Integrating patient-reported outcomes and electronic health record data to improve clinical decision support for depression treatment

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Abstract

Purpose: The objective of this study, named EffectRx, was to develop, implement, and assess a scalable system of patient data collection and clinician feedback in multiple primary care practices.

Scope: Primary care physicians (PCPs) diagnose and treat a substantial amount of depression among adults. We aimed to address barriers to effective depression treatment primary care by electronically collecting medication-related side effect and depression severity data from patients and providing automated feedback to clinicians.

Methods: EffectRx involved the development and implementation of a system of patient data collection and clinician feedback. We collected data on medication-related side effects, depression severity, medication adherence, and receipt of cognitive behavioral therapy (CBT) from patients taking an antidepressant for depression using an existing health information technology system at the University of Colorado. Patient-specific data were then provided to clinicians in automatically-generated reports to use at the point-of-care.

To pilot test the system, EffectRx used a prospective cohort design and was implemented in three primary care practices within the University of Colorado Healthcare system. Adult (age 18+) patients prescribed an antidepressant to treat depression were eligible and recruited on a rolling basis throughout the funding period. Data collection was ongoing for 3-6 months per patient. Electronic medical record data for all participants will be obtained approximately one year after patient enrollment ended.

Results: Overall clinician and patient feedback about the data collection and clinician feedback process was positive, and the data collection and automated report generation system worked successfully throughout the study period. Twenty patients were enrolled in the pilot study and completed at least one survey (average age=38 years). The majority of patients (65%) indicated they had filled their antidepressant at baseline. The most common side effects at baseline were agitation and headaches (reported by 75% of patients). Frequency of side effects decreased over the study for the majority of patients who completed more than one survey (n=13). The mean PHQ-9 score at baseline was 10.1 (median=10.5, range=0-22). Among patients who completed more than one survey, 69% reached remission and 77% reached treatment response by the time they completed their last survey. Note that because final data is not available for all participants, data analysis is preliminary. An updated final report will be submitted upon completion.

Key words: antidepressants; primary care; side effects; depression severity; tolerability; adherence; patient-reported outcomes; electronic data capture; health information technology

PURPOSE

The objective of this study was to develop, implement, and assess a scalable system of patient data collection and clinician feedback to improve depression care management in multiple primary care practices. We leveraged the Electronic National Quality Improvement and Research Network (eNQUIRENet), a network of non-integrated primary care practices within the American Academy of Family Physicians. We collected data on medication-related side effects, depression severity, medication adherence, and receipt of cognitive behavioral therapy (CBT) from patients taking an antidepressant for depression and reported the patient-specific data into feedback provided to clinicians at the point-of-care. We assessed the system of data collection from patients and enhanced feedback to clinicians using surveys and semi-structured interviews with patients and clinicians. The study was named EffectRx and had two specific aims:

Specific Aim 1: Enhance an existing clinician feedback report by integrating novel data collected electronically from patients between clinical visits with medication adherence and EHR data; pilot test the data collection and enhanced report in eight eNQUIRENet primary care practices.

Specific Aim 2: Using semi-structured interviews with up to 12 patients and up to 8 clinicians who participate in Specific Aim 1, assess the feasibility and utility of the patient data collection and enhanced clinician feedback by obtaining: (1) patients' reactions to completing the online surveys and the usefulness of their clinician receiving the information from those surveys; and (2) clinicians' opinions regarding the feedback's content, format, timing, and associated resource burden.

SCOPE

Background

Depression is a common and burdensome health condition with many barriers to treatment, even though effective treatment options exist. The estimated lifetime prevalence of depression is over 20% in the United States general population.[1,2] Depression is also the leading cause of disability worldwide as measured by the number of years lived with a disabling condition.[1,3] Up to 60% of depressed patients have severe to very severe symptoms, resulting in decreased productivity at home and work, more frequent use of healthcare, and overall economic costs estimated at several billion dollars per year.[1,4-6] Beyond the avoided loss in productivity and economic burden, effectively-treated depression results in decreased risk of physical disability, medical conditions such as coronary heart disease and diabetes, suicidality and mortality.[7-14] Antidepressants are an effective first line treatment for adults with depression, yet non-adherence is common. A recent study of e-prescriptions found that 26% of new prescriptions for antidepressants were never filled.[15] Non-adherence after initial fill is also high, with up to 68% of patients stopping their antidepressant within three months of its initiation.[16] Tolerability--the occurrence, severity and burden of side effects--is known to be associated with decreased treatment adherence.[17,18] In particular, side effects felt to be very bothersome may double the risk of discontinuation.[19] Many clinicians are not aware a patient is experiencing side effects or that the patient has discontinued their medication.[17,20,21] These barriers to effective pharmacologic treatment of depression represent an area for needed intervention, particularly in primary care practices.

Primary care physicians (PCP) diagnose and treat a substantial amount of depression among adults, making primary care practices an ideal setting for testing and implementing strategies for improved clinical decision support and patient-centered depression care management. Nearly 50% of people with mental health problems receive all of their health care from their PCP, including depression treatment.[22,23] Depression is listed as a diagnosis for nearly 10% of office visits in primary care, and up to 14% of primary care patients are estimated to have major

depressive disorder at any point in time.[24-26] Nearly half of all antidepressant-related visits are with a PCP, and at least 60% of first antidepressant prescriptions are written by a PCP.[27-30]

Context

Our system of electronically collecting data from patients and providing automated and actionable feedback to the clinician has the potential to decrease the burdens on the practice and lead to an increase in effective depression treatment compared to care-as-usual. The automated system will also be scalable for implementation in a wide variety of practice settings.

We aimed to address barriers to effective antidepressant treatment of depression, such as non-adherence, while decreasing the burden on practices by electronically collecting data from patients and providing automated feedback to the clinician in a timely manner. The conceptual basis of this proposal was based on the measurement based care framework in that we provided enhanced feedback to clinicians that included specific measurement-based data elements collected from the patient. We developed and tested the online data collection tool and system, and enhanced feedback report for clinicians to use at the point-of-care and between patient visits (Specific Aim 1). We will also assess the data collection and enhanced feedback system from the perspective of both patients and clinicians (Specific Aim 2).

