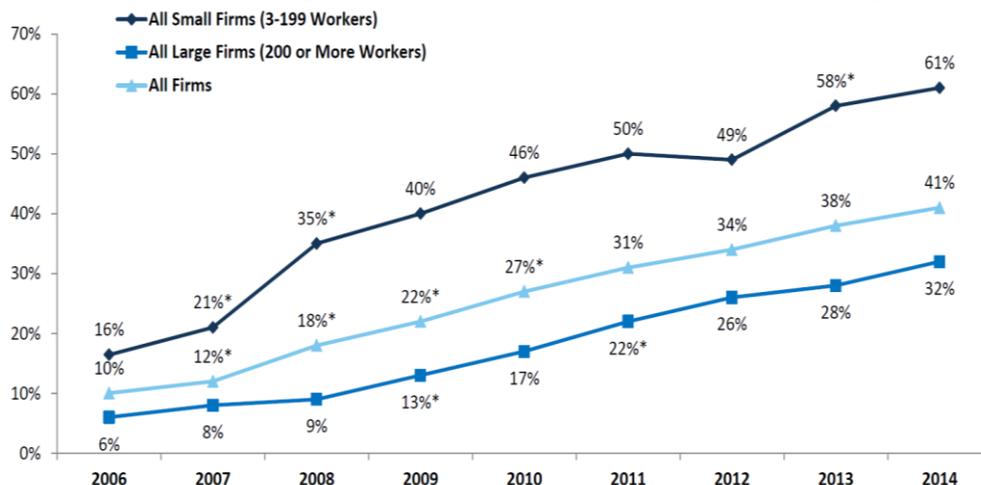
Administrative barriers are designed to encourage physicians and patients to substitute lower cost for higher cost services. Our studies in Medicaid/Medicare populations suggest that these policies can create unintended adverse effects among patients with mental illness (e.g., reductions in treatment initiation, premature discontinuation of therapy, unintended switching among medications) without appreciable cost savings to the program.⁴¹⁻⁴⁵

In addition, certain patient subgroups are at a higher risk of non-adherence. Factors such as comorbidity burden, race/ethnicity, and income may influence adherence. Co-occurring somatic conditions put patients with mental illness at a greater risk of adverse health events and high health care costs.^{46,47} Black Medicaid patients with schizophrenia are less likely to have adequate medication adherence in either the acute or maintenance treatment phase.⁴⁸ Similar racial/ethnic disparities in both treatment and adherence exist among patients with bipolar disorder.^{49,50} Although the effect of income on adherence among the mentally ill is not clear, it has been established that low-income patients with a chronic somatic illness are more sensitive to copayment changes than comparable high-income patients.⁵¹

A.5. Modern HDHPs Might Reduce both Appropriate and Inappropriate Health Care [RQ-5]: The landmark RAND Health Insurance Experiment of the 1970-80s found that cost sharing reduces use of both appropriate and inappropriate health care, including diagnostic testing, treatment, and hospitalizations.⁵² The poorest and sickest individuals subject to high cost-sharing had a 10% projected increase in mortality.⁵² The RAND study suggested that individuals with poorer mental health status had a relatively more favorable response to free mental health care.⁵³ Nevertheless, this study, with a total sample size of only ~2000 adults, could not assess outcomes for individuals with less common conditions such as bipolar disorder. In addition,

Figure 1. Growth of HDHPs

(from The Kaiser Family Foundation, Employer Health Benefits Annual Survey 2014¹)



the RAND experiment occurred in an era with a vastly different range of medications, tests, and services.

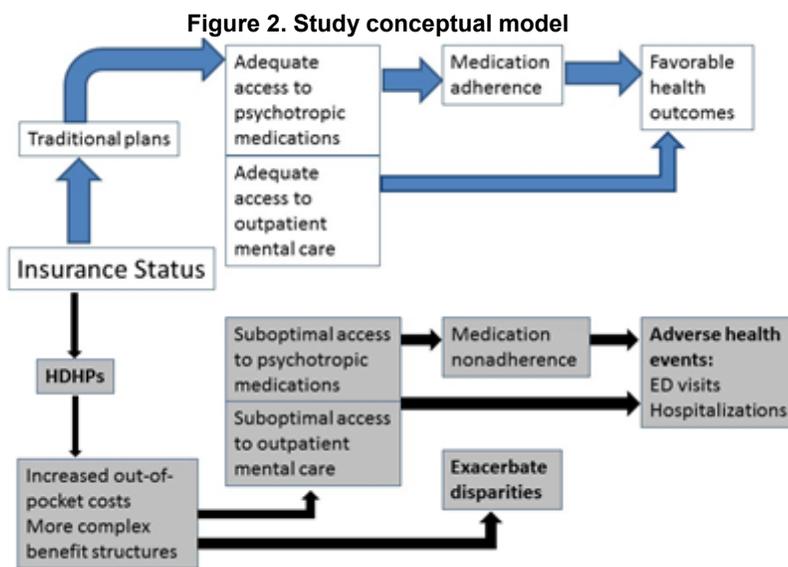
There are few well-controlled longitudinal studies of the impacts of modern HDHPs and, to our knowledge, no controlled studies of HDHPs among the chronically mentally ill. Our research group has used rigorous research designs to study patients' utilization of health care after transition to HDHPs (see Section F below). We found that HDHPs reduced hospitalizations and emergency department (ED) visits, primarily for low severity medical problems.⁵⁴ We also identified a trend toward reduced colorectal cancer screening, with HDHP patients more likely to receive a lower-cost, less sensitive test.⁵⁵ With respect to medication use, other investigators have found that subjecting medications to full cost-sharing under HDHPs reduced use of chronic illness medications including cardiovascular and asthma drugs.^{56,57} Our study found that adherence is largely preserved when HDHP designs include more generous medication copayments as in traditional plans.⁵⁸ This is important from a policy perspective because it suggests that tailored health plans could preserve access to essential treatments. Difficulties affording medications could be followed by complications such as hospitalizations, representing increased suffering from the patient perspective. Among patients with mental illness, it is not known how HDHPs impact quality of care, patient outcomes, and cost burden. Figure 2 shows the theoretical basis for our research, illustrating how considerable increases in patient cost-sharing and complex benefit structures under HDHPs may affect mental health care.

A.6. Patients Perspectives on Access to Treatment for Bipolar Disorder [RQ-3; RQ-6]: Few published studies explore patients' perspectives on either the impact of HDHPs or the role of patient cost-sharing in treatment for bipolar illness. No studies,

quantitative or qualitative, specifically examine the impact of HDHPs on bipolar patients. A general survey of new HDHP enrollees found low awareness of the deductible, and over half of those who were aware of their deductible anticipated forgoing medical care in response.⁵⁹ Our previous survey found that lower-income families in HDHPs were more likely to report forgone care, compared to higher-income families;⁶⁰ among all families with a chronic condition, half had difficulty paying for care – more than twice the rate among families in traditional plans, even after controlling for other factors.⁶¹ A focus group study of persons with disabling physical or mental health conditions found that HDHPs limited patients' ability to afford basic health services and medications;

participants reported forgoing care, taking medical risks, and experiencing anxiety about healthcare choices.⁶² A qualitative study found that bipolar patients rarely mentioned medication costs as “concerns or fears;”⁶³ however, in a follow-up study of those with poor adherence, 60% reported problems accessing care including inability to pay.⁶⁴ Our patient partners at the Depression and Bipolar Support Alliance consider access and cost issues to be leading concerns, as did a large majority of respondents to a recent DBSA web survey.⁶⁵

A.7. Need for the Proposed Research [RQ-3]: The proposed study addresses several important gaps in current evidence about mental illness and HDHPs. First, decision-makers at all levels (consumers, employer-sponsors, and private and public sector policymakers) lack reliable information about the quality and continuity of care for the hundreds of thousands of individuals living with mental illness in commercial insurance plans and about their out-of-pocket costs.⁶⁶⁻⁶⁸ Moreover, there is essentially no information about how commercially-insured mentally ill patients respond to different cost-sharing arrangements, let alone the much higher levels in HDHPs. Third, prior research suggests that HDHPs reduce careseeking and treatment adherence (see above).



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Patients with mental illness might be at particular risk for disruptions in treatment because expensive psychotropic medications and mental health visits are subject to full cost-sharing in many HDHPs. Adherence is already low among patients with bipolar disorder (~35%³⁴) and further financial pressures could exacerbate nonadherence, resulting in adverse outcomes such as hospitalization. Finally, many previous studies of the impact of HDHPs have included subjects with a choice of health plans, thereby increasing individual-level selection bias, a major threat to validity.⁶⁹⁻⁷¹

Our research will address these important gaps in understanding, while overcoming common research limitations. We will include a longitudinal, national, and socioeconomically diverse population, allowing us to draw solid and generalizable conclusions about the impact of HDHPs on patients with bipolar disorder. Through previously funded studies, we have already constructed many complex variables and algorithms needed for the proposed research, and have obtained 9 of the 11 years of insurance claims data from a large US insurer. We have also developed cutting-edge analytical methods to better understand the intended and unintended consequences of transitioning to HDHPs. Employer-mandated switches to an HDHP provide an ideal natural experiment for comparing modern health insurance designs on quality of care, access and adherence to medications, burden of out-of-pocket costs, and adverse outcomes such as preventable hospitalizations. Moreover, ongoing involvement of patients and patient advocates in our proposed study, including incorporation of patients' perspectives through a range of mechanisms, will ensure a richness that has been lacking in previous research.

B. SIGNIFICANCE

The rapid expansion of "value-based" HDHPs that include major cost sharing could have very detrimental effects on patients with bipolar disorder. We will take advantage of a massive insurance claims dataset that captures the increasingly common "natural experiment" of employers mandating that all employees enter HDHPs. We will compare three distinct insurance designs: traditional low-deductible insurance plans and HDHPs with and without medications subject to the deductible. We will evaluate (1) changes in medication adherence, health services utilization, and quality of care; (2) changes in adverse events; and (3) changes in patient out-of-pocket costs after the switch from traditional to HDHP insurance. We will assess these effects in the overall population of patients with bipolar illness and in specific vulnerable subgroups, including racial/ethnic minorities, poorer patients, rural patients, and patients with high comorbidity burdens.

The voices of patients -- especially vulnerable patients with mental illness -- have largely been excluded when determining which "valuable" services should be exempt from high cost sharing under HDHPs. We will address this critical gap by conducting in-depth interviews with a sample of patients and holding ongoing reciprocal dialogue with stakeholders, including a community of patients with bipolar disorder. Stakeholders will help to refine our quantitative analyses and complement them with a deeper understanding -- one that cannot be readily derived from claims data alone -- of key issues surrounding access to mental health treatment.

