

Analysis of Medication Possession Ratio for Improved Blood Pressure Control – Towards a Semantic Web Technology Enabled Workbench

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Abstract

Using a patient management ontology developed on Semantic Web technologies, we have provided a framework and workbench to identify hypertensive patients with inadequate systolic blood pressure (SBP) control. We have populated our ontology with production electronic medical record data from a general medical practice in New Zealand. Medication Possession Ratio (MPR) is used as a key concept in grouping patients whose SBP control can be improved. We also provide a prescription timeline visualisation scheme to aid a clinician in understanding a patient's antihypertensive prescribing patterns. Both to validate our workbench and to enable immediate care improvement and research, we have utilised our framework to model the association of prescribing-based MPR to SBP. While the aggregate observed improvement in SBP is 18.55 mmHg from full as compared to nil MPR, there are poorly controlled patients among both high and low MPR groups, indicating distinct cohorts for quality improvement follow-up.

1. Introduction

Cardiovascular disease (CVD) is a leading cause of death worldwide. In 2005, in the United States alone, the adult population affected by CVD was estimated to be 80.7 million (37.1% of total population), out of which 73 million (33.6%) were estimated to have uncontrolled high blood pressure (BP) [1]. The same report estimates the direct and indirect costs related to high BP to be USD 69.4 billion for 2008. CVD related statistics from other parts of the world tell a similar story, with CVD causing over 1.9 million deaths (42% of all deaths) in the European Union (EU) in 2005 with an overall CVD related cost burden of €169 billion per year to the economy [2]. In New Zealand (NZ), CVD accounts for 40% of all deaths making it the leading cause of death [3]. Since hypertension (HT) is a chronic condition with a significant contribution towards increased CVD risk, these statistics motivate continued investigation into ways of better managing hypertensive patients.

The relationship between BP and risk of CVD events is continuous, consistent and independent of other risk factors – the higher the BP, the greater the chance of having a heart attack, heart failure, stroke and kidney disease [4]; and the shorter the life expectancy [1]. With the discovery of new drugs and increasing effectiveness of pharmacologic treatment techniques, proven therapy to control high BP and reduce CVD events exists, but studies indicate only around 50-60% of treated patients achieve their target BP [1, 5]. The precise reasons for patients not achieving target BP despite being treated are not clear, but one key factor is lack of adherence to the prescribed BP-lowering medications [6].

To provide clinicians with better tools to help close the gaps in BP control, we have developed an ontology-based architecture and workbench using semantic web based technologies [7]. Herein we illustrate our approach in the context of examining the association of Medication Possession Ratio (MPR) to systolic blood pressure (SBP) with the agenda of immediate quality improvement follow-up to patients, and further research on adherence issues. This study was approved under the University of Auckland Human Participants Ethics Committee protocol number 2007/078.

2. Methodology

We used electronic medical record (EMR) data stored in a Patient Management System (PMS) from a general medical practice in metropolitan Auckland, New Zealand which serves a predominantly Pacific population. We focus on providing practice specific patient information that will make it feasible for a practice staff to follow-up the patients and take immediate action to improve BP control.

De-identified patient data was extracted from the practice’s commercial PMS (MedTech32 <http://www.medtechglobal.com/>). 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, classifications (diagnosis codes, and some procedure codes), relevant laboratory test results, and blood pressure measurements. The data extract spanned from the 29th of January 2008 to 18 months prior (i.e. till 29th July 2006) with the exception of classifications, which are relevant for an indefinite time with respect to chronic illness and hence were extracted for five years back.

The data extract involved 9710 patients (6991 enrolled and funded), with 48651 prescriptions (13% antihypertensive medications), 11865 BP measurements and 31716 patient classification codes (encoding 1193 HT and 1041 diabetes mellitus classifications). The present study concerns quality assurance of a one-year analysis period (AP) from 29th January 2007 – 29th January 2008. Inclusion criteria were a diagnosis of HT (based on Read Clinical Codes), having had an antihypertensive (AHT) prescription before the beginning of the AP and an AHT prescription during the AP, and to have had at least one BP measurement during the AP.

