Copyright Statement

The digital copy of this thesis is protected by the Copyright Act 1994 (New Zealand).

This thesis may be consulted by you, provided you comply with the provisions of the Act and the following conditions of use:

- Any use you make of these documents or images must be for research or private study purposes only, and you may not make them available to any other person.
- Authors control the copyright of their thesis. You will recognise the author’s right to be identified as the author of this thesis, and due acknowledgement will be made to the author where appropriate.
- You will obtain the author’s permission before publishing any material from their thesis.

To request permissions please use the Feedback form on our webpage. [http://researchspace.auckland.ac.nz/feedback](http://researchspace.auckland.ac.nz/feedback)

General copyright and disclaimer

In addition to the above conditions, authors give their consent for the digital copy of their work to be used subject to the conditions specified on the Library Thesis Consent Form and Deposit Licence.

Note: Masters Theses

The digital copy of a masters thesis is as submitted for examination and contains no corrections. The print copy, usually available in the University Library, may contain corrections made by hand, which have been requested by the supervisor.
ChronoMedIt – A Computational Quality Audit Framework for Better Management of Patients with Chronic Disease

by

Thusitha Dananjaya De Silva Mabotuwana

Abstract

Chronic disease is a leading cause of death worldwide accounting for around 60% of all deaths. An important aspect of successful chronic disease management is quality audit and feedback to clinicians. However, due to the complex temporal relationships inherent in chronic disease, formulating clinically relevant queries is difficult using the querying tools often built into commercial practice management systems.

The onset of this PhD research involved working with staff of a general practice clinic to develop a set of explicit quality audit indicators for blood pressure control. Eight indicators were identified as most relevant to the practice. The ability to compute these indicators reliably from routinely collected electronic medical records (EMRs) was validated by clinical panel assessment. These eight indicators informed formulation of a model of chronic disease audit with four broad classes of indicators: (1) persistence to indicated medication; (2) timely measurement recording; (3) time to achieve target; and (4) measurement contraindicating therapy.

The four broad indicator classes have been implemented within the ChronoMedIt (Chronological Medical auditIt) framework as an extensible and configurable architecture. The main components of the ChronoMedIt architecture are: an XML based specification for indicator formulation (with an associated XML-Schema), a drug and classification knowledge base maintained using Semantic Web technologies, a C# based criteria processing engine, a SQL-Server based patient database with related stored procedures and a graphical user interface to formulate queries and generate reports. ChronoMedIt can produce patient-specific audit reports as well as reports to benchmark an entire practice for a given evaluation period. A visualisation tool has been developed to provide an alternate representation of patient prescribing and measurement histories. By modifying the indicator specification and knowledge base an analyst can address a wide array of chronic disease management queries as specific instances of the four broad indicator classes. The framework’s core computation has been verified using redundant query implementations on a battery of simulated case data and is illustrated against the EMRs of several practices.
ChronoMedIt has been applied in several real-world settings; notably, identifying patients with poor antihypertensive medication adherence profiles for a feasibility study of nurse-led adherence promotion.
Acknowledgements

It has been a long journey to get to the point of this thesis submission and I would like to express my sincere thanks to several people. First and foremost I would like to express my utmost gratitude to my PhD supervisor, Prof. Jim Warren for all his support during my PhD years. I certainly cannot imagine having a better supervisor than him and I cannot thank him enough for all his guidance, patience, knowledge, motivation and integrity. Having 15+ peer-reviewed publications is by no means easy for a PhD student to achieve within three years and I attribute this success to Jim since I could not have achieved this without his constant support and feedback with quick turnaround times on manuscripts. It has been a privilege working with Jim and I would also like to thank him for giving me the fantastic opportunity to work as an Assistant Research Fellow for the National Institute for Health Innovation (NIHI).

I would also like to thank my associate supervisor A/Prof. Tim Kenealy for all his support, encouragement and guidance, especially on clinical matters.

My sincere thanks also go to our clinical collaborators, especially Dr. John Kennelly whom I have been working with from the beginning of my PhD. John has been a clinical lead and getting access to production patient data in a timely manner would have been a much more daunting task without his support. Also, special thanks to Tim and Dr. Stewart Wells for assisting me in gaining access to patient data from their respective practices.