B.1. Our Proposed Study Addresses Major Research Gaps [RQ-1; RQ-6]: Our proposed study aligns closely with recently published PCORI research priorities. PCORI has prioritized research about bipolar illness because of its prevalence and severity, treatment complexity, and evidence gaps in treatment approaches.⁷²

PCORI's 2012 "National Priorities for Research and Research Agenda"⁷³ calls for studies on "Improving Health Systems," especially on "new system-level strategies ... that have not been rigorously evaluated", "comparative studies on the use of incentives," and "alternative system-level approaches to improving patient access to care." Our comparison of traditional plans and HDHPs, which include benefit features intended to influence patient utilization, responds to this call. Our interviews (Aim 4) exploring patient views on the value of different services directly respond to the PCORI agenda's emphasis on outcomes that "patients experience and think are important". Finally, our analyses of vulnerable patients addresses the PCORI agenda by examining "differences in patient response" across "socioeconomic, demographic, and other patient characteristics."

In April 2013, PCORI's Advisory Panel on Improving Healthcare Systems identified five topics for special consideration, including studies comparing "different insurance features on chronically ill patients' access to care and quality of care;" the PCORI brief specifically noted that the impact of HDHPs "remains unknown for

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access, quality, and outcomes.” Another brief, “Mental Health and Primary Care Co-Location,” made particular note of the high risks of medical comorbidity, nonadherence, treatment complications, and hospitalization among patients with mental illness, especially those in rural areas. Our proposal includes a special focus on patients with bipolar disorder who live in rural areas and who have high comorbidity levels. Similarly, the Institute of Medicine’s (IOM) priority list⁷⁴ calls specifically for studies that: (1) compare strategies for enhancing medication adherence, (2) compare effects of alternate benefit designs and cost-sharing arrangements on chronically ill patients, and, (3) delineate barriers to care for populations that experience health disparities. Our research plan aligns closely with these IOM priorities.

The two most prominent clinical guidelines for treating bipolar disorder (from the American Psychological Association¹⁴ and the VA/Department of Defense⁷⁵) both emphasize medication adherence to prevent adverse outcomes (such as relapse, hospitalization, and suicide), and consistent clinical follow-up to ensure optimal medication adherence. Patient advocacy organizations frequently voice concerns about financial barriers to access and the importance of expanded insurance coverage.⁷⁶ In a 2010 survey⁶⁵ conducted by our study partner, the Depression and Bipolar Support Alliance (DBSA), 71% of respondents reported that psychiatric medication costs were a barrier to their treatment. DBSA’s report concluded that the data did not support “the common (mis)conception that people with bipolar disorder or depression are in denial and think they don’t need their medication;” rather, side effects and out-of-pocket costs play very prominent roles. The priorities laid out by both the professional guidelines and advocacy organizations point to the significance of our study, which will examine important potential barriers to medication adherence and other mental health services.

B.2. Our Proposal Has Several Innovations and Major Potential to Influence System Policies [RQ-3]:

The proposed project features several innovations in the areas of mental health systems research that promise to inform future policies and insurance designs. We will construct the largest and most geographically diverse observational dataset of commercially-insured patients with serious mental illness, including plan members from all 50 states over 11 years. The national setting is more generalizable than typical settings such as regional health systems. Our study would also be the first controlled, longitudinal study comparing the impacts of HDHPs and traditional plans on patients with a serious mental illness. No current literature exists on changes in medication use, outpatient visits, quality of care, or adverse outcomes associated with HDHPs in patients with bipolar disorder.

The large sample size (~109,000 patients with bipolar disorder aged 12-64 years who match our study criteria, described below) in our claims data will permit us to compare major contemporary insurance designs. This will be the first rigorous study to compare the impacts of HDHPs with and without full drug cost-sharing among the mentally ill; subjecting chronic medications to deductibles might profoundly impact treatment continuity and quality. Our study will also be the first large enough to examine the HDHP effects on subgroups of patients with bipolar disorder who might be particularly vulnerable, including racial minorities, patients with high comorbidity, and those in rural areas or with low income. Our unique dataset includes individual-level socioeconomic status (SES) measures, enabling more precise inference of SES effects on outcomes. HDHPs may exacerbate the health inequalities faced by these vulnerable groups, who may be more likely to forego essential care under HDHPs.

Our quasi-experimental, longitudinal study design will be uniquely rigorous in addressing the question of HDHP effects on patients with bipolar disorder. We will use aggregated and patient-level interrupted time series regression modeling, adjusted difference-in-differences, and a two-stage propensity matching approach to create a closely matched control group. Accumulating evidence⁷⁷ suggests that our matching approach leads to effect estimates that closely approximate randomized controlled trials. Another distinct advantage will be our inclusion of individuals offered no choice of insurance plans, minimizing member-level selection bias, a major limitation of research in this field.

Our thorough patient engagement component, which includes a study co-investigator based at DBSA, in-depth interviews with patients currently enrolled in insurance plans comparable to those in our claims dataset, and regular feedback from both our Patient/Stakeholder Advisory Panel and the broader DBSA community, will

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provide our study with energy, ideas for protocol enhancements, a wealth of lived experience for interpreting results, and myriad opportunities for disseminating results as they emerge.

B.3. Pathways toward Improvements in Care [RQ-3]: HDHPs could cause disruptions in treatment of bipolar illness due to cost-related nonadherence or confusion about coverage details. HDHPs could also cause reductions in outpatient and inpatient care, or increased psychiatric hospitalizations due to treatment disruptions. Because of the rapid growth in HDHPs, our study is highly relevant to policymakers at all levels. Both types of HDHPs (with and without medications subject to the deductible) as well as traditional plans with no deductible are all highly prevalent in the US. This wide “practice variation” in insurance benefits design implies a crucial need to understand the impacts of design differences in order to optimize patient health. Prior research indicates that even small differences in insurance design can have powerful consequences for vulnerable patients.

Opportunities to implement policy recommendations would be readily available. Insurers redesign benefit offerings every year and respond quickly to shifting pressures from employers. Our study potentially includes an immediately-available “policy intervention,” if HDHPs with generous medication coverage promote bipolar medication adherence and better health outcomes, employers and health insurers could quickly shift to such designs. Evidence that exempting mood stabilizing drugs from full cost-sharing preserves appropriate utilization could also contribute to amendments to the 2003 Medicare Modernization Act that requires HSA-eligible HDHPs to subject all medications to the deductible.²⁴ State and federal regulators closely examine insurer practices and set standards for benefits packages. We expect that policy makers will use our results to introduce health plan designs that promote high quality care among patients with mental illness.

Given the timely and policy-relevant nature of our research, we expect to share preliminary results at scientific conferences, through reports and meetings with stakeholders (PCORI, DHHS, CMS, AHRQ, NIMH, MHRN/HMORN, NAMI, major health insurers), and with the DBSA community through news updates and other communications. We anticipate 7 published reports in medical and health policy journals with broad circulation. Our research group has had considerable success informing health policy decisions. For example, our past studies of drug benefit limits among the chronically ill elderly and those with schizophrenia have informed policies to improve drug coverage in Medicaid populations, provide Medicare Part D drug coverage subsidies for the near poor, close the Medicare drug coverage gap, and include benzodiazepines in the Medicare drug benefit.^{36-38,78,79} This research will continue our tradition of innovative academic/policymaker partnership.

Our collaborator, DBSA, enhances our capacity to translate study findings to practice. DBSA is a national mental health advocacy organization created by and for people who live with mood disorders. DBSA has multiple avenues for disseminating research findings and mobilizing patients and caregivers to press for needed changes, including 800 local support groups, a popular internet site, a Facebook page with >100,000 followers, and the Care For Your Mind blog with ~5,000 user sessions per month. DBSA is also soon to launch its Parity Campaign, informing patients of new policies (including the Affordable Care Act) that seek to increase access to mental health care, and working to ensure that these policy goals are realized. DBSA leaders have expressed confidence that the goals of our proposed research align well with their Parity Campaign, and will disseminate our study results in tandem with the Campaign as appropriate (see Letters of Support).

C. STUDY APPROACH [RQ-2]

Our study objective is to determine the effects of two types of HDHPs (with and without medications subject to the deductible), compared with traditional commercial insurance, on adolescents and adults with bipolar disorder. To accomplish this, we will conduct quantitative analyses using a very large, geographically diverse dataset of insurer claims complemented by in-depth interviews with individual patients. Insights gained from these interviews, from our Patient/Stakeholder Advisory Panel, and from our ongoing partnership with a major patient advocacy organization (DBSA) will shape and inform the quantitative analyses.

Aims 1-3 will use insurance claims data to examine the impacts of ongoing natural experiments whereby some employers shift their entire employee populations from traditional insurance to HDHPs with two distinct benefit structures. In **Aim 1**, we will evaluate changes in medication adherence, and in the intensity and quality

of other health care following this shift. In **Aim 2**, we will assess changes in adverse events such as preventable psychiatric hospitalizations. In **Aim 3**, we will evaluate changes in patient out-of-pocket cost burden. In each of these first three aims, we will first examine HDHP effects in the overall population of patients with bipolar illness, then compare differences in effects between the two types of HDHPs, and finally examine changes in specific vulnerable subgroups, including racial/ethnic minorities, poorer patients, rural patients, and patients who have high comorbidity burdens. In **Aim 4**, using interviews, we will explore patient experiences coping with complex insurance benefits and gather their views on higher- and lower-value care, contrasting these to standard definitions and conceptions of healthcare “value.”

Throughout the three years of study, we will rely on our Patient/Stakeholder Advisory Panel and our investigative partnership with DBSA to monitor our progress, to continuously bring in fresh community perspectives on our work and its relevance, and to help us refine our study approach.

C.1. Overview of Design and Methods: In **Aims 1-3**, we will use 11 years of insurance claims data on more than 109,000 patients with bipolar disorder. Outcomes will include adherence to bipolar medications, rates of laboratory-based medication monitoring, psychotherapy visits, use of acute services such as emergency department visits and hospitalizations, and out-of-pocket costs (total, by type of service, and per service unit). We will first examine trends over calendar time among the overall population and vulnerable subgroups defined by income, race/ethnicity, rural residence, and comorbidity burden. We will then rigorously evaluate HDHP effects by examining changes in the above outcomes before and after the mandated switch from traditional plans to HDHPs. Our studies will generate the first empirical evidence regarding the comparative effectiveness of alternative insurance designs in preserving quality and continuity of care among the mentally ill.