2.1. Adherence to Medication

Medication Possession Ratio (MPR) is widely used as a measure of adherence to long-term medication, such as AHT medication [5, 8, 9]. Our work is based on the premise that general practice prescribing data can be used to determine MPR, and that MPR can be used as a marker of patient adherence to prescribed medication; however, whether the patient duly collected the prescribed medication and consumed it as directed is unknown.

For our purposes we defined MPR as:

$$\frac{\text{\#of days supply held during AP}}{\text{\#of days in AP}} \times 100 \quad (1)$$

where AP refers to the period from 29th January 2007 – 29th January 2008, with the prior 6 months of extracted prescribing data forming a run-in period for the analysis. The term *held* (as opposed to the more commonly used term *obtained* [9]) in (1) indicates that we explicitly account for the boundary prescriptions (i.e. prescription coverages that fully subsume AP start or AP end dates) and include only the supply that falls within AP.

Following past MPR-related studies [5, 8, 9], we take a patient as *adherent* to therapy when their MPR is $\geq 80\%$.

2.2. An Ontology based Approach

Semantic Web is an evolving extension to the World Wide Web (WWW) that allows semantics of information to be defined for automated processing by machines. In order to define the semantics and make the domain assumptions and relationships explicit, in our previous work [7] we used the Web Ontology Language (OWL) [10] (i.e. one of the Semantic Web based technologies) to create an ontology to transform the extracted PMS data into a unified patient management ontology. We used the Protégé-OWL [11] development environment and Java for the ontology creation and transformation process. The developed ontology was further refined for our current work to include a MPR over AP (i.e. one year) for each of several major AHT drug classes – ACEi/ARBs, beta-blockers, diuretics and Calcium-Channel-Blockers (CCBs), as well as an overall AHT MPR, based on the latest data extract. Overall MPR is calculated based on the percent of days covered by *any* AHT prescription (i.e. irrespective of the AHT drug class) during the AP.

In addition to MPR, mean patient BP, based on the BP measurements a patient had during the analysis period, was mapped into the ontology. We decided to do this processing in the data transform stage (i.e. the preprocessing stage – reader is referred to previous work [7] for details of this mapping process) as opposed to creating a SWRL (Semantic Web Rule Language) [12] rule to calculate average BP within Protégé-OWL. The justification behind this was that if required, it is easier to set a requirement such as ‘patients who had at least two BP measurements during AP’ in the Java based preprocessor than in a SWRL rule (as of Protégé-OWL build 126, it is not possible to pose restrictions on SWRL *aggregate* functions – count of BP should be ≥ 2 during AP in this case). Further, OWL supports efficient description logic (DL) based reasoning; however reasoner inferred knowledge, querying and SWRL built-ins [12] are currently not integrated, and therefore we have used mainly SWRL (to write inference rules) instead of DL based reasoning. Figure 1 shows the resulting ontology with data for a selected patient.

3. Results

After populating the ontology with the extracted data, SQWRL (Semantic Query-enhanced Web Rule Language) [13] was used to query the ontology knowledge base to determine the required patients. We identified 280 HT patients who satisfied our inclusion criteria, and for these patients, we queried the ontology for overall MPR and average SBP. Analysis was based on SBP only noting that JNC7 [4] says “impressive evidence has accumulated to warrant greater attention to the importance of SBP as a major risk factor for CVDs [and the] rise in SBP continues throughout life, in contrast to DBP [i.e. diastolic BP], which rises until approximately 50 years old.”