Settings

The EffectRx project was implemented within a national distributed network of non-integrated primary care practices, demonstrating the scalability of the resulting system to diverse primary care settings. The Electronic National Quality Improvement and Research Network (eNQUIRENet) is a health data network that links EHR data across non-integrated primary care practices. In 2005, the Agency for Healthcare Research and Quality (AHRQ) created the Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) Network to support and carry-out research with a focus on comparative clinical effectiveness and outcomes of different treatment approaches. eNQUIRENet, developed by the Colorado DEcIDE (CO-DEcIDE) Center in collaboration with the American Academy of Family Physicians National Research Network (AAFP NRN), is a federated network that links EHR data across 345 non-integrated primary care practices representing over 3 million patients and 2,000 clinicians. The network captures, codes and standardizes approximately 100 unique data elements per patient for up to 10 years of time, with an average of over 48 months of data across all member practices.

Once funding was confirmed, efforts were made to recruit practices through eNQUIRENet. Appropriate practices were identified and contacted by Dr. Wilson Pace (Co-Investigator and Director (at the time) of the AAFP NRN). They were provided with detailed information about the study and were able to ask questions for Dr. Pace and Dr. Heather Anderson about the study. Ultimately, EffectRx was successfully implemented in three primary care practices, all members of eNQUIRENet, within the University of Colorado Healthcare system (UCH): (1) Women's Integrated Services in Health (WISH) is a clinic designed specifically for women's healthcare needs and is located on the Anschutz Medical Campus in Aurora, Colorado; (2) UCHealth Primary Care – Family and Internal Medicine is a NCQA patient-centered medical home located in Lone Tree, a suburb of Denver, Colorado; (3) AF Williams Family Medicine Center is a NCQA patient-centered medical home located in metro Denver, Colorado. A fourth practice enrolled in the study but never successfully recruited any patients.

Participants

To pilot test the electronic data collection and point-of-care report (Specific Aim 1), patients who met the following eligibility criteria were recruited from the primary care practices described above: (1) age 18+; (2) taking an antidepressant to treat depression; (3) not pregnant; (4) had a personal e-mail address and regular access to the internet.

Recruitment methods

Three recruitment methods were used in this study. The original recruitment method involved medical staff within the clinics identifying eligible patients and telling them about the study. Fliers were also posted in common areas (restrooms, exam rooms). Medical staff were provided with copies of the Study Enrollment guide, which was a one-page perforated sheet that included a brief checklist of eligibility criteria on the top half and information for patients on the bottom half. For interested patients, medical staff completed the bottom half of the Study Enrollment Guide by filling-in the patient's medical record number (which they needed to register for the study). The bottom half of the Study Enrollment Guide was then given to the patient to take with them. There were blank spaces on the Study Enrollment Guide for the patient to write the user name and password that they chose during the online registration process. Interested patients were given access to either a tablet or computer at their clinician's office from which they could access the study website to consent and register. They could also access the website once they left the clinic visit. The online consent process was secure and approved by the Colorado Multiple Institutional Review Board (COMIRB). This patient recruitment method did not result in the number of participants as originally anticipated.

The second recruitment method was made available in May 2015. On a weekly basis, an automated query of the Clinical Data Repository (CDR; described below) was used to identify all patients meeting study inclusion criteria in the past 7 days. A pdf report was automatically generated and placed in a secure file folder behind the practice's firewall. Only staff at the practice had access to the folder. The Practice Champion accessed the report on a weekly basis and sent e-mails to or called patients that met study eligibility criteria. The email indicated that the patient was eligible for a study being conducted by the University Of Colorado School Of Pharmacy based on a medication that was prescribed at their last visit. It did not mention depression or antidepressants. It briefly described the study and included an electronic link to the website where the patient could register and consent for the study and complete their first survey. This recruitment was not successful in recruiting new patients because the Practice Champions rarely had enough time to contact patients on a weekly basis.

The third recruitment option was introduced in February 2016 and involved a research assistant from the study team sending an e-mail to the Practice Champion at each practice on a weekly basis, listing patients eligible for the study (identified from the query described above). The Practice Champion responded to the e-mail with an indication for each patient of whether or not it was OK to contact the patient regarding the study. The study's research assistant then mailed eligible, practice-approved patients a letter on behalf of the practice inviting them to participate in the study. Several new patients were recruited using this method.

The first recruitment method was most successful in that the majority of patients were recruited using this method. However, it was also implemented for a longer period of time than the latter two methods. The third recruitment method is likely to have been most successful if it had been implemented for longer. The second method was not successful because of the time burden it placed on the Practice Champion to contact the patients.

Patients were compensated with a $10 electronic gift card (www.icardgiftcard.com) after consenting and registering for the study and completing their first survey, an additional $20 electronic gift card after completing the study (i.e., all required side effect and PHQ-9 surveys), and an additional $10 for completing the end-of-study assessment survey.

METHODS

Pilot Study design

EffectRx used a prospective cohort design. Eligible patients were recruited from participating primary care practices using methods as described above from June 2014 through July 2016.

Once a patient was enrolled in the study, data collection was ongoing for up to six months. These data collection procedures are described in more detail below.

Data sources/collection

Specific Aim 1

Once a patient was enrolled in the pilot study, data collection was ongoing for at least three months and up to six months. At each data collection time point, patients received an e-mail asking them to complete the set of instruments (described below) online. The instruments were presented to the patients as one continuous instrument, with one question presented on each screen. Data was collected outside the point-of-care, at the following time points based on clinical recommendations and pending appointment dates: (1) at baseline (i.e., when the patient consented and registered for the study); (2) three to four days prior to each scheduled clinical visit; and (3) monthly, if a patient did not have a clinical visit scheduled within the subsequent month AND had not reached remission based on their prior PHQ-9 score. A patient's study period ended once they had been in the study for at least three months and they reached remission (PHQ-9 total score < 5), or had been in the study for six months.

