

A Framework for Assessing Adherence and Persistence to Long-Term Medication

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Abstract. Poor adherence and persistence to long-term medication is a growing concern worldwide. Despite their importance, tools that facilitate the identification of patients who show poor adherence and persistence rates are limited. Herein we present a framework we have developed to assist in assessing adherence and persistence rates. We demonstrate the framework's features using production electronic medical record data from a general medical practice in the context of analysis of antihypertensive and antidepressant prescribing. The framework is flexible and extensible and has the potential to be used as a tool to improve the management of patients on long-term medication either to benchmark quality over a specified evaluation period or for the direct identification of specific patients that would benefit from immediate follow-up.

Keywords. ambulatory care information systems, clinical audit, long term care, non-adherence, quality indicators

1. Introduction

A recent report by the World Health Organization (WHO) [1] reports that around 60% of all deaths worldwide are due to chronic diseases. Clinical research has shown impressive efficacy rates for improving patient well-being by properly administering prescribed medication, yet patient adherence to long-term medication is poor, averaging around 50% in developed countries and even lower rates in developing countries [1].

It has been reported that physicians often do not enquire about patient adherence in some settings, are not accurate in predicting adherence, and often overestimate adherence [2]. Although poor adherence to therapy has been recognised as an important factor in the management of patients with chronic illness, tools that support clinicians to systematically identify patients who show poor adherence are limited. In light of the large magnitude of the issue, and the ongoing need to formulate successful adherence improvement strategies, we have developed a flexible and extensible framework capable of successfully identifying patients with poor adherence to their long-term medication. Our framework enables analysis of patterns in electronic prescribing from electronic medical records (EMRs). The framework presented herein is flexible in terms of the specific criteria of interest with respect to medications, adherence

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thresholds, time periods of interest and defining characteristics of cohorts of interest. The work is illustrated in terms of antihypertensive and antidepressant prescribing – relating to major chronic conditions routinely managed through long-term prescribing in the community.

2. Methods

2.1. Adherence and Persistence to Medication

Adherence refers to the extent to which a patient’s behaviour to take the prescribed medications aligns with the instructions and recommendations from the prescriber [1]. In this paper we employ possession based adherence measures of proportion-of-days-covered based on the prescribing in the patient’s general practice EMR, which we will refer to as the medication possession ratio (MPR) [3]. In our previous work, we identified issues related to summing the durations of prescriptions (which is a common way of calculating MPR). The reader is referred to [4] for a discussion on temporal relations and how the edges of the period of interest need to be handled for a more accurate measure of MPR. We define an *evaluation period* (EP, e.g., 12 months) for which the MPR is to be computed, preceded by a *run-in period* (usually, e.g., six months) so that prescription coverages that run into the evaluation period can be properly accounted for. For the purposes of this paper we use the definitions:

If no prescription record during the run-in period:

$$\text{MPR} = \frac{\text{Number of days supply held during EP}}{\text{Number of days between first prescription date and end of EP}} \times 100 \quad (1)$$

else:

$$\text{MPR} = \frac{\text{Number of days supply held during EP}}{\text{Number of days in EP}} \times 100 \quad (2)$$

On the other hand, the medical literature uses the term *persistence* to refer to the time of continuous therapy – a “permissible gap” of specified number of days which is the maximum allowable period patients could go without a dose and not anticipate reduced or suboptimal outcomes [5]. Patients who have gaps (also referred to as a ‘lapse’) in treatment exceeding this duration are deemed non-persistent.

2.2. Protocol for Data Extraction

We collaborated with a general medical practice in metropolitan Auckland, New Zealand that has an ethnically diverse patient population. We extracted production EMR data stored in the practice’s Patient Management System (PMS). The data extract consisted of a practice-specific patient identifier (through which practice staff, but not the external researchers, could identify the patient for follow-up), demographics (age in years, ethnicity and gender), prescribing (but not dispensing) details and classifications (diagnosis codes, and some procedure codes). Patient data was extracted for the 18-month period from 01-October-2005 to 31-March-2007 providing a 12-month EP and a six-month run-in period (with the exception of classifications, which are relevant for an indefinite time with respect to chronic illness, extracted for five years back). The dataset included 2713 patients, 29772 prescriptions and 8365 patient classifications.

