Implementation and Evaluation of the Pathway Platform:
A Digitally Enabled Care Pathway to Improve Depression Key Performance Indicators and Patient Outcomes in Primary Care Clinics

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Mobile App for Patients and Care Team Interface
Powered by Fora Health, a Ctrl Group Ltd Product

TABLE OF CONTENTS

SUMMARY

Study Title

Implementation and Evaluation of a Digitally Enabled Care Pathway to Improve Depression Key Performance Indicators and Patient Outcomes in Primary Care.

Objectives

The primary objective of this study is to determine whether implementing the Pathway Platform in primary care improves adherence to measurement-based care practices.

Secondary objectives include determining whether implementing the Pathway Platform improves additional clinical process measures and depression response and remission outcomes.

Design and Outcomes

A pre- and post- study design is utilized to assess the impact of implementing the Pathway Platform in the primary care setting. Up to 20 primary care sites will be identified to participate in the study. Care team members involved in depression management will receive education on evidence-based clinical practices for depression care, such as measurement-based care practices and shared-decision making. Clinics with behavioral resources will also receive additional education on behavioral health integration. Training on how to onboard patients to use the Pathway Platform and utilize electronic medical records to view data collected in the Pathway Platform will also be provided. Study outcomes identified in this protocol will be assessed among 200 patients who will be enrolled in the Pathway Platform (post-implementation cohort). Outcomes will also be assessed in another 200 patients from the same participating clinics prior to study implementation (pre-implementation cohort). Implementation success will be evaluated by comparing study outcomes among the two cohorts with a total sample size of 400 patients (of which 200 will receive the intervention and 200 will not). The primary outcome is PHQ-9 utilization over six months and will be compared between the pre- and post- implementation cohorts. Additional process measures will be compared, including shared-decision making, medication adjustments, referrals to behavioral health, primary care follow-up post hospitalizations, and remission and response. Data collected in the Pathway Platform will also be evaluated to explore pre-defined patient outcomes. Additional outcomes will be explored in data captured from patients who continue to use the app beyond the initial 6 month study period.

Sample Size and Population

The study will take place in up 20 primary care clinics within Advocate Aurora Health Care that are representative of different geographic locations, patient populations, and care models for

depression management, including behavioral health integration models.

The Pathway Platform consists of a mobile app for patients and a care team interface that can be accessed through Epic. We intend to enroll 200 patients who meet the eligibility criteria for this study and agree to download the Pathway Platform. An additional 200 patients will be identified from the same participating clinics to form the pre-implementation cohort. These are patients who visited the participating clinics at least 6 months prior to study implementation; they will not be actively enrolled into the study and their data will be collected retrospectively through chart reviews and electronic data pulls.

LIST OF ABBREVIATIONS

AE	Adverse Event
APA	American Psychiatric Association
APPS	Mobile Health Applications
ASEX	Arizona Sexual Experience Scale
CCM	Collaborative Care Model
DSST	Digit Symbol Substitution Test
ED	Emergency Department
EMR	Electronic Medical Record
GAD	Generalized Anxiety Disorder
GAS	Goal Attainment Scale
GAD	Generalized Anxiety Disorder
IRB	Institutional Review Board
IQR	Interquartile Range
MBC	Measurement Based Care
MDD	Major Depressive Disorder
PAM-13	Patient Activation Measure
PDQ-D5	Perceived Deficits Questionnaire- Depression
PHQ-2	Patient Health Questionnaire-2
PHQ-9	Patient Health Questionnaire Depression
PROMIS	Patient-Reported Outcomes Measurement Information System
PSD-6	PROMIS Sleep Disturbance 6a
PTSD	Post-Traumatic Stress Disorder
SAE	Serious Adverse Event
SD	Standard Deviation
SDM	Shared-Decision Making Model
SSR	Special Situation Report
WSAS	Work and Social Adjustment Scale
WHO-5	World Heart Organization- Five Well Being Index

1 STUDY OBJECTIVES

1.1 Primary Objective

The primary objective of this study is to determine whether implementing the Pathway Platform in primary care improves adherence to measurement-based care practices. We hypothesize improved clinical processes in measurement-based care, measured by PHQ-9 utilization among patients attending clinics post-implementation compared to those attending clinics pre-implementation.

1.2 Secondary Objectives

Secondary objectives include determining whether implementing the Pathway Platform improves additional clinical process measures and MDD response and remission outcomes. Patient outcomes and Pathway Platform utilization will be explored among patients using the Pathway Platform.

2. BACKGROUND AND RATIONALE

2.1 Background

Health-related technology solutions that utilize mobile phones, known as mobile health applications (apps), have the potential to expand health interventions beyond the traditional face-to-face patient visit. For the healthcare provider, mobile apps can offer low cost and easily scalable interventions to monitor and improve services to patient populations that are difficult to retain in treatment and may promote better health.[1] Uptake of health-related mobile apps has increased in recent years as technology barriers such as access, knowledge, and product usability have improved, reducing obstacles for 'digitally excluded' subpopulations (e.g., poor, rural, and older).[2] Consensus exists that the availability of a mobile app for depression management that is user friendly and aligns with busy office practice would likely be adopted by end users.[3-4] Patients with depression and their treating provider may benefit from the use of a mobile health app to assist in disease management.

American Psychiatric Association (APA) clinical guidelines recommend measurement-based care (MBC) in treating depression, defined as a psychiatric evaluation including quantitative measures of symptoms, level of functioning, and quality of life. APA guidelines cite several studies that have shown benefits in using quantitative measures during an initial screening and also for monitoring depression throughout treatment.[5]A mobile app may promote MBC by allowing patients to remotely answer quantitative instruments, such as the PHQ-9, which can be uploaded into their electronic medical records (EMR) for in office visits and physician monitoring.[5] A study

by Torous et al. found that while in person paper scores and app scores were strongly correlated (r=.84), PHQ-9 app scores were consistently higher over a 30 days period.[6] An overall conclusion of this study was that collecting PHQ-9's through a mobile app may be more sensitive than the traditional PHQ-9.[6] Increased consultation times are often cited as a barrier to MBC implementation.[5,7] An app may save time as the physician will only need to review PHQ-9 instead of administering the questions during the visit. Although the validity of the PHQ-9 has been shown in studies, further research is needed to assess its ability to track outcomes of depression therapy over time.[7] This systematic approach to treatment may have positive effects on the patient-physician relationship and enhance shared decision making.[5]

A shared decision-making (SDM) model of interaction can foster patient provider engagement as well as increase patient satisfaction.[8] Several studies have found that individuals suffering from a mental illness want a larger part in the treatment decision making process.[9] A common barrier for SDM is a physician choosing a treatment plan that is not mutually agreed on by both the physician and patient. This can be overcome by increasing education and further clarifying the benefits of a specific treatment plan to align with the patient's values.[9] Incorporating a SDM model may help increase adherence to drug treatment in a primary care setting.[8] Mobile technology can enhance SDM.

A collaborative care model (CCM) that involves behavioral health integration within primary care is another evidence-based practice that enhances depression management. Collaborative care is a systematic approach that improves patient education and integrates mental health professionals or other care extenders, such as nurses, into the primary care clinic to help primary care physicians provide treatment in conformity with evidence-based guidelines.[10] CCM's have been shown to improve outcomes of patients with major depression.[11]

We hypothesize that integrating the Pathway Platform to support measurement- based care and shared decision- making, will improve the clinic workflow, depression management, adherence to medication, patient-provider engagement and improve depression outcomes and care.

2.2 **Study Rationale**

Major Depressive Disorder (MDD) is a serious public health concern worldwide with ample documentation demonstrating that it is one of the leading contributors to the global burden of disease and is currently the leading cause of disability worldwide.[12-13] Moreover, the economic burden of MDD is estimated to total $210.5 billion with approximately 50% of the cost being attributable to impairment in role function.[13-15]

A selection of mobile apps has been developed and are available for depression management.

However, many are patient facing only and have not implemented a care team interface. Most of these apps have been assessed for effectiveness in a research setting only and have not been integrated within clinic workflow resulting in lack of adoption by the care team and by healthcare systems.

This study builds on prior work that piloted a mobile App for feasibility and depression management, the *Pathway app*. The first iteration of the Pathway App included patient reported outcomes related to depression, wellbeing, cognitive symptom tracking, medication adherence and side effects. Pilot results confirmed the feasibility of using the Pathway app in patients with depression and showed a trend in patient engagement in the app arm, albeit in a small sample size. The Pathway pilot and feasibility study included qualitative assessments with patients and clinicians that highlight the need to enhance the flow of real time data shared with the care team and the need to integrate within the care team work flow including real time data sharing of the patient's app data within the EMR[16]. It also highlighted the need for care team education on measurement-based care, shared-decision making, and collaborative care and on how to utilize the Pathway App to improve these processes. Building on these results we created the *Pathway Platform* which includes a newer iteration of the Pathway App along with real time patient level data shared with the EMR integration in real-time and educational program both care team and patient facing.

We aim to implement a digitally enabled care pathway referred to as the *Pathway Platform* and assess its impact on measurement-based care and other evidence-based processes. The primary objective is to determine whether PHQ-9 utilization, a measurement- based practice, is greater after is the Pathway Platform implemented.

3. STUDY DESIGN

We will use a pre- post- study design to assess the impact of implementing the Pathway Platform in the primary care setting. Clinic performance and select patient outcomes will be compared before and after implementation. Additional patient outcomes will be assessed after implementation among patients using the Pathway Platform (**Figure 1**).

This study will be performed within primary care clinics in Advocate's Health Care System. Advocate is the largest healthcare provider in the state of Illinois with 12 hospitals, 20 health centers, and 250+ care sites. It is one of the largest Accountable Care Organizations in the United States caring for over 2 million patients annually. General practitioners provide diagnoses, treatment, and clinical care for adults ages 18 and over with chronic diseases, which often includes MDD.

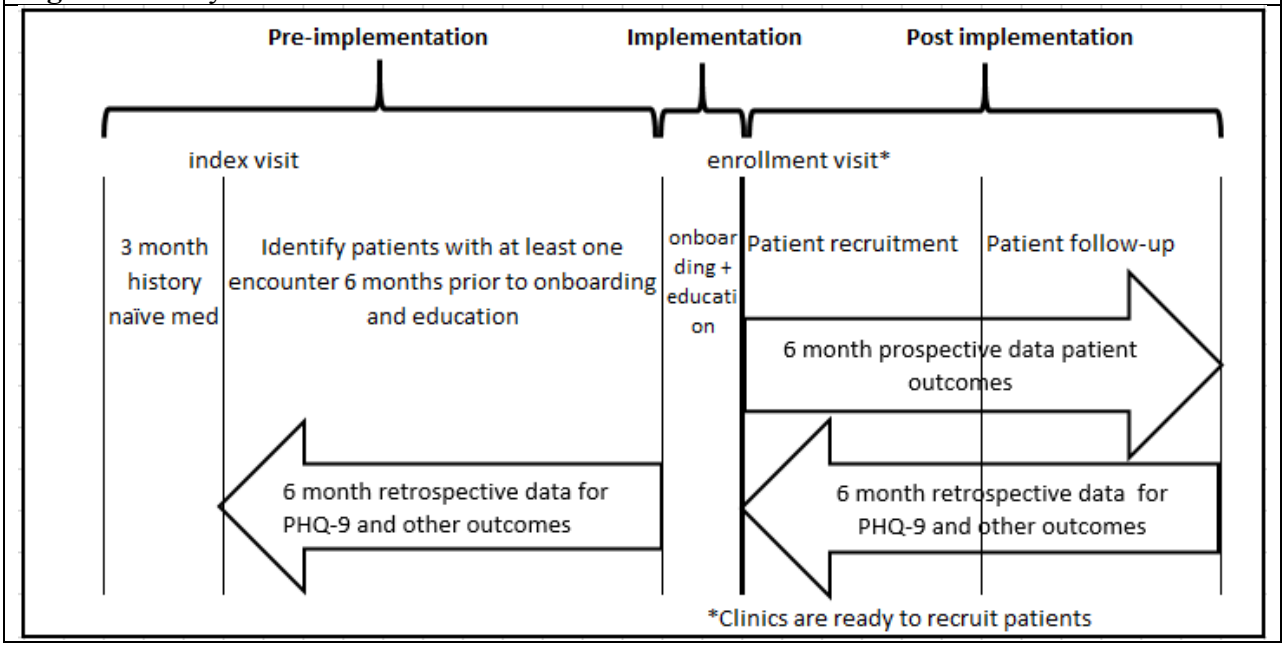
3.1 Performance among participating clinics post-implementation

The Pathway Platform will be implemented in up to 20 primary care sites within the Advocate Aurora Health system and enroll a total of 200 patients for six-month duration. The visit where the patient has been onboarded to the Pathway Platform will be the enrollment visit (Figure 1). During the post- implementation period, data on patient outcomes will be collected through the Pathway Platform. At the end of the study an electronic and manual chart review for patients using the Pathway Platform will be conducted among participating clinics and performance related to measurement-based care, shared decision making and collaborative care, where applicable, will be assessed over the post-implementation period.