The specific timing of data collection was a dynamic process using an algorithm based on several factors including time from last completed survey, next pending appointment, time from initial survey and change in PHQ-9 score between initial and last survey. Participating practices were involved in decisions regarding these algorithms. Pending/upcoming appointment dates were obtained from the CDR using the point-of-care protocol engine on a nightly basis and used in the algorithm that determined on a patient-by patient basis exactly when they received an e-mail notification to complete the study instrument. The system was "smart" in requesting data from patients only when necessary, based on the algorithms defined by the study team and participating practices. Patients who provided data more frequently were those who did not respond to treatment and did not have regular follow-up appointments scheduled, or had very frequent follow-up visits scheduled.

A final extract of EHR data will be obtained for all study subjects 12 months after patient recruitment ended (August 1, 2017) and will be linked to their study data. This will allow for at least six months of follow-up data after the last enrolled patient's study period ends. In addition, EHR data will be extracted for all patients with a diagnosis of depression during the study period from the clinics participating in the study. This limited dataset will be de-identified prior to being made available to the study team. The data will be used to compare baseline characteristics of patients who participated in the study to those who did not participate, and to compare clinical outcomes if available. The following EHR data elements will be obtained: Demographic Information (Year of birth, Gender, Race/Ethnicity; Prescribed Medications; Diagnoses (Problem List, Encounter-Level Diagnoses linked to visit record; Vital Signs (Systolic Blood Pressure, Diastolic Blood Pressure, Height, Weight); PHQ-2 results; PHQ-9 results. An updated final report will be submitted upon completion of all analyses.

Specific Aim 2

All patients were asked to complete a final survey asking them about their experiences during the study. Questions covered the following topics:

- ease of online consent and registration process
- ease of online completion of the PHQ-9 and side effects survey instrument
- frequency of data collection
- motivation to complete online instruments
- helpfulness of patient-centered feedback at the end of each online session
- utilization during encounters with their clinician of the information they provided online throughout the study

Now that patient enrollment has ended, we will interview at least one clinician from each of the participating practices. The interview has been developed to collect information from clinicians regarding the following:

- timing of data collection and receipt of report
- online method of data collection from patients
- clinical utility of information added to the Patient Recommendation Report
- utility of immediate alerts and ad hoc, non-urgent updates
- suggestions for improvement of feedback report
- associated resource burden (for example, staff time to print/download reports; clinician time to review reports; staff and clinician time to respond to immediate alerts)

Intervention

We leveraged health information technology systems already in place to collect and integrate key pieces of patient-centered information into a patient-specific report for clinicians to use at the point-of-care.

Clinical Data Repository

Every eNQUIRENet practice included in this study used an EHR and also housed a local relational database referred to as the Clinical Data Repository (CDR). The CDR is a standardized database drawn from the EHR that includes relevant clinical information such as: appointment dates and reasons; diagnosis dates, codes, and descriptions; family history; insurance coverage details; medications ordered (type, date, dose, refills allowed); dates and types of procedures ordered and completed; vital signs, lab dates and results; and standardized instruments such as the PHQ-9. For this project, all data mapping and data extraction-transfer-load processes were conducted using tools from DARTNet Institute, Inc. DARTNet, Inc. abstracts data from multiple eNQUIRENet practices and standardizes the data elements across the different EHR products into a local CDR. De-identified data extracts are then shared across practices within eNQUIRENet using DARTNet, Inc. and other vendors as trusted third parties. This system allows the network to act as a virtual data warehouse, while allowing each clinical organization to keep control over its own data while they have the ability to securely share data with other practices within the network.

Collection of patient-reported data

An online instrument was used to collect data from patients regarding their frequency, intensity, and burden of medication-related side effects; their depression severity and symptoms (PHQ-9); and whether they were referred to or received CBT and filled their antidepressant prescription. Additional items to screen for increased suicide risk were also included. See Figure 1 for example screen shots from the online instrument. Data was collected from patients using the existing iHealth Connect system. iHealth Connect was developed and is maintained and operated by the University of Colorado Department of Family Medicine Information Services group, under the direction of Wilson Pace, MD, a co-investigator in this proposal and a primary architect of eNQUIRENet. iHealth Connect has provided researchers across the USA and in Canada access to secure data collection, feedback and clinical alerting systems utilizing the web, mobile web, IVR, text messaging and email as indicated for each study. The system has been in continuous operation for over seven years hosting multiple clinical and research applications. A web-based secure data exchange was enhanced to link iHealth Connect with DARTNet CDRs across the country.

