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Using primary care prescribing data to improve GP awareness of antidepressant adherence issues

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ABSTRACT

Background Adherence to antidepressant therapy remains a major issue worldwide. Most people with depression are treated in a general practice setting, but many stop taking antidepressants before completing a six-month course as recommended by guidelines.

Objectives To determine antidepressant adherence rates as indicated in primary care prescribing data and pharmacy dispensing data; to demonstrate commonly occurring patterns related to non-adherence, using a prescription visualisation tool we have developed; and to determine whether prescribing data is a good predictor of dispensing based adherence.

Methods We analysed general practice electronic prescribing data for the year ending 31 December 2006 and linked pharmacy dispensing records by National Health Index. We calculated medication adherence for patients starting antidepressants using a six-month evaluation period and a gap-based adherence measure. Patients with a gap of more than 15 days in antidepressant therapy were considered non-adherent. Using a prescription visualisation tool, we described common modes of non-adherence.

Results Out of 2713 patients, 153 satisfied our inclusion criteria. Thirty-nine percent of patients showed poor adherence based on prescribing and 68% showed poor adherence on dispensing. Prescribing based non-adherence had a positive predictive value of 98% (95% CI 92%–99%) and negative predictive value of 51% (CI 47%–52%) for dispensing based non-adherence. Three broad categories of non-adherence were identified: 1) failure to return for re-prescription, 2) failure to maintain adherence despite initial attempts and 3) failure to return for re-prescription in a timely manner.

Conclusions Prescribing data identifies substantial adherence issues in antidepressant therapy. Clinicians should consider adherence issues as part of the overall treatment regime and discuss such issues during consultations.

Keywords: ambulatory care information systems, clinical audit, patient non-adherence, quality indicators

Introduction

Depression is among the most treatable of mental disorders – between 80 and 90% of people eventually respond well to treatment and return to their normal lives,[1] yet a major issue in the management of depression is poor adherence to antidepressant therapy.[2] Treatment guidelines provide guidance on optimal choice of medicine[3] and guidelines such as the ones by the National Institute for Health and Clinical Excellence in the UK[4] and the New Zealand (NZ) Guidelines Group[5] suggest a minimum of six months of continuous antidepressant therapy for the first episode of depression and longer for subsequent episodes. However, research indicates that 44% of patients stop taking medication by the third month of therapy.[6] Although not all patients can be expected to benefit, high rates of adherence to evidence-based treatment can be expected to deliver the best health outcomes for a population with the given condition.

Most people with depression are treated in a general practice setting, either by a general practitioner (GP) alone or, for more serious depression, in partnership with specialist mental health services.[7] Therefore, we work on the premise that routinely collected prescribing data stored in the electronic medical record (EMR) in a general practice setting can be used to detect patients who show poor adherence to antidepressant therapy (and hence on suboptimal therapy). Nearly 100% of GPs in NZ use an EMR. In a survey of GP EMRs in 11 countries, NZ had the highest rate of provision of 14 desirable computer functions.[8] This presents an excellent foundation for use of EMR data to support quality improvement efforts, and in particular to actively identify and manage non-adherent patients. In this paper we attempt to combine high quality EMR data with a novel visualisation tool that can be used to enhance GP–patient communication on adherence issues and assist GPs and patients to be more aware of non-adherence.

Most antidepressant adherence related studies in the past have been carried out using pharmacy dispensing claims data,[2,9–11] and therefore we also investigate adherence rates as indicated in dispensing records. In NZ, the government pays a substantial amount of the overall pharmaceutical expenses (this was 67% in 2008,[12] but has been considerably more since September 2008 when patient co-payments were dropped to NZ $3 or less for all patients) as determined by a Pharmaceutical Schedule set by the Pharmaceutical Management Agency (PHARMAC). Community pharmacies submit electronic claims for reimbursement of the government funded components of dispensed medicines to a centralised reimbursement system. Almost all NZ pharmacies use computers as part of their business.[13] NZ also benefits from a National Health Index (NHI) – a unique patient identifier which provides an opportunity to uniquely match a general practice's prescribing data to pharmacy dispensing data from across the country.