3.2 Retrospective Assessment: pre-implementation performance at the clinic level (before Pathway Platform implementation)

To assess Advocate's primary care sites performance pre-implementation, an electronic and manual chart review will be conducted from the same Advocate primary care clinics participating in the implementation study. Patients with a clinic visit at least 6 months prior to implementation (index visit) of the Pathway Platform and meeting the inclusion criteria for enrollment in the study, will be included in this analysis (figure 1). Patient history will be evaluated for three months prior to index visit to confirm eligibility. The goal is to capture patients with a new start, dose adjustment or switch of an antidepressant medication 6 months prior to the implementation index date (three-month inclusion window for patient identification). Six months of patient history will be "retrospectively" collected for this baseline patient cohort to assess the primary outcome, defined as PHQ-9 utilization, and other secondary outcomes outlined in the protocol. This analysis will serve as the comparison control for the primary and secondary outcomes to compare performance at the same clinics pre and post-implementation of the Pathway Platform. Depending on the number of eligible patients identified per site (20 per site), group level matching for age and sex may be conducted. The primary endpoint will be the proportion of patients with at least 2 PHQ-9 scores.

Figure 1: Study schematic



* Primary and secondary outcomes will be evaluated at 6 months, data collected beyond 6 months will be used for exploratory analysis

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

Patients will be recruited from up to 20 primary care clinics within Advocate Aurora Health that have agreed to implement the Pathway Platform. We aim to identify clinics that are representative of different geographic locations, patient populations, and care models for depression management, including behavioral health integration models. We will balance clinic diversity with feasibility to conduct this study. For example, we will only include clinics that have integrated Epic within their workflow so that the care team can easily access data collected from the patient in the Pathway Platform. We will also focus on clinics that have a large volume of patients diagnosed with depression as well as clinics that have care team members that are interested and engaged in depression care.

All care team members who care for patients with depression will be invited to participate in this implementation study and will have access to an online educational resource center. Patients fulfilling the following criteria will be eligible to download and use the Pathway Platform:

4.1 Inclusion

1. Adult aged 18 and above

2. Diagnosis with major depressive disorder or reference to "clinical depression" in patient charts. See **Appendix 1** for ICD codes for major depressive disorders
3. Recently prescribed monotherapy antidepressant medication (defined as new start, medication switch, or dose change in the past 3 months (**Appendix 2**).
4. Patients with inadequate response or tolerability concerns determined based on A PHQ-2 score of 3 or greater, or a PHQ-2 <3 with a PHQ-9 score of 5 or greater recorded in medical records in the past 6 weeks or during screening,
5. Able and willing to provide informed consent
6. Able to use the Pathway Platform based on clinician's judgment, e.g. owns an iPhone version 5 or later or smartphones with Android operating systems, have an active data plan or regular WiFi access.

4.2 Exclusion

1. Missing PHQ-2/PHQ-9 score in the past 6 weeks and/or unable to perform PHQ-2/PHQ-9 at index visit
2. Diagnosis with bipolar depression, schizophrenia, and/or schizoaffective disorder, (**Appendix 1**).
3. Patient no longer under primary care for depression and has transitioned to a psychiatric care team (i.e., Psychiatrist, Advance Practice Psychiatric Nurse, Psychiatric Nurse Practitioner, Psychiatric Physician Assistant).
4. Lack of functional English literacy (indicated by primary language in EMR).

4.3 Study Enrollment Procedures

This is a real-world implementation study with minimal interaction between the study team and patients. To address recent virtual visits in primary care due to COVID-19 and for the safety of the study team, study methods were developed to adapt virtual patient recruitment and e-consent during existing virtual visit processes. An in person consenting process is also available for in person clinic visits, when safe and appropriate, and will be supported by a study team member present at recruiting clinics.

Study team will review clinic schedules routinely for visits scheduled the next day and will flag potentially eligible patients and will discuss the list with the health care team. These patients will be introduced to the study opportunity by care team members during routine clinic visits.

- Consenting in person: If the patient is interested, they will be roomed with a study team member who will confirm study eligibility and provide written informed consent. If the patient is eligible and provides consent, the study team will share a secure message with a link for the Pathway App with the patient and the patient will be able to activate the Pathway App and start entering data. The secure message will be shared with the patient via AAH's secure patient portal. Or through an email for patients who have not activated their portal. The invitation message in the email will include an individualized link to download the App with a unique code specific to that patient to ensure security.
- e-Consenting virtually: If the patient is interested, the care team member will inform the research team, who will confirm eligibility and send a secure invitation to the patient (AAH patient portal or email with unique link and code). The invitation message includes a link to start the e-consenting process and that includes study contact information to allow patients to reach out to the study team with any questions during e-consenting or during the study. The link in the message will direct the patient to start the e-consenting process. The patient will not be able to download the app until they have completed the e-consenting process. Patient e-consent will be obtained in REDCap using a finger or stylus-directed signature on the mobile phone, with data including attestation of individual identity and time and date of signing. Upon completion, participants will be able to download a pdf copy of the signed e-consent form. The patient will then be invited to download the Pathway App via another secure message with a link including details for the patient to activate the mobile app and start entering data.

4.4 Pathway Platform

The Pathway Platform consists of three components:

4.4.1 Pathway App

Pathway is a mobile application designed to gather health information related to the management of depression to enhance patient clinical engagement and guide patient care. The patient facing interface includes a digital assistant that allows patients to interact with the Pathway Platform in a chat-based conversational text interface. The information collected from the patient is intended to assist the care team in managing the patient's depression through enhancing measurement-based care and shared-decision making - enhancing patient-provider engagement and ultimately patient outcomes. The study will deploy the most recent iteration of the Pathway Platform. Earlier iterations were piloted in four primary care clinics.[16] Feedback from this pilot was used to enhance Pathway Platform functionality. The current iteration of the Pathway Platform, which is the version that will be used in the implementation study described in this protocol, prompts patients to complete four scales to assess depression status biweekly (Patient Health Questionnaire [PHQ-9] and Perceived Deficits Questionnaire-Depression [PDQ-D5]), quality of life (World Health Organization- Five Well Being Index [WHO-5]), and cognition (Digit Symbol Substitution Test [DSST]).[7,17,18,19] The Pathway Platform also includes a daily evening check-in with the patient to collect information on medication adherence and side effects. Patients reporting side effects related to sleep are prompted to complete the PROMIS Sleep Disturbance 6a and patients reporting side effects related to sexual dysfunction are prompted to complete the Arizona Sexual Experience Scale (ASEX).[20,21] An optional functionality of the Pathway Platform is to set and track goals using the Goal Attainment approach adapted for depression during clinic visits with a healthcare provider.[22] In addition, the Pathway Platform includes patient facing education for the patient on how to use the Pathway Platform to collect data as well as how to prepare for a visit with health care providers, set and assess progress towards goals and self-management. For purposes of evaluating this implementation study three additional scales assessing patient-provider engagement and functional improvement will be deployed through the Pathway Platform at baseline and subsequently every 6 months until the end of the study (Patient Activation Measure - 13[PAM-13], CollaboRATE, and Work and Social Adjustment Scale [WSAS]).[23,24,25]

4.4.2 Electronic Medical Record integration

Data collected in the Pathway Platform is electronically transmitted and stored in the patient's EMR. This data is accessible to the care team and provides a longitudinal summary that may assist in decision making and depression management. Providers can view this data either before or during the patient visit and use it to discuss future depression management.

4.4.3 Educational Scaffolding

An online Educational training program was developed using evidence-based medicine building

on measurement-based care and shared-decision making concepts as they relate to depression management. Educational material describes how the Pathway Platform can help care team members in clinical processes related to these process improvement measures. In clinics using a collaborative care model additional education material specific to this care model is provided. Educational material housed in an online resource center which includes reading material, presentations, and videos. Additionally, up to three audit and feedback sessions will be conducted for each participating clinic. The objectives of audit and feedback sessions are to benchmark performance measures, including shared decision making, reflect on current clinical practice and improvement strategies, and setting team-based action plans. Care team members who manage depression must complete specific training before they are able to enroll patients and begin using the Pathway Platform.

A training manual was also developed for patients. The manual describes the Pathway Platform functionality, as well as, how to use and interpret the data collected.

3.3 Study Duration

Patients will be enrolled in the study for a minimum duration of 6 months with the option to continue using the app at that time to a common study end date of January 7, 2023 (access to in-app final study evaluations will end January 21, 2023). Data from the Pathway Platform will be collected prospectively for the duration of the patient's participation. Process measures will be collected retrospectively from the EMR and through manual chart review after 6 months of enrollment and at the end of the study(post-implementation) and over a 6-month period prior to implementation (pre-implementation).

5. STUDY PROCEDURES

5.1 Schedule of events

Table 1: Schedule of evaluations								
	Pre-electronic and manual chart reviews	**Complete education by care team**	**Screening**	**Baseline assessment**	**6 month Assessment**		**Final assessment**	
Study Day/Week:		**Day -1**	**Day 0**	**Day 1**	**Day 168 - 172^**		**Study end**	
Visit Windows (Days):								
Source			**EMR/ patient scheduling**	**Pathway Platform**	**Pathway Platform**	**EMR and Manual Review**	**Pathway Platform**	**EMR and Manual Review**
Patient electronic screening			X					
Informed consent			X					
Onboarding			X					
Demographic characteristics	X							
Number of PHQ-9 scores documented	X				X	X	X	X
Treatment adjustments	X				X	X	X	X
Shared decision making (OPTION-12 and CollaboRATE)	X				X	X	X	X
Referral to behavioral health	X					X		X
PHQ-9 scores	X				X		X	
Emergency room visits	X					X		X
Emergency room visits due to mental illness	X					X		X
Hospital admissions	X					X		X
Follow up after emergency room and hospital visits	X					X		X
Hospital admissions due to mental illness	X					X		X
Healthcare resource utilization								
Outpatient visits including phone calls	X					X		X
Outpatient visits including phone calls due to mental illness	X					X		X
Remission and response (using PHQ-9 data)	X				X		X	
PAM 13 ***				X	X		X	
CollaboRATE**, ***				X	X		X	
WSAS ***				X	X		X	
PHQ-9				X	X	X	X	X
WHO-5				X	X		X	
PDQ-D5				X	X		X	
Medication adherence				X	X		X	
Side effects				X	X		X	
PSD-6 (only if reporting side effects of sleep problems)				X	X		X	
ASEX (only if reporting side effects of sexual problems)				X	X		X	
Goal Setting				X				
Goal Attainment					X		X	
App analytics				X	X		X	
Report analytics				X	X		X	
Educational material analytics				X	X		X	
In depth interviews (Patients and Clinicians)							X	
Adverse Events*	X		X	X	X		X	X
Serious Adverse Events	X		X	X	X		X	X
^Day 168 reflects end of initial 24 week study period in which the final set of care questionnaires are available for completion (PHQ-9, WHO-5 and PDQ-D5), these expire within 3 days. Day 172; The off-boarding process is available, including the research questions (PAM-13, WSAS,								

CollaboRATE), these expire after 30 days.
*If during the conduct of the study, a health care professional or patient spontaneously reports an Adverse Event or a serious adverse event to a Takeda product; such information should be reported to the sponsor. As such reports are spontaneously notified, causality of any AEs should be assumed unless there is evidence to the contrary; **CollaboRATE will also be asked within the App at Day 84 with a 30 day window for completion during patient enrollment. ***PAM 13, CollaboRATE and WSAS; the App will trigger response to these questionnaires every 6 months until study end (note; if patient completed these questionnaires within 4 weeks of study end point, they will not be re-deployed for completion at end of study).