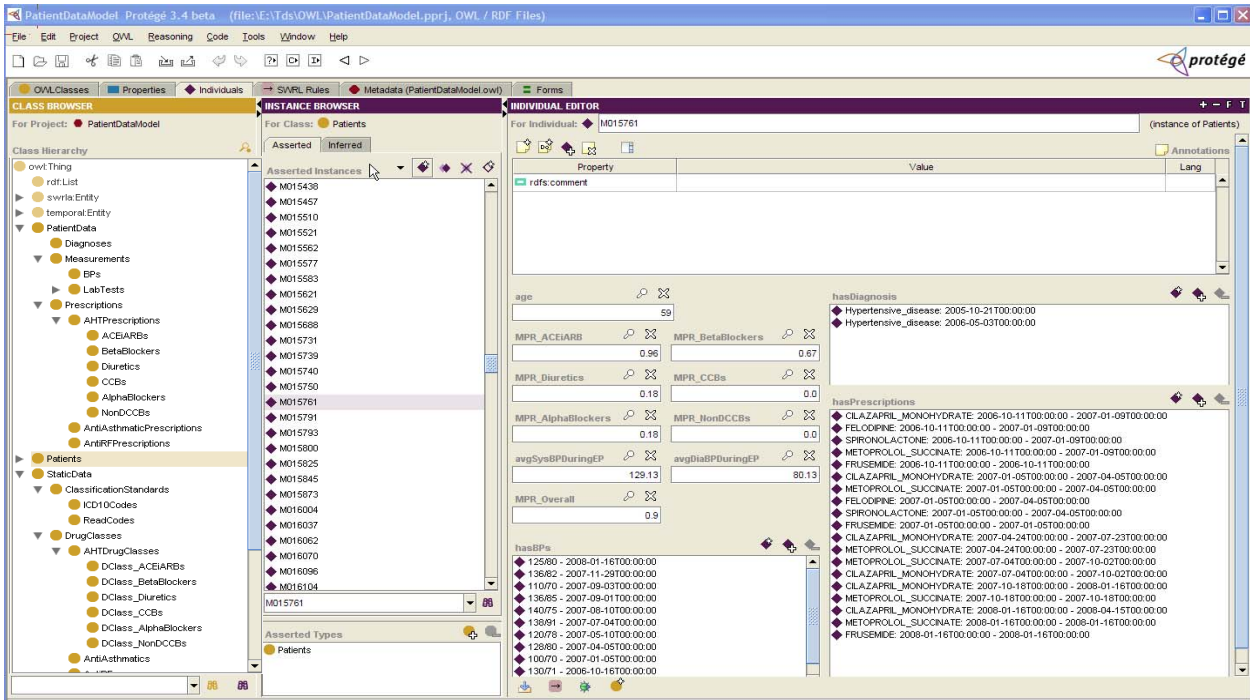


Figure 1. A selected patient instance within the unified patient management ontology

3.1. Relationship of Adherence to BP Control

Following JNC7 recommendations, to have controlled SBP, we used the condition $SBP < 140$ mmHg for HT only patients and $SBP < 130$ mmHg for patients with HT and diabetes mellitus (DM). Summarised in Table 1 is a comparison between overall AHT adherence and control of average SBP for HT only patients. Table 2 shows the average SBP and overall MPR comparison of HT patients with DM. It needs to be noted that herein we present an analysis using overall MPR, but the same analysis can be carried out on a drug class specific basis as well (using the drug class specific MPRs) if required.

MPR Condition	SBP < 120	$120 \leq SBP < 140$	$140 \leq SBP < 160$	$160 < SBP$
$80\% \leq MPR$	6	52	34	3
$60\% \leq MPR < 80\%$	3	13	16	1
$40\% \leq MPR < 60\%$	0	7	10	2
$MPR < 40\%$	0	3	3	4

Table 1. Comparison of average SBP (in mmHg) and MPR for patients with HT only (N=157). The dark-solid lines indicate the division between adherent and controlled (top left quadrant), adherent and not-controlled (top right), non-adherent and controlled (bottom left) and non-adherent and not-controlled (bottom right) patients.

MPR Condition	SBP < 110	$110 \leq SBP < 130$	$130 \leq SBP < 150$	$150 < SBP$
$80\% \leq MPR$	2	26	37	13
$60\% \leq MPR < 80\%$	0	5	20	7
$40\% \leq MPR < 60\%$	0	2	4	1
$MPR < 40\%$	0	2	1	3

Table 2. Comparison of average SBP (in mmHg) and MPR for patients with HT and DM (N=123). The interpretation of the dark-solid lines is the same as in Table 1.

We can now combine the information in Tables 1 and 2 to form a more concise 2x2 matrix as shown in Table 3.

	Controlled SBP (SBP < 140 or SBP < 130 if DM present)	Uncontrolled SBP
Adherent (MPR ≥80%)	86	87
Non-adherent	35	72

Table 3. Adherence vs having controlled SBP (in mmHg).