We will use a range of analytical methods tailored to our study outcomes. Specifically, we will use two strong quasi-experimental, longitudinal research designs: an **interrupted time series with comparison series design** and a **pre-post with propensity-matched comparison group difference-in-differences design**. The Cochrane Collaboration (an independent organization that produces and disseminates systematic reviews of health care interventions) considers both to be strong research designs that permit causal inference.^{80,81} Moreover, we will use a range of statistical methods including generalized linear mixed models,^{82,83} and interrupted aggregate and patient-level time series models^{58,84} as appropriate for each of our study outcomes. Study design features that strengthen the internal validity of the proposed research and reduce member- and employer-level selection biases include (i) selecting only employers that offer only one health plan type to employees, (ii) using a validated two-level (employer and member) **propensity score matching approach**,^{77,85} and (iii) propensity score matching on baseline population characteristics, including the functional form of the baseline outcome trends.⁷⁷ Cutting-edge research has shown that this matching approach leads to effect estimates that closely approximate randomized controlled trials.⁷⁷ These approaches will reduce baseline differences between employers choosing among the three possible types of insurance and control for potential patient-level differences in employee populations.

In **Aim 4**, we will conduct in-depth interviews with approximately 40 commercially insured individuals with bipolar disorder or their family caregivers to explore how they navigate deductibles, copayments, and other complex insurance features. We will also determine the health care services that patients most value and assess how they prioritize difficult health care cost tradeoffs.

C.2 Sources of Data and Access [IR-1]: Our OptumInsight **health insurance claims data**, spanning 11 years (2004-2014), is from one of the largest and most geographically diverse commercial health plan in the US. This insurer has membership in all 50 states and annual enrollment of ~33 million members; this insurer was among the first to offer modern HDHPs. In addition to pharmacy and medical service claims, the de-identified datasets contain enrollment information and Credit Report data linked to the member file, including indicators of individual-level SES rarely used in health care research (household income, net worth, and educational attainment). To address the concern of the adequacy of this data source, we note this standard health insurance claims dataset is directly from a large national health insurer. Health insurance claims datasets have been used for decades in health services research and their use has been validated for

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capturing cohorts of patients with bipolar disorder. Our group⁸⁶⁻⁸⁸ and others have published multiple studies using these data.

To assess the efficiency of data linkage between claims data and credit report data and implications for bias based on proportion of total sample that may not have these data [IR-2], data vendor Optum will link patient addresses to geocoded 2000 and 2010 census data, a process that has previously yielded <1% unlinked data. Information on member race and ethnicity is also included, based on geocodes, US census data, and an imputation strategy incorporating member surname. [MD-2] We will also have detailed benefit information for ~80% of employers, including individual and family deductible levels, HDHP type (HSA, Health Reimbursement Arrangement, or non-account), and copay and coinsurance amount by service type. For employers with missing deductible levels, [MD-2] we have developed an imputation algorithm that has 97.0% sensitivity and 96.2% specificity. To determine employer deductible levels, we will use a benefits type variable that we have for smaller employers (with approximately 100 or fewer employees). For larger employers, we will take advantage of the fact that health insurance claims data are the most accurate source for assessing out-of-pocket obligations among patients who utilize health services. Our claims data contain an in-network/out-of-network deductible payment field. For patients who use expensive or frequent services, the sum of their yearly deductible payments will add up to clearly identifiable exact amounts such as \$500.00, \$1000.00, \$2000.00, etc. When several members have these same amounts, it provides strong evidence that the employer offered such an annual deductible level. It will also be possible to detect employers that offer choices of deductible levels when multiple employees have deductibles at two or more levels, such as 20 employees with an annual amount of \$1000.00 and 12 employees with \$500.00. For employers with at least 10 workers, we therefore will sum each employee's in-network deductible payments and number of claims over the enrollment year and plan to assess other key characteristics such as percentage with Health Savings Accounts. On a randomly selected half of the employer data set that contained our calculated employer characteristics (such as the percentage of patients with deductible levels between \$1000-\$2500) as well as actual deductible amounts, we will use a logistic model that predicts the 3-level outcome of deductible <=\$500/\$500-\$999/>\$1000 based on multiple aggregate employer characteristics such as the first and second most common whole number deductible value, the percentage with Health Savings Accounts or Health Reimbursement Arrangements, the median deductible payment, the percentage of employees using services, the employer size, the percentage of employees with deductible levels between \$100-\$500/ \$500-\$1000/ \$1000-\$2500/ >\$2500, etc. This predictive model will output the probability that employers had deductibles in the three categories (summing to 1) and we will assign the employer to the level that had the highest probability. If we detect employers that had 10 or more employees with whole number deductible levels both above and below \$500 (e.g. \$250.00 and \$1500.00), we will assign the employers' category as "choice." If 100% of employees had Health Savings Accounts, we will overwrite any previous assignment to classify the employer as a high-deductible employer. We will test the predictive model on the other half of the sample for which we have actual deductible levels. At employers with 75-100 workers, we anticipate to find sensitivity and a specificity of over 96%. We will have all study years (2004-2014) available in-house. The sample size (see section C.10) will be sufficient to investigate HDHPs' effects within carefully selected employer groups, as well as within vulnerable patient subgroups.

Our patient partner, DBSA, will help recruit **Aim 4 interview respondents** through local chapter meetings and social media platforms. Interested individuals will contact DBSA, who will screen for eligibility. Participants will be non-elderly adult patients with bipolar illness enrolled in commercial plans or caretaking family members, able to converse in English; respondents will give informed consent for recorded telephone interviews of approximately 1 hour, each conducted using a semi-structured interview guide.

C.3 Interventions and Comparators [RQ-5; HT-1 to HT-4]: Our analyses in **Aims 1-3** will include members of traditional health plans (including low-deductible Health Maintenance Organization, Preferred Provider Organization, and Point of Service plans) and HDHPs. We define traditional health plans as those having annual deductibles of \$500 or less for individuals and copayments of less than \$50 for most services. We

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define HDHPs as those requiring individuals to spend at least \$1000 out-of-pocket annually for most clinical services before more comprehensive coverage begins, but which typically have exemptions for preventive care.

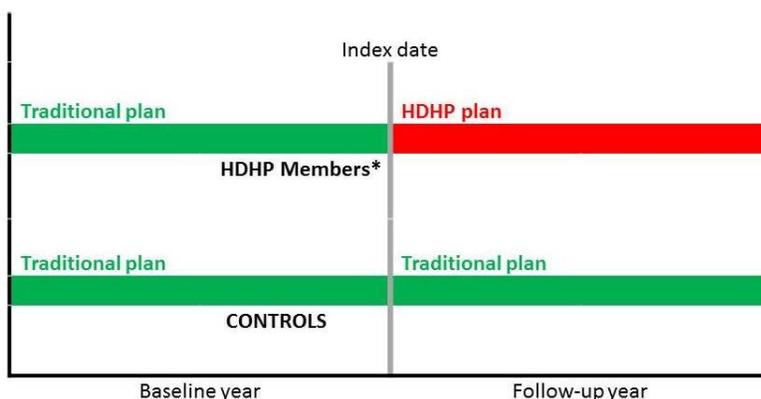
We will further classify HDHPs as HSA-eligible and HSA-ineligible. HSA-eligible HDHPs subject most medical services (including psychotropic medications and all mental health visits) to the annual deductible; only “preventive” health care (a limited set of services such as check-ups and screenings) are under first-dollar coverage, either for free or with a modest copayment. By contrast, HSA-ineligible HDHPs also subject many services to the deductible, but they generally include more generous coverage for medications (i.e., tiered copayments, as in traditional plans) and primary care visits might require only a modest copayment. These coverage differences for key services create a natural experiment that will permit us to answer crucial questions regarding optimal insurance designs for patients with bipolar illness.

For **Aim 4** in-depth interviews, we will sample respondents with either traditional insurance or HDHPs in order to explore this contrast. However, we recognize that many respondents may not fully understand the design of their insurance plan, and we expect new themes to emerge regarding lack of benefits clarity.

C.4 Enrollment Period and Follow-up Duration for Aims 1-3:

Our study period will extend 11 years (January 2004 to December 2014), a period of rapid growth of HDHPs,²² capturing an unprecedented sample size of patients with bipolar disorder transitioning to HDHPs. The intervention cohorts will include individuals who transitioned to HDHPs between January 2005 (after a minimum one year baseline period in a traditional plan) and December 2013 (to allow one year of follow-up). We will follow all subjects for 1 year before and 1 year after the index month of switching (*Figure 3*). Matched controls will be drawn from employers who chose to remain in a traditional plan in the same calendar year, and our matching approach will ensure calendar month of switch is also balanced across the study groups. We will require continuous enrollment for the 24 month study period for both groups.

Figure 3. Study design of HDHP members and controls



* A subgroup of members are “forced switchers” whose employers mandate that they transition from a traditional to a high-deductible health plan

C.5 Study Population for Aims 1-3 [RQ-3; CI-1 to CI-4; HT-1 to HT-4]: Inclusion Criteria: We will include health plan members aged 12 to 64 years at the beginning of the baseline period. Consistent with prior research,⁸⁹⁻⁹¹ we will use medical claims data and a validated algorithm^{36,41,43-45,92,93} to identify members who had at least two ambulatory encounters or one hospital encounter with a diagnosis of bipolar disorder (ICD-9 diagnostic codes: bipolar-I: 296.0, 296.1, 296.4-296.7; bipolar-II: 296.89; and bipolar-other: 301.11 and 301.13^{43-45,89-91}). The first advisory panel committee meeting in October 2015 directly shaped our cohort definition stream of work; advisors agreed that bipolar inclusion criteria should include requiring at least 1 inpatient or 2 outpatient diagnoses, to better ensure that the diagnosis is valid and relevant to the planned analyses. Despite the tightening of our diagnostic criteria, our newest cohort totals remain on target with the estimates in our original power analysis. Eligibility for the study is predicated on the principal diagnosis of bipolar disorder (any diagnosis) not just diagnosis at the first position, as advised by our stakeholder panel. The study cohort was derived through applying the following inclusion rules, therefore defining individuals as eligible for our study:

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Study cohort: Of 41,638,597 members enrolled in the national insurer during 2004-2012, we found 18,184,556 have a 2-year enrollment span, a study inclusion criterion. Among these, 148,706 have at least 1 inpatient or 2 outpatient diagnoses of bipolar disorder; this reflects a prevalence of 1% members with bipolar disorder, which is consistent with expectation among the commercially insured population. Among 148,706 members with bipolar disorder, 57,028 matched our age criterion (12 to 64 years of age). (We will conduct sensitivity analyses of our main results varying our bipolar diagnosis criteria [e.g., requiring diagnosis prior to index date, requiring only one diagnosis; [CI-5](#)]) To minimize selection bias, our study cohorts will include individuals whose employers offer only a single benefit type with no choice. Our intervention cohorts will include traditional plan members with bipolar illness who experience an employer-mandated switch to HSA-eligible HDHPs with full drug cost-sharing (i.e., out-of-pocket medications payments until the deductible limit is reached), or to HSA-ineligible HDHPs that subject medications only to copayments as in traditional health plans. The control cohort will include members with bipolar illness whose employers offered only a traditional plan for the follow-up year. We estimate that 7,227 have HDHP insurance and 49,801 have traditional plan insurance. **Exclusion Criteria:** We will exclude members age 65 years or older who could be eligible for Medicare benefits, including drug coverage through Medicare Part D. We will also exclude members whose employer offered a choice of health plan. This strengthens our design by reducing potential selection bias due to, for example, healthier members selecting HDHPs or individuals anticipating discretionary utilization. . Input from our panel advisory meetings led to the decision to exclude from our cohort those individuals with a diagnosis of schizoaffective disorder or schizophrenia in order to identify a clinically homogenous group for our study, as advised by our clinical psychiatrist co-investigator Alisa Busch, MD. This criterion was further supported by our advisors at DBSA. According to sources at DBSA, schizophrenia and schizoaffective disorder are not comorbidities seen in their peer population. In their judgment, people living with schizophrenia and schizoaffective disorder are unlikely to come to DBSA meetings and would have their needs better met in other settings. The ineligibility criteria therefore included the 3 categories: 1) patients with only 1 outpatient bipolar diagnosis, 2) 1 inpatient or 2 outpatient diagnosis of schizophrenia diagnosis, and 3) 1 inpatient or 2 outpatient diagnosis of schizoaffective disorder. We estimate 3,731 individuals were excluded from the study cohort due to evidence of schizoaffective disorder and schizophrenia. There have been no changes in identifying eligible individuals to enroll in our approved research plan beyond the stakeholder advisory panel decision to exclude schizoaffective disorder and schizophrenia, calculate their overlap with the bipolar population, and exclude them from the final cohort.

Subgroups [IRQ-4]: We will stratify our analyses by additional characteristics to permit evaluation of vulnerable subgroups: comorbidity level (e.g., highest tertile versus intermediate and lowest tertiles of validated Adjusted Clinical Groups score^{94,95}), SES (e.g., highest versus lowest tertile household income), rural versus urban residency, and race/ethnicity group¹⁵²⁻¹⁵³(non-Hispanic white versus black, Asian, Hispanic, and other). These variables are described in section C.8. For Rural versus non-rural areas; non-rural areas will be the reference group. We will use Rural-Urban Commuting Area (RUCA) codes that reflect travel and shopping patterns at the county level. Using an established probabilistic ZIP code-to-county file,¹⁴⁸ we will assign patients by their residential ZIP codes to RUCA groups. Similar to previous research,¹⁴⁹⁻¹⁵¹ we will categorize the 10-point RUCA classification into: “rural” (RUCA codes 7-10) and “non-rural”, comprising large rural cities/towns (RUCA codes 2-6) and urban areas (RUCA code 1).

C.6 Matching Strategy for Aims 1-3 [CI-5]: For comparing effects among insurance designs, we will use propensity score matching based on both employer- and member-level characteristics to balance the study and control groups on observed characteristics as in our prior work.⁹⁶⁻⁹⁸ We will first match similar employers (to minimize employer selection effects) and then match individuals within groups of similar employers to ensure high comparability between study groups. The individual match will include matching on the baseline outcome measure, an approach crucial to generating estimates comparable to randomized controlled trials.^{77,85}

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We will use the sample selected with this method for interrupted time-series analyses and for pre-post with comparison group difference-in-differences (Section C.9). Use of comparison groups matched at both the employer- and individual-level will increase comparability between HDHP and traditional plan cohorts in baseline employer characteristics, member demographic characteristics, and baseline health care utilization. This offers a further degree of control for any potential contemporaneous changes that may influence specific study outcomes.^{41-44,54,55,80,99}

Employer-level Propensity Matching: The study population will include employees of firms that mandated a switch to HDHPs and others that kept traditional plans as their sole insurance option. While this minimizes member-level selection into health plans, our previous work indicates that some employers might select HDHPs based on employee characteristics.¹⁰⁰ To create strata of employers with similar baseline characteristics, we will generate scores predicting the propensity of an employer switching to an HDHP in a given year among all employers making such a decision. Propensity scoring is a well-established method that assists in generating a comparison group with a similar likelihood of being exposed to a given “intervention” (in this case, shifting to HDHP coverage) based on measured characteristics when subjects have not been randomly allocated into study groups.¹⁰¹⁻¹⁰⁴ We will use logistic regression to predict an employer’s likelihood of switching to an HDHP (versus remaining in a traditional plan). Candidate predictors in our propensity score models will include baseline employer-level covariates (Section C.8). We will use results from this model to divide employers into four strata according to propensity score, then match HDHP members with bipolar illness to traditional plan members with bipolar illness within each stratum (see immediately below).¹⁰⁴

Individual-level Propensity Matching: To identify closely matched patient controls for each of our HDHP study members with bipolar illness, we will use member-level propensity score matching¹⁰¹ to select members within the eligible pool of employees from each stratum of matched employers. Based on individual-level covariates (Section C.8) and similar enrollment dates, we will match four contemporaneous controls with bipolar disorder to each HDHP member with bipolar disorder within a pre-defined propensity score caliper (0.6 of the standard deviation of the pooled baseline propensity score).¹⁰⁵

C.7 Outcome Measures for Aims 1-3 [RQ-6]: We will examine a range of validated outcomes^{58,89,90,106-108} that, based on the literature, are regarded by clinical experts and policymakers as important. Each outcome domain has also been identified as important to patients and caregivers, based on the literature⁶³⁻⁶⁵ and advice from our Patient/Stakeholder Advisory Panel. Aim 4 interviews and community feedback throughout the study will provide further information about the importance to patients of these and potential alternative measures.

(Aim 1) Access to Appropriate Outpatient Treatment: We will measure several domains of outpatient care:

- (i) **Use of outpatient services:** We will measure overall access to outpatient services with monthly prevalence and counts of different categories of outpatient visits (total, primary care non-mental health, primary care mental health, and mental health provider/substance abuse specific [defined by Current Procedural Terminology psychiatric codes (908xx series) and ICD-9 codes 290-310¹⁰⁹]). DBSA advisors on our advisory panel have also contributed to the decision to include and examine use of psychotherapy visits.
- (ii) **Regular mental health follow-up visits:** While patients with bipolar disorder may have asymptomatic periods, episodes of clinical instability are common^{18,19} thus periodic monitoring is recommended even for those who are euthymic. As a measure of treatment quality, we will examine changes in receiving at least one outpatient mental health/substance abuse visit per quarter.
- (iii) **Medication adherence for bipolar disorder:** As a measure of overall access to medications, we will examine overall monthly and annual prevalence rates of treatment with medications that are either guideline recommended or indicated by the Food and Drug Administration for bipolar disorder, including 1st and 2nd generation antipsychotics, anticonvulsants, and lithium^{14,16,17}. Our measures of quality of care will include two patient-level monthly measures of medication availability^{58,106,107}: the average standardized dose of bipolar medications available per day, and the proportion of days with each type of bipolar medication available (i.e., proportion of days covered^{106,107}). We can use these to assess the association between switching to an HDHP and changes in the average dose of medications available, or a change in the likelihood of skipping days of

treatment with a particular medication (e.g., proportion of days covered by a mood-stabilizing agent).^{89,90,110}

(iv) **Guideline-recommended clinical monitoring:** The American Psychiatric Association¹⁴ recommends routine drug level monitoring for a number of bipolar disorder medications. Our quality measures will include: for lithium, carbamazepine and valproate users: testing for drug serum level at least once in a year;¹¹¹ for lithium users: renal and thyroid function tests every 6 months; and for valproate and carbamazepine users: blood counts and hepatic function tests every 6 months.^{14,111} In addition, use of 2nd generation antipsychotics may be associated with cardiometabolic risk through effects on body weight, and lipid and glucose metabolism.^{112,113} Consensus guidelines recommend that patients receiving 2nd generation antipsychotics be monitored for lipid and glucose levels every 3 months to ascertain risk of diabetes and cardiovascular disease.¹¹⁴ Thus, we will also assess lipid (total cholesterol and triglycerides) and serum glucose testing every 6 months in users of these medications, as in previous research.¹⁰⁸

(Aim 2) Adverse Patient Clinical Outcomes: We will examine changes in rates of: (i) psychiatric and non-psychiatric ED visits and day hospitalizations to determine if cost-sharing under HDHPs resulted in adverse short-term health events among patients with bipolar disorder, and (ii) psychiatric and non-psychiatric hospitalizations and hospitalization days as evidence of the impact of HDHPs on overall rates of serious morbidity. As in our prior work, we will define psychiatric-related events as those associated with a primary diagnosis of bipolar disorder (ICD-9: 296.0, 296.1, 296.4-296.8, 301.11 and 301.13^{43-45,90}), depression (ICD-9: 296.2, 296.3, 298.0, 300.4, 309.1, and 311⁴²), or schizophrenia (ICD-9: 295^{36,41}), substance abuse (ICD-9: 291, 292, 303-305.0, 305.2-305.7, 305.9¹⁰⁹), or events in psychiatric hospitals.⁴⁵

(Aim 3) Patient Out-of-Pocket Cost Burden: We will examine annual patient out-of-pocket costs (paid deductible, coinsurance, and copayment amounts), summing these discretely for prescription fills, outpatient visits, and other major service categories. We will calculate both the overall annual burden of costs per patient, and measures such as average cost per fill or per month of medication, and per behavioral health visit, which may be easier for lay consumers of our research results to consider and compare. To control for price inflation, we will convert all patient costs to current year US dollars using the Consumer Price Index.¹¹⁵

C.8 Covariates for Aims 1-3: We will use (i) employer-level and (ii) individual-level covariates to propensity match, adjust, or stratify our analyses.