5.2 Description of study evaluations

1. EMR data pulls and manual chart reviews: EMR data and manual chart review data will be collected from two cohorts of patients: (1) patients attending clinics after implementation (post- implementation cohort) and (2) patients attending clinics before implementation (pre-implementation). For the pre-implementation cohort, data will be collected over a six-month period. For the post-implementation cohort, data will be collected from the time of study implementation until the end of the study.

2. Pathway Platform data and analytics: Data on patient outcomes and Pathway Platform usage will be collected throughout the study starting at day 1 and ending on the final day of the patient's participation (i.e. 6 months, common study end date or patient withdrawl). Similarly, data on report usage by care team will be collected throughout the study.

3. Educational resource center analytics: The number of times material in the resource center is viewed will be recorded between day 1 and the end of the study.

6. SAFETY ASSESSMENTS

6.1 Adverse Events Related to the Pathway Platform

No adverse events (AEs) are expected in this minimal risk study related to the Pathway Platform; however, all serious adverse events (SAEs) that are spontaneously reported during the study period will be collected.

A SAE is defined as an adverse event, reported during the implementation study of the Pathway Platform, in the view of either the investigator or sponsor, results in any of the following outcomes:

a. Death
b. Life-threatening adverse event
c. Inpatient hospitalization or prolongation of existing hospitalization (for > 24 hours)
d. Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
e. Congenital anomaly/birth defect.

f. Important medical events that may not result in death, be life-threatening or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

The following information will be collected for any SAE that is reported:

- Event details
- Start and stop date
- Frequency
- Intensity
- Investigator's opinion of the causal relationship to study procedure(s), including the details of the suspected procedure
- Outcome of event
- Severity

Causality to study procedures will be determined for all SAEs and deemed "related" or "not related" to the intervention. Severity will be assessed as mild (event is transient and easily tolerated by the subject), moderate (event causes the subject discomfort and interrupts the subjects' usual activities), or severe (event causes considerable interference with the subject's usual activities). The start date of the SAE is the date that the first signs or symptoms were noted. The stop date is the date on which the subject recovered, the event resolved, or the subject died.

All SAEs, along with the information bulleted above, will be compiled and included in the final study report. SAEs will be reported to Takeda within 24 hours of becoming aware of the event.

6.2 Change in Participant Suicidal Ideation

Patients using the Pathway Platform will answer biweekly PHQ-9 surveys, during which Item 9 asks about the frequency of suicidal ideation. It is possible that a patient will report a change in suicidal ideation in the course of responding to this question. In the event that a patient responds affirmatively to this question, the patient will receive a pop-up notification that s/he should contact his/her health care provider or emergency services immediately. This instruction is what is given in routine clinical practice. The

data from the Pathway Platform is not monitored in real time by care teams. Patients will be informed via consent that the information provided to the Pathway Platform is not directly or continuously monitored. As an additional item of note, data from the Pathway Platform may be delayed and/or not received by the EMR if device is unable to transmit data.

This information will also be included in the patient consent and will be explained to the patient by the Care Team during the consent process.

7. INTERVENTION DISCONTINUATION

Patients are not required to use the Pathway Platform and can choose to discontinue at any time. Adherence to use will be tracked and reported for analytical purposes.

8. STATISTICAL CONSIDERATIONS

8.1 General Design and Hypothesis

The following hypotheses will be examined:

Primary hypothesis: PHQ-9 utilization will be greater after implementation compared to before implementation of the Pathway Platform.

Secondary hypothesis: Provider processes and patient depression related outcomes will have greater improvements in patient outcomes after implementation of the App compared to previous practice patterns.

8.2 Sample size and randomization

The primary outcome for this study is PHQ-9 utilization. Assuming 75% PHQ-9 utilization prior to implementation of the Pathway Platform and 90% PHQ-9 utilization after implementation of the Pathway Platform, we will need 100 patients per group, for a total of 200 patients, assuming 80% power and a 2-sided alpha of 0.05 using Pearson chi square test for two independent proportions. To allow for subgroup analyses the sample will include 200 patients per group, for a total of 400 patients; 200 patients will comprise the "post-implementation" cohort and 200 will comprise the "pre-implementation" cohort. **Table 2** presents additional sample size calculations based on different assumptions of PHQ-9 utilization.

Table 2: Sample size calculations based on different assumptions of PHQ-9 utilization, alpha = 0.05, Power = 80%.

PHQ-9 utilization pre-implementation	PHQ-9 in Pathway post-implementation	N patients per group
75%	80%	1,094 per group
75%	90%	100 per group
75%	95%	49 per group
50%	65%	170 per group
50%	80%	30 per group
50%	90%	20 er group

8.3 Outcomes

8.3.1 Primary outcome

The primary process outcome is PHQ-9 utilization over a six-month period. For purposes of this study, PHQ-9 utilization will be defined as documentation of at least 2 PHQ-9 scores in the EMR over the initial 6-month study period. The proportion of patients who meet this definition will be compared between patients attending clinics pre- and post- implementation of the Pathway Platform. Additional analyses exploring the number of PHQ-9s over the study period will also be conducted.

8.3.2 Secondary outcome

Process outcomes: The following secondary process outcomes will be compared between patients attending clinics pre- and post- implementation of the Pathway Platform.

- Measurement- based care: The proportion of patients reflecting measurement-based care informed MDD treatment adjustments in their charts, defined as at least one dose change, medication switch, or add on medication during the study period. The frequency and types of treatment adjustments will also be explored.
- Shared- decision making: The proportion of patients reflecting shared-decision making, using the OPTION12 Tool framework.[26] The tool will be modified by adding a thirteenth domain inquiring about goal setting (Asking the patient or caregiver about goals of treatment). The frequency and domains of shared-decision making will also be explored in a manual chart review and a variable added to assess if the clinician documented asking the patient about their goals of treatment.

- Referrals to behavioral health: The proportion of patients with at least one referral will be compared. The frequency and types of referrals will also be explored.
- Follow-up after hospitalization for mental illness: The proportion of hospitalized adults who receive follow-up within 7 days of discharge and within 30 days of discharge.
- Follow-up after emergency department visit for mental illness: The proportion of adults

who receive follow-up within 7 days of discharge and within 30 days of ED visit.

- Healthcare resource utilization: Number and costs associated with hospital admission, length of stay, emergency room admissions, and encounters with outpatient clinics. Costs will be calculated using USA national average costs for inpatient and outpatient visits or using an average Advocate Health Care system cost.

Patient clinical outcomes: The following outcomes will be compared between patients attending clinics pre- and post- implementation of the Pathway Platform, keeping in mind that the number of patients with these measures in the pre- implementation patient group will be limited:

- MDD remission: The proportion of patients with PHQ-9 <= 5 at the end of the study period. The last measurement available during the study period will be used to calculate remission.
- MDD response: The proportion of patients with a 50% or greater reduction in PHQ-9 scores. The first and last scores available during the study period will be used to calculate response.
- Diagnosis progress notes stating change from mild, moderate, or sever, to in remission or partial remission will be assessed descriptively.

Patient reported outcomes: The difference in scores between baseline, and 6-month follow up will be compared among patients using the Pathway Platform who completed the following measures:

- PAM-13
- CollaboRATE (this questionnaire is also included as a 3-month post-enrollment assessment and will be analyzed across all available time points)
- WSAS

8.3.3 Exploratory outcomes

Patient clinical and reported outcomes:

- The following patient reported outcomes will be collected in the Pathway Platform throughout the study. The difference in scores between the baseline measure, 6-months, and end of the studywill be compared. This will be restricted to patients who completed these scales at these two-time points. To be inclusive of all patients, additional analyses will be conducted to compare first and last scores available:
    - PHQ-9
    - WHO-5
    - PDQ-D5

- The following patient reported outcomes will be collected in the Pathway Platform and described at 6-months and end of the study:
    - Antidepressant Medication adherence
    - Antidepressant Medication dose adjustment and switches
    - Side effects
    - Depression remission
    - Depression response
    - Goal attainment
    - Patient reported outcomes (PAM-13, CollaboRATE and WSAS) will also be explored at 6 months and end of the study.

Pathway Platform and report utilization: Pathway Platform analytics will be explored to understand patient adherence to the platform which includes frequency of logging into the Pathway Platform and frequency of completing each of the Pathway Platform functionalities. Care-team utilization of Pathway Platform reports will also be explored, including describing type of care team members who viewed the Pathway Platform reports as well as frequency of viewing the reports.

Education utilization: Frequency of viewing material in the resource education center will be described by patient and by care-team members. Commonly viewed educational material will be highlighted.

Subgroup analysis: primary, secondary, and exploratory outcomes will be compared across a number of patient demographic and clinical characteristics, including PHQ-9 severity at baseline, comorbidities (see appendix 3 for comorbid conditions and ICD codes), app utilization by patients, and EMR report utilization by providers. Additional subgroup analysis will be conducted by type of care model at the site level (e.g. collaborative care vs. non collaborative care sites).

8.3.4 Patient and provider in-depth interviews

In-depth interviews will be conducted at the end of the study period with approximately 20 patients and 15 care team members who have used the Pathway Platform. Interviews will involve discussing reactions and feedback on the Pathway Platform, education material, care team interface, and overall implementation of the Pathway Platform. These semi-instructed in-depth interviews will allow patients to reflect on the process and identify higher level causes behind any difficulties or challenges, explore any suggested changes and to gather general feedback regarding the participant's experience during the study. Findings from this sub-study will complement the main study analysis and explore the use of the Pathway Platform App and what this could mean for ongoing development of the Pathway Platform.

8.3.5 System level performance

Performance and patient outcomes evaluated in this study will be evaluated at the system level covering all primary care clinics. Data will be collected retrospectively on patients attending any primary care clinic during the study period. This data will be used to understand performance at the system level.

8.4 Data analysis

For primary and secondary hypothesis testing, process measures, patient clinical outcomes, and health care resource utilization will be compared pre- and post- implementation of the Pathway Platform.