The odds ratio (OR) based on Table 3 is 2.03 (95% CI, 1.23-3.36), indicating (unsurprisingly) a significant positive association between MPR and controlled SBP. We also plotted the distribution of average SBP against MPR (Figure 2) for our cohort consisting of 280 HT patients (with or without DM). Using a linear regression model, the regression coefficient for MPR was 0.1855 (95% CI, 0.1005-0.2706) while the intercept was 154.15 (model $R^2=0.062$) – an observed mean reduction in SBP for being adherent from 0% to 100% of 18.55 mmHg.

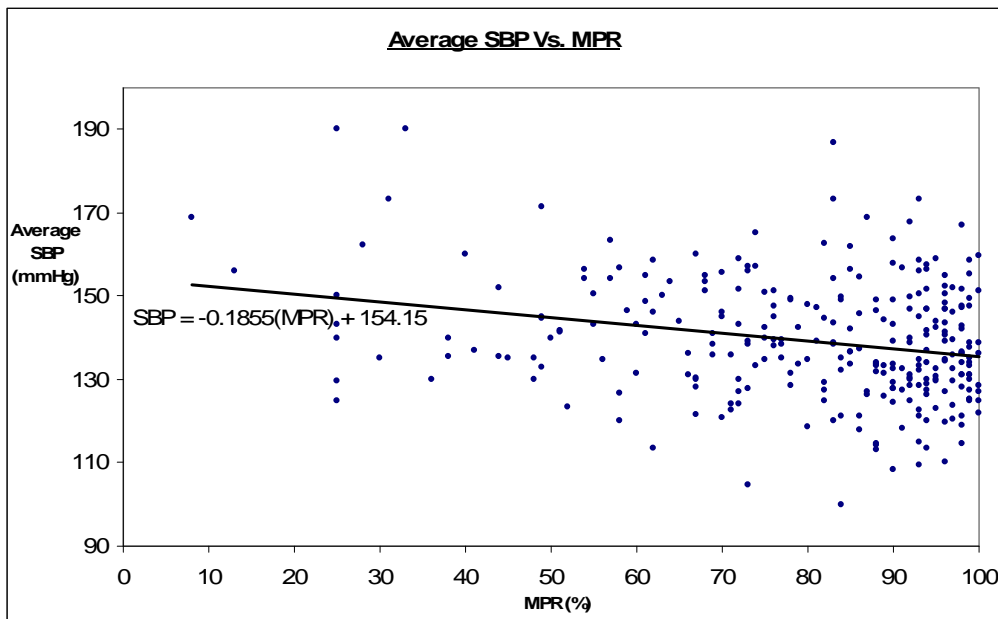


Figure 2. Plot of SBP versus MPR for HT patients.

3.2. Using the Data for Quality Assurance

Patients falling into the right-hand column of Table 3 (i.e. patients with uncontrolled SBP) presents an opportunity for the clinicians to improve SBP control of the practice's HT patient population. The patients who have uncontrolled SBP while having an adequate MPR (i.e. the notably large number of patients in the top-right quadrant) are expected to constitute a mix of those for whom the prescribing from the physicians is not sufficiently aggressive and those who are not taking the medication as directed. These patients require a different kind of follow-up from those in the lower-right quadrant (for whom the starting point will be attention to timely recall to the practice).

To identify patients with HT and DM who have uncontrolled SBP, for example, we can write a SQWRL query as shown in Figure 3. Here, *PatientsWithHT* and *PatientsWithDM* are other SWRL rules used to determine patients with HT and patients with DM respectively. These concepts are defined such that a patient with HT is a patient who has at least one associated HT diagnosis (based on Read Clinical Codes), and likewise for a patient with DM. *PatientsWithPrBeforeAP* and *PatientsWithPrDuringAP* are two other SWRL rules used to satisfy our inclusion criteria of having an AHT prescription before and during AP.

Name
qryUncontrolledSBPWithHTandDM
SWRL Rule
PatientsWithHT(?p) ^ PatientsWithDM(?p) ^ PatientsWithPrBeforeAP(?p) ^ PatientsWithPrDuringAP(?p) ^ avgSysBPDuringEP(?p, ?avgSys) ^ swrlb:greaterThanOrEqual(?avgSys, 130) ^ MPR_Overall(?p, ?mpr) → sqwrl:select(?p, ?avgSys, ?mpr)

Figure 3. A SQWRL query to determine patients with HT and DM who have uncontrolled SBP.