Employer-level Covariates include: employer size, health plan expenditure quintile, employee out-of-pocket cost quintile, median employee age, median employee comorbidity score, and proportions of employees who are women, have family coverage, and reside in high-poverty or low-education neighborhoods. Our ongoing research has found that health plan and employee out-of-pocket costs independently predict employer HDHP enrollment. We will calculate baseline expenditures by summing standardized amounts paid by the health plan for all services utilized by all employees; the data vendor provides these standardized cost amounts. We will use median employee Adjusted Clinical Groups scores^{94,95} to estimate comorbidity; the ACG algorithm uses age, sex, and ICD-9-CM codes to calculate a morbidity score relative to a reference population average of 1.0.⁹⁴ Researchers have validated the index against premature mortality.⁹⁵

Member-level Covariates include: bipolar disorder type, age, sex, SES, race/ethnicity, state of residence, rurality, Dartmouth Atlas Hospital Referral Region of residence, baseline out-of-pocket and health plan expenditures, number and month (relative to index date) of outpatient/ED/hospital visits, and enrollment in individual versus family coverage. To derive indicators of race/ethnicity, we will first use a variable supplied by the data vendor that applies surname analysis to categorize members as Hispanic or Asian. We will then use US Census block group data¹¹⁶ (geocoding) to indicate predominantly black or white neighborhoods. We will combine both techniques because geocoding is not sensitive in detecting ethnicity¹¹⁷ and surname analysis is non-informative regarding race. **[MD-2]** This validated approach has a high positive predictive value.¹¹⁸⁻¹²² We will have access to individual-level Credit Report-derived variables for income and net worth, which is a major advance over previous studies that used only neighborhood SES measures. We will also determine neighborhood SES (geocoded poverty and education levels) and use principal components approach to calculate a neighborhood SES index.^{99,123,124,125} Adjusted Clinical Groups scores^{94,95} will estimate comorbidity.

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To account for SES variables' data missingness among HDHP and traditional plan adult members, we will use 3 methods to accommodate missingness: (a) multiple imputation, (b) modeling missingness as a member-level characteristic, and (c) excluding members with missing data. If findings differ, we will present results using all 3 methods in manuscripts or attached appendices. We will use SAS procedures PROC MI and PROC MIANALYZE to impute the missing individual level covariates and conduct the statistical analyses under the assumption of missing at random. The SAS procedure PROC MI will impute the missing variables (including individual net worth, income level, poverty level and education level) using other available variables such as age, gender, census block level income, poverty, education and etc. Then we will use PROC MIANALYZE to analyze the imputed data. We will also explore certain Bayesian imputation techniques to handle missing data in case missing is not at random and compare the results.^{146,147}

C.9 Analysis Plan for Aims 1-3 [IR-3; HT-1 to HT-4]: Overview: These analyses will determine how specific outcomes change after employer-mandated switching from traditional plans to HDHPs. To address methodological standard IR-3, we plan to use the most rigorous quasi-experimental retrospective longitudinal designs and analyses available for AIMS 1-3, namely interrupted time series with comparison series matched on multiple baseline covariates as well as the baseline trend of outcome measures. For Aim 4 we will use appropriate standard techniques for qualitative analyses of interview data (detailed below). We will first compare the characteristics of our matched cohorts (HSA-eligible and HSA-ineligible HDHP members, and traditional plan controls) using chi-square tests, t-tests and Poisson or quantile regression.¹²⁶ We will contrast sociodemographic characteristics, employer characteristics, and baseline health care utilization. Subsequent analyses will use time-series plots and rigorous analytical methods appropriate for each outcome, described below. Data collected on the same individuals in successive years are correlated (“repeated observations”). The extended general linear models—generalized estimating equations (GEE) and generalized linear mixed models (GLMM) for binary, count, or continuous measured outcomes—are appropriate methods for estimating parameters to adjust for these correlations within subjects.^{82,83} The term of interest in our GEE or GLMM models will be the interaction between *time* (pre versus post) and *cohort* (HDHP versus traditional plan). Statistical analyses in Aims 1-3 will first compare those transitioning to HDHPs with patients remaining in traditional plans; then contrast effects between HDHP members with full drug cost-sharing (HSA-eligible plans) and those transitioning to HDHPs without full drug cost-sharing (HSA-ineligible HDHPs). Each HDHP group will have as controls only those traditional plan members paired to a given HDHP member during the propensity score match. To examine possible selection effects due to applying our enrollment criteria and propensity matching approaches (see C.10), we will also compare our analytic population to members with bipolar disorder who were excluded from the sample.^[MD-4; CI-2]

(Aim 1) Access to Appropriate Outpatient Care: We will assess changes before and after the index month in the *utilization and adherence* outcomes listed in C.7 for Aim 1 using patient-level *interrupted time series with comparison series*. The interrupted time series design includes multiple observations over time both before and after an intervention (i.e., the plan switch) and adjusts for most threats to internal validity (e.g., secular changes in prescribing, aging of the population) because it adjusts for baseline trends in study outcomes that are unrelated to the intervention.⁸⁰ Furthermore, our strategy of matching on the baseline outcome trend should generate highly robust causal estimates. We will use patient-level segmented linear regression models^{58,84} to statistically estimate patient-level changes in both level and trend in outcomes after the switch to HDHPs, while controlling for autocorrelation of the data and individual-level covariates. The segmented regression models include a constant term; an integer variable indicating *time* in months (t) from the start of the observation period to estimate baseline trend; a binary variable, *intervention*, indicating the period after the index month, to estimate change in level; and an interaction between *intervention* and *time*, to estimate change in trend. We will test the statistical significance of level or trend changes, adjusting for first-order autocorrelation between sequential monthly measurements using the empirical sandwich estimator in GEE.⁵⁸

For selected quality measures (i.e., likelihood of a quarterly outpatient mental health visit or receiving

guideline-recommended lab monitoring when using lithium, valproate, carbamazepine, and 2nd generation antipsychotics; C.7), our approach will be a pre-post with comparison group and difference-in-differences design. Logistic regression models will assess the independent effect of HDHPs on these outcomes, while controlling for patient-level covariates and secular utilization trends (by including index month).^{54,55,99}

(Aim 2) Adverse Patient Clinical Outcomes: To examine the impact of transitioning to HDHPs on changes in rates or risk of psychiatric/non-psychiatric ED visits and hospitalizations, we will use a pre-post with comparison group difference-in-differences design. We will control for patient-level covariates in the models. We will use GLMM to model the effect of HDHPs on annual hospitalization days.

(Aim 3) Patient Out-of-Pocket Costs Burden: Analysis of changes in patient costs will rely primarily on a pre-post with propensity-matched comparison group design and a difference-in-differences analytical framework. We will model costs to patients using two-part general linear models. We will select the conditional mean and variance functions based on the actual data, potentially using a log link with a Gamma error distribution.^{127,128} To inform the final model specification, we will employ specification tests including the Pregibon Link test for non-linearity¹²⁹ and a modified Park test to select the conditional variance function.¹²⁷

Stratified Analyses to Assess Effects on Vulnerable Subgroups: We will compare outcomes between HDHP and traditional plan members among strata defined by four covariates: comorbidity burden (e.g., higher versus low tertiles of Adjusted Clinical Groups score,^{81,82} SES (higher versus low tertiles); race/ethnicity (non-Hispanic white versus black, Asian, Hispanic, and other), and rural versus urban residency. We will use GEE or GLMM to express relative changes in outcomes among HDHP member subgroups compared to changes among controls.¹³⁰ If statistical power permits, we will add three-way interaction terms (e.g. study_group*study_period*SES) to assess whether the HDHP switch was associated with a change in baseline disparities in outcomes.

C.10 Sample Size Estimates and Power Calculations [HT-1 to HT-4]: Using 10 years of data (2003-2012), we found 42 million unique adolescents and adults aged 12-64, approximately 450,000 of whom (~1%) had at least one bipolar disorder diagnosis. This is consistent with our expectation of a lower disease prevalence among commercially-insured adults compared with the 3% prevalence estimated by epidemiological surveys,³ because individuals with bipolar disorder less commonly have private insurance.¹³¹ A total of 109,012 of the 450,000 with a bipolar diagnosis met our inclusion criteria of 2 years continuous enrollment, with the first year in a traditional plan, the second in a traditional or HDHP, and no choice from the employer at any point regarding plan type. Projecting to 2014, our sample will include over 10,800 HDHP members (1525 HSA and 9275 non-HSA) and 43,200 matched traditional plan controls with bipolar illness (1:4 matching). Our smallest HDHP subgroups examined for primary outcomes will include 1525 HSA members (smallest medication adherence cohort) and 2160 non-white members (smallest emergency department and hospitalization outcome cohort).

For interrupted time series analyses of medication adherence, based on assumptions including 12 months of follow-up, autocorrelation of less than 0.3, and 0.05 type I error,¹³² we will have greater than 90% power to detect a 6% relative decrease in adherence in our smallest medication outcome subgroup (HSA-HDHP members). For example, we could detect an adherence rate change from 49% (as seen in previous literature¹³³) to 46% with a standard deviation of 1.5%. This is a *smaller* change in adherence than has been observed previously in HDHP-HSA studies.⁵⁷

We will use generalized estimating equations to model difference-in-differences analyses of our least frequent outcomes, including emergency department visits and hospitalizations. Based on the smallest subgroup of 2160 non-white HDHP members and their 8640 matched traditional plan controls, a baseline psychiatric hospitalization rate of 10% per year,⁸⁹ (the lowest rate among our measures), 0.05 type I error, 80% power, and a conservative repeated observations correlation assumption of 1, we will be able to detect a 20% relative decrease (e.g., from 10% to 8%). This is smaller than the 27% hospitalization decline we detected in a previous HDHP study.⁵⁴ We will have more power to detect changes for all other outcomes. The power estimates were calculated using PASS software.¹³⁴

C.11 Study Population and Methods for Aim 4 [RQ-3; PC-2]: Ours will be the first qualitative study to explore views of patients with bipolar illness regarding insurance-related barriers to care and experiences with commercial insurance benefits. Qualitative results will complement and inform our quantitative claims-based analyses in Aims 1-3. For Aim 4, DBSA will assist in recruiting **individuals living with bipolar disorder or close family members** to participate in semi-structured telephone interviews. The opportunity to volunteer for participation in interviews will be presented in local DBSA chapter in the form of a flyer for attendees. These flyers will be distributed by DBSA to chapter leadership by means of US mail, email, and routine in-person outreach visits by DBSA officials to chapter meetings. Interested individuals who see the flyer will telephone our co-investigator Phyllis Foxworth at DBSA in Chicago. Ms. Foxworth will conduct an initial screening for eligibility, focused on insurance coverage type, English competence, and achieving a rough US geographic balance. Ms. Foxworth will transmit contact details of individual interested in participating to the DPM/HPHCI team. We anticipate identifying ~100 candidate respondents at DBSA, to allow for drop-out due to additional screening, scheduling conflicts, non-consent, etc. In order to achieve full saturation of themes, we anticipate needing 40 completed interviews, as described below. We will schedule more interviews (~60 in total) in order to pilot test our instrument and to account for partial or non-informative interviews.