Additional patient reported outcomes will be compared among patients using the Pathway Platform only at baseline and end of study. For pre-implementation, outcomes will be assessed among patients who visited one of the study clinics at least once over the pre-implementation study period and were eligible to use the Pathway Platform, if it had been available. For the post-implementation period, the Pathway Platform will be the data source for paired t-test analysis, assessing change in continuous variables including PHQ-9 scores. Categorical outcomes will be presented as proportions and compared using Pearson Chi2 test. Continuous outcomes will be assessed for normality and presented as means and standard deviations (SD) or medians and interquartile ranges (IQR); continuous outcomes will be compared using Student's t test for independent groups. Two-tailed tests using a significance threshold of $p < 0.05$ will be used for all tests.

Exploratory outcomes: will be described among patients attending the pathway platform clinics only and will be compared between baseline, 6-month and extended follow up. Change in these outcomes overtime, including utilization analytics will also be explored. Categorical outcomes will be presented as proportions and compared using McNemars' test. Continuous outcomes will be assessed for normality and presented as means and standard deviations (SD) or medians and interquartile ranges (IQR); continuous outcomes will be compared using Student's Paired t test for single group comparison. Two-tailed tests using a significance threshold of $p < 0.05$ will be used for all tests. Goal attainment will be summarized by proportion of patients who achieve their identified goals based on the set time bound duration of the goal (i.e., GAS Score ≥50).[29,30] The goal attainment scale adapted for depression yields a norm-based score (standardized to a mean of 50, SD of 10) at baseline and at the end of the time bound goal; the change from score from baseline will also be summarized.

System level performance: Process outcomes will be evaluated at the system level (all primary

care clinics) among patients fulfilling eligibility criteria, if the app were available. Descriptive analysis will be utilized to describe process outcomes across all clinics.

In depth interviews: Interpretative Phenomenological Analysis will be used to analyze the qualitative data. To increase the rigor and validity of the analysis, and as a form of triangulation, the analysis will be conducted by 3 members of the research team (the lead qualitative researcher and 2 others). Analysis will involve 2 stages: (1) Data management, which will include, familiarization with the data, reading notes, and/or listening to the audio dialogue in order to extract main themes and ideas and thematic framework development, identifying the key issues and concepts present in the data and creating themes both inductively, based on the data, and deductively, based on the research questions, (2) Interpretation stage, which will include focused defining the main concepts and mapping the ways in which different parts of the data are related to each other.

4. 9.4 PARTICIPANT RIGHTS AND CONFIDENTIALITY

4.1 9.4.1 Institutional Review Board (IRB) Review

This protocol, the informed consent document, and any subsequent modifications will be reviewed and approved by the Advocate's IRB, who is responsible for oversight of the study.

4.2 9.4.2 Informed Consent Forms

A signed consent form will be obtained from each participant by the Advocate Research Team. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy will be given to each participant and will be documented in the participant's record.

4.3 9.4.3 Participant Confidentiality

Data will be extracted from an EMR data pull as well as chart reviews and shared only with the clinic and research staff that are needed to identify eligible patients for the study in a password-protected MS Excel sheet. For clinic staff, shared patient information will be limited to only the patients seen at that clinic location. All paper copies of study data collection forms will be stored in a secure location at Advocate Research Institute to maintain subject confidentiality.

A subject ID will be assigned to each study participant; this will serve as a unique subject identifier for the study and Pathway Platform data. Data management for Pathway Platform data will have security processes in place that are service organizational control

or SOC2 compliant. This comprises data storage and transmission between the Pathway Platform, servers, and EMR system. Data collected for the study will be maintained and monitored while the study is active and the identifying link will be destroyed upon study close.

4.4 **9.4.4Study Discontinuation**

The study may be discontinued at any time to ensure that research patients are protected.

5. 10. TAKEDA MARKETED PRODUCT ADVERSE EVENT REPORTING REQUIREMENTS

An AE is any untoward medical occurrence in a subject administered a Takeda medicinal product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, a new disease or worsening in severity or frequency of a concomitant disease, temporally associated with the use of a Takeda medicinal product, whether the event is considered causally related to the use of the Takeda product.

10.1 Special Situation Reports and Product Quality Issues

A special situation report (SSR) includes any of the following events:

- Pregnancy: Any case in which a pregnant patient is exposed to a Takeda product or in which a female patient or female partner of a male patient becomes pregnant following treatment with Takeda product. Exposure is considered either through maternal exposure or via semen following paternal exposure.
- Breastfeeding: Infant exposure from breast milk.
- Overdose: All information of any accidental or intentional overdose.
- Drug abuse, misuse or medication error: All information on medicinal product abuse, misuse or medication error (potential or actual).
- Suspected transmission of an infectious agent: All information on a suspected (in the sense of confirmed or potential) transmission of an infectious agent by a medicinal product.
- Lack of efficacy of Takeda product.
- Occupational exposure.
- Use outside the terms of the marketing authorization, also known as “off-label”.
- Use of falsified medicinal product.

A product quality issue refers to defects related to the safety, identity, strength, quality, or purity of the product or with the physical characteristics, packaging, labeling, or design of the product.

10.2 Procedures

Collection and Reporting of Spontaneous AEs, SSRs, and Product Quality Issues Related to a Takeda Product: If during the conduct of the study, a health care professional or patient spontaneously reports an AE, SSR, or product quality issue where the event/issue pertains to a Takeda product (or unbranded generic); such information should be reported to the sponsor. As such reports are spontaneously notified, causality of any AEs should be assumed unless there is evidence to the contrary.

AEs, SSRs or products complaints relating to any Takeda products received spontaneously must be reported via email or by telephone within 24 hours of awareness and no later than by the next working day. The preferred method for reporting is via email. If a report is received via telephone it should be backed up with an email. Advocate may submit Reportable Information to Takeda at medicalinformation@tpna.com. Alternatively, Advocate may submit Reportable Information to Takeda's Call Center by calling 1-877-Takeda7.

6. 11. PUBLICATION OF RESEARCH FINDINGS

Publication of the results of this study will be governed by the policies and procedures developed by the Steering Committee, which will include representatives from Advocate Health Care and the Takeda/Lundbeck Alliance. Any presentation, abstract, or manuscript related to the data resulting from this study will be made available for review by Advocate Health Care and the Takeda/Lundbeck Alliance prior to submission.

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Appendix 1: Selection criteria ICD codes		
Code Type	**Code**	**Description**
ICD-9-CM DX	296.26	Major depressive disorder, single episode in full remission
ICD-9-CM DX	296.25	Major depressive disorder, single episode, in partial or unspecified remission
ICD-9-CM DX	296.21	Major depressive disorder, single episode, mild
ICD-9-CM DX	296.22	Major depressive disorder, single episode, moderate
ICD-9-CM DX	296.24	Major depressive disorder, single episode, severe, specified as with psychotic behavior
ICD-9-CM DX	296.23	Major depressive disorder, single episode, severe, without mention of psychotic behavior
ICD-9-CM DX	296.20	Major depressive disorder, single episode, unspecified
ICD-9-CM DX	296.36	Major depressive disorder, recurrent episode, in full remission
ICD-9-CM DX	296.35	Major depressive disorder, recurrent episode, in partial or unspecified remission
ICD-9-CM DX	296.31	Major depressive disorder, recurrent episode, mild
ICD-9-CM DX	296.32	Major depressive disorder, recurrent episode, moderate
ICD-9-CM DX	296.34	Major depressive disorder, recurrent episode, severe, specified as with psychotic behavior
ICD-9-CM DX	296.33	Major depressive disorder, recurrent episode, severe, without mention of psychotic behavior
ICD-9-CM DX	296.30	Major depressive disorder, recurrent episode, unspecified
ICD-9-CM DX	296.x	Manic depression/bipolar disorder (Episodic Mood Disorder)
ICD-9-CM DX	295.9x	Schizophrenia
ICD-10-CM DX	F325	Major depressive disorder, single episode, in full remission
ICD-10-CM DX	F324	Major depressive disorder, single episode, in partial remission
ICD-10-CM DX	F320	Major depressive disorder, single episode, mild
ICD-10-CM DX	F321	Major depressive disorder, single episode, moderate
ICD-10-CM DX	F323	Major depressive disorder, single episode, severe with psychotic features
ICD-10-CM DX	F322	Major depressive disorder, single episode, severe without psychotic features
ICD-10-CM DX	F25.x	Schizoaffective disorders
ICD-10-CM DX	F328	Other specified depressive disorder
ICD-10-CM DX	F329	Major depressive disorder, single episode, unspecified
ICD-10-CM DX	F332	Major depressive disorder, recurrent severe without psychotic features
ICD-10-CM DX	F3342	Major depressive disorder, recurrent, in full remission
ICD-10-CM DX	F3341	Major depressive disorder, recurrent, in partial remission
ICD-10-CM DX	F3340	Major depressive disorder, recurrent, in remission, unspecified
ICD-10-CM DX	F330	Major depressive disorder, recurrent, mild
ICD-10-CM DX	F331	Major depressive disorder, recurrent, moderate
ICD-10-CM DX	F333	Major depressive disorder, recurrent, severe with psychotic symptoms
ICD-10-CM DX	F339	Major depressive disorder, recurrent, unspecified
ICD-10-CM DX	F31.x	Manic depression/bipolar disorder
ICD-10-CM DX	F20.x	Schizophrenia
ICD-10-CM DX	F43.1	Persistent depressive disorder
ICD-10-CM DX	F43.21	Adjustment d/o with depressed mood
ICD-10-CM DX	F43.23	Adjustment d/o with mixed anxiety and depressed mood