In this paper, we focus on the use of prescribing EMR data to identify patients on suboptimal therapy using a gap-based adherence measure. We then discuss several patterns of non-adherence that we have observed in our dataset. We also analyse community pharmacy dispensing records to determine how antidepressant prescription data compares to pharmacy claims data.

Methods

We examine adherence rates of antidepressant medicines, each of which is listed on the Pharmaceutical Schedule and is therefore fully or partly funded by government. The medications that were considered were among the 20 different antidepressant medicines recognised by the NZ Ministry of Health.[14]

Adherence to medication

Adherence refers to the extent to which a patient follows the medical instructions and recommendations from the prescriber.[15] In this paper we employ a gap-based adherence measure which is an indication of the time of continuous therapy. For our purposes, we allow a 'permissible gap' of 15 days, which is the maximum allowable period patients could go without a dose and not anticipate reduced or suboptimal outcomes;[16] patients who have gaps (also referred to as 'lapses') in treatment exceeding this duration are deemed non-adherent.

Our adherence computation is based on whether the patient was covered by *any* antidepressant medication on a given day within the evaluation period (EP), with no consideration of stockpiling of supply between prescriptions. Although somewhat rare, we have seen cases where, for example, amitriptyline and paroxetine or doxepin and fluoxetine have been prescribed as concurrent medications. Simple addition of durations may be accurate for patients on monotherapy, however, in the former example, if amitriptyline and paroxetine were both prescribed for 90 days, 120 days prior to the end of our EP, our analysis would show that a patient had a 30-day gap towards the end of the EP. Therefore our adherence computation scheme can handle not only patients on monotherapy, but also cases where patients are on multiple agent therapy, which is often the case with complex patients. This has been acknowledged by

other researchers and often only patients on monotherapy are considered in order to 'reduce the complexity in measuring medication adherence'[17] and patients on concurrent therapy are excluded due to the fact that it is difficult 'to define adherence for more than one medication concurrently'.[9] We have previously shown that taking such factors into consideration provides a more effective measure of adherence.[18]

Analysis protocol

Unlike a chronic condition such as diabetes, many patients with depression can be successfully withdrawn from treatment after an initial treatment period and therefore do not need to be on antidepressants for the rest of their lives. We used a six-month period, from 1 July 2006 to 31 December 2006, as our EP. We included only patients who had had an antidepressant-free period of six months prior to the start of our EP, i.e. no antidepressant prescription during the period from 1 January 2006 to 30 June 2006. Using this protocol, we examine the prescribing of antidepressant medicines and their community pharmacy dispensing. Only funded patients enrolled at the practices were included (all New Zealand citizens and permanent residents can be enrolled with one primary healthcare organisation (PHO), which is funded for the management of that person; each general practice is associated with a PHO). The analysis included the following steps:

1 separation of the cases with a therapy gap exceeding the 15-day threshold based on prescribing data into the 'adherent' and 'non-adherent' groups
2 visual inspection of the patterns of treatment and lapse in the non-adherent group
3 comparison of adherence status with prescribing to that based on dispensing, including computation of the positive predictive value (PPV) and negative predictive value (NPV) of non-adherence with prescribing for non-adherence on dispensing
4 computation of a logistic regression model of dispensing adherence based on demographic factors (using the Microsoft Excel 2010 Data Analysis tools) with and without the inclusion of prescribing adherence as a factor.