Once the required patients are identified, the prescribed medication can be visualised using a Microsoft Excel based tool we have developed (Figure 4). This can help identify whether uncontrolled SBP is due to potential lapse in prescribing, or due to patient specific reasons, such as non-adherence despite claiming a prescription; and thereby appropriate action taken to improve patient SBP.

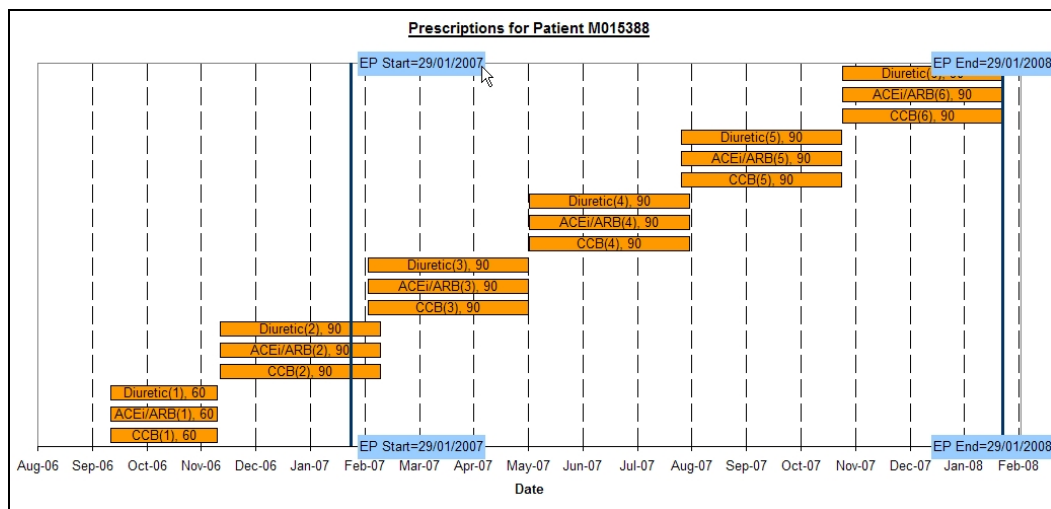


Figure 4. Prescribed medication for (an adherent) HT patient with uncontrolled SBP. The labels indicate the prescribed AHT drug class, prescription sequence number for that AHT drug class (in parentheses), and prescription coverage in days.

4. Discussion

In this paper we have presented an ontology based framework and workbench that can be used to determine HT patients whose BP control can be improved, based on prescribed medication and average SBP. The approach identifies individual patients within a practice, who can then be followed up by a clinician. The workbench provides a simple prescription timeline visualisation tool to aid determination of potential causes of uncontrolled SBP. We have used our architecture to model association of adherence (based on possession of prescriptions) to SBP control, finding both an (expected) significant positive correlation, and a promising area of contra-hypothesis cases for a quality assurance follow-up and further research.

Limitations of our study include the consideration of a single clinical practice (and therefore a relatively small sample of patients) and use of an MPR based on prescribing (as compared to dispensing) as a working measure of adherence. The software, coding and mode of practice, however, is substantially similar to the majority of practices in New Zealand and would have strong similarity to other countries with high uptake of electronic prescribing in the community (e.g., Australia and the UK).

The user interface of the workbench, consisting of Protégé with Java-based helper code (and some analysis presented herein via Microsoft Excel), is still under development. Our aim is to allow an end-user (e.g., a practice manager) to select from a range of SQWRL-based queries and to choose among a selection of definitions and parameter values to support their immediate quality assurance and/or research goals.

AHT has been the subject of considerable decision support systems research, notably the PRODIGY [14] and ATHENA [15] systems. The present research differs chiefly in emphasis on analysis of patient management over a fixed time period and with application to quality improvement over a cohort of patients rather than as interactive decision support at the point of care.

Our immediate research goal is to use the approach presented herein to identify (1) a cohort of non-adherent patients with uncontrolled SBP, and look into identifying patient reasons for non-adherence and; (2) a cohort of adherent patients with uncontrolled SBP and understand possible causes (study submitted to the Northern X Regional Ethics Committee protocol number NTX/08/17/EXP).

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