Appendix 2: List of antidepressant medication classes			
MEDICATION_ID	**NAME**	**GENERIC_NAME**	**ORDER_COUNT**
30792	SERTRALINE HCL 50 MG PO TABS	Sertraline HCl Tab 50 MG	364265
30791	SERTRALINE HCL 100 MG PO TABS	Sertraline HCl Tab 100 MG	344586
49150	ESCITALOPRAM OXALATE 10 MG PO TABS	Escitalopram Oxalate Tab 10 MG (Base Equiv)	279295
27521	FLUOXETINE HCL 20 MG PO CAPS	Fluoxetine HCl Cap 20 MG	250226
25473	CITALOPRAM HYDROBROMIDE 20 MG PO TABS	Citalopram Hydrobromide Tab 20 MG (Base Equiv)	246662
49151	ESCITALOPRAM OXALATE 20 MG PO TABS	Escitalopram Oxalate Tab 20 MG (Base Equiv)	191759
52482	BUPROPION HCL ER (XL) 150 MG PO TB24	Bupropion HCl Tab ER 24HR 150 MG	191523
54838	DULOXETINE HCL 60 MG PO CPEP	Duloxetine HCl Enteric Coated Pellets Cap 60 MG (Base Eq)	179414
41375	VENLAFAXINE HCL ER 75 MG PO CP24	Venlafaxine HCl Cap ER 24HR 75 MG (Base Equivalent)	140523
54837	DULOXETINE HCL 30 MG PO CPEP	Duloxetine HCl Enteric Coated Pellets Cap 30 MG (Base Eq)	140369
52483	BUPROPION HCL ER (XL) 300 MG PO TB24	Bupropion HCl Tab ER 24HR 300 MG	136883
41377	VENLAFAXINE HCL ER 150 MG PO CP24	Venlafaxine HCl Cap ER 24HR 150 MG (Base Equivalent)	129493
26233	CITALOPRAM HYDROBROMIDE 40 MG PO TABS	Citalopram Hydrobromide Tab 40 MG (Base Equiv)	128087
14668	SERTRALINE HCL 25 MG PO TABS	Sertraline HCl Tab 25 MG	126081
1130	AMITRIPTYLINE HCL 25 MG PO TABS	Amitriptyline HCl Tab 25 MG	111075
31120	FLUOXETINE HCL 40 MG PO CAPS	Fluoxetine HCl Cap 40 MG	110799
6802	BUPROPION HCL ER (SR) 150 MG PO TB12	Bupropion HCl Tab ER 12HR 150 MG	110322
3069	MIRTAZAPINE 15 MG PO TABS	Mirtazapine Tab 15 MG	101445
29473	PAROXETINE HCL 20 MG PO TABS	Paroxetine HCl Tab 20 MG	93100
45710	CITALOPRAM HYDROBROMIDE 10 MG PO TABS	Citalopram Hydrobromide Tab 10 MG (Base Equiv)	88045
1127	AMITRIPTYLINE HCL 10 MG PO TABS	Amitriptyline HCl Tab 10 MG	84142
27520	FLUOXETINE HCL 10 MG PO CAPS	Fluoxetine HCl Cap 10 MG	76319
41370	VENLAFAXINE HCL ER 37.5 MG PO CP24	Venlafaxine HCl Cap ER 24HR 37.5 MG (Base Equivalent)	64038
46525	FLUOXETINE HCL 20 MG PO TABS	Fluoxetine HCl Tab 20 MG	47822
43380	PAROXETINE HCL 10 MG PO TABS	Paroxetine HCl Tab 10 MG	46591
1131	AMITRIPTYLINE HCL 50 MG PO TABS	Amitriptyline HCl Tab 50 MG	42808
3068	MIRTAZAPINE 30 MG PO TABS	Mirtazapine Tab 30 MG	41887
43381	PAROXETINE HCL 40 MG PO TABS	Paroxetine HCl Tab 40 MG	41484
53289	ESCITALOPRAM OXALATE 5 MG PO TABS	Escitalopram Oxalate Tab 5 MG (Base Equiv)	40429
21941	TRAZODONE HCL 150 MG PO TABS	Trazodone HCl Tab 150 MG	40137
15185	NORTRIPTYLINE HCL 10 MG PO CAPS	Nortriptyline HCl Cap 10 MG	38909
33067	VENLAFAXINE HCL 75 MG PO TABS	Venlafaxine HCl Tab 75 MG (Base Equivalent)	35559
15186	NORTRIPTYLINE HCL 25 MG PO CAPS	Nortriptyline HCl Cap 25 MG	33918
54836	DULOXETINE HCL 20 MG PO CPEP	Duloxetine HCl Enteric Coated Pellets Cap 20 MG (Base Eq)	33170
49138	LEXAPRO 10 MG PO TABS	Escitalopram Oxalate Tab 10 MG (Base Equiv)	25964
29474	PAROXETINE HCL 30 MG PO TABS	Paroxetine HCl Tab 30 MG	25543
24234	ZOLOFT 50 MG PO TABS	Sertraline HCl Tab 50 MG	24619
6801	BUPROPION HCL ER (SR) 100 MG PO TB12	Bupropion HCl Tab ER 12HR 100 MG	23869
54049	MIRTAZAPINE 7.5 MG PO TABS	Mirtazapine Tab 7.5 MG	23111
30269	FLUOXETINE HCL 10 MG PO TABS	Fluoxetine HCl Tab 10 MG	22273

25491	BUPROPION HCL 75 MG PO TABS	Bupropion HCl Tab 75 MG	21540
33068	VENLAFAXINE HCL 37.5 MG PO TABS	Venlafaxine HCl Tab 37.5 MG (Base Equivalent)	21070
24233	ZOLOFT 100 MG PO TABS	Sertraline HCl Tab 100 MG	20074
16385	PAXIL 20 MG PO TABS	Paroxetine HCl Tab 20 MG	18434
25490	BUPROPION HCL 100 MG PO TABS	Bupropion HCl Tab 100 MG	17921
18059	PROZAC 20 MG PO CAPS	Fluoxetine HCl Cap 20 MG	16426
7035	DOXEPIN HCL 10 MG PO CAPS	Doxepin HCl Cap 10 MG	16384
1128	AMITRIPTYLINE HCL 100 MG PO TABS	Amitriptyline HCl Tab 100 MG	16341
72022	DESVENLAFAXINE SUCCINATE ER 50 MG PO TB24	Desvenlafaxine Succinate Tab ER 24HR 50 MG (Base Equiv)	15946
26237	CELEXA 20 MG PO TABS	Citalopram Hydrobromide Tab 20 MG (Base Equiv)	15281
15187	NORTRIPTYLINE HCL 50 MG PO CAPS	Nortriptyline HCl Cap 50 MG	14927
48727	BUPROPION HCL ER (SR) 200 MG PO TB12	Bupropion HCl Tab ER 12HR 200 MG	14897
20977	EFFEXOR XR 75 MG PO CP24	Venlafaxine HCl Cap ER 24HR 75 MG (Base Equivalent)	14669
29905	MIRTAZAPINE 45 MG PO TABS	Mirtazapine Tab 45 MG	12852
7038	DOXEPIN HCL 25 MG PO CAPS	Doxepin HCl Cap 25 MG	12040
49140	LEXAPRO 20 MG PO TABS	Escitalopram Oxalate Tab 20 MG (Base Equiv)	10718
54830	CYMBALTA 60 MG PO CPEP	Duloxetine HCl Enteric Coated Pellets Cap 60 MG (Base Eq)	10331
1132	AMITRIPTYLINE HCL 75 MG PO TABS	Amitriptyline HCl Tab 75 MG	9606
20979	EFFEXOR XR 150 MG PO CP24	Venlafaxine HCl Cap ER 24HR 150 MG (Base Equivalent)	9586
72023	DESVENLAFAXINE SUCCINATE ER 100 MG PO TB24	Desvenlafaxine Succinate Tab ER 24HR 100 MG (Base Equiv)	9391
6825	WELLBUTRIN SR 150 MG PO TBCR	NULL	7725
7039	DOXEPIN HCL 50 MG PO CAPS	Doxepin HCl Cap 50 MG	7042
52480	WELLBUTRIN XL 150 MG PO TB24	Bupropion HCl Tab ER 24HR 150 MG	6968
52481	WELLBUTRIN XL 300 MG PO TB24	Bupropion HCl Tab ER 24HR 300 MG	6922
80523	VILAZODONE HCL 40 MG PO TABS	Vilazodone HCl Tab 40 MG	6849
43371	PAXIL 10 MG PO TABS	Paroxetine HCl Tab 10 MG	6813
44901	MIRTAZAPINE 15 MG PO TBDP	Mirtazapine Orally Disintegrating Tab 15 MG	6798
10582	IMIPRAMINE HCL 25 MG PO TABS	Imipramine HCl Tab 25 MG	6650
74599	VENLAFAXINE HCL ER 150 MG PO TB24	Venlafaxine HCl Tab ER 24HR 150 MG (Base Equivalent)	6585
103956	TRAZODONE HCL PO	traZODone HCl	6562
54831	CYMBALTA 30 MG PO CPEP	Duloxetine HCl Enteric Coated Pellets Cap 30 MG (Base Eq)	6485
26238	CELEXA 40 MG PO TABS	Citalopram Hydrobromide Tab 40 MG (Base Equiv)	6402
27552	FLUVOXAMINE MALEATE 100 MG PO TABS	Fluvoxamine Maleate Tab 100 MG	6244
101719	SERTRALINE HCL PO	Sertraline HCl	5893
10583	IMIPRAMINE HCL 50 MG PO TABS	Imipramine HCl Tab 50 MG	5647
33064	VENLAFAXINE HCL 25 MG PO TABS	Venlafaxine HCl Tab 25 MG (Base Equivalent)	5629
33066	VENLAFAXINE HCL 100 MG PO TABS	Venlafaxine HCl Tab 100 MG (Base Equivalent)	5403
54119	FLUOXETINE HCL 20 MG/5ML PO SOLN	Fluoxetine HCl Solution 20 MG/5ML	4766
31386	TRAZODONE HCL 300 MG PO TABS	Trazodone HCl Tab 300 MG	4706
48243	PAROXETINE HCL ER 25 MG PO TB24	Paroxetine HCl Tab ER 24HR 25 MG	4651
74598	VENLAFAXINE HCL ER 75 MG PO TB24	Venlafaxine HCl Tab ER 24HR 75 MG (Base Equivalent)	4581

74600	VENLAFAXINE HCL ER 225 MG PO TB24	Venlafaxine HCl Tab ER 24HR 225 MG (Base Equivalent)	4467
6241	DESIPRAMINE HCL 25 MG PO TABS	Desipramine HCl Tab 25 MG	4466
27553	FLUVOXAMINE MALEATE 50 MG PO TABS	Fluvoxamine Maleate Tab 50 MG	4418
20976	EFFEXOR XR 37.5 MG PO CP24	Venlafaxine HCl Cap ER 24HR 37.5 MG (Base Equivalent)	4403
15188	NORTRIPTYLINE HCL 75 MG PO CAPS	Nortriptyline HCl Cap 75 MG	4326
52739	WELLBUTRIN SR 150 MG PO TB12	Bupropion HCl Tab ER 12HR 150 MG	4203
12168	ZOLOFT 25 MG PO TABS	Sertraline HCl Tab 25 MG	4075
18058	PROZAC 10 MG PO CAPS	Fluoxetine HCl Cap 10 MG	3984
91500	FLUOXETINE HCL PO	FLUoxetine HCl	3908
37510	EFFEXOR 75 MG PO TABS	Venlafaxine HCl Tab 75 MG (Base Equivalent)	3893
43372	PAXIL 40 MG PO TABS	Paroxetine HCl Tab 40 MG	3812
87235	CITALOPRAM HYDROBROMIDE PO	Citalopram Hydrobromide	3777
105378	WELLBUTRIN PO	buPROPion HCl	3710
16386	PAXIL 30 MG PO TABS	Paroxetine HCl Tab 30 MG	3705
121792	VORTIOXETINE HBR 10 MG PO TABS	Vortioxetine HBr Tab 10 MG (Base Equiv)	3563
32736	PROZAC 40 MG PO CAPS	Fluoxetine HCl Cap 40 MG	3537
107520	FLUOXETINE HCL 60 MG PO TABS	Fluoxetine HCl Tab 60 MG	3446
80522	VILAZODONE HCL 20 MG PO TABS	Vilazodone HCl Tab 20 MG	3292
105801	ZOLOFT PO	Sertraline HCl	3283
33065	VENLAFAXINE HCL 50 MG PO TABS	Venlafaxine HCl Tab 50 MG (Base Equivalent)	3224
37994	SERTRALINE HCL 20 MG/ML PO CONC	Sertraline HCl Oral Concentrate for Solution 20 MG/ML	3209
1129	AMITRIPTYLINE HCL 150 MG PO TABS	Amitriptyline HCl Tab 150 MG	3202
48254	PAXIL CR 25 MG PO TB24	Paroxetine HCl Tab ER 24HR 25 MG	3169
74597	VENLAFAXINE HCL ER 37.5 MG PO TB24	Venlafaxine HCl Tab ER 24HR 37.5 MG (Base Equivalent)	3046
94580	LEXAPRO PO	Escitalopram Oxalate	2822
44902	MIRTAZAPINE 30 MG PO TBDP	Mirtazapine Orally Disintegrating Tab 30 MG	2795
7036	DOXEPIN HCL 100 MG PO CAPS	Doxepin HCl Cap 100 MG	2779
10581	IMIPRAMINE HCL 10 MG PO TABS	Imipramine HCl Tab 10 MG	2602
121793	VORTIOXETINE HBR 20 MG PO TABS	Vortioxetine HBr Tab 20 MG (Base Equiv)	2559
84163	AMITRIPTYLINE HCL PO	Amitriptyline HCl	2520
48242	PAROXETINE HCL ER 12.5 MG PO TB24	Paroxetine HCl Tab ER 24HR 12.5 MG	2485
86048	BUPROPION HCL PO	buPROPion HCl	2454
48253	PAXIL CR 12.5 MG PO TB24	Paroxetine HCl Tab ER 24HR 12.5 MG	2367
88576	CYMBALTA PO	DULoxetine HCl	2273
4753	CLOMIPRAMINE HCL 50 MG PO CAPS	Clomipramine HCl Cap 50 MG	2260
99459	PROZAC PO	FLUoxetine HCl	2168
45716	CELEXA 10 MG PO TABS	Citalopram Hydrobromide Tab 10 MG (Base Equiv)	2162
48244	PAROXETINE HCL ER 37.5 MG PO TB24	Paroxetine HCl Tab ER 24HR 37.5 MG	2150
128150	DESVENLAFAXINE SUCCINATE ER 25 MG PO TB24	Desvenlafaxine Succinate Tab ER 24HR 25 MG (Base Equiv)	1978
115687	BUPROPION HCL ER (XL) 450 MG PO TB24	Bupropion HCl Tab ER 24HR 450 MG	1965
72176	PRISTIQ 50 MG PO TB24	Desvenlafaxine Succinate Tab ER 24HR 50 MG (Base Equiv)	1951
37511	EFFEXOR 37.5 MG PO TABS	Venlafaxine HCl Tab 37.5 MG (Base Equivalent)	1899

