

Fostering the use of clozapine in the severely mentally ill through academic detailing

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ABSTRACT

Academic detailing is an educational program in which independent researchers and clinicians evaluate available literature to develop up-to-date, unbiased, evidence-based recommendations for a given therapeutic area. Pharmacists, nurses, and physicians trained as academic detailers then disseminate this information to providers. This is one means to foster the greater use of clozapine in patients with treatment-resistant schizophrenia. The Veterans Health Administration (VHA) Academic Detailing Service meets with mental health providers at each facility to identify barriers and healthcare systems solutions, provide feedback about prescribing and patterns of care, and develop and distribute educational materials to improve veteran health outcomes. Preliminary results include a reduction in polypharmacy antipsychotic use from 17% of patients on antipsychotics to 12.2% of patients ($p < 0.001$). Although there was a numeric increase clozapine new starts in the 5-month interim analysis, the increase was not significant in this analysis. Analysis for 12-month data is underway. The early success of this program demonstrates there may be opportunity for this type of educational intervention in the Veterans Affairs Healthcare System.

KEYWORDS

academic detailing, clozapine

INTRODUCTION

Pharmaceutical companies are one of the highest revenue-generating industries, owing much of their success to effective marketing strategies. In 2005, the pharmaceutical industry spent \$29.9 billion on marketing, of which \$7.2 billion was spent directly targeting physicians through detailing and journal advertising.¹ Often, sales representatives are the only sources from which providers receive drug information about newly available medications. In turn, practitioners may be influenced to prescribe new FDA-approved drug therapies which may not be as safe, effective, or economical as alternative treatments. How then can practitioners be educated on not just the new treatment options, but evidence-based recommendations?

WHAT IS ACADEMIC DETAILING?

Academic detailing is an educational program that seeks to use the "successful marketing strategies of industry but without its sales-oriented spin" to promote guidelines and best practices.² Independent researchers and clinicians evaluate available literature to develop up-to-date, unbiased, evidence-based recommendations for a given therapeutic area.³ Pharmacists, nurses, and physicians trained as academic detailers disseminate this information through the use of key messages delivered to providers during individual or group educational outreach visits. Academic detailing aims to influence prescribing

behaviors to employ the safest and most effective treatment modalities, frequently resulting in cost-savings.⁴

WHAT IS THE EVIDENCE BEHIND IT AND WHY DOES IT WORK?

Academic detailing has demonstrated effectiveness in changing prescribing practice in a variety of healthcare settings. In one of the earliest studies on academic detailing, the inappropriate prescribing of vasodilators, oral cephalexin, and propoxyphene decreased by 14% ($p = 0.001$) compared to controls after physicians in primary care offices were visited twice by academic detailers and received a series of "unadvertisements" (counter-advertisements of these agents).⁵ Geriatric nursing homes participating in an educational academic detailing program reduced the excessive use of sedating drugs by 27% compared to 8% in the control group ($p = 0.02$) without negatively affecting the overall behavior and level of functioning of their residents.⁶ Furthermore, a Cochrane Review of sixty-nine randomized controlled trials found that educational outreach visits resulted in increases in clinically appropriate or decreases in clinically inappropriate prescribing.⁷ Some of the mechanisms by which academic detailing offers advantages compared to traditional educational methods include visiting healthcare providers to ensure better market penetration,

tailoring communication to the individual participant, and engaging participants in discussion to determine their baseline knowledge, attitudes, and likelihood for behavior change.^{2,8} While published reports have described the effects of educational outreach programs targeting mental health diagnoses in primary care, no information is available evaluating effects in the specialty setting of psychiatry. Nonetheless, applying the principles above which have made academic detailing successful in other areas may lead to similar achievements in mental healthcare.

WHY DOES THE VA WANT TO IMPLEMENT THIS?

The Veterans Health Administration (VHA) has made a major commitment in recent years to improving care for mental health conditions and encouraging adherence to evidence-based practice. Typical mental health prescribing does not follow clinical practice guidelines, and this is consistent amongst multiple healthcare systems. The evaluation of atypical antipsychotics has been one of the most active areas of research. Of particular significance, these agents are being prescribed more frequently, often for off-labeled indications including above FDA-approved maximum doses and polypharmacy in treatment resistant schizophrenia. Evidence is lacking for the effectiveness of antipsychotic polypharmacy and studies indicate increased morbidity and mortality.⁹⁻¹² Consensus guidelines clearly agree that patients with schizophrenia who have not responded to at least two adequate trials of antipsychotics should be offered clozapine, which has been found to be more effective than other antipsychotics in treatment-refractory patients.¹³⁻¹⁶ Despite these published guidelines, it is estimated that clozapine is used in 14% to 50% of eligible candidates; it is used by less than 5% of VHA patients diagnosed with schizophrenia.¹⁷⁻¹⁹ Academic detailing is one means to foster the greater use of clozapine in patients with treatment-resistant schizophrenia.