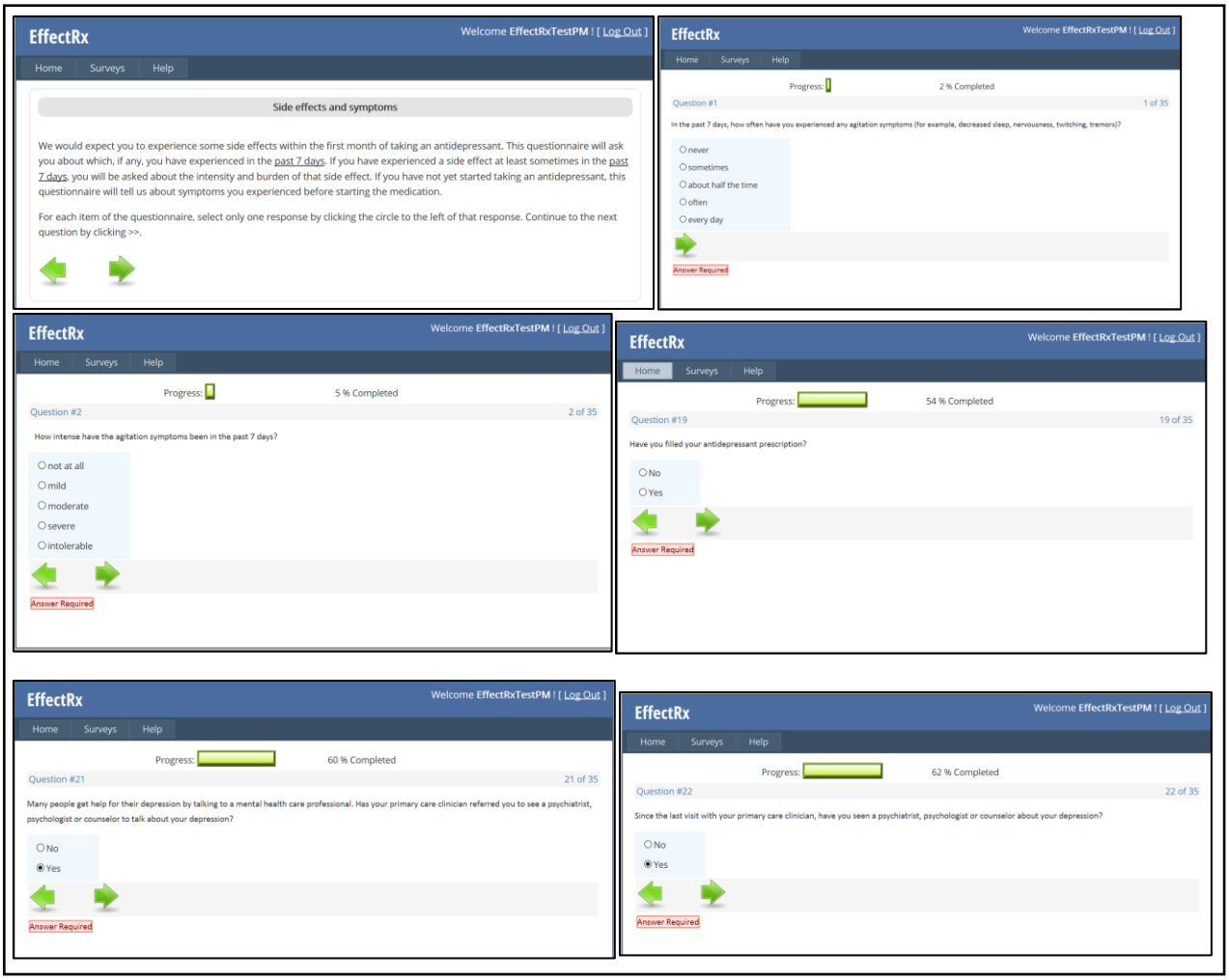

Figure 1. Example screen shots from the online data collection instrument completed by patients

Medication-related side effects

The instrument implemented in EffectRx to collect information from patients about medication-related side effects was developed and pilot tested as part of Dr. Anderson's AHRQ Comparative Effectiveness Career Development Award. The instrument asks patients about the frequency, intensity (i.e., severity) and burden (i.e., interference with daily life) of side effects they may have experienced in the past week. It was modeled after two existing instruments: the Frequency, Intensity, and Burden of Side Effects Rating (FIBSER), a three-item instrument created for and validated during the STAR*D practical clinical trial of pharmacologic treatment for new cases of depression;[31] and the Toronto Side Effects Scale (TSES), a 32-item instrument used by clinicians to elicit side effect experiences from patients.[32] However, these two instruments were each lacking an important component. While the FIBSER asks patients about three characteristics (frequency, intensity and burden) of side effects in general, it does not link these characteristics to any particular side effect or group of side effects. The TSES asks about the frequency and severity of 32 specific side effects but does not ask about the burden of the events, found to be the most useful tolerability characteristics in monitoring depression treatment.[33] Specifically, the instrument used in EffectRx asks about frequency, intensity and burden of specific groups of side effects (agitation, gastrointestinal, sedation, headache, sexual

dysfunction, and other). These groups of side effects are consistent with those most commonly reported with use of selective serotonin reuptake inhibitors.[34]

Depression severity and symptoms

The PHQ-9 is a validated instrument used to measure the severity of depression symptoms in a primary care setting.[35] The PHQ-9 can be used to screen for depression and to measure the baseline severity of depression at the time of diagnosis, while the repeated use of the PHQ-9 yields change scores and absolute thresholds to measure treatment outcomes such as response and remission. The PHQ-9 also includes one item that asks the patient about thoughts of death or hurting themselves. For the current study, two additional items were asked of patients who indicated any thoughts of death or hurting themselves on the PHQ-9: had these thoughts worsened, and did their clinician know about them.

Receipt of CBT, medication adherence

Participants were asked if they had been referred by their PCP to a psychiatrist, psychologist or counselor for CBT for their depression, and if they had actually seen a psychiatrist, psychologist or counselor for their depression since their last visit with their PCP. They were also asked if they had filled their antidepressant prescription, and if so, how many doses of their antidepressant they had missed in the past 7 days.

Point-of-care feedback to clinicians

A patient-specific point-of-care report (Figure 2) was developed that included a summary of the patient's depression scores, along with their responses to each item of the online instrument described above. The depression summary information included the baseline PHQ-9 score, most recent prior PHQ-9 score, current PHQ-9 score, current depression severity category (mild, moderate, moderately severe, or severe), and whether they had reached treatment response or remission. Thresholds were determined for all side effect intensity (severe or intolerable) and burden (severe or unable to function) items, with any responses above the threshold highlighted in the report. PHQ-9 items with a response of "more than half the days" or more often were also highlighted in the report.

A point-of-care report was generated every time a patient completed an online instrument. The pdf containing the report was automatically placed within a secure file folder behind the UCH firewall and was only accessible by clinicians specified for each practice site. Practice Champions distributed the reports to clinicians.

An algorithm was implemented within an existing secure action messaging system within IHealth Connect to alert study team members to patients who may be at imminent risk for a suicide attempt. The algorithm would have prompted an immediate text message alert to Drs. Heather Anderson and Wilson Pace for any patient who met the following criteria: (1) indicated they had thoughts of death or hurting themselves (from the PHQ-9); indicated these thoughts has worsened; and (3) indicated their clinician did not know they were having these thoughts. No such urgent messages were ever generated during the study.

Measures

Specific Aim 1

The primary outcome measures for Specific Aim 1 were created from data collected through the online instrument described above and administered to patients throughout the study period.