128921	DULOXETINE HCL 40 MG PO CPEP	Duloxetine HCl Enteric Coated Pellets Cap 40 MG (Base Eq)	1710
44894	REMERON SOLTAB 30 MG PO TBDP	Mirtazapine Orally Disintegrating Tab 30 MG	1696
26357	CLOMIPRAMINE HCL 25 MG PO CAPS	Clomipramine HCl Cap 25 MG	1674
6242	DESIPRAMINE HCL 50 MG PO TABS	Desipramine HCl Tab 50 MG	1638
3093	REMERON 15 MG PO TABS	Mirtazapine Tab 15 MG	1593
80521	VILAZODONE HCL 10 MG PO TABS	Vilazodone HCl Tab 10 MG	1563
44893	REMERON SOLTAB 15 MG PO TBDP	Mirtazapine Orally Disintegrating Tab 15 MG	1518
7491	ELAVIL 25 MG PO TABS	Amitriptyline HCl Tab 25 MG	1500
7488	ELAVIL 10 MG PO TABS	Amitriptyline HCl Tab 10 MG	1450
7040	DOXEPIN HCL 75 MG PO CAPS	Doxepin HCl Cap 75 MG	1436
3094	REMERON 30 MG PO TABS	Mirtazapine Tab 30 MG	1391
6823	WELLBUTRIN SR 100 MG PO TBCR	NULL	1388
6238	DESIPRAMINE HCL 10 MG PO TABS	Desipramine HCl Tab 10 MG	1360
72177	PRISTIQ 100 MG PO TB24	Desvenlafaxine Succinate Tab ER 24HR 100 MG (Base Equiv)	1336
54829	CYMBALTA 20 MG PO CPEP	Duloxetine HCl Enteric Coated Pellets Cap 20 MG (Base Eq)	1308
90158	EFFEXOR PO	Venlafaxine HCl	1307
23872	WELLBUTRIN 100 MG PO TABS	Bupropion HCl Tab 100 MG	1266
104831	VENLAFAXINE HCL PO	Venlafaxine HCl	1255
53337	LEXAPRO 5 MG PO TABS	Escitalopram Oxalate Tab 5 MG (Base Equiv)	1189
80922	VIIBRYD 40 MG PO TABS	Vilazodone HCl Tab 40 MG	1167
36044	NEFAZODONE HCL 100 MG PO TABS	Nefazodone HCl Tab 100 MG	1121
122218	LEVOMILNACIPRAN HCL ER 40 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 40 MG (Base Equivalent)	1079
90794	ESCITALOPRAM OXALATE PO	Escitalopram Oxalate	1059
38018	CITALOPRAM HYDROBROMIDE 10 MG/5ML PO SOLN	Citalopram Hydrobromide Oral Soln 10 MG/5ML	1041
50590	ESCITALOPRAM OXALATE 5 MG/5ML PO SOLN	Escitalopram Oxalate Soln 5 MG/5ML (Base Equiv)	1022
36046	NEFAZODONE HCL 200 MG PO TABS	Nefazodone HCl Tab 200 MG	982
36045	NEFAZODONE HCL 150 MG PO TABS	Nefazodone HCl Tab 150 MG	977
17917	FLUVOXAMINE MALEATE 25 MG PO TABS	Fluvoxamine Maleate Tab 25 MG	965
89706	DULOXETINE HCL PO	DULoxetine HCl	940
7037	DOXEPIN HCL 150 MG PO CAPS	Doxepin HCl Cap 150 MG	929
97999	PAXIL PO	PARoxetine HCl	913
26358	CLOMIPRAMINE HCL 75 MG PO CAPS	Clomipramine HCl Cap 75 MG	911
23873	WELLBUTRIN 75 MG PO TABS	Bupropion HCl Tab 75 MG	875
30321	PROTRIPTYLINE HCL 5 MG PO TABS	Protriptyline HCl Tab 5 MG	860
97988	PAROXETINE HCL PO	PARoxetine HCl	852
38229	SERZONE 150 MG PO TABS	Nefazodone HCl Tab 150 MG	837
30320	PROTRIPTYLINE HCL 10 MG PO TABS	Protriptyline HCl Tab 10 MG	828
95905	MIRTAZAPINE PO	Mirtazapine	820
121791	VORTIOXETINE HBR 5 MG PO TABS	Vortioxetine HBr Tab 5 MG (Base Equiv)	817
52738	WELLBUTRIN SR 100 MG PO TB12	Bupropion HCl Tab ER 12HR 100 MG	804
72073	FLUVOXAMINE MALEATE ER 100 MG PO CP24	Fluvoxamine Maleate Cap ER 24HR 100 MG	764

122219	LEVOMILNACIPRAN HCL ER 80 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 80 MG (Base Equivalent)	764
86679	CELEXA PO	Citalopram Hydrobromide	752
48255	PAXIL CR 37.5 MG PO TB24	Paroxetine HCl Tab ER 24HR 37.5 MG	740
52740	WELLBUTRIN SR 200 MG PO TB12	Bupropion HCl Tab ER 12HR 200 MG	712
45394	MIRTAZAPINE 45 MG PO TBDP	Mirtazapine Orally Disintegrating Tab 45 MG	695
38228	SERZONE 200 MG PO TABS	Nefazodone HCl Tab 200 MG	661
45212	PROZAC WEEKLY 90 MG PO CPDR	Fluoxetine HCl Cap Delayed Release 90 MG	653
90159	EFFEXOR XR PO	Venlafaxine HCl	653
113119	VILAZODONE HCL 10 & 20 & 40 MG PO KIT	Vilazodone HCl Tab Starter Kit 10 (7) & 20 (7) & 40 (16) MG	620
122220	LEVOMILNACIPRAN HCL ER 120 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 120 MG (Base Equivalent)	596
38227	SERZONE 100 MG PO TABS	Nefazodone HCl Tab 100 MG	589
45213	FLUOXETINE HCL 90 MG PO CPDR	Fluoxetine HCl Cap Delayed Release 90 MG	561
72074	FLUVOXAMINE MALEATE ER 150 MG PO CP24	Fluvoxamine Maleate Cap ER 24HR 150 MG	553
122217	LEVOMILNACIPRAN HCL ER 20 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 20 MG (Base Equivalent)	547
29910	REMERON 45 MG PO TABS	Mirtazapine Tab 45 MG	526
6239	DESIPRAMINE HCL 100 MG PO TABS	Desipramine HCl Tab 100 MG	510
7041	DOXEPIN HCL 10 MG/ML PO CONC	Doxepin HCl Conc 10 MG/ML	495
29648	PHENELZINE SULFATE 15 MG PO TABS	Phenelzine Sulfate Tab 15 MG	487
7492	ELAVIL 50 MG PO TABS	Amitriptyline HCl Tab 50 MG	469
119146	DESVENLAFAXINE ER 50 MG PO TB24	Desvenlafaxine Tab ER 24HR 50 MG	465
97070	NORTRIPTYLINE HCL PO	Nortriptyline HCl	439
82218	TRAZODONE HCL ER 150 MG PO TB24	Trazodone HCl Tab ER 24HR 150 MG	431
37509	EFFEXOR 100 MG PO TABS	Venlafaxine HCl Tab 100 MG (Base Equivalent)	430
29178	NORTRIPTYLINE HCL 10 MG/5ML PO SOLN	Nortriptyline HCl Soln 10 MG/5ML	410
99177	PRISTIQ PO	Desvenlafaxine Succinate	404
24605	PAROXETINE HCL 10 MG/5ML PO SUSP	Paroxetine HCl Oral Susp 10 MG/5ML (Base Equiv)	401
48739	WELLBUTRIN SR 200 MG PO TBCR	NULL	379
132523	TRINTELLIX 20 MG PO TABS	Vortioxetine HBr Tab 20 MG (Base Equiv)	361
30290	PROZAC 10 MG PO TABS	Fluoxetine HCl Tab 10 MG	358
105380	WELLBUTRIN XL PO	buPROPion HCl	343
80921	VIIBRYD 20 MG PO TABS	Vilazodone HCl Tab 20 MG	338
6243	DESIPRAMINE HCL 75 MG PO TABS	Desipramine HCl Tab 75 MG	337
100750	REMERON PO	Mirtazapine	336
132522	TRINTELLIX 10 MG PO TABS	Vortioxetine HBr Tab 10 MG (Base Equiv)	324
37507	EFFEXOR 25 MG PO TABS	Venlafaxine HCl Tab 25 MG (Base Equivalent)	311
119147	DESVENLAFAXINE ER 100 MG PO TB24	Desvenlafaxine Tab ER 24HR 100 MG	283
19392	NEFAZODONE HCL 50 MG PO TABS	Nefazodone HCl Tab 50 MG	269
82549	VIIBRYD PO	Vilazodone HCl	266
53826	BUDEPRION SR 150 MG PO TB12	Bupropion HCl Tab ER 12HR 150 MG	263
37508	EFFEXOR 50 MG PO TABS	Venlafaxine HCl Tab 50 MG (Base Equivalent)	258
27929	IMIPRAMINE PAMOATE 75 MG PO CAPS	Imipramine Pamoate Cap 75 MG	245
27926	IMIPRAMINE PAMOATE 100 MG PO CAPS	Imipramine Pamoate Cap 100 MG	238