Data extraction

We collaborated with a multi-physician NZ general medical practice from metropolitan Auckland. Prescribing data, patient gender, age, ethnicity and socio-economic coding were extracted from this practice's proprietary EMR (MedTech32 – www.medtechglobal.com/ (accessed 29 June 2011)) into a password-protected research database, retaining NHI but removing other identifying information including name and address. The pharmacy dispensing records for government subsidised medicines for these patients were extracted from the national claims database, as matched on NHI, by the NZ Health Information Service (now part of the Information Directorate) of the Ministry of Health, and then merged into the research database. Data were analysed by non-proprietary, generic, active ingredient in order to account for brand and generic substitution.

The EMR data extracted from the practice management system (PMS) contained prescribing records for the 12-month period from 1 January 2006 to 31 December 2006. Patient ethnicity data (i.e. whether a patient identified himself or herself as Maori, Pacific, European or Asian) as well as socio-economic quintile data (based on census data and patient address) were also extracted for these patients. The data extract involved 2713 enrolled and funded patients and 21 868 prescriptions (around 4.2% of these for antidepressants). The pharmacy dataset included dispensing data for the 15-month period from 1 January 2006 to 31 March 2007 for these 2713 patients, linked by their NHI. In NZ, a prescription (with refills) is valid for a period of three months before it expires (medication may be dispensed as three months supply at once, or a one-month supply at a time may be collected from a single three-month prescription); hence the pharmacy dispensing data was extracted for an additional three months beyond the date of the last prescription. The dispensing dataset included data for 2452 of the 2713 patients identified in the prescribing dataset and 49 716 dispensing records (around 5% of these for antidepressants). This data extraction and analysis process was approved under the Northern Regional Ethics Committee protocol number NTX/07/55/EXP.

Results

Medication lapses in antidepressant therapy

We first analysed prescribing data to identify adherence issues in antidepressant therapy, as indicated in the practice's EMR. One hundred and fifty-three patients satisfied our inclusion criteria and were therefore inferred to have started their antidepressant therapy during the EP. Out of these patients, 59 were identified as being non-adherent.

Using the prescription visualisation tool we developed as part of the ChronoMedIt framework,[19] we then visually inspected the various antidepressant

prescribing patterns for the non-adherent patients (Figure 1).

The top timeline in Figure 1 shows a case where there was only a single 90-day prescription. The second case is consistent with the GP deciding to start the patient on a short, 30-day course (perhaps to check on efficacy and whether the patient had any adverse reactions) and then prescribing a normal 90-day script when the patient returned for the next prescription. However, this patient has not had a full six months of antidepressant therapy, hence the guideline has not been complied with. The last case is a typical scenario where the patient appears to have failed to return on time for the second prescription, possibly as a result of using medication intermittently such that the supply lasted longer than it would have if taken regularly. These three cases represent three broad categories of non-adherence, which we respectively identify as 1) failure to return for re-prescription, 2) failure to maintain adherence despite initial attempts (note that there is only a single re-prescription for 90-days with respect to the second case in Figure 1, but this could have even been three 30-day re-prescriptions, still having the same affect) and 3) failure to return for re-prescription in a timely manner. Through visual inspection of the individual cases, all other cases of non-adherence were concluded to be a variation or a combination of these three categories.

Figure 2 shows several cases related to adherent patients. The first case satisfies the minimum guideline requirements while the other two patients have been on antidepressants for a longer duration. The second patient in Figure 2 and the second patient in Figure 1 have some similarity as the patient was started on a shorter 30-day duration script and then moved onto a standard 90-day script, and it is possible that the prescribing pattern seen in the second patient in Figure 2 was the GP's intention for the second patient in Figure 1 as well.

Prescribing vs dispensing based adherence

The results of matching the patients satisfying our inclusion criteria to their dispensing via NHIs are shown in Table 1.

