Medicines Optimisation for patients with Treatment Resistant Schizophrenia: designing and implementing an automated clozapine prescription ordering system

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Abstract

Introduction
Clozapine is the only antipsychotic that is licensed for use in Treatment Resistant Schizophrenia. There are several practical issues with regard to clozapine supply, namely that treatment is long term and repeat prescriptions are required every 6 months. In Devon, around 365 patients are prescribed clozapine. The previous supply process had a number of concerns that meant patient safety could be at risk. A process for transitioning to an automated system to reduce system error and improve patient safety was devised.

Methods
The change to a fully automated electronic system was done in three steps:

- Requesting new prescriptions go direct to the mental health trust pharmacists allowing:

  - proactive management of the 'soon to expire' lists

  - a meaningful clinical screening using the electronic notes

  - checks for a valid medical review within the last 12 months

- Replacing the monthly manual expiry checks with a date-ordered filing system.

- Replacing the manual filing system with a more secure and efficient electronic system.

The team involved with the design and implementation of the new system consisted of two pharmacists, one technician and one member of the IT team.

Results
The new automated system was successfully implemented resulting in a number of improvements. A safer system was created by having a clinical screen completed with access to patients' notes; serious errors were detected and corrected quickly. Fewer prescriptions go out of date and soon to expire prescriptions are known in advance. Time dedicated to clozapine increased due to clinical screening however time spent chasing prescriptions dramatically decreased. Time use was therefore most cost efficient and appropriate. Patients benefited from fewer prescribing errors, supply delays and more accurate recording.

Conclusion
An automated system to ensure up to date and appropriate clozapine prescriptions was successfully designed and implemented. This has multiple system process benefits but also, more importantly, benefits to patient safety.

Keywords: clozapine, treatment resistant schizophrenia, medicines optimisation

Background

Clozapine is the only antipsychotic that is licensed for use in Treatment Resistant Schizophrenia[1] (TRS) – defined as when at least two other antipsychotics have been tried at an adequate dose for an appropriate amount of time without a satisfactory response.

After clozapine's initial introduction onto the market in 1971 it was discovered that it could cause neutropenia and agranulocytosis - a sudden and potentially fatal decrease in white blood cells.

Agranulocytosis occurs in approximately 0.7% of patients treated with clozapine,[1] the majority of cases occurring within the first year. Clozapine was withdrawn and then subsequently reintroduced to the market in 1989 with a new UK licence that stipulates that the individual, responsible consultant and supplying pharmacist must all be registered with the manufacturer and the individual must undertake regular blood monitoring as outlined in Table 1. In Devon we are registered with the Clozaril Patient Monitoring System (CPMS).

Clozapine can cause a number of other serious side-effects that require careful monitoring in order to minimise their impact on the individual's quality of life (see Table 2).[2] Although agranulocytosis is now well detected and managed by regular blood tests, constipation and cardiac side effects can also result in death – clozapine induced gastrointestinal obstruction occurs in approximately 3 cases in 1,000[3] and myocarditis in between 0.7-1.2%.[4] Regular medical reviews are therefore warranted.

Despite the side-effect burden, clozapine remains the only antipsychotic with proven efficacy in TRS and, therefore, it has a unique and valuable role in its management.

There are several practical issues with regard to clozapine supply:

- Treatment is long term and repeat prescriptions are required every 6 months.

- Doses need to be titrated up slowly over a number of weeks to avoid complications from over-sedation and postural hypotension.

- If doses are missed for more than 48 hours, treatment needs to be re-titrated.

- Medical reviews with a doctor must happen at least once a year (this is a Trust standard).