23796	VIVACTIL 10 MG PO TABS	Protriptyline HCl Tab 10 MG	235
1156	AMOXAPINE 50 MG PO TABS	Amoxapine Tab 50 MG	235
37925	LUVOX 100 MG PO TABS	Fluvoxamine Maleate Tab 100 MG	228
16153	PAMELOR 10 MG PO CAPS	Nortriptyline HCl Cap 10 MG	226
89586	DOXEPIN HCL PO	Doxepin HCl	225
53112	PAROXETINE MESYLATE 20 MG PO TABS	Paroxetine Mesylate Tab 20 MG (Base Equiv)	221
31385	TRANYLCYPROMINE SULFATE 10 MG PO TABS	Tranylcypromine Sulfate Tab 10 MG	216
129677	VILAZODONE HCL 10 & 20 MG PO KIT	Vilazodone HCl Tab Starter Kit 10 (7) & 20 (23) MG	203
7493	ELAVIL 75 MG PO TABS	Amitriptyline HCl Tab 75 MG	197
1153	AMOXAPINE 100 MG PO TABS	Amoxapine Tab 100 MG	195
61428	BUDEPRION XL 300 MG PO TB24	Bupropion HCl Tab ER 24HR 300 MG	192
122246	LEVOMILNACIPRAN HCL ER 20 & 40 MG PO C4PK	Levomilnacipran HCl Cap ER 24HR 20 & 40 MG Therapy Pack	192
19852	SERZONE 50 MG PO TABS	Nefazodone HCl Tab 50 MG	183
1155	AMOXAPINE 25 MG PO TABS	Amoxapine Tab 25 MG	183
72990	BUDEPRION XL 150 MG PO TB24	Bupropion HCl Tab ER 24HR 150 MG	181
59776	SELEGILINE 6 MG/24HR TD PT24	Selegiline TD Patch 24HR 6 MG/24HR	175
38259	NEFAZODONE HCL 250 MG PO TABS	Nefazodone HCl Tab 250 MG	157
16154	PAMELOR 25 MG PO CAPS	Nortriptyline HCl Cap 25 MG	156
37926	LUVOX 50 MG PO TABS	Fluvoxamine Maleate Tab 50 MG	150
7489	ELAVIL 100 MG PO TABS	Amitriptyline HCl Tab 100 MG	146
103953	TRAZAMINE PO	NULL	143
132712	TRINTELLIX PO	Vortioxetine HBr	141
122242	FETZIMA 80 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 80 MG (Base Equivalent)	138
12816	MAPROTILINE HCL 50 MG PO TABS	Maprotiline HCl Tab 50 MG	138
27928	IMIPRAMINE PAMOATE 150 MG PO CAPS	Imipramine Pamoate Cap 150 MG	134
6240	DESIPRAMINE HCL 150 MG PO TABS	Desipramine HCl Tab 150 MG	134
80920	VIIBRYD 10 MG PO TABS	Vilazodone HCl Tab 10 MG	126
53114	PAROXETINE MESYLATE 40 MG PO TABS	Paroxetine Mesylate Tab 40 MG (Base Equiv)	124
24603	PAXIL 10 MG/5ML PO SUSP	Paroxetine HCl Oral Susp 10 MG/5ML (Base Equiv)	122
115898	FORFIVO XL 450 MG PO TB24	Bupropion HCl Tab ER 24HR 450 MG	122
45380	REMERON SOLTAB 45 MG PO TBDP	Mirtazapine Orally Disintegrating Tab 45 MG	117
53111	PAROXETINE MESYLATE 10 MG PO TABS	Paroxetine Mesylate Tab 10 MG (Base Equiv)	117
1230	ANAFRANIL 50 MG PO CAPS	Clomipramine HCl Cap 50 MG	112
122245	FETZIMA 40 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 40 MG (Base Equivalent)	109
12815	MAPROTILINE HCL 25 MG PO TABS	Maprotiline HCl Tab 25 MG	106
16155	PAMELOR 50 MG PO CAPS	Nortriptyline HCl Cap 50 MG	105
59778	SELEGILINE 12 MG/24HR TD PT24	Selegiline TD Patch 24HR 12 MG/24HR	103
116927	BUPROPION HBR ER PO	buPROPion HBr	99
97071	NORTRIPYTLINE HCL PO	Nortriptyline HCl	93
122243	FETZIMA 120 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 120 MG (Base Equivalent)	92
105379	WELLBUTRIN SR PO	buPROPion HCl	89
38230	SERZONE 250 MG PO TABS	Nefazodone HCl Tab 250 MG	86

14441	NARDIL 15 MG PO TABS	Phenelzine Sulfate Tab 15 MG	82
117245	VENLAFAXINE HCL ER PO	Venlafaxine HCl	82
86043	BUPROPION HBR PO	buPROPion HBr	80
20758	SURMONTIL 50 MG PO CAPS	Trimipramine Maleate Cap 50 MG	78
38025	CELEXA 10 MG/5ML PO SOLN	Citalopram Hydrobromide Oral Soln 10 MG/5ML	78
37993	ZOLOFT 20 MG/ML PO CONC	Sertraline HCl Oral Concentrate for Solution 20 MG/ML	74
116013	BUPROPION HCL ER (SR) PO	buPROPion HCl	74
53113	PAROXETINE MESYLATE 30 MG PO TABS	Paroxetine Mesylate Tab 30 MG (Base Equiv)	73
53251	PEXEVA 20 MG PO TABS	Paroxetine Mesylate Tab 20 MG (Base Equiv)	71
59777	SELEGILINE 9 MG/24HR TD PT24	Selegiline TD Patch 24HR 9 MG/24HR	70
1229	ANAFRANIL 25 MG PO CAPS	Clomipramine HCl Cap 25 MG	69
21746	TOFRANIL 25 MG PO TABS	Imipramine HCl Tab 25 MG	69
75930	BUPROPION HBR ER 522 MG PO TB24	Bupropion HBr Tab ER 24HR 522 MG	66
82219	TRAZODONE HCL ER 300 MG PO TB24	Trazodone HCl Tab ER 24HR 300 MG	66
93521	IMIPRAMINE HCL PO	Imipramine HCl	64
132521	TRINTELLIX 5 MG PO TABS	Vortioxetine HBr Tab 5 MG (Base Equiv)	63
122496	FETZIMA PO	Levomilnacipran HCl	61
116014	BUPROPION HCL ER (XL) PO	buPROPion HCl	60
21747	TOFRANIL 50 MG PO TABS	Imipramine HCl Tab 50 MG	58
400628	VENLAFAXINE(COMPOUNDED) 15 MG/ML PO SUSP	venlafaxine (compounded) 15 mg/mL po susp	57
117239	TRAZODONE HCL ER PO	traZODone HCl	55
6271	DESYREL 150 MG PO TABS	Trazodone HCl Tab 150 MG	54
1154	AMOXAPINE 150 MG PO TABS	Amoxapine Tab 150 MG	53
15182	NORPRAMIN 25 MG PO TABS	Desipramine HCl Tab 25 MG	53
95046	LUVOX CR PO	fluvoxaMINE Maleate	53
12817	MAPROTILINE HCL 75 MG PO TABS	Maprotiline HCl Tab 75 MG	51
55184	PROZAC 20 MG/5ML PO SOLN	Fluoxetine HCl Solution 20 MG/5ML	49
75223	CITALOPRAM & DIET MANAGE PROD 10 MG PO MISC	Citalopram Tab 10 MG & Dietary Management Cap Pack	47
32005	NORTRIPYTLINE HCL 25 MG PO CAPS	Nortriptyline HCl Cap 25 MG	47
121979	BRINTELLIX PO	Vortioxetine HBr	46
87415	CLOMIPRAMINE HCL PO	clomiPRAMINE HCl	46
128151	PRISTIQ 25 MG PO TB24	Desvenlafaxine Succinate Tab ER 24HR 25 MG (Base Equiv)	45
72075	LUVOX CR 100 MG PO CP24	Fluvoxamine Maleate Cap ER 24HR 100 MG	45
15737	LUVOX 25 MG PO TABS	Fluvoxamine Maleate Tab 25 MG	43
91526	FLUVOXAMINE MALEATE PO	fluvoxaMINE Maleate	43
122244	FETZIMA 20 MG PO CP24	Levomilnacipran HCl Cap ER 24HR 20 MG (Base Equivalent)	42
76881	BUPROPION HBR ER 174 MG PO TB24	Bupropion HBr Tab ER 24HR 174 MG	41
6272	DESYREL 300 MG PO TABS	Trazodone HCl Tab 300 MG	41
18060	PROZAC 20 MG/5ML PO LIQD	NULL	38
132397	ELAVIL PO	Amitriptyline HCl	37
123813	DESVENLAFAXINE FUMARATE ER 50 MG PO TB24	Desvenlafaxine Fumarate Tab ER 24HR 50 MG (Base Equiv)	33
27522	FLUOXETINE HCL 20 MG/5ML PO LIQD	NULL	33

2057	TRAZODONE HCL POWD	Trazodone HCl Powder	33
1126	AMITRIPTYLINE HCL 10 MG/ML IM SOLN	NULL	33
75929	BUPROPION HBR ER 348 MG PO TB24	Bupropion HBr Tab ER 24HR 348 MG	32
22238	TRIMIPRAMINE MALEATE 25 MG PO CAPS	Trimipramine Maleate Cap 25 MG	32
22239	TRIMIPRAMINE MALEATE 50 MG PO CAPS	Trimipramine Maleate Cap 50 MG	32
16156	PAMELOR 75 MG PO CAPS	Nortriptyline HCl Cap 75 MG	32
7490	ELAVIL 150 MG PO TABS	Amitriptyline HCl Tab 150 MG	32
72076	LUVOX CR 150 MG PO CP24	Fluvoxamine Maleate Cap ER 24HR 150 MG	31
22237	TRIMIPRAMINE MALEATE 100 MG PO CAPS	Trimipramine Maleate Cap 100 MG	30
19544	SINEQUAN 50 MG PO CAPS	Doxepin HCl Cap 50 MG	29
50589	LEXAPRO 5 MG/5ML PO SOLN	Escitalopram Oxalate Soln 5 MG/5ML (Base Equiv)	29
119271	DESVENLAFAXINE ER PO	Desvenlafaxine	27
27927	IMIPRAMINE PAMOATE 125 MG PO CAPS	Imipramine Pamoate Cap 125 MG	27
121840	BRINTELLIX 10 MG PO TABS	Vortioxetine HBr Tab 10 MG (Base Equiv)	27
121841	BRINTELLIX 20 MG PO TABS	Vortioxetine HBr Tab 20 MG (Base Equiv)	27
96617	NEFAZODONE HCL PO	Nefazodone HCl	26
53253	PEXEVA 40 MG PO TABS	Paroxetine Mesylate Tab 40 MG (Base Equiv)	26
82550	VILAZODONE HCL PO	Vilazodone HCl	26
19545	SINEQUAN 75 MG PO CAPS	Doxepin HCl Cap 75 MG	25
97998	PAXIL CR PO	PARoxetine HCl	24
23797	VIVACTIL 5 MG PO TABS	Protriptyline HCl Tab 5 MG	22
89055	DESYREL PO	traZODone HCl	21
97989	PAROXETINE MESYLATE PO	PARoxetine Mesylate	20
53633	BUDEPRION SR 100 MG PO TB12	Bupropion HCl Tab ER 12HR 100 MG	20
53252	PEXEVA 30 MG PO TABS	Paroxetine Mesylate Tab 30 MG (Base Equiv)	19
59804	EMSAM 6 MG/24HR TD PT24	Selegiline TD Patch 24HR 6 MG/24HR	19
89011	DESIPRAMINE HCL PO	Desipramine HCl	19
113548	VIIBRYD 10 & 20 & 40 MG PO KIT	Vilazodone HCl Tab Starter Kit 10 (7) & 20 (7) & 40 (16) MG	19
84224	ANAFRANIL PO	clomiPRAMINE HCl	18
76061	APLENZIN 522 MG PO TB24	Bupropion HBr Tab ER 24HR 522 MG	18
20756	SURMONTIL 100 MG PO CAPS	Trimipramine Maleate Cap 100 MG	18
20757	SURMONTIL 25 MG PO CAPS	Trimipramine Maleate Cap 25 MG	17
53250	PEXEVA 10 MG PO TABS	Paroxetine Mesylate Tab 10 MG (Base Equiv)	17
123815	DESVENLAFAXINE FUMARATE ER 100 MG PO TB24	Desvenlafaxine Fumarate Tab ER 24HR 100 MG (Base Equiv)	17
99446	PROTRIPTYLINE HCL PO	Protriptyline HCl	17
116975	DESVENLAFAXINE SUCCINATE ER PO	Desvenlafaxine Succinate	16
97884	PAMELOR PO	Nortriptyline HCl	15
1231	ANAFRANIL 75 MG PO CAPS	Clomipramine HCl Cap 75 MG	15
21751	TOFRANIL-PM 75 MG PO CAPS	Imipramine Pamoate Cap 75 MG	15
122259	FETZIMA TITRATION 20 & 40 MG PO C4PK	Levomilnacipran HCl Cap ER 24HR 20 & 40 MG Therapy Pack	14
16338	PARNATE 10 MG PO TABS	Tranylcypromine Sulfate Tab 10 MG	14
129681	VIIBRYD STARTER PACK 10 & 20 MG PO KIT	Vilazodone HCl Tab Starter Kit 10 (7) & 20 (23) MG	14