INITIATIVE TO INCREASE USE OF CLOZAPINE

Clozapine is the only antipsychotic that has been found to be superior to both first generation and second-generation antipsychotics in the treatment refractory schizophrenia. The CATIE phase 2E effectiveness study demonstrated the median time to discontinuation for patients on clozapine to be significantly longer compared to those on olanzapine, quetiapine, or risperidone (10 months versus 2-3 months). Discontinuation due to lack of efficacy was also lower in the clozapine group (11%) compared to olanzapine (35%), quetiapine (43%), and risperidone (43%).¹⁵ In the CUTLASS 2 trial, clozapine

showed significant enhancement in symptom improvement over one year compared to other atypical antipsychotics, reducing the total PANSS score by five points ($p=0.013$).¹⁶ Furthermore, several studies suggest that using clozapine may reduce suicidal behavior in patients with schizophrenia.²⁰⁻²⁴

PROVIDER SURVEY ON PERCEIVED BARRIERS

To identify the principle reasons for the underutilization of clozapine within our VHA facilities, the Academic Detailing Service (ADS) conducted a survey assessing providers' beliefs about clozapine and prescribing practices in treatment resistant schizophrenia. One hundred and eighteen mental health providers in two regional areas (Veterans Integrated Service Networks 21 and 22) completed the survey. Fifty-five percent of providers responded that they would prescribe in-line with clinical practice guidelines, considering a trial of clozapine after two antipsychotic treatment failures; an overwhelming 80% would consider this option after three antipsychotic treatment failures. Despite these attitudes, 52% had not initiated clozapine therapy in over one year. Sixty-seven percent of respondents agreed they would use two or more antipsychotics prior to a trial of clozapine. Providers' range of comfort in starting a patient on clozapine varied widely, which could be due to several perceived barriers. The top three barriers identified were the mandatory blood monitoring, patient acceptance, and patient registration for clozapine use. Seventy percent of providers believed that local support with registration, side effect monitoring and management, and psychotic symptom management would increase the use of clozapine. Finally, respondents were asked about patient attitudes towards clozapine treatment. Eighty-five percent of providers felt that patients' primary barrier to initiating therapy was blood monitoring. Additionally, survey results conveyed an interest in the development of patient and provider educational materials.

INTERVENTIONS

The VHA Academic Detailing Service meets with mental health providers at each facility to identify barriers and healthcare systems solutions, provide feedback about prescribing and patterns of care, and develop and distribute educational materials to improve veteran health outcomes.

REGISTRATION AND PRESCRIBING PROCESSES

Numerous strategies have been employed thus far to address the complicated processes of initiating clozapine treatment. The initial step taken to increase utilization

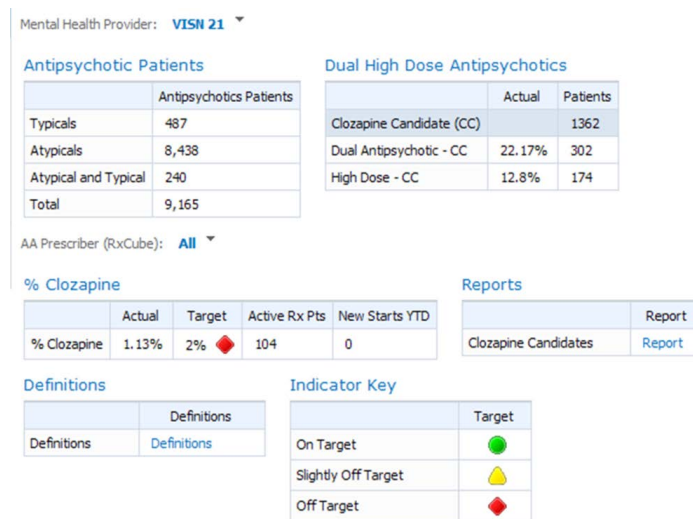
was to enroll more providers with the VHA's National Clozapine Coordinating Center (NCCC) for clozapine prescriptive authority. The only providers within VHA authorized to prescribe clozapine are American Board of Psychiatry and Neurology certified or Board-eligible psychiatrists or neurologists.²⁵ Consequently, the VHA ADS is requesting an expansion of the individuals authorized to prescribe clozapine to other mental healthcare providers with prescribing privileges (i.e. psychiatry residents, nurse practitioners, physician's assistants, pharmacists). Additionally, in an effort to streamline the patient registration process, protect patient confidentiality, and serve as documentation in the electronic medical record, the NCCC is progressing toward the use of an electronic interfacility consult rather than faxed applications. Lastly, an order set has been implemented in the computerized physician order entry to facilitate clozapine titration upon treatment initiation and order associated labs.