3. Results

3.1. Framework Architecture

Patient data is extracted from the PMS to flat files via its in-built reporting tool. The data is then imported into a SQL Server database. An ontology-based representation of the different drug and patient classification information needed to formulate the query criteria (see Section 3.2) is specified using the Web Ontology Language (OWL) [6]. An XML document is created to specify the query criteria – e.g., for a given EP, ‘patients classified with hypertension who have an MPR < 80% with a lapse >30 days for antihypertensive medication’ (requiring the system to recognise ‘hypertension’, ‘MPR<80%’, ‘lapse>30 days’ and ‘antihypertensive’). The criteria, specified in XML, is validated against an XML-Schema document we have created. The overall framework is implemented in C# .NET and various stored procedure and user-defined function calls are used to retrieve required patient data from the database.

3.2. Drug and Classification Ontology

The drug and classification information was modelled using the Protégé-OWL [7] development environment (Figure 1).



Figure 1. Two views of the drug and problem ontology. The *Antidepressants* and *Problems* classes are expanded in the left view and part of the *Antihypertensives* class is expanded in the right view.

Drug_Classes is a high-level concept under which different drug classes such as Antihypertensives and Antidepressants have been created. Antihypertensives class further refines to different subclasses of antihypertensive medication. Similarly, the Problems class represents the different classifications of interest – in this case we have included only depression, diabetes and hypertension. In NZ, the Read Clinical Codes [8] are used to classify patients, and most of the commonly used Read Codes have been created in the *Read_Codes* class which is under *ClassificationSchemes*. To indicate that a particular Read Code denotes a condition, the corresponding condition class

(Hypertension for example) is also made a parent class of that Read Code (i.e., multiple inheritance) [6]. The grayish number within parenthesis indicates the number of OWL individuals [6] in each class – for example, four Read Codes are associated with hypertension (represented by the *Hypertension* class in the ontology).

3.3. Adherence/Persistence Reports

Once a query has been formulated in the XML document using the domain level concepts specified in the ontology, the framework can produce an adherence/persistence report in a .txt or .pdf format with patient specific details indicating the reasons behind why the patient was returned in the query result. For a query such as ‘patients classified with *hypertension* and *diabetes* who have an MPR < 80% with a lapse >30 days for *ACEi-Inhibitor* or *ARB* medication for the EP 01-April-2006 to 31-March-2007’ for example, an identified patient’s details are shown in Figure 2.

53 X013983			
<u>MPR</u>			
Value	Denominator		
32.97%	01-Apr-2006 to 31-Mar-2007		
<u>Medication Lapse(s):</u>			
Lapse in Medication	Lapse Start	Lapse End	Lapse Duration (days)
Cilazapril	16-Mar-2006	06-Jun-2006	82
Cilazapril	06-Jul-2006	07-Sep-2006	63
Cilazapril	07-Oct-2006	01-Dec-2006	55
Cilazapril	31-Dec-2006	16-Feb-2007	47
<u>After Classified with:</u>			
Classification Description	Classification Code	Classified on	
Diabetes mellitus	C10.00	22-Nov-2002	
Essential hypertension	G20.00	22-Aug-2005	

Figure 2. A report with adherence/persistence details

The report indicates the different lapse durations that occurred during the specified EP, patient MPR (32.97%) as well as the relevant patient classification details.