87234	CITALOPRAM & DIET MANAGE PROD PO	NULL	12
19541	SINEQUAN 100 MG PO CAPS	Doxepin HCl Cap 100 MG	12
59874	EMSAM 12 MG/24HR TD PT24	Selegiline TD Patch 24HR 12 MG/24HR	11
103954	TRAZODONE & DIET MANAGE PROD PO	NULL	10
76060	APLENZIN 348 MG PO TB24	Bupropion HBr Tab ER 24HR 348 MG	10
15183	NORPRAMIN 50 MG PO TABS	Desipramine HCl Tab 50 MG	10
15179	NORPRAMIN 10 MG PO TABS	Desipramine HCl Tab 10 MG	10
19543	SINEQUAN 25 MG PO CAPS	Doxepin HCl Cap 25 MG	10
84189	AMOXAPINE PO	Amoxapine	9
21745	TOFRANIL 10 MG PO TABS	Imipramine HCl Tab 10 MG	8
96477	NARDIL PO	Phenelzine Sulfate	8
68121	FLUOXETINE & DIET MANAGE PROD 10 MG PO MISC	Fluoxetine HCl Cap 10 MG & Dietary Management Cap Pack	8
59871	EMSAM 9 MG/24HR TD PT24	Selegiline TD Patch 24HR 9 MG/24HR	7
1891	ASENDIN TABS 50 MG PO	Amoxapine Tab 50 MG	7
98330	PEXEVA PO	PARoxetine Mesylate	7
19540	SINEQUAN 10 MG PO CAPS	Doxepin HCl Cap 10 MG	7
108627	BUPROPION HCL (XL) PO	buPROPion HCl	7
117143	PAROXETINE HCL ER PO	PARoxetine HCl	6
108626	BUPROPION HCL (SR) PO	buPROPion HCl	6
15180	NORPRAMIN 100 MG PO TABS	Desipramine HCl Tab 100 MG	6
7487	ELAVIL 10 MG/ML IM SOLN	NULL	6
27338	ISOCARBOXAZID 10 MG PO TABS	Isocarboxazid Tab 10 MG	6
97986	PARNATE PO	Tranylcypromine Sulfate	5
85979	BUDEPRION XL PO	buPROPion HCl	5
85978	BUDEPRION SR PO	buPROPion HCl	5
75165	AMITRIPTYLINE & DIET MANAGE PR 25 MG PO MISC	Amitriptyline HCl Tab 25 MG & Diet Manage Prod Cap Pack	5
105240	VIVACTIL PO	Protriptyline HCl	5
84461	APLENZIN PO	buPROPion HBr	5
122087	VORTIOXETINE HBR PO	Vortioxetine HBr	5
99460	PROZAC WEEKLY PO	FLUoxetine HCl	4
130049	VIIBRYD STARTER PACK PO	Vilazodone HCl	4
103824	TOFRANIL PO	Imipramine HCl	4
117032	FLUVOXAMINE MALEATE ER PO	fluvoxaMINE Maleate	4
21750	TOFRANIL-PM 150 MG PO CAPS	Imipramine Pamoate Cap 150 MG	4
98385	PHENELZINE SULFATE PO	Phenelzine Sulfate	4
16157	PAMELOR 10 MG/5ML PO SOLN	Nortriptyline HCl Soln 10 MG/5ML	4
19542	SINEQUAN 150 MG PO CAPS	Doxepin HCl Cap 150 MG	3
21749	TOFRANIL-PM 125 MG PO CAPS	Imipramine Pamoate Cap 125 MG	3
104125	TRIMIPRAMINE MALEATE PO	Trimipramine Maleate	3
97063	NORPRAMIN PO	Desipramine HCl	3
103921	TRANYLCYPROMINE SULFATE PO	Tranylcypromine Sulfate	3
2099	NORTRIPTYLINE HCL POWD	Nortriptyline HCl Powder	3

148925	ESKETAMINE HCL (56 MG DOSE) 28 MG/DEVICE NA SOPK	Esketamine HCl Nasal Soln 28 MG/Device x 2 (56 MG Dose Pack)	3
100571	RAPIFLUX PO	FLUoxetine HCl	3
86042	BUPROPION & DIET MANAGE PROD PO	NULL	3
91770	GABOXETINE PO	NULL	3
91498	FLUOXETINE & DIET MANAGE PROD PO	NULL	3
90276	EMSAM TD	Selegiline	2
82404	OLEPTRO 300 MG PO TB24	Trazodone HCl Tab ER 24HR 300 MG	2
82403	OLEPTRO 150 MG PO TB24	Trazodone HCl Tab ER 24HR 150 MG	2
100751	REMERON SOLTAB PO	Mirtazapine	2
93522	IMIPRAMINE PAMOATE PO	Imipramine Pamoate	2
95225	MAPROTILINE HCL PO	Maprotiline HCl	2
121507	KHEDEZLA PO	Desvenlafaxine	2
148927	ESKETAMINE HCL (84 MG DOSE) 28 MG/DEVICE NA SOPK	Esketamine HCl Nasal Soln 28 MG/Device x 3 (84 MG Dose Pack)	2
1881	IMIPRAMINE HCL POWD	Imipramine HCl Powder	2
68122	GABOXETINE 10 MG PO MISC	Fluoxetine HCl Cap 10 MG & Dietary Management Cap Pack	2
21748	TOFRANIL-PM 100 MG PO CAPS	Imipramine Pamoate Cap 100 MG	2
27248	MARPLAN 10 MG PO TABS	Isocarboxazid Tab 10 MG	2
15181	NORPRAMIN 150 MG PO TABS	Desipramine HCl Tab 150 MG	1
103825	TOFRANIL-PM PO	Imipramine Pamoate	1
116112	FORFIVO XL PO	buPROPion HCl	1
97358	OLEPTRO PO	traZODone HCl	1
149210	SPRAVATO (84 MG DOSE) NA	Esketamine HCl	1
121369	KHEDEZLA 100 MG PO TB24	Desvenlafaxine Tab ER 24HR 100 MG	1
121368	KHEDEZLA 50 MG PO TB24	Desvenlafaxine Tab ER 24HR 50 MG	1
121839	BRINTELLIX 5 MG PO TABS	Vortioxetine HBr Tab 5 MG (Base Equiv)	1
101698	SENTRAVIL PM-25 PO	NULL	1
89054	DESVENLAFAXINE SUCCINATE PO	Desvenlafaxine Succinate	1
Notes: Trazodone less than 150mg, Amitriptyline, Nortriptyline, Imipramine, and Amoxapine may be excluded. NULL = Medication record is not linked to Generic Name.			

Appendix 3: ICD codes to identify patients with comorbidities		
Code Type	**Code or Code Range**	**Condition**
ICD-9-CM DX	3310	Alzheimer's
ICD-10-CM DX	G30.x	Alzheimer's
ICD-9-CM DX	14.x- 209.x	Cancer
ICD-10-CM DX	C0.x-C96.x	Cancer
ICD-9-CM DX	43.x-44.39; 7854, V434	Cerebrovascular disease
ICD-10-CM DX	E08.x-E13.x; G45.x- 46.x; 60.x-I79.x; I96; Z9582.x	Cerebrovascular disease
ICD-9-PROC	3848	Cerebrovascular disease
ICD-10-PROC	04R.x-04RY4KZ	Cerebrovascular disease
ICD-9-CM DX	338.x	Chronic pain
ICD-10-CM DX	G89.x	Chronic pain
ICD-9-CM DX	428.x	Congestive heart failure
ICD-10-CM DX	I09.x-I13.x; I50.x; R57.x	Congestive heart failure
ICD-9-CM DX	49.x; 5064; 51.x; 7702	COPD/asthma
ICD-10-CM DX	J4.x- J479	COPD/asthma
ICD-9-CM DX	410.x-4149; 433.x	Coronary artery/heart disease
ICD-10-CM DX	I20.x-I259; 63.x-I6529; Z955; Z9861	Coronary artery/heart disease
ICD-9-CM DX	250.x	Diabetes
ICD-10-CM DX	E10.x; E11.x; E13.x	Diabetes
ICD-9-CM DX	345.x	Epilepsy
ICD-10-CM DX	G40.x-G40B19	Epilepsy
ICD-9-CM DX	00.x-129; 2515; 271.x-2892; 3064; 4474; 45.x; 53.x-57.x; 61.x; 75.x; 78.x; 893.x; 997.x	GI disorders
ICD-10-CM DX	A0.x; A2.x; A4.x; A5.x; B0x; B3.x; B6.x; B7.x-B8.x; E164; E73.x-E74.x; I85.x-1880; K2.x-K6.x; K9.x; N8.x; Q3.x-Q4.x; Q7.x; R10.x-R198	GI disorders
ICD-9-CM DX	V08, 042, 07953	HIV
ICD-10-CM DX	Z21, B20, B9735	HIV
ICD-9-CM DX	401.x-404.93	Hypertension
ICD-10-CM DX	I10.x-I132	Hypertension
ICD-9-CM DX	346.x	Migraine
ICD-10-CM DX	G430.x-G324B1	Migraine
ICD-9-CM DX	278.0x	Obesity
ICD-10-CM DX	E66.x	Obesity
ICD-9-CM DX	715.x; 7330.x	Osteoarthritis/osteoporosis
ICD-10-CM DX	M15.x-M19.x; M800.x; M81.x	Osteoarthritis/osteoporosis
ICD-9-CM DX	331.82-33.2x	Parkinson's disease
ICD-10-CM DX	G20.x-G3183	Parkinson's disease
ICD-9-CM DX	240.x-2469	Thyroid disease
ICD-10-CM DX	E00.x-E079	Thyroid disease

Appendix 4: OPTION-12 Questionnaire

1	The clinician *draws attention to* an identified problem as one that requires a decision making process.	Yes 1	No 0
2	The clinician *states* that there is more than one way to deal with the identified problem ('equipoise').	Yes 1	No 0
3	The clinician *assesses* the patient's preferred approach to receiving information to assist decision making (e.g. discussion, reading printed material, assessing graphical data, using videotapes or other media).	Yes 1	No 0
4	The clinician *lists* 'options', which can include the choice of 'no action'.	Yes 1	No 0
5	The clinician *explains* the pros and cons of options to the patient (taking 'no action' is an option).	Yes 1	No 0
6	The clinician explores the patient's *expectations* (or ideas) about how the problem(s) are to be managed.	Yes 1	No 0
7	The clinician explores the patient's *concerns* (fears) about how problem(s) are to be managed.	Yes 1	No 0
8	The clinician checks that the patient has *understood* the information.	Yes 1	No 0
9	The clinician offers the patient explicit *opportunities* to ask questions during the decision making process.	Yes 1	No 0
10	The clinician elicits the patient's *preferred level of involvement* in decision-making.	Yes 1	No 0
11	The clinician indicates the need for a *decision making* (or *deferring*) stage.	Yes 1	No 0
12	The clinician indicates the need to review the decision (or *deferment).*	Yes 1	No 0