EffectRx POC Report — Completed: **3/14/2014**

Practice:	Patient Name:	DOB:	ID:
AF Williams Family Medical Center	**Zzzztestfifty, Zzzztestfifty**	**1/1/1980**	**2303392**

Baseline PHQ-9 total score:	**2**	on	3/5/2014		
Prior PHQ-9 total score:	**11**	on	3/14/2014		
Current PHQ-9 total score:	**7**	on	3/14/2014	Current depression severity:	**Mild**
Patient has reached **response.**				*High-risk items: **#27, #29**	

#	Question	Answer
1	In the past 7 days, how often have you experienced any agitation symptoms (for example, decreased sleep, nervousness, twitching, tremors)?	never
2	How intense have the agitation symptoms been in the past 7 days?	N/A
3	How much have the agitation symptoms interfered in your daily life over the past 7 days?	N/A
4	In the past 7 days, how often have you experienced any gastrointestinal symptoms (for example, abdominal pain, nausea, diarrhea, constipation)?	never
5	How intense have the gastrointestinal symptoms been in the past 7 days?	N/A
6	How much have the gastrointestinal symptoms interfered in your daily life over the past 7 days?	N/A
7	In the past 7 days, how often have you experienced any sedation symptoms (for example, drowsiness, increased sleep, dizziness)?	never
8	How intense have the sedation symptoms been in the past 7 days?	N/A
9	How much have the sedation symptoms interfered in your daily life over the past 7 days?	N/A
10	In the past 7 days, how often have you experienced any headaches?	never
11	How intense have the headaches been in the past 7 days?	N/A
12	How much have the headaches interfered in your daily life over the past 7 days?	N/A
13	In the past 7 days, how often have you experienced any sexual dysfunction (for example, decreased sexual drive, problems achieving orgasm, erectile dysfunction)?	never
14	How intense has the sexual dysfunction been in the past 7 days?	N/A
15	How much has the sexual dysfunction interfered in your daily life over the past 7 days?	N/A
16	In the past 7 days, how often have you experienced any other symptoms (for example, sweating, flushing, fluid retention, blurred vision, dry mouth, weight gain/loss, change in appetite)?	never
17	How intense has the other symptom(s) been in the past 7 days?	N/A
18	How much has the other symptom(s) interfered in your daily life over the past 7 days?	N/A
19	Have you filled your antidepressant prescription?	No
20	Are you taking your antidepressant as prescribed?	N/A
21	Many people get help for their depression by talking to a mental health care professional. Has your primary care clinician referred you to see a psychiatrist, psychologist or counselor to talk about your depression?	No
22	Since the last visit with your primary care clinician, have you seen a psychiatrist, psychologist or counselor about your depression?	No
	PHQ-9 Items:	
23	Little interest or pleasure in doing things	Not at all
24	Feeling down, depressed, or hopeless	Several days
25	Trouble falling or staying asleep, or sleeping too much	Not at all
26	Feeling tired or having little energy	Several days
27	Poor appetite or overeating	*More than half the days
28	Feeling bad about yourself – or that you are a failure or have let yourself or your family down	Not at all
29	Trouble concentrating on things, such as reading the newspaper or watching television	*Nearly every day
30	Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	Not at all
31	Thoughts that you would be better off dead, or of hurting yourself in some way	Not at all
32	If you indicated any problems above, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Somewhat difficult

Figure 2. Patient-specific point-of-care report

Depression severity, response, and remission. The PHQ-9 total score ranges from 0 to 27. Category of baseline depression severity was based on previously validated thresholds of the total score: mild (0-4), moderate (5-9), moderately severe (10-14) or severe (15+).[35] Depression remission was defined as a PHQ-9 total score < 5 (assuming a prior score ≥ 5), while treatment response was defined as a PHQ-9 total score < 10 (assuming a prior score ≥ 10) and/or a 50% decrease in PHQ-9 total score (Table 1).[33,36]

Suicidal ideation. The last item of the PHQ-9 asks respondents if they have had "thoughts that they would be better off dead, or of hurting themselves in some way" in the past two weeks, with responses ranging from "not at all" (0) to "nearly every day" (3). An indication of several days or more on this item has been found to accurately reflect suicidal ideation.[37] *Emergent suicidal ideation* was defined as a score ≥ 1 (several days or more), with prior score(s) equal to zero. *Worsening suicidal ideation* was defined as any increase in the current suicidal ideation score compared to the prior score (Table 1).

Side effect tolerability. The patient-reported side effect tolerability instrument collected information on the frequency, intensity, and burden of specific side effects experienced in the past seven days. The intensity and burden of specific side effects were included in the patient-specific point-of-care report because each implies the side effect occurred at some frequency. Side effect intensity and burden are collected on a scale from "none/not at all" to "intolerable/unable to function." (Table 1)

Receipt of CBT. Two questions were included at the end of the side effect tolerability instrument that asked patients if: (1) they have been referred to see a psychiatrist, psychologist or counselor to talk about their depression, and (2) they have seen a psychiatrist, psychologist or counselor to talk about their depression since their last visit with their PCP (Table 1).