We constructed a logistic regression model of dispensing based non-adherence to determine what factors were associated with adherence to antidepressant dispensing for our cohort of 153 patients. Out of these, 21 patients had only prescribing records

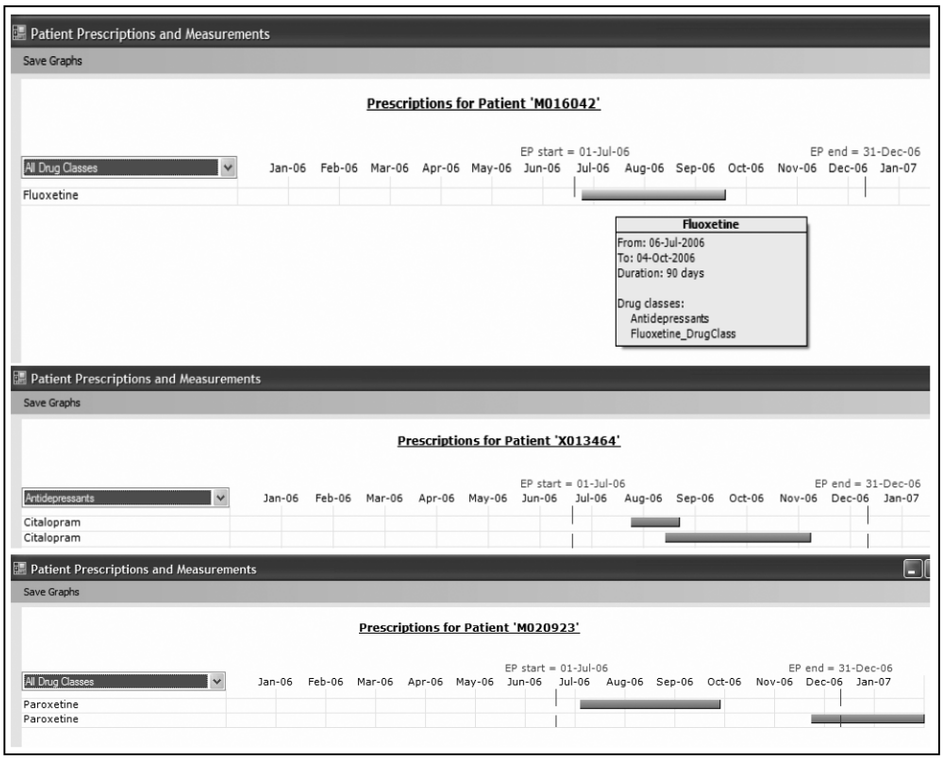

Figure 1 Commonly occurring patterns related to non-adherence. The tooltip in the top figure shows further details related to the selected prescription