The constant support from the NIHI team – Malcolm, Chris, Koray, Rekha, Martin, Karen, Deb and Terri is also much appreciated. Also, special thanks to Rekha whose initial work with Jim gradually led to my PhD work. My fellow PhD students – Mehnaz, Priyesh, Helen and Jose – it has been great working with you all, worrying about ‘getting our PhDs done’ as well as sharing the somewhat regular setbacks/disappointments we have had together. I am sure our PhD years will always remain a great learning experience for us all. Also, thanks to my good friends Duleepa (special thanks to you for the tips on various PhD related matters), Saeyorn, Kushil, Thiranjith, Kasun, Charaka, Ruchira and Sasanka & Sasanka for organising various get-togethers and gaming sessions; they have been a good source of distraction from continuous thesis work.
I could not have completed this research without the financial support I received from The University of Auckland Doctoral Scholarship as well as NIHI and I thank both institutes for their support. Also, I have had the privilege of attending three local conferences and three international conferences during my PhD years and this was only made possible by the kind financial backing from Jim through his HoD account as well as the conference travel support grants from BuildIT, National Heart Foundation, The Royal Society of New Zealand and The University of Auckland’s PReSS funding for postgraduate students.

Last but not least, I would like to thank my loving family – mum Karnika, dad Thusantha and sister Hasini for putting up with me over the last so many years, providing me with absolutely all the support I can think of as well as encouraging me to start a PhD when I was in two minds. Working for long hours and then chatting/playing around with my little sister when I needed a break has kept me going, and I need to thank her for that. Aththa (grand-dad) and ammamma (grandma) – your encouragement is also very much appreciated and I hope I have made you proud by continuing your line of ‘educated children’. Finally, I would not have had the energy to work with so much perseverance without the continuous love, care, patience and support of one person who always admired and appreciated what I did and that is my loving wife Venuka. Special thanks for her patience and putting up with me no matter what.

Thusitha Mabotuwana

4th May 2010
2.3.3 The Medical Database Adaptor Framework ................................................................. 33
2.3.4 IDAN/KNAVE II Project ............................................................................................... 34
2.3.5 VISITORS System ....................................................................................................... 37
2.3.6 Temporal Extensions to Relational Databases ............................................................ 39
   2.3.6.1 Chronus and Chronus-II ....................................................................................... 40
   2.3.6.2 TimeDB ................................................................................................................ 41
   2.3.6.3 DXtractor ............................................................................................................. 41
2.3.7 Temporal Rule Mining ................................................................................................. 42
2.4 Quality Indicators in Primary Care .................................................................................. 44

3.0 DEVELOPMENT OF QUALITY AUDIT CRITERIA FOR CHRONIC DISEASE MANAGEMENT ... 52
   3.1 Background – the Therapeutic State Transition Model .................................................. 52
   3.2 Development of Audit Criteria and The Quality Audit Report ......................................... 56
   3.3 An Initial Implementation of the Audit Criteria .............................................................. 59
       3.3.1 Data Extraction, Data Cleaning and Pre-Processing .............................................. 59
       3.3.2 Quality Audit Report Generation ............................................................................ 64
   3.4 Criteria Validation – The 20/20 Study .......................................................................... 66
   3.5 Four Categories of Quality Audit Criteria ..................................................................... 72

4.0 PRELIMINARY RESULTS – AN ONTOLOGY BASED APPROACH ......................................... 74
   4.1 Limitations of Using an Entirely SQL-based Approach (the Previous Implementation) ...... 74
   4.2 Domain-Modelling and Methods ................................................................................... 76
       4.2.1 An Ontology-Based Approach .............................................................................. 76
       4.2.2 A Unified Patient Management Ontology ........................................................... 77
       4.2.3 PMS Data Extraction ............................................................................................ 79
       4.2.4 Patient Data Pre-processing and Dynamic Creation of OWL Properties ............... 79
   4.3 Identifying Patients with Hypertension on Suboptimal Therapy using the Ontology Based Approach .......................................................... 83
       4.3.1 Disease Management Ontology ............................................................................ 83
       4.3.2 Patient Data Ontology .......................................................................................... 86
       4.3.3 Best Practice Violation Taxonomy ........................................................................ 87
       4.3.4 Querying the Ontology using SQWRL ................................................................. 89
       4.3.5 An Excel-based Prescription Timeline Visualisation Tool ...................................... 92
   4.4 Other Ontology Related Work and Limitations of a Pure Ontology Based Approach ....... 93

5.0 CHRONOMEDIT FRAMEWORK ARCHITECTURE .................................................................. 97
   5.1 The Need for a Novel Criteria Model ............................................................................ 97
   5.2 Framework Verification ................................................................................................. 98
   5.3 Introducing Medication Adherence as an Audit Criterion ............................................. 99
5.4 The Criteria Model

5.5 The Computational Framework

5.5.1 Creating Audit Criteria

5.5.2 The Drug and Classification Knowledge Base

5.5.3 ChronoMedit’s Database Structure and Parsing BPs and Lab Test Results

5.5.4 Implementation of the Criteria Model

5.5.5 Framework Outputs

5.5.5.1 Adherence/Persistence to Indicated Medication

5.5.5.2 Timely Measurement Recording

5.5.5.