Table 1. Definitions of measurements and point-of-care report elements

Measurement	Source	Definition
Depression		
Baseline severity	PHQ-9 total score (baseline)	0-4 = mild 5-9 = moderate 10-14 = moderately severe 15+ = severe
Response	PHQ-9 total score	(1) Current score < 10 (assuming a prior score ≥ 10) OR (2) 50% decrease from prior to current score
Remission	PHQ-9 total score	Current score < 5 = remission (assuming a prior score ≥ 5)
Suicidal ideation		
Emerging	PHQ-9 suicidal ideation item	Current score > 0 with prior score(s) = 0
Worsening	PHQ-9 suicidal ideation item	Any increase in current score compared to prior score
Side effect tolerability		
Intensity	Side effect instrument	Intensity rated as "severe" or "intolerable"
Burden	Side effect instrument	Burden rated as "severe" or "unable to function"
Referral to/ receipt of CBT	Side effect instrument	Referred to CBT (yes/no) Received CBT since last clinical visit (yes/no)

Specific Aim 2
The outcome measures from the second stage of EffectRx (Specific Aim 2) will come from patient surveys and semi-structured interviews with clinicians who participated in Specific Aim 1. Measures will include the following:

According to patients:

- ease of online consent and registration process
- ease of online completion of the PHQ-9 and side effects survey instrument
- frequency of data collection
- motivation to complete online instruments
- helpfulness of patient-centered feedback at the end of each online session
- utilization during encounters with their clinician of the information they provided online throughout the study

According to clinicians:

- timing of data collection and receipt of report
- online method of data collection from patients
- clinical utility of information added to the Patient Recommendation Report
- utility of immediate alerts and ad hoc, non-urgent updates
- suggestions for improvement of feedback report
- associated resource burden (for example, staff time to print/download reports; clinician time to review reports; staff and clinician time to respond to immediate alerts)

Limitations
Limitations of EffectRx were primarily related to practice recruitment, patient recruitment, and availability of fulfillment data for study participants. The original intent was to recruit eight primary care practices, and at least that many expressed interest in the study during the development of the proposal. There were two main barriers to participation once funding was received and practices were being actively recruited: (1) practices had already started incorporating use of the PHQ-9 into their regular depression care and did not want their patients completing too many PHQ-9s, resulting in survey fatigue; and (2) practices had already engaged in one or more other research studies and did not want to burden their practice population with an additional study.

Every effort was made to enroll 30 patients at each practice and obtain complete follow-up on all enrolled patients. After nearly one year using the original recruitment method, we were not on track to reach our goal of 30 patients at each site so new recruitment methods were approved by COMIRB and implemented in order to kick start patient recruitment. However, neither method resulted in successful recruitment that met our original goals. While the semi-structured interviews with clinicians have not yet been completed, informal conversations with clinicians throughout the study indicate that a major reason for low recruitment was that clinicians did not think about the study when with patients and therefore did not tell them about the study. Another potential explanation for low recruitment was the fact that eligible patients were all being prescribed an antidepressant to treat depression. We recognize that this is a challenging population from which to collect data, particularly online. We believe the ideal primary care practice in which to implement our patient recruitment was one in which behavioral health care was integrated. In retrospect, better recruitment could have been obtained by having a full-time Research Assistant interact with the participating practices on a regular basis and do in-person recruitment and consenting of patients at the practices on a regular basis.

The original study included the obtainment of medication fulfillment data to be linked with patient data collected during the study. However, valid and complete fulfillment data was not ultimately

feasible so it was excluded from the final project. However, two questions were added to the data collection instrument that asked if the patient had filled their antidepressant and if so, how many doses they had missed in the past week. These items were used to describe adherence.

RESULTS

Principal findings

Specific Aim 1

The objective of this aim was to develop, implement, and pilot test a system to electronically collect data from patients taking an antidepressant to treat depression and incorporate that patient-reported information into an automatically-generated report for their clinician to use at the point-of-care. The study team was successful in developing and implementing the system, which was comprised of four parts:

1. the online study registration and consent process, which was housed in iHealthConnect
2. an online instrument completed by patients through iHealthConnect that included questions about medication-related tolerability, medication adherence, and the PHQ-9
3. the patient-reminder algorithm that sent participants an email when it was time to complete a survey; the timing of these requests was based on upcoming appointment dates and the amount of time since their last survey completion
4. automatically-generated reports in PDF format that included all information provided by the participants and were provided to clinicians to be used at the point-of-care

The success of the development and implementation of the system was evident by the fact that participants in the pilot study were able to register and consent for the study online and subsequently complete online surveys when logged into iHealthConnect; reminder e-mails were automatically sent to participants at appropriate times; and patient-specific reports were generated for clinicians when their patients completed the online instrument. The process involved trouble-shooting and testing by the study team before being implemented during the pilot test at the three primary care practices.

Twenty patients were recruited into the pilot study and completed at least one survey (mean=2.85 surveys, median=2 surveys, range=1-19 surveys). Only one of these 20 participants was male. The average age at study baseline was 37.3 years (median=33.7 years, range=21.9-64 years). The majority of patients (65%) indicated they had filled their antidepressant at baseline; only three patients indicated missing any doses in the past week. The majority (65%) had been referred to a mental health professional by their PCP.

The most commonly reported side effects at baseline were agitation and headaches, each reported by 75% of patients (Figures 2a-2c). Agitation occurred more frequently, with 20% of patients indicating they experienced the side effect nearly every day in the past week. Gastrointestinal (GI) symptoms and sexual dysfunction were the most intolerable side effects, followed by agitation and headache. With respect to burden, GI symptoms were reported to be severe by 15% of patients. None of the types of side effects were reported to have caused the patients to be unable to function.

Over the course of the study, frequency of side effects decreased for the majority of patients who completed more than one survey (n=13). Frequency of agitation decreased for 54% of patients; frequency of GI symptoms decreased for 38% of patients; frequency of sedation decreased for 31%; frequency of headaches decreased for 31%; frequency of sexual dysfunction decreased for 38%; and frequency of other symptoms decreased for 62%.

The mean PHQ-9 score at baseline was 10.1 (standard deviation=7.0, median=10.5, range=0-22). The mean PHQ-9 score at baseline was significantly higher for patients who had not yet filled their antidepressant (n=7, mean PHQ-9 score=14.7) compared to patients who had filled

their antidepressant (n=13, mean PHQ-9 score=7.5; t-value=2.47, $p<0.05$). Thirty-percent (n=6) of patients were categorized as mild depression, 15% (n=3) as moderately depressed, 30% (n=6) as moderately severely depressed, and 25% (n=5) as severely depressed at baseline. Twenty-percent (n=4) indicated they had thoughts they would be better off dead or of hurting themselves on several of the days in the past week. No patients indicated these thoughts had worsened and no patients indicated that their clinician did not know about these thoughts. Among the patients who completed more than one survey (n=13), 69% reached remission and 77% reached treatment response by the time they completed their last survey of the study.