- Clozapine cannot be released by the pharmacies without an in-date prescription and an in-date blood result showing that white blood cell levels are within range.
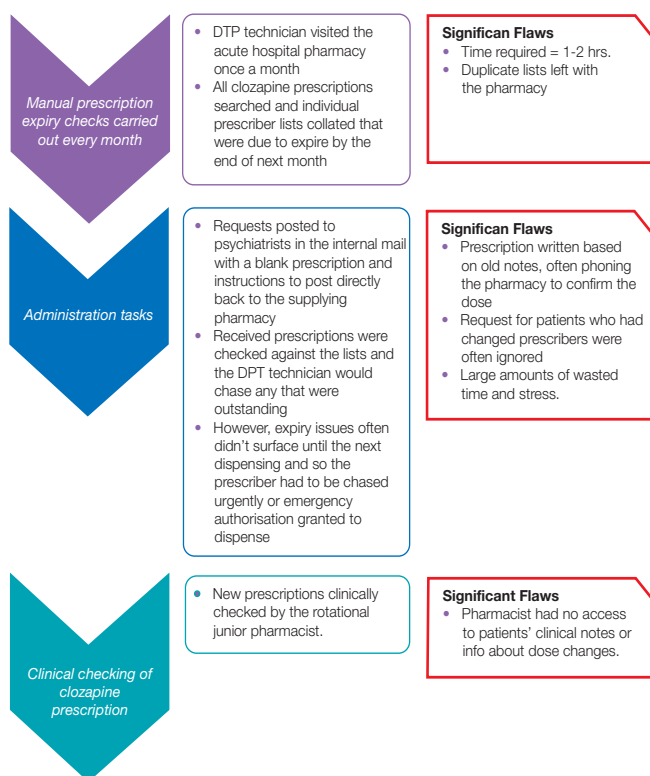
Local Issues

In Devon (as in most of the UK), consultant psychiatrists are responsible for the repeat prescriptions and the pharmacies registered for clozapine supply are based in acute NHS Hospital Trusts (four locally). At Devon Partnership NHS Trust (DPT) there are over 365 clozapine patients (from a population of 850,000):

- 168 patients in Exeter, East and Mid Devon
- 107 patients in South Devon
- 23 patients in West Devon
- 67 patients in North Devon

The historical supply pathway

Prior to the Medicines Management (MM) team's intervention, the supply pathway in Exeter, East and Mid Devon was as follows:

Manual prescription expiry checks carried out every month
- DTP technician visited the acute hospital pharmacy once a month
- All clozapine prescriptions searched and individual prescriber lists collated that were due to expire by the end of next month

Significan Flaws
- Time required = 1-2 hrs.
- Duplicate lists left with the pharmacy

Administration tasks
- Requests posted to psychiatrists in the internal mail with a blank prescription and instructions to post directly back to the supplying pharmacy
- Received prescriptions were checked against the lists and the DPT technician would chase any that were outstanding
- However, expiry issues often didn't surface until the next dispensing and so the prescriber had to be chased urgently or emergency authorisation granted to dispense

Significan Flaws
- Prescription written based on old notes, often phoning the pharmacy to confirm the dose
- Request for patients who had changed prescribers were often ignored
- Large amounts of wasted time and stress.

Clinical checking of clozapine prescription
- New prescriptions clinically checked by the rotational junior pharmacist.

Significant Flaws
- Pharmacist had no access to patients' clinical notes or info about dose changes.

Time after starting clozapine	Full blood count monitoring frequency
First 18 weeks	Weekly
Week 19 – 52	Fortnightly
Week 52 onward (while maintained on clozapine)	4 weekly
Table 1. Blood monitoring requirements with clozapine	

Frequency (% of patients treated)	Side-effect
Very common (>10%)	Drowsiness, tachycardia, constipation, hypersalivation
Common (<10%, >1%)	Weight gain, blurred vision, tremor, hypertension, postural hypotension, nausea
Uncommon (<1%, >0.1%)	Agranulocytosis
Rare (<0.1%, >0.01%)	Diabetes mellitus, myocarditis, blood clots
Very rare (<0.01%)	Thrombocytopenia, cardiomyopathy, cardiac arrest, obsessive compulsive symptoms
Table 2. Potential side-effects of clozapine (not exhaustive)	

Ongoing safety concerns

Clearly this pathway had a number of flaws that resulted in both wasted time and safety concerned, namely:

- As new prescriptions were returned directly to the pharmacy, the DPT MM team were unaware of what had been received and were unable to proactively chase outstanding prescription requests.

- As all prescriptions were physically located at the acute Trust, the mental health team (pharmacists and consultants) had no access to the information contained on them after posting.

- The pharmacists' clinical check of new prescriptions was not fit for purpose due to lack of access to the patients' clinical notes, meaning that the pharmacist was unaware of any recent clinically significant changes including new medications, side-effects, blood assay results or smoking habits.

- The supply of the prescription was not connected to the annual medical review and, therefore, many requests for dose changes were received outside of the prescription renewal system and many people did not receive a regular annual review as there was no prompt for psychiatrists to carry them out.