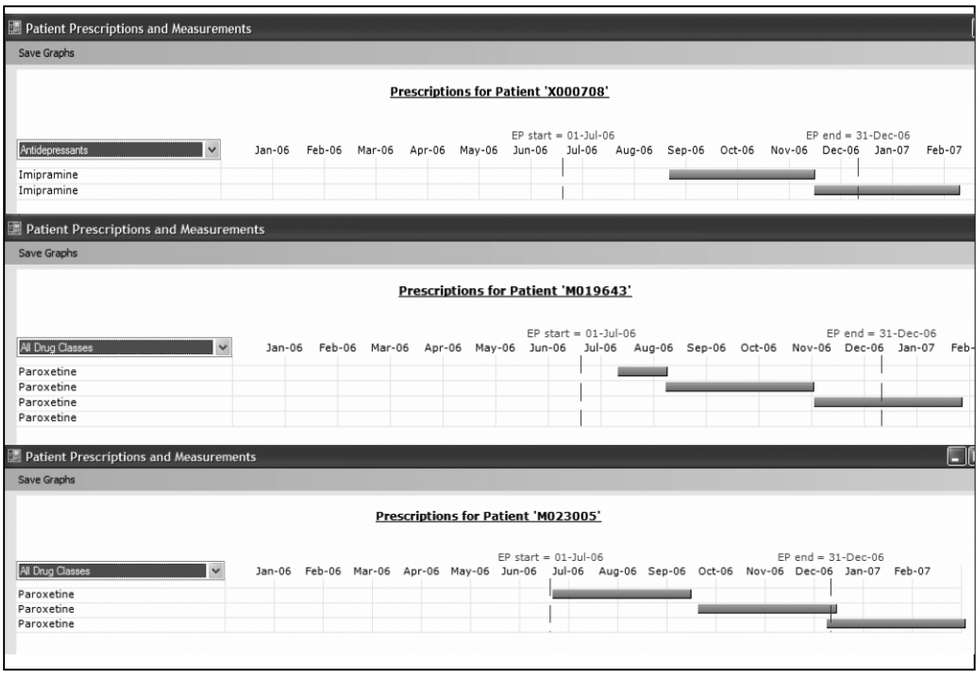

Figure 2 Several prescribing patterns for adherent patients

Table 1 Association of prescribing based non-adherence and dispensing based non-adherence (*n*=153)

Prescribing	Dispensing		PPV	NPV
	>15-day lapse	No lapse	(95% CI)	(95% CI)
>15-day lapse	58 (38%)	1 (1%)	0.98	0.51
No lapse	46 (30%)	48 (31%)	(0.92–0.99)	(0.47–0.52)

(i.e. no dispensing), and a lapse of more than 15 days in dispensing was ascribed to them. Characteristics of the included patients are shown in Table 2.

The dependent variable for regression was a binary indicator for lapsed versus not lapsed based on dispensing data. Independent variables, shown in Table 2, were: age categories; gender; ethnicity (treated as a series of binary indicators with European omitted as the reference); and being in the most depressive socio-economic quintile. None of the independent variables were statistically significant in the model.

We then extended our model by including prescribing based adherence (zero/one for presence of a lapse of more than 15 days) for each patient. This model has an adjusted *R*-squared of 0.2143. The one significant variable is the prescribing adherence (P <0.001; coefficient=0.44, 95% CI 0.31–0.58).

Discussion

This study analysed antidepressant non-adherence using general practice prescribing data and pharmacy dispensing data. Prescription-based non-adherence was observed to provide 98% PPV and 51% NPV for dispensing based non-adherence. Thus, an adherence problem revealed in prescribing appears worthy of action (note in Table 1 that only one person out of 153 was adherent in dispensing despite being non-adherent in prescribing). While the PPV is very good, it is notable that prescribing only detects about half of the potential problems as compared to dispensing data (and of course both prescribing and dispensing are only surrogates for knowledge of whether the patient actually took the medication). Moreover, a regression model of adherence found no simple demographic

Table 2 Characteristics of patients prescribed antidepressant medication (*n*=153)

Characteristic	Number of patients (%)	Number of non-adherent patients (as a % of non-adherent patients, *n*=59)
Age (years)		
<30	23 (15%)	9 (15%)
30–44	36 (24%)	12 (20%)
45–59	45 (29%)	20 (34%)
60–74	31 (20%)	11 (19%)
75+	18 (12%)	7 (12%)
Gender		
Female	111 (73%)	40 (68%)
Male	42 (27%)	19 (32%)
Ethnicity		
Maori	8 (5%)	4 (7%)
Pacific	2 (1%)	0 (0%)
European	138 (90%)	53 (90%)
Asian	1 (1%)	0 (0%)
Other	4 (3%)	2 (3%)
Most deprived quintile	30 (20%)	13 (22%)

predictors (from age, gender, ethnicity or socio-economic status) that could substitute for prescribing data.