Data will not be available for a control group of patients (i.e., patients not enrolled in the study) until a final EHR data extract is received in August 2017, allowing for at least six months of follow-up data after the last enrolled patient's study period ends. These results are considered preliminary until the most recently recruited patient has completed the study and a control group is identified and analyzed.

Specific Aim 2

Six participants have completed an end-of-study survey assessing their time in the study. Half of the respondents indicated their clinician used the information they provided during their surveys at the point-of-care. Two respondents felt that their clinician having their information "definitely" improved the care they received; three patients felt it "somewhat" improved the care they received; and one did not think it improved their care at all. All but one respondent indicated they had completed at least one PHQ-9 during a clinical visit prior to joining the study, indicating familiarity with the instrument. Respondents indicated they had no problems with the online consent and registration problems, or that any problems they did have were quickly resolved. All six respondents registered and consented for the study using the tablet provided at their doctor's office, rather than doing so on their own time after the visit.

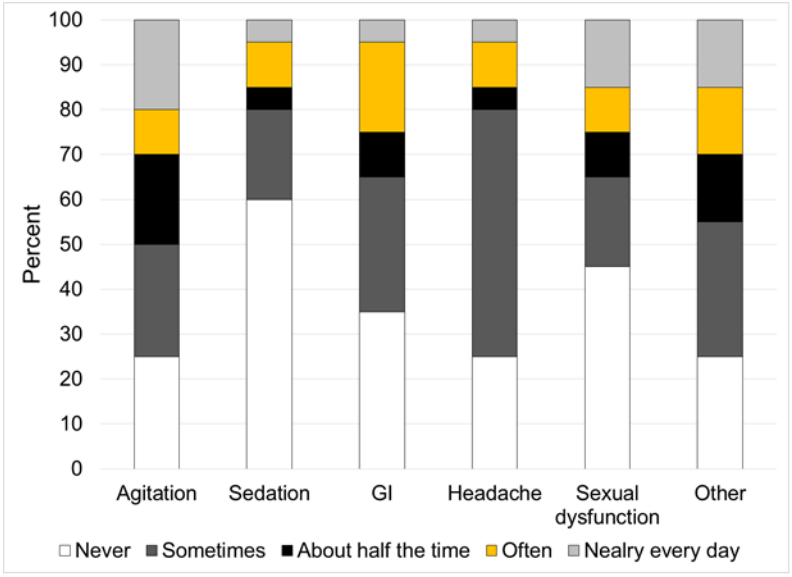

Figure 2a. Frequency of each type of side effect at baseline

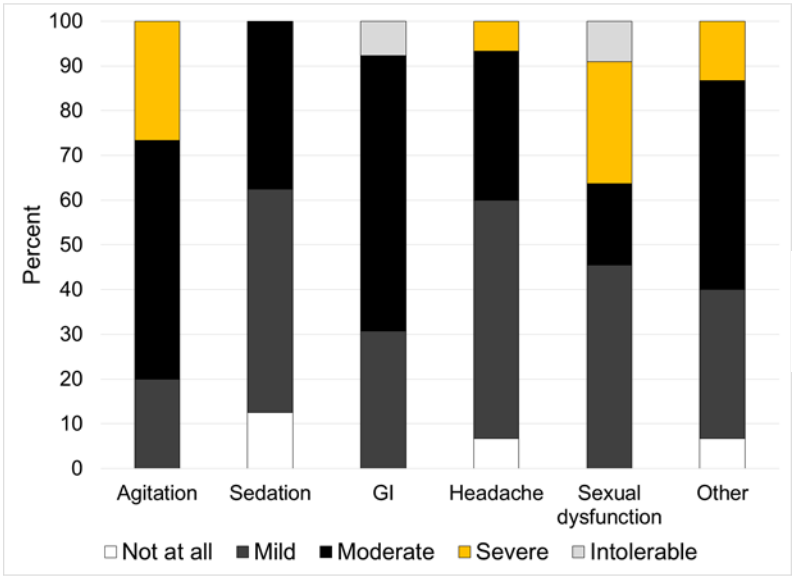

Figure 2b. Intensity of each type of side effect at baseline

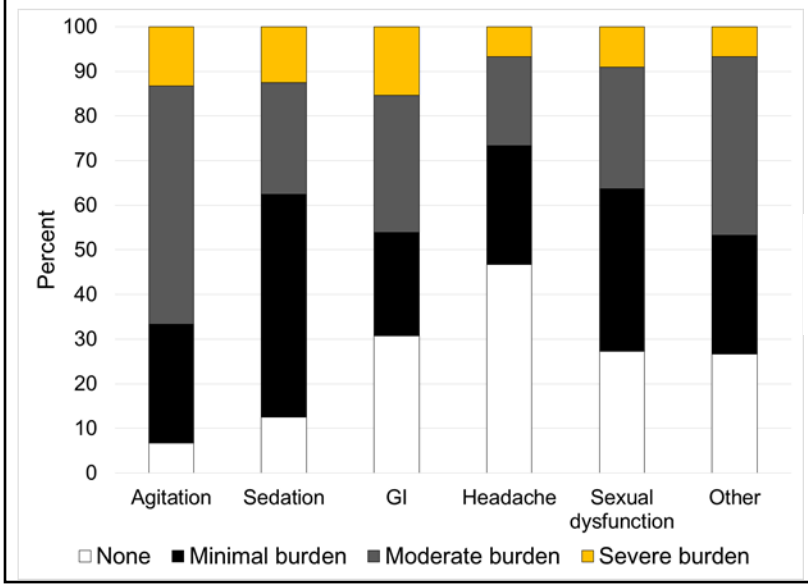

Figure 2c. Intensity of each type of side effect at baseline

Outcomes

The study team was successful in developing and implementing a system to electronically collect data from patients taking an antidepressant to treat depression and incorporate that patient-reported information into an automatically-generated report for their clinician to use at the point-of-care. The system included four parts:

5. the online study registration and consent process, which was housed in iHealthConnect
6. an online instrument completed by patients through iHealthConnect that included questions about medication-related tolerability, medication adherence, and the PHQ-9
7. the patient-reminder algorithm that sent participants an email when it was time to complete a survey; the timing of these requests was based on upcoming appointment dates, the amount of time since their last survey completion, and changes in PHQ-9 scores
8. automatically-generated reports in PDF format that included all information provided by the participants and were provided to clinicians to be used at the point-of-care

The pilot study implementation at three primary care practices provided data from participants that will be analyzed more thoroughly upon receipt of final data for all participants in August 2017. Informal feedback from clinicians throughout the study indicated they appreciated the patient-specific reports, and feedback from participants indicated they were not burdened by completing the instruments and liked knowing that their clinicians had this information about them. The formal clinician and patient assessments will be completed by August 2017 and results will be included in the updated final report at that time.