All **interview respondents** will be English-speaking adults. We plan to stratify the sample by patients with bipolar disorder and family members who may be able to provide perspectives about patients whose illness is more severe. In all cases, the patients themselves will be insured through an employer’s commercial plan. Patients with Medicare, Medicaid, military, or self-purchased coverage will be excluded. We will also stratify the sample along two other dimensions to facilitate

contrasts of interest [RQ-4; RQ-5]: (1) low/no deductible insurance plan vs high deductible plan; (2) no major illness other than bipolar vs another major condition requiring continuous treatment. We initially plan to sample 5 individuals per subgroup, resulting in 20 individuals per stratum for contrast analyses. We expect that this sample will allow us

	Patients		Family members	
	Low deductible insurance	High deductible insurance	Low deductible insurance	High deductible insurance
Bipolar illness only	5	5	5	5
Other major comorbidities	5	5	5	5

to achieve saturation of response theme in each of the three sample strata. We will seek diverse geographic residence, age, sex, and race/ethnicity, but not compare across these characteristics.

The interview domains [RQ-6; PC-3] will include accessing treatment for bipolar disorder and comorbidities, affordability of treatment, how patients learn about their insurance coverage, the types of care patients consider "high-value" (i.e. most important for their health and well-being), and making choices about care in the context of cost-sharing requirements.

C.12 Analysis Approach for Aim 4 [IR-3]: The semi-structured interview instruments were developed with inputs from our Advisory Panel. The domains of inquiry have arisen from discussions during protocol development and from previous research on treatment for bipolar disorder. These domains represent questions not easily answered with claims data, such as patient learning and coping around insurance benefits, affordability of care, and making choices among services (see Appendix). Dr. Madden, senior co-Investigator Dr. Ross-Degnan, and Ms. Foxworth will lead and guide this activity.

The interviews will be conducted by an experienced, well-trained research assistant interviewer based at the Department of Population Medicine at the Harvard Pilgrim Health Care Institute/Harvard Medical School. The interviewer will be equipped with a digital voice recorder (Olympus WS-852, with TP-8 telephone pick-up microphone). Interviews will be scheduled at the convenience of both the interviewer and the interviewee, and the interviewer will conduct these from a quiet, private space at either the DPM office or another location, using either a DPM phone or a personal phone. The voice recorder device will have been password-encrypted due to prior connection to the HPHCI computer network. The brief written notes (e.g., noting date, time, general impressions of the interview, any methods concerns) from the interviewer and MP3 audio filenames will have only study IDs and no actual personal identifiers. The interviewer will endeavor to avoid introduction of proper

names of individuals or places into the interviews. Written notes will be stored securely as soon as possible at HPHCI, where they will also be entered electronically and stored in secure data files on a restricted server directory. MP3s will be uploaded from the recorder to a restricted server directory for storage. MP3s will also be copied onto encrypted USB drives and sent by FedEx (or hand delivery) to a professional transcription service in downtown Boston that has been used in many prior department studies (Audio Transcription Center). The transcription service will transcribe the MP3 interviews verbatim, except that the service has agreed to replace all proper names with, e.g., “[NAME]”, thereby creating written transcripts in MSWord format, containing only study IDs as identifiers. These MSWord files will be returned on the same encrypted USB drives to HPHCI via FedEx or hand delivery, and uploaded to the restricted server directory.

We will code transcribed interview data by reviewing each transcript for responses in a range of conceptual categories, using the structure of our interview guide to define initial categories and domains. We will employ both deductive codes (themes identified *a priori*) and inductive codes (additional themes that emerge from the data). The study team will conduct a coding validation exercise on an initial transcript. The lead investigator (Dr. Madden) and the research assistant interviewer will then independently review 2 transcripts and create additional codes as necessary for the emerging themes. All study investigators and the Advisory Panel will review and revise the initial coding scheme. We will develop a codebook with a detailed description of each code, inclusion and exclusion criteria, and examples. We will then code the remaining transcripts, iteratively refining the coding scheme as necessary until all transcripts are coded and no new or important themes emerge.

We will apply thematic analysis to summarize the interview material using standard qualitative techniques and a grounded theory approach.¹³⁵⁻¹³⁷ Recurrence, similarities, and differences will be noted across transcripts. Using the coded data, we will describe each theme in detail, noting strength and predominance of opinions, patterns and linkages between themes, as well as similarities and differences across the subgroups. We will seek to detect divergent views among participants and contrast observations between respondent categories. Data coding and the analytic process will be conducted using QDA Miner Lite software.¹³⁸

C.11 Potential Generalizability and Limitations: This research has several possible limitations.

Differential dropout: Because vulnerable populations such as those with low SES might choose to forego employer health insurance coverage when offered only an HDHP, we will analyze whether differential dropout by group occurred after employer-mandated coverage changes. We will minimize its potential impact on our analyses by performing individual-level propensity matching based on multiple employee-level factors including SES to develop tightly-matched control groups. We will restrict our follow-up duration to 12 months because differential dropout from HDHPs could become more pronounced after the first enrollment year. We expect that we will be able to detect even small changes in utilization soon after the HDHP switch among our very large sample (Section C.10), so that 12 months should be sufficient follow-up to generate policy-relevant insights.

Financial incentives: We will also be unable to track amounts in Health Savings or Health Reimbursement Accounts because these data are only available from employers or financial institutions. This could lead to uncertainty regarding members’ financial incentives or disincentives to seek care. However, the presence of these accounts would bias results toward the null, so that any differences detected are likely to be robust.

Identification of clinical cohort: We will use claims data to identify bipolar disorder. Structured clinical interviews are the gold standard for identifying bipolar illness with high accuracy and inter-rater reliability. Enrollees misdiagnosed as *not having* bipolar disorder (i.e., false negatives) will not be in our cohort and we will be unable to comment on the impact of HDHPs in this group. However, several studies have demonstrated that administrative data can be highly accurate in establishing bipolar disorder for quality assessment, finding that among those identified as having bipolar disorder, 94% are confirmed by chart review.^{66,92,93}

Generalizability: Our inclusion criteria require traditional plan membership for at least a year at baseline, making our results applicable largely to health plan members familiar with the general structure of traditional insurance benefits. This limits generalizability of our results to populations such as previously uninsured low income employees who enter HDHPs. However, given the substantial percentage of employers that are

considering introducing HDHPs,²² our results will be highly relevant to a major segment of the private health insurance market. Our findings may also be generalizable to traditional plan members switching to HDHPs offered in the state health insurance exchanges mandated by the Affordable Care Act.

D. PROJECT MILESTONES AND TIMELINE

This project will take 36 months to complete. We will obtain Institutional Review Board approval prior to conducting the studies. We arrange for re-licensing the insurance claims datasets, all years of which by the time of award will be available in-house. Below we list specific milestones by 6-month study period:

Months 1-6 Refine study protocols with input from Advisory Panel and DBSA community feedback activities.

(Review and refinement as needed of the protocols is considered necessary throughout the study. Any substantive revisions to the protocols must be submitted to the IRB for approval before action.)

Aims 1-3. Identify intervention and comparison cohorts. Identify insured members with diagnosed bipolar disorder who match inclusion criteria. Create employer-level and member-level covariates. Extract pharmacy, outpatient, and inpatient claims. Develop outcome measures of access to appropriate outpatient treatment, adverse patient health outcomes, and patient out of cost burden.

Aim 4. Develop consensus around initial interview guide. Preparation and training for recruitment of interview respondents and on interview procedures.

Months 7-12 Additional refinement of protocols with Advisory Panel input and DBSA community feedback.

Aims 1-3. Data cleaning, validation, and error checking by characterizing 2004-2014 bipolar prevalence and outcome trends in members with bipolar disorder. Create study design by stratifying HDHP and control employers according to propensity to switch to an HDHP. Member-level propensity match of HDHP members and contemporaneous control members with bipolar disorder. Compare baseline characteristics of the 3 study groups and against broader population of insured members with bipolar illness. Preliminary analyses of changes in access to appropriate outpatient treatment (Aim 1) following switching to HDHPs. Stratify analyses contrasting HDHP members with and without full drug cost-sharing. Early dissemination of results through conference abstract submissions, additional stakeholder meetings, DBSA avenues of communication.

Aim 4. Pilot test and refine interview procedures and guide. Recruit 75% of interview respondents. Complete 50% of interviews. Ongoing transcription and create coding scheme for interview analysis.

Months 13-18 Additional refinement of protocols with Advisory Panel input and DBSA community feedback.

Aims 1-3. Finalize Aim 1 main analyses and draft **manuscripts 1 and 2** reporting changes in access to appropriate outpatient treatment and quality of care. Additional dissemination activities. Preliminary Aim 2 analyses of changes in adverse patient outcomes (psychiatric/non-psychiatric ED visits and hospitalizations) following switching to HDHPs. Contrast HDHP members with and without full drug cost-sharing. Early dissemination of Aim 2 results through conference abstract submissions, additional stakeholder meetings, and DBSA avenues of communication.

Aim 4. Refine coding for interview analysis. Completion of remaining interviews, attaining theme saturation. Ongoing transcription and analysis of interviews. Early dissemination of interview findings through conference submissions, stakeholder meetings, and DBSA avenues of communication.

Months 19-24 Additional refinement of protocols with Advisory Panel input and DBSA community feedback.

Aims 1-3. Finalize Aim 2 main analyses and draft **manuscript 3** reporting changes in adverse patient outcomes (psychiatric/non-psychiatric ED visits and hospitalizations) following switching to HDHPs. Additional dissemination activities from Aim 2. Preliminary Aim 3 analyses of changes in patient out-of-cost burden. Stratify analyses contrasting HDHP members with and without full drug cost-sharing. Early dissemination of Aim 3 results through conference abstract submissions, additional stakeholder meetings, DBSA avenues of communication.

Aim 4. Finalize analyses of interviews and draft **manuscript 4** on patient perspectives on access to

appropriate treatment of bipolar in the context of commercial plans. Dissemination of results.

Months Additional refinement of protocols with Advisory Panel input and DBSA community feedback.