Our results also indicate, as expected, that antidepressant adherence problems in the community are very commonplace, irrespective of whether prescribing or dispensing data are used as the indicator. Our results indicate that poor adherence rates were 39% and 68% based respectively on prescribing and dispensing. The increase in non-adherence from dispensing as compared to prescribing is unsurprising; for example, Bailey *et al*[20] report that refill failure occurred in 33% of refill opportunities. Moreover, our non-adherence rates are consistent with the high rates of non-adherence other researchers have reported. Using a ten-day grace period for maximum lapse duration allowed, Bambauer *et al*[9] reported that around 75% of the patients showed poor adherence in dispensing data. Cantrell *et al*[2] reported that approximately 57% of patients were non-adherent to antidepressant therapy using a six-month EP, while Doesschate *et al*[21] reported antidepressant non-adherence rates ranging from 39.7% to 52.7%, with a mean of 46.5% over two years.

A main goal of this study is to inform GPs so that they become more aware of antidepressant non-adherence in the community and to demonstrate a few commonly occurring types of prescribing patterns. Our intention is not to criticise any (in)action by the collaborating practice, but to make clinicians (and health information technology innovators) more aware of the existing high prevalence of non-adherence, and its detectability from electronic prescribing and dispensing records. This provides a fertile ground for useful interventions, either in the form of interactive decision support alerts during the doctor–patient encounter, or more proactively through study of population patterns to devise targeted adherence promotion strategies.

Within the scope of this study, we identified three broad patterns related to non-adherence: 1) failure to return for re-prescription, 2) failure to maintain adherence despite initial attempts and 3) failure to return for re-prescription in a timely manner. Each of these would probably be amenable to a distinct adherence promotion strategy and serves to inform a further development of a model of medication adherence. We also demonstrated the use of a prescription visualisation tool to support clinicians in seeing the nature of adherence problems as indicated in the data (which may be difficult to discern in a tabular list of prescribing dates). Such a visual representation could act as a prompt and a facilitator of discussion with patients to determine factors that may have contributed to the non-adherence pattern and/or regarding how long to continue medication.

If previous dispensing data is readily available at the point of prescribing, clinicians can have even more informed conversations with patients (i.e. regarding their refill adherence) as compared to when using prescribing data alone. This use of dispensing data could entail ethical implications with respect to the patient's

privacy which would need to be resolved in advance of the use of such a network. Conversely, we see no issue in the use of practice-based prescribing data since this only involves the GPs of a practice exercising awareness of the records of their own actions.

Although depression is recognised as one of the most treatable of mental disorders and adherence to treatment identified as a key factor in recovery, the diagnosis and management of depression is not without contention and complexity.[22] Primary care physicians manage a wide range of human experience and suffering including grief, adjustment, personality disorders, substance abuse, medical illness, pain and sleep disorders that can merge in a less than discrete way with the concept of depression. Both the clinician and patient may have different understandings and levels of conviction as to the appropriate diagnosis and most available and optimal treatment, but agree that depression is a valid working model to describe the patient's experience and that it is appropriate to trial an antidepressant. Exclusively categorising depression is not definitive (e.g. the NZ depression guidelines[5] refer to severe, moderate and mild depression – medication is considered compulsory for severe, a good option for moderate and not initially indicated for mild depression); in practice there are often important triggering or exacerbating factors such as relationship or work difficulties that vary over time. The natural history of depression is that it often resolves over time (and, on the other hand, that it also recurs), and that it is common for patients to come for help when they have been depressed for a long time and may therefore be approaching natural recovery. Moreover, it is common for patients to stop medication because they feel themselves to be recovering, or not recovering despite medication. Also, culture, context, prior experience, personal and family biases and preferences, trust and therapeutic alliance, memory, judgement and motivation, level of side effects and patient response are all factors that may impact on ongoing adherence. Tools and techniques such as the ones discussed herein are promising to provide support, but the complexity of the task must be kept in mind.