Regardless of low patient enrollment, the study was successful in the development of a system to electronically collect patient-reported frequency, intensity and burden of medication-related side effects; depression severity; and medication adherence. The system of algorithms to prompt patients to complete an online instrument based on upcoming appointments and changes in PHQ-9 scores was dynamic and designed to decrease survey burden on patients while maximizing patient-reported information available to clinicians for use at the point-of-care.

Discussion and Conclusions

The objective of this project was to develop, implement, pilot test, and assess a system to electronically collect data from patients taking an antidepressant to treat depression and incorporate that patient-reported information into an automatically-generated report for their clinician to use at the point-of-care. The goal was to develop a less burdensome method for primary care practices to monitor patients taking an antidepressant to treat their depression. Existing depression care management programs that involve case management and detailed feedback to clinicians in primary care practices can be effective in improving depression symptoms and medication adherence, but may be impractical for larger practices.[38-40] Major drawbacks to these programs include the time required on behalf of clinic nurses and other staff and the monetary burdens on the practice.

EffectRx developed, implemented, pilot tested, and will assess a potentially less burdensome system of electronically collecting patient-reported data and integrating the data into a patient-specific report for clinicians to use at the point-of-care. While patient recruitment was low, the system was successfully used to consent participants, electronically collect information from the participants regarding their tolerability of medication-related side effects and depression severity, and provide the information to the clinician at the point-of-care. While the formal assessment has not yet been completed (results will be included in an updated final report when available after August 2017), preliminary analysis of participant end-of-study surveys indicates they did not feel burdened by completing the online instruments and felt better knowing their clinician received the information they provided. Informal feedback from clinicians throughout

the study indicated they appreciated receiving the information about their patients between clinic visits. Such a system is scalable to practices with existing electronic patient-clinician information exchange systems and stands to be a less-burdensome method for monitoring depressed patients throughout their treatment.

Significance

Our system of electronically collecting data from patients and providing automated and actionable feedback to the clinician has the potential to decrease the burdens on the practice and lead to an increase in effective depression treatment compared to care-as-usual. The Health Information Technology for Economic and Clinical Health Act (HITECH), part of the American Recovery and Reinvestment Act, will significantly increase widespread use of health information technology and electronic data within primary care over the next several years. Through HITECH, the government is offering incentive payments totaling up to $27 billion over 10 years to hospitals and physicians who demonstrate meaningful use of electronic health record (EHR) data.[41] By 2015, health care providers were expected to adopt and be actively using electronic health records and be in compliance with meaningful use (http://www.healthit.gov/policy-researchers-implementers/meaningful-use). Meaningful use ranges from less complex data capture and sharing in Stage 1 (2011-2012) to more advanced clinical processes in Stage 2 (2014) and evidence of increased functionality and improved outcomes in Stage 3 (2015). HITECH will lead not only to an increase in adoption of EHRs but also to an increase in the inclusion of e-prescribing, use of patient portals, and access to advanced data capture, integration, and sharing technologies. Each of these elements will support the use of automated systems to collect patient-reported outcomes between clinic visits and provide enhanced clinician feedback in a timelier manner.

The use of rating scales, side effect monitoring, medication prescribing and dosing based on guidelines, and decision support-guided care are all components of measurement based care.[42-44] The American Psychiatric Association's *Practice Guideline for the Treatment of Patients With Major Depressive Disorder* recently recommended that measurement based care be used when treating depressed patients with antidepressants.[44] Our inclusion of data on depression severity and side effect tolerability in the clinician feedback is consistent with the measurement based care framework of providing feedback to clinicians about patients taking an antidepressant.. Clinician feedback systems often rely on the EHR for patient-specific data. However, measures of depression symptoms and severity and medication-related side effects are poorly documented in the EHR. The ability to use health information technology to collect patient-reported outcomes provides enhanced feedback for clinicians within the measurement based care framework. Importantly, these patient-reported outcomes can be measured and reported to clinicians between visits, when patients often experience changes to their health or treatment of which the clinician may not be aware. The collection of these data also enhances information available for observational comparative effectiveness research.

Implications

We aimed to address barriers to effective antidepressant treatment of depression, such as non-adherence, while decreasing the burden on practices by electronically collecting data from patients and providing automated feedback to the clinician in a timely manner. We were successful in developing a smart HIT system to request information from patients electronically and integrate the patient-reported information into actionable feedback for their clinicians to use at the point-of-care. Such a system is scalable to practices with existing electronic patient-clinician information exchange systems and stands to be a less-burdensome method for monitoring depressed patients throughout their treatment.

Further work is needed by the study team. We will obtain electronic medical record data for all participants and a sample of non-participating patients in August 2017, providing at least six months of follow-up for all participants beyond the end of their time in the pilot study. This data will be analyzed as described above in the Methods section. We will also complete the formal assessment with clinicians and will complete a final analysis of all end-of-study patient surveys. Finally, while patient recruitment into the pilot study was low, the project resulted in pilot data that will be used to design a subsequent pragmatic trial that will test the effectiveness of the patient-centered feedback to increase antidepressant adherence and improve treatment response for depressed patients being treated in primary care.

LIST OF PUBLICATIONS AND PRODUCTS FROM THE STUDY

None to report

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