25-30 **Aims 1-3.** Finalize Aim 3 main analyses and draft **manuscript 5** reporting changes in patient out-of-cost burden following switching to HDHPs. Additional Aim 3 dissemination activities. Conduct stratified analyses for Aims 1-3 by vulnerable subgroups (race/ethnicity, SES, rural residence, comorbidity burden). Early dissemination of results of stratified analyses through conference abstract submissions, additional stakeholder meetings, DBSA avenues of communication.

Aim 1-4. Develop framework for **manuscript 6** on our study's experiences in patient engagement.

Months Ongoing inputs from Advisory Panel and DBSA community feedback, including recommendations for future policy and research. Prepare and submit final report; final dissemination activities.

31-36

Aims 1-3. Finalize analyses of disparities in outcomes (Aims 1-3) following switching to HDHPs among particularly vulnerable subgroups (race/ethnicity, SES, rural residence, comorbidity burden). Draft **manuscript 7** on disparities in outcomes; additional dissemination activities.

Aim 1-4. Draft **manuscript 6** on our study's experiences in patient engagement.

E. PATIENT POPULATION [RQ-3; PC-2]

E.1 Populations Affected: Aims 1-3 analyze retrospective de-identified data from 2004-2014 insurance claims. The characteristics and numbers of insurance plan members whose claims data will be analyzed in Aims 1-3 are described in Sections C.2, C.5, and C.10. We seek to determine the impacts of switching to HDHPs within the insured population that yielded these claims. This population is very minimally affected by the research itself because we are observing events that took place in the recent past, and the data have been de-identified. However, people living with bipolar illness and their families have significant potential to benefit when our study findings are disseminated, in terms of better public understanding of the challenges these patients face, and improvements in health system policies.

In **Aim 4**, interview respondents will voluntarily share their experiences on treatment of bipolar disorder in the context of commercial insurance coverage. Following DBSA recruitment efforts, we will contact ~100 individuals to potentially participate in the study, and we plan to interview up to 60 patients or family members representing a range of geographic locations, both genders, patients aged 12-64, different race/ethnicities, and levels of socioeconomic status. Through the interview process, respondents may develop deeper awareness of the attendant issues of insurance coverage and treatment choices, or they may experience mild emotional distress discussing sensitive topics, but we expect no significant impacts on this population (see Protection of Human Subjects). Our analyses will emphasize answers to the following types of questions: "Does your insurance help you pay for therapist visits?", "How did you learn about these aspects of your coverage?", and "When you have to make difficult choices, what do you prioritize?"

Patient partners in our study will participate as equals on our team and, hopefully, derive net benefits in terms of collegiality, learning, and compensation. The broader population of the DBSA community (i.e., users of DBSA social media, etc.) and patients and stakeholders in the public at large will be able to learn about study results and provide feedback (see Section G), but these would not differ substantially from the effects of existing DBSA outreach activities and routine publication of research.

F. RESEARCH TEAM AND ENVIRONMENT

Our proposed study will assess how patients with bipolar disorder fare when required to pay much higher out-of-pocket costs under HDHPs. It will be conducted primarily at the Department of Population Medicine (DPM), which resides within the Harvard Pilgrim Health Care Institute (HPHCI), and is a department of Harvard Medical School. The study capitalizes on DPM's expertise using administrative data and strong quasi-experimental study designs to evaluate the impacts of cost-containment and coverage policies on medical and psychiatric outcomes. We have conducted both early regional and ongoing large national HDHP studies analyzing health care utilization, costs, and outcomes in general health populations and populations defined by somatic conditions. Our experience with rigorous designs and innovative methods will produce reliable,

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generalizable results invaluable for policymakers in designing insurance benefits that improve the health of patients with bipolar disorder.

F.1 Research Team Capability to Accomplish The Goals of The Proposed Research: The study personnel are ideally situated to address the study goals, and include nationally recognized leaders in the realms of mental health services research, HDHP health impacts, and quasi-experimental designs. **J. Franklin Wharam, MB, BCh, BAO, MPH, Co-Principal Investigator** is a general internist and Assistant Professor at DPM. Dr. Wharam is a leading national expert in the designs and outcomes of HDHPs, has published multiple studies reporting effects of HDHPs on appropriate health care, and leads four R01-level projects examining a national HDHP. He also leads four projects assessing the impact of health policies on patients living with mental illness or substance use disorders. **Christine Y. Lu, MSc, PhD, Co-Principal Investigator** is a pharmacoepidemiologist, clinical pharmacologist, health services researcher, and Instructor at DPM, with expertise in mental health research, health policy analysis and evaluation, disparities, quasi-experimental research designs, longitudinal data analysis, and qualitative research. She is a Co-Investigator of four related studies examining HDHP impacts. **Jeanne Madden, PhD, Co-Investigator** is an Instructor with extensive experience in the use of claims and survey data to address financial access to medications and other health services, in directing large projects, and in measurement and validation. **Alisa Busch, MD, MS, Co-Investigator/Subcontract**, is a psychiatrist, Assistant Professor of Psychiatry and HealthCare Policy, and hospital-based clinical leader and administrator in psychiatry. She is a national expert in investigations of severe mental illness using insurance claims data. **Stephen Soumerai, ScD, Co-Investigator** is a Professor with decades of experience in mental health research and policy evaluation, well known globally for his work on coverage policies, quality of care, and patient outcomes. **Dennis Ross-Degnan, ScD, Co-Investigator** is an Associate Professor, health services researcher, and methodologist who is highly recognized for studies of the impacts of insurance benefit changes, pioneering longitudinal evaluation methods, and conducting surveys in many traditional and non-traditional settings. **Fang Zhang, PhD, Biostatistician and Co-Investigator** is an Assistant Professor and the nation's expert in constructing observational research designs to study HDHP impacts. He was among the first to construct interrupted times series designs matched on the functional form of the baseline outcome, closely approximating randomized controlled trial results. **Phyllis Foxworth, BS, Co-Investigator/Subcontract**, is an organizational leader and public speaker who works with patients and caregivers throughout the country, helping people meet the multitude of personal and system-related challenges of living with bipolar disorder and building local capacities for grassroots advocacy.

F.2 Appropriateness of the Research Environment and Study Sites [PC-4]: Our study team has extensive connections to public and private policymakers (through, e.g., HPHC, HMORN, MHRN, Optum/United, Blue Cross, CMS, NIH, AHRQ, professional associations) and a history of major successes translating research findings into policy advances. The DPM research environment has a rich structural and intellectual capacity for research (see People and Places Template) and it has proven conducive not only to carrying out groundbreaking cost containment and HDHP studies, but also to informing policymakers and affecting policy change. Dr. Soumerai has frequently advised state and federal government entities. Prior DPM studies have helped shape Medicaid and Medicare Part D drug coverage policies regarding extra subsidies for vulnerable groups, closing the Part D coverage gap, and coverage of specific medication classes. Dr. Wharam's studies demonstrating that HDHPs reduce colonoscopy use were followed by an HPHC decision to exempt colonoscopies from deductibles. If we were to detect, for example, that more generous drug coverage within HDHPs protects patients from adverse HDHP outcomes, our research team is ideally situated to inform policymakers for appropriate reforms to optimize patient outcomes.

The Depression and Bipolar Support Alliance (DBSA), our patient partner, is the leading grassroots organization advocating for people living with bipolar disorder, with rich prior research collaboration experience and a tremendous, multi-channel capacity to interact with the types of patients who are the focus of this study. Dr. Busch is a practicing psychiatrist and lead researcher at McLean Hospital, the largest psychiatric affiliate of Harvard Medical School and the premier US facility dedicated to improving the lives of persons with psychiatric

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illness. She will provide not only expertise in clinical psychiatry and health services research, but also access to high-level local and national leaders in mental illness policymaking.

Our psychiatrist consultants are superb, long-time colleagues who are optimally positioned to bring additional vital perspectives to our work as it progresses and then turn our results into action. Dr. Simon is the director of the Mental Health Research Network and works closely with NIMH and 13 health system research centers on practical, feasible ways to improve mental health care in the US. Dr. Duckworth is the Medical Director for the National Alliance on Mental Illness, the other leading advocacy organization concerned with mental illness issues in the US. He is also an Associate Medical Director for Behavioral Health at a major health insurer and many years of leadership experience in public agencies and professional organizations.

F.3 Our Research Populations Represent the Real World of Patients Living with Bipolar Disorder [PC-3]

We selected the claims data resource for our HDHP studies because the major national insurer from which the claims derive was the first to promote HDHPs, and is now the largest seller of HDHPs and HSA-associated plans. Our data include about 25% of all HDHP members in the US, allowing us to examine rare outcomes, and facilitating the use of rigorous longitudinal designs. The demographics are nearly identical to those of privately insured respondents in the American Community Survey,¹³⁹ on characteristics such as age and poverty level. The South and Midwest are somewhat over-represented, but zipcode information allows us to adjust for geographic influences. We have identified well over 100,000 individuals aged 12-64 and diagnosed with bipolar disorder who match our strict enrollment criteria in this large dataset.

A major study advantage is that the experiment we will assess has already happened in the real world (and is continuing to occur). Over the last decade, many employers have required all employees to join HDHPs, generating a rigorous "natural experiment" with workers exogenously selected into different plan types. Moreover, we can contrast two built-in "interventions" because there is more generous drug coverage in one subset of HDHPs.

Our qualitative study will gather perspectives from patients with bipolar disorder coping with varied insurance benefits, in the present day and across the US. Findings from our in-depth telephone interviews will round out the results from our claims analyses, providing stories of what choices individuals make, and why, when faced with cost-sharing requirements. Our patient representatives, including Ms. Foxworth and the two advisory panel members she identified, will bring these perspectives to our study on a deeper and longer-term basis; they will be fully familiar with our goals, methods, and progress, and provide their insights on specific study issues as they arise. Finally, we will be reaching out, through DBSA and our series of broader patient engagement activities, to thousands more patients and caregivers who are, unequivocally, the real world of people experiencing bipolar disorder and experiencing the modern US health care system.