3.4. Prescription Plots

We developed a graphical tool that can assist a clinician to easily visualise patient prescribing patterns (independent of a patient’s adherence/persistence rate). If a clinician needs to see the prescribing patterns for patient ‘M017131’ or ‘M016169’ for example, this identifier can be entered into the framework which will produce the corresponding prescribing plot as shown in Figure 3. The plots show the different medications the patients have been prescribed using a different colour for each medication. The prescription lists can then be filtered by selecting the required drug or drug class as shown in the drop-down menu in the top figure in Figure 3. It can be seen from Figure 3. that patient ‘M017131’ was adherent to prescribed antihypertensives (cilazapril and metoprolol) as well as antidepressants (amitriptyline) while patient ‘M016169’ showed poor adherence and persistence to the prescribed antidepressant medication (paroxetine), with two significant lapses in therapy – one during the EP and one at the end of the EP (i.e., an ongoing lapse).

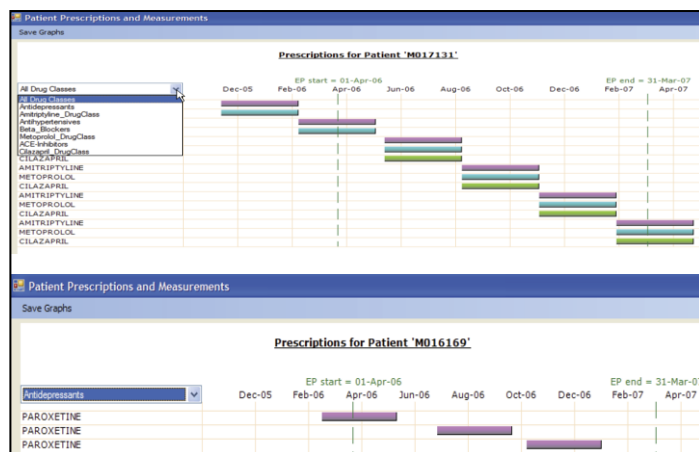


Figure 3. Two prescription plots – an adherent patient at the top and a non-adherent patient at the bottom

4. Conclusion

We have developed a generic, extensible framework that can be used to assess patient adherence and persistence rates from production EMR data. Our focus is on providing practice-specific patient information to make it feasible for practice staff to assess the quality of their management of patients on long-term medications over time. This may serve either to support assessment of a quality improvement program or, by examination of the specific cases exhibiting sub-optimal adherence and persistence, to act as a tool to support immediate follow-up on those patients. Further work is necessary to develop a graphical user interface for specification of the XML that defines the reporting requirements, improved interfacing to production EMR systems, and possible extension to support analysis of dispensing records to gain further sensitivity in detecting adherence and persistence problems.

References

- [1] Sabaté, E. (2003) *Adherence to Long-Term Therapies, Evidence for Action*. World Health Organization, Geneva.
- [2] Miller, L.G., Liu, H., Hays, R.D. et al. (2002) How well do clinicians estimate patients' adherence to combination antiretroviral therapy? *Journal of General Internal Medicine* 17(1):1–11.
- [3] Andrade, S.E. et al. (2006) Methods for evaluation of medication adherence and persistence using automated databases. *Pharmacoepidemiology and Drug Safety* 15(8):565–574; Discussion 575–577.
- [4] Mabotuwana, T.D.S., Warren, J. (2008) A semantic web technology based approach to identify hypertensive patients for follow-up/recall. In *Proceedings of the 21th IEEE International Symposium on Computer-Based Medical Systems (CBMS)*, IEEE CS Press, Finland, 318–323.
- [5] Cramer, J.A., Roy, A., Burrell, A. et al. (2008) Medication compliance and persistence: Terminology and definitions. *Value in Health* 11(1):44–47.
- [6] McGuinness, D.L., Harmelen, F.V. (2004) *OWL Web Ontology Language Overview*. <http://www.w3.org/TR/owl-features/>.
- [7] Knublauch, H., Fergerson, R.W., Noy, N.F., Musen, M.A. (2004) The Protégé OWL plugin: An open development environment for semantic web applications. In McIlraith, S.A. et al (Eds.) *Proceedings of the Third International Semantic Web Conference ISWC 2004, Hiroshima, Japan*, Springer, 229–243.
- [8] Chisholm, J. (1990) The Read clinical classification. *British Medical Journal* 300(6732):1092.