Low adherence is a complex issue without a single solution, however, low adherence is an indication of the need for improved communication between GPs and patients; possibly the clinician needs to engage the patient more in a joint 'problem-solving' approach in relation to underlying adherence barriers and use novel tools (e.g. the visualisation tool discussed herein) to explain optimal prescribing patterns to patients. This is an important issue as there is evidence to suggest that providers often do not ask about medication adherence from patients, and may not use the most effective communication strategies when they do.[23] Research has shown that patients prefer graphical representations the most (compared to numerical values such as number needed to treat) when encouraging patients to take medication, and that consideration should be given to developing visual aids to support shared clinical decision making.[24] Educating and discussing issues is also supported by a recent study in NZ where the researchers investigated patient beliefs about medication and found that 'patient concerns with medications were positively associated with (self-reported) non-adherence'.[25] Other investigators also have demonstrated that 'interpersonal process variables (such as greater levels of patient–provider collaboration) are important in influencing antidepressant adherence'.[26]

Studies to date that match prescribing to dispensing in an open-loop healthcare system (i.e. where prescribing and dispensing do not operate from a single central database) have been limited. We have matched prescribing data to dispensing data based on the NHI number, providing a simple and robust means of matching patients between general practice and community pharmacy. Previous research investigated success rates of linking prescribing records to dispensing records (using probabilistic matching techniques) based on a combination of patient characteristics, such as gender, year of birth and postal code, and prescription characteristics, including prescription date and Anatomical Therapeutic Chemical-codes; this resulted in a smaller dispensing-to-prescribing data linkage proportion of 64.8%.[27] We believe our matching, based on the NHI number, provides a more accurate indication of the value of prescribing data to indicate adherence in dispensing.

Good adherence has been associated with lower yearly medical costs,[2] less likelihood of experiencing short-term disability events,[28] lower risk of hospitalisation and emergency room visits[11] and fewer recurrent episodes of depression.[29] Our work presents an opportunity for practices to enhance the capacity for having better conversations with patients. A possible intervention can be designed for identified patients to educate them on the importance of medication adherence. GPs can use a tool such as the one presented herein to discuss adherence issues with patients, and perhaps even print a copy of the individual patient graphs at the end of each encounter to make patients more aware of individual adherence. We have discussed how analysing prescribing data is a reasonably good measure of dispensing adherence and can be used to identify patients with good/bad adherence, and intuitively the absence of timely prescription in the general practice EMR should be a strong indicator of an underlying problem in medication supply and adherence and could ultimately lead to better clinical outcomes.

We acknowledge several limitations in our investigation:

1 Our study was based on a relatively small sample of patients from a single general practice. Extracting data from several general practices or a large PHO that manages several general practices would provide a more robust assessment.
2 Our data was based on general practice prescribing data and it is possible that not all prescriptions were issued by the general medical practice from which we extracted the EMR data. It is possible that some prescriptions were issued during a patient's stay in hospital, or from the community specialist mental health service, in which case the record would appear in the dispensing data but not in the prescribing data – in fact, there were 195 patients identified in our dispensing dataset as being eligible and satisfying our inclusion criteria, however, only 153 had prescriptions issued by the collaborating practice. Further, some medication may have been stopped by the GP (perhaps after three months), but such information is not recorded in the EMR, and therefore is not accounted for in our analysis.
3 Clinical assessments such as the Patient Health Questionnaire-9 (PHQ-9)[30] can be used to monitor response to treatment and if such information is made available within an EMR system, outcomes of identified patients can be closely correlated to medication adherence. However, PHQ-9 data is not available within the PMS at the moment and therefore this study has not investigated any direct patient outcomes.

Conclusions

Patient adherence to antidepressant treatment is poor. There is evidence to suggest that substantial adherence issues can be identified by analysing prescribing data, and therefore clinicians need to consider poor adherence to antidepressant therapy as common and should at least discuss such issues with patients during consultations. Linking dispensing data to corresponding prescribing records confirms that there is merit in analysing a patient's prescribing record; such analysis at the point of prescribing should be promoted, possibly including the support of graphic tools. Further work is needed to determine what type of clinical interventions would be best suited to improving patient adherence to antidepressant therapy.

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CONFLICTS OF INTEREST

None.

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