AUDIT AND FEEDBACK TOOLS

Audit of providers' clinical practices and feedback regarding their performance can produce small to moderate effects in changing practice.²⁶ In Australia and New Zealand, a combined approach using academic detailing and audit and feedback techniques successfully increased the use of clozapine in patients with schizophrenia.²⁷ Of note, monitoring requirements in these two countries are similar to the United States and in the VHA.²⁸ The VHA ADS developed a Clozapine Dashboard which mental health providers and administrative staff can access via a secure website (Figure 1). The dashboard serves as a screening tool to identify patients who may be candidates for a trial of clozapine, based on a diagnosis of schizophrenia and a history of two or more antipsychotic trials in the last five years. Patients on antipsychotic polypharmacy or high dose antipsychotics are also highlighted, as these patients may be experiencing side effects from their current medication regimen.

Reports are available for providers to screen patients for their distance to the closest medical facility within VA from their home, a complete VA medication history of antipsychotics previously tried, duration of time on therapy and their medication refill rates on their active antipsychotics. This summary information allows the provider to review for potential clozapine candidates and provide a starting point for discussion with the patient on how previous treatment trials managed symptoms and side effects of their therapies.

Figure 1. Clozapine Dashboard



EDUCATIONAL MATERIALS

The VHA ADS acknowledges that several opportunities exist for educational outreach, developing evidence-driven materials for both providers and patients. Multiple provider-specific educational pieces have been created. **"The symptomatic management of schizophrenia: a review of the evidence"** pamphlet is used to guide discussion between academic detailers and mental health providers to promote the appropriate use of antipsychotics, considering efficacy, safety, and all other things equal, cost. Clozapine "toolkits," concise reference cards detailing the administrative and clinical requirements for clozapine use, have also been created and used to guide in-service discussions with providers and residents. Additionally during in-services attendants were provided a recently published article by Agid et al, which reviews the risks and benefits for clozapine and the appropriate place in therapy.²⁹ Lastly, a conversational piece has been developed to aid mental health providers in beginning the discussion of clozapine as an option with patients.

RESULTS AS OF SEPTEMBER 2011

When comparing baseline year of October 1, 2009 through September 30, 2010 to October 1, 2010 through September 30, 2011, the program implementation steps were completed are as follows:

1. Increase of newly registered providers for clozapine
2. Decrease in Polypharmacy for patients who are candidates for clozapine monotherapy.
3. Decrease in Supratherapeutic Dosing Antipsychotics for patients who are potential candidates' for clozapine monotherapy.
4. Increase in new clozapine patients registered/started

5. Increase in # sites implementing order sets for appropriate prescribing of titration
6. Increase in # sites implementing IFC consult for NCCC to process new patients
7. Increase # of in-services completed –with orientation to the tool kit educational support

A relevant increase in newly registered providers from 2009 to 2010 was 43 additional VA psychiatry providers. Overall, polypharmacy antipsychotic use reduced from 17% of patients on antipsychotics to 12.2% of patients ($p < 0.001$). Supratherapeutic dosing was not changed during the measurement period. Although there was a numeric increase clozapine new starts in the 5-month interim analysis the increase was not significant through February of 2011. Analysis for 12-month data is underway following an assessment of patients started in inpatient continuing to outpatient maintenance. Individual sites such as the VA Sierra Nevada Healthcare System and VA San Diego Healthcare System saw a rise in prescribing of clozapine during the 12-month period, although the sustained impact outside of inpatient new starts was not found in identification of outpatient prescription data. Some of the limits to this analysis include patients in long-term care facilities transferred from VA inpatient units will not be recorded as maintenance clozapine patients if VA outpatient pharmacies do not service the LTC with prescription benefits.

Five sites implemented order sets to enhance appropriate prescribing of the 11 sites in the academic detailing service network. Six sites completed the implementation of the electronic registration consult (IFC) of new patients placed on clozapine through the VA National Clozapine Coordinating Center. All major medical centers in the network received in-service with the clozapine tool kit and academic detailing educational materials.

CONCLUSIONS

This quality improvement program was tasked with developing a model for the delivery of a national Academic Detailing Service. The model developed in VISN 21/22 follows evidence based practices and integrates models of change shown to be reliable in changing prescribing behavior. Our model provides critical path sequences to direct activities efficiently. We also provide timelines when results should become evident if the program is producing the intended results. Preliminary results have been consistent with our model (e.g., changes in clozapine prescribing habits in individual sites, adoption of the dashboard to identify high-risk prescribing practices, increased NCCC registrations). We

have successfully identified key barriers to clozapine use and have developed tools (provider handouts, patient handouts, online dashboards) to address these barriers within the context of our model. As these barriers are resolved at individual sites, we expect practice patterns of mental health providers to converge with clinical guidelines. One of the findings of the PEW Prescription Project indicated, "savings are realized only when the information is translated into changes in clinical practice. That is what academic detailing helps to achieve."³⁰ The early success of this program demonstrates there may be opportunity for this type of educational intervention in the Veterans Affairs Healthcare System.

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How to cite this editor-reviewed article

Farhadian S, Yee M, Christopher MLD. Fostering the use of clozapine in the severely mentally ill through academic detailing. *Ment Health Clin* [Internet]. 2011;1(5):94-8. Available from: <http://dx.doi.org/10.9740/mhc.n87507>