- Potential delays or interruption in supply could result in missed doses and subsequently a destabilising of the patients' mental health. This could result in patients requiring re-titration onto clozapine and possible admission to an inpatient ward

Aim

The DPT Medicines Management team wanted to improve the efficiency and governance of the system by introducing automated systems where possible and ensuring that staff had access to appropriate information to enable them to carry out their roles proficiently. Additionally, and more importantly, the team wanted to avoid the potential harm and impact to patients of running out of clozapine and the impacts of this including loss of psychiatric control, possible need to re-titrate dose and, therefore, potential re-admission to inpatient wards. There was a high risk of patient care being compromised by inefficient systems.

The specific aims for the project were to:

- reduce the number of prescriptions that expired prior to receipt of replacement prescription

- improve the quality of clinical screening

- ensure staff have access to the information they need to carry out their role proficiently including timely reminders for prescription rewrites and medical reviews.

Method

It was recognised that the best way to achieve the necessary changes with the system would be via small, stepwise improvements at one site (Exeter, East and Mid Devon). The changes were therefore broken down into three distinct stages:

Step 1
- Request prescriptions go direct to DPT pharmacists allowing:
  - proactive management of the 'soon to expire' lists
  - a meaningful clinical screening using the electronic notes
  - checks for a valid medical review within the last 12 months.

Step 2
- Replace the monthly manual expiry checks with a date-ordered filing system that enables a more robust repeat prescription system.

Step 3
- Replace manual filing system with a more secure and efficient electronic system.

The team involved with the design and implementation of the new system consisted of two pharmacists, one technician and one member of the IT team.

Step One: Transferring responsibility for the clinical screen to the DPT pharmacists

The greatest concern with the original pathway was with the standard of the clinical screen. It was decided that a specialist DPT pharmacist with full access to the patients' electronic clinical notes must replace the junior acute Trust dispensary pharmacist. This would ensure all new prescriptions were checked against reports of changes in the person's mental state, reports of side-effects, interactions, smoking behaviour, assay results and any unexpected changes in doses. If the DPT pharmacist had any concerns they could document these in the person's electronic notes and contact the prescriber.

After clinically checking the prescription, the pharmacist would then deliver the prescription to the pharmacy, at the same time communicating any important information.

This step was successfully implemented with minimal disruption. Initially, some prescriptions continued to go directly to the acute Trust hospital but these quickly stopped. This change resulted in a large number of errors being addressed which previously would have been missed (see Figure 1). It was also noted by the DPT pharmacists that the number and severity of errors significantly decreased after 6 months (i.e. once all prescription had been through the new system).

Additionally, the checking pharmacist could now check via the electronic records when the last medical review was and could prompt the psychiatrist's secretaries to make appointments for those who hadn't had a review in the past 12 months.

- *Prescription written for a patient de-registered on CPMS*

- *Prescription written for 400mg nocte when dose should have been 250mg nocte*

- *Dose continued for a patient with an assay level of 0.07mmol/ml (range 0.35-0.5mmol/ml)*

Figure 1: Examples of errors detected by the clinical screening of prescriptions

Step Two: Replacing the monthly manual prescription checks with a date ordered filing system

The next step was to develop a robust repeat prescription system that did not rely on physical visits to the acute Trust pharmacy. The initial iteration of this system involved a card-based system, which contained basic details such as name, dose and expiry date of the prescription (see Figure 2). The DPT technician updated the information on the cards after each clinical screening. Patients were filed according to the month their prescription renewal was due creating six sections: January/July, February/August, March/September, April/October, May/November and June/December.

As the card system was with the DPT team, it was possible to proactively chase prescriptions before they expired without needing to visit the acute Trust, thus saving time and improving efficiency.

Whilst this system had a number of advantages, there were still some drawbacks. For example, it was not easy to find a specific patients details without searching though all the patients.

Once we were confident that the card data was accurate it was transferred onto an Excel spreadsheet that could be hosted on the MM shared drive. This spreadsheet benefited from being fully searchable and accessible from any networked computer.
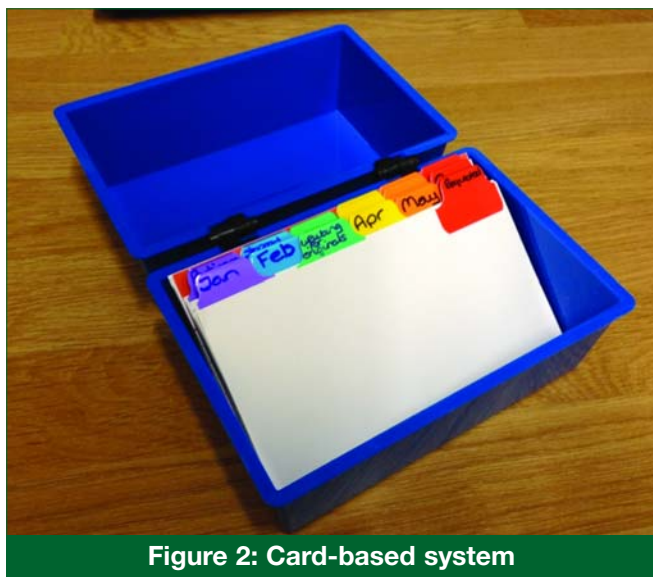

Figure 2: Card-based system

Whilst safety concerns for the ordering of clozapine prescriptions had now been addressed, the amount of time required to send the prescription requests and maintain the database was still an issue.

Step Three: Replacing the spreadsheet with a more secure and efficient automated system

At this point, the DPT performance team became involved and we progressed from a spreadsheet to the Trust's SharePoint database hosted on the Trust's 'Orbit' site – a cloud-based data-hosting site. The 'live' system runs by automatically counting down to when a prescription is due to expire. When a prescription is within four weeks of expiry, the system automatically sends an email to the consultant and their secretary with the patient's details requesting a new prescription. The consultant then completes a prescription,

uploads a copy to the patient's electronic notes and emails a specific clozapine email address verifying its completion.

The DPT pharmacist completes the clinical screening using the patient's notes resolving any issues directly with the consultant. They document the process in the patient's notes, print out the prescription, sign to confirm the clinical check and deliver it to the acute Trust pharmacy. Finally, the pharmacist updates the database with the new expiry date of the prescription (along with any additional information found whilst screening), resetting the countdown in the process. The process is repeated every six months or after a dose change.

If the expiry date has not been updated within seven days of prescription expiry, the system will automatically send daily reminders to the consultant, copying in the Medicines Management team. Through this process the MM team are informed of all soon to expire prescriptions and proactively chase them before they expire.

A screenshot of the 'Clozapine Register' is provided in Figure 3. The system contained the same data fields as the Excel spreadsheet but also extra space for recording when medical reviews have been conducted, results of clozapine assay tests and a free-text comments box.
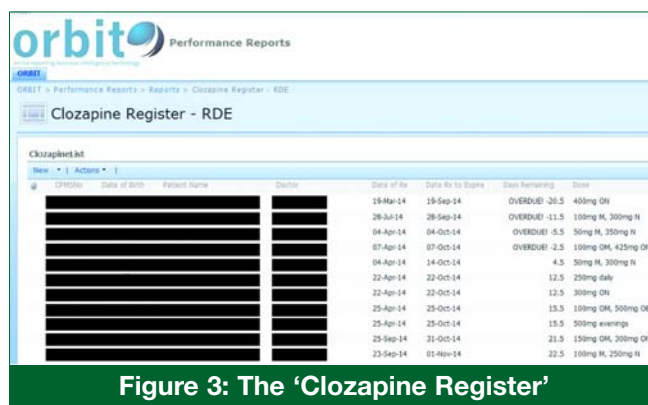

Figure 3: The 'Clozapine Register'

Practical improvements

First wave

Monthly prescription requests were generated automatically, with daily reminders if necessary.

Consultants, pharmacists and clozapine clinic nurses can all access the register and read/write access levels can be set to maintain integrity. A full history of all edits to data provides firm governance and audit reassurance.

The new system enabled the introduction of a new electronic clozapine prescription that could be uploaded onto patients' electronic clinical notes. This significantly reduced time delays from postage as well as reducing paper waste and ensuring that everyone involved in the individual's care could see the most up to date prescription.

Second wave

The medical review date was added to the reminder letters to give the prescribers advanced warning of when a new medical review was required. This reduced the screening pharmacists' workload as without this intervention they would screen the new prescription but short-date the expiry of the prescription to one

month to provide opportunity for the medical review. Although this process ensured that there was an in-date prescription and an annual medical review it did mean that two clinical screenings took place so the advanced notice to the prescribers helped to reduce this occurrence.

We were aware of incidents where the GPs were not aware that their patients were prescribed clozapine as it was not listed on the GP's prescribing screen. We therefore designed a standard letter to advise all GPs to add a note on their prescribing screen for each patient and recorded the delivery of this letter on the database. Checking this had been done has become a standard part of the pharmacists' clinical check. This is a further patient safety feature to prevent potential missed doses on admission to hospital and avoid the risk of inadvertently prescribing interacting medicines.

The practical benefits of the new system

- **Safer.** Having a clinical screen carried out by a pharmacist with access to patient's notes results in serious errors detected and corrected quickly.

- **Fewer out of date prescriptions.** Importantly, expired or soon to expire prescriptions are known to the team in advance. Previously, the Mental Health team were only made aware at the time of dispensing.

- **More efficient input from Mental Health Team.** While time dedicated to clozapine has increased due to clinical screening, the time spent chasing prescriptions and searching paper records has dramatically decreased. Time used is, therefore, more cost-efficient and appropriate.

Patient focused benefits of the new system

- **Safer.** Clozapine use is safer; reported side effects are now proactively chased with the consultant by the screening pharmacist. Changes in smoking habit that have not been followed up can be flagged and assay results can be used to recommend dose increases or decreases. All of these benefits have resulted in a reduced number and impact of side effects, therefore improving quality of life.

- **Reliable supply chain.** Avoiding supply problems has meant that patients are spared having to make multiple journeys to collect their medication. This also reduces the risk of missing doses and the potential knock-on effects on mental state and possible re-titration.

- **Error prevention.** Actively detecting and rectifying dose change errors before they are supplied prevents patients being accidentally under-dosed and the potential of symptom control problems or overdose and associated additional side effects.

- **Accurate recording.** GPs accurately recording the use of clozapine on their systems will reduce the risk of prescribing interacting medicines and also reduce the risk of clozapine being missed on admission to hospitals.

Problems created

- **Doctors.** Whilst not a new problem, prescribers getting used to new systems of working initially created a few problems including continuing to post prescriptions to the wrong acute hospital, not uploading prescriptions correctly and electronic signatures.

- **Electronic systems.** General issues around the database including associated IT issues and lack of IT skills of prescribers.

- **More clinical screening.** The creation of an additional 168 prescriptions to clinically check every six months results in additional time and, therefore, cost pressures. The workload is currently spread between three pharmacists.

The Future

Going forwards, there are minor improvements that could be done to further advance the system:

- Minimising pharmacist input into the system to just the clinical screening and dealing with clinical queries will improve the cost effectiveness of the system.

- Community mental health teams and prescribers should be able to take ownership of parts of the system and update data for their individual patients. This had already begun to some extent with the specialist clozapine nurse now responsible for the uploading of blood assay results onto the system and contacting prescribers with any issues.

- Electronic transmission of the prescriptions through to the pharmacies would be advantageous so that the final printing out stage after the screening could be avoided. This would enable one Devon-wide screening service.

- Seamless data transfer between the Trust's electronic patients notes and the database is a current aspiration. Although not possible with our current system, the Trust is introducing a new system this summer and we hope to be able to progress with this.

- Once the above point has been achieved we would like to investigate how we can pull through physical health monitoring data into the database, not only from within DPT but from Primary Care. This may be possible in the short term using hand held 'Wellbeing Passports' that we have recently developed.

The feedback from the consultants has been excellent. At first they were not enthusiastic about the automated electronic nagging but within the one prescription cycle (6 months) they began to understand the benefits and we have had regular comments such as "I have no idea how we ever managed to keep up to date in the past". It has also saved individual mental health community teams time as many of them had developed their own databases in an attempt to manage the workload but struggled to keep these up to date.

Conclusion

In conclusion, an automated system to ensure up to date and appropriate clozapine prescriptions was successfully designed and implemented. This has multiple system process benefits but also, more importantly, benefits to patient safety. The system is now running in the Exeter, East, Mid, South and West Devon areas and, currently, we are in the process of setting this up in North Devon. The aim is to soon roll this out to include the local forensic unit to ultimately include all patients prescribed clozapine in the county.

Declaration of interests

None

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