G. ENGAGEMENT PLAN [RQ-3; PC-1; PC-2]

G.1. Planning the Study: The research team is fortunate to have had key stakeholders in bipolar illness involved throughout the development of the proposed research. We summarize our engagement to date and our post-award plans. **Background.** Senior team members (Drs. Soumerai, Ross-Degnan, and Simon) have long histories researching patient access and barriers to appropriate mental illness treatment. Drs. Soumerai and Ross-Degnan's well-known studies of the effects of state Medicaid payment policies on medication and service use among vulnerable beneficiaries with mental illness^{36-38,41,44,140} were conducted with feedback from local patient advocacy groups in New Hampshire and experts in community psychiatry. The National Alliance on Mental Illness has used these studies in advocating for broader access to effective medications and in testimony before state and national legislatures. Drs. Lu, Madden, and Soumerai are affiliated with the NIMH-funded Mental Health Research Network, led by Dr. Simon,^{66,141,142} which was established to advance mental health research in health plans.^{143,144} Drs. Wharam, Ross-Degnan, and Soumerai have spearheaded a series of groundbreaking studies on the impact of HDHPs.^{32,54,55,96,145} With this background, we began planning a national study of the effects of HDHPs on patients with bipolar disorder that would incorporate patient views in a more meaningful way than previous research.⁴³⁻⁴⁵

Development. At the suggestion of NAMI Medical Director Ken Duckworth (an in-kind consultant on this

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project), we engaged with DBSA in developing the proposal. During this collaboration, the proposed study has grown more ambitious, incorporating DBSA's excellent ideas. In addition to facilitating access to patient respondents for in-depth interviews, co-investigator Phyllis Foxworth, the DBSA Director of Advocacy, and patient representatives Kimberly Allen and Kristin Olbertson have strengthened our recruiting strategy and suggested better ways to engage patients. They identified a need for Aim 4 interviews to focus on how patients adapt to benefits over time and on the complicating factor of provider networks. They suggested that we elicit input on study protocols and findings from the larger DBSA community. The patient partners have emphasized how much importance they attach to this study. As Ms. Allen stated, "Claims, finance, benefits, payment, and misinformation about all of it – this is the single most important item in mental health care!"

Post-Award. Although our protocols for Aims 1-3 are rooted in decades of experience in claims-based research and methodological choices are restricted by the types of data in claims, our selection of outcomes will continue to be informed by patient perspectives on their importance. Patients will also help us identify aspects of preliminary findings that merit deeper exploration. These inputs will come from our DBSA co-Investigator and patient partners, but we will also elicit input from the broader DBSA community on the areas covered by the draft interview guide for Aim 4. Some questions may be "tested" for relevance in brief surveys done via DBSA's chapter groups or Facebook page. Also, the iterative nature of in-depth interviews means that the direction of inquiry in Aim 4 will be shaped gradually over time by the respondents themselves.

G.2. Conducting the Study: Our co-investigator Phyllis Foxworth and Patient/Stakeholder Advisory Panel members will participate in all stages of the proposed project. Ms. Foxworth will attend monthly and ad hoc meetings, reviewing all study protocols and result summaries. She will meet face-to-face in Boston in Year 1 with Boston-based team members. She will have a central role in Aim 4 and in study-wide patient engagement activities (more below.) The Advisory Panel will meet with the full team four times each year by telephone (~90 minutes) and also be available for modest, intermediate requests for study feedback (~monthly).

For **Aims 1-3**, the Advisory Panel will review claims-based measures and help to identify high versus low-value care. Specifically, our clinicians (Drs. Wharam, Busch, Simon, and Duckworth) will clarify which clinical services are supported by evidence and guideline recommendations. However, we will rely on our patient partners to help us understand which metrics represent high- or low-value care from a patient perspective, and the meaning of different outcomes in terms of impact on daily living.

In **Aim 4**, Ms. Foxworth will lead interview respondent recruitment through DBSA. Working with DBSA's Directors of Chapter Relations and Communications, she will train selected chapter leaders in appropriately presenting the study opportunity and directing interested individuals to Ms. Foxworth at DBSA in Chicago. Ms. Foxworth will act as primary contact, provide additional preliminary information and screening, and pass contacts along to Dr. Madden and the interviewer. Drs. Madden and Ross-Degnan, and Ms. Foxworth will review analysis plans, coding, themes, and results as the interviews proceed, refining ongoing recruitment procedures as needed to ensure sample balance and theme saturation.

For **all Aims**, we will request the Panel's advice on interpreting preliminary findings and framing the results in presentations and manuscripts to be meaningful to their audiences. All panel members will have opportunities to co-author study papers, if interested. DBSA, MHRN, and NAMI will be actively involved in planning and implementing the dissemination of our results.

Throughout the study, we will engage patients through DBSA chapters, campaigns, and social media platforms. With guidance from the Advisory Panel, we will identify aspects of the study that can benefit from feedback from the broader DBSA community. In each instance, the team will identify the best vehicle for feedback; DBSA already uses multiple outreach tools, including quarterly web surveys, a Facebook page with over 100,000 followers, and the Care For Your Mind blog with 5,000 user sessions per month. Other potential avenues include the local chapters and a network of 10 regional DBSA-affiliated grassroots advocacy organizations. We will also consider whether these channels could be used to gather additional data that might supplement or inform our primary research findings. With additional IRB review and approval, we may ask community members about their experiences with insurance, access to care, and choices in healthcare.

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In addition, we will take advantage of DBSA’s previously-established “Peer Council” to serve as a standing community feedback panel for our study. On a quarterly basis, starting in the 4th quarter of the study, we will begin engaging this Peer Council by informing them about our study and requesting that they represent their DBSA peer community by commenting on selected study outputs and informational queries. This standing panel, in the form of DBSA’s Peer Council (anticipated N~100), will thus combine longitudinal study engagement with broader representation than our more intensive Advisory Panel.

We will monitor the dynamics of Advisory Panel meetings to ensure that the voices of all participants are heard. We will periodically check in with patient representatives and other Advisory Panel members by phone or e-mail to assess their experiences in the project and to obtain their suggestions for improving patient/stakeholder engagement. Advisory Panel inputs, both scientific and procedural, will be carefully documented and a report on patient engagement will be developed toward the end of the study.

G.3. Disseminating the Study Results [PC-4]: Our Advisory Panel will advise the study team about which findings would be of greatest interest to patient communities, how to frame these findings effectively for patients, and what channels would be the most effective for reaching individuals living with bipolar illness and people involved in their care. DBSA’s wide range of outreach channels (such as the social media platforms, chapters, website, and monthly e-Update newsletter) offer promising opportunities for dissemination to patients. Due to DBSA’s dedication to the study, we anticipate being able to collect patient reactions to study findings and recommendations. We will assemble commentary from the community regarding the salience and acceptability of our work, and their ideas for health system change and future inquiries.

G.4. Principles for Engagement: Reciprocal Relationships. We will foster a mutually beneficial collaboration toward shared goals among the team of investigators, consultants, and patient representatives. Each patient and stakeholder partner will provide perspective as an individual and a representative of other similar stakeholders. Our DBSA co-investigator Ms. Foxworth has been instrumental in shaping our proposal, intensifying our respondent recruitment strategy, and encouraging the inclusion of a range of community feedback activities. Our psychiatrist co-Investigator (Alisa Busch) is a national leader in mental health services research who will oversee clinical inputs to the study. Consultant psychiatrists Greg Simon and Ken Duckworth are each national leaders with close affiliations to health systems, academic institutions, and major mental health patient advocacy organizations. Kimberly Allen, a patient representative, has professional expertise in employee assistance and chemical dependency programs, and holds insurance licensure. Kristin Olbertson, a patient family representative, holds doctoral degrees in law and US history. Three additional stakeholders were added to the advisory panel in the period between our initial application for funding and the announcement of our award; these additions were made in response to PCORI reviewers. The additional panel members provide more voices for health insurers, employers, clinicians, and patients. Ken Dolan-DelVecchio is Vice President for Health and Wellness at Prudential Financial, Inc. He has 17 years of experience helping to ensure that Prudential’s employees with mental illnesses receive essential health insurance benefits and health services. Dr. Jim Sabin is Director of the Harvard Pilgrim Health Care Ethics Program, an internationally-renowned ethicist, and a psychiatrist. He has spent many years convening employers and health insurance representatives to discuss challenging ethical issues in the health insurance industry, including issues around mental health benefits. He therefore has a deep understanding of the challenges of optimizing mental health care from the perspective of both an employer and health insurer. Francisca Azocar, PhD, is Vice President of Research and Evaluation for Behavioral Health Sciences at Optum Behavioral Health, the nation’s largest behavioral health network that serves to address employee mental health issues. She has extensive experience working with academic institutions to conduct research that advances care for patients with severe mental illness. We will acknowledge the contributions of our Advisory Panel in all manuscripts and also offer the opportunity for co-authorship.

Co-Learning. Advisory Panel meetings will represent a forum for co-learning. Study investigators will learn patient and stakeholder perspectives, while patient representatives will learn about the research process. Individual check-in sessions afterward will offer opportunities for patient representatives to further educate the

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team about their perspective and to clarify questions. Selected DBSA chapter leaders will participate in Aim 4 recruitment. Ms. Foxworth will directly participate in analyses of interviews, lending her insights as a patient representative and organizer. She will educate the Boston-based team on DBSA's use of community outreach tools, how messages are selected and shaped, and pitfalls to avoid, and she will inform the team on how the issues raised in our research resonate with DBSA's grassroots activities. Our Aim 4 interview respondents and community members (through feedback activities) will help to fill information gaps inherent in claims data and help us to infuse our findings with patient perspectives.

Partnership. In engaging the Advisory Panel as partners, the research team will balance the desire for more input with the need to be respectful of advisor's jobs, families, and other commitments. Phyllis Foxworth will be a co-Investigator at 7% effort per year. Patient advisors will receive a \$500 honorarium per year to compensate them for four 90-minute Advisory panel meetings, pre-meeting review of materials, after-meeting check-ins, and ad hoc communications. One psychiatrist consultant will receive up to \$3000 per year for 3 days of advice including his participation on our panel, while the other will be available for the panel meetings and additional ad hoc advice on an in-kind basis. Advisory Panel meetings will be conducted by telephone conference (due to our geographic diversity) and scheduled far in advance at members' convenience.

Trust, Transparency, Honesty. We are privileged to partner with the diverse and highly experienced Advisory Panel members. Their involvement represents a commitment to a relationship based on mutual respect for the contributions of the entire study team. Open and honest communication will be crucial in facilitating effective collaboration. All members of our study team are accustomed to adhering to these principles within their own organizations and in past collaborations. Decisions about the study will be made by consensus with input from all partners; major study decisions will be discussed at Advisory Panel meetings and Advisory Panel members will be apprised of key decisions made outside of meetings. We will share study findings with DBSA, MHRN, NAMI, and other stakeholders, obtaining their inputs, while continuing the tradition of academic freedom whereby investigators can communicate unbiased findings and publish without censoring.

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For detailed instructions, refer to the Application Guidelines for your PFA. Do not exceed 10 pages.

Following scholarly citation practice, list the source material cited in this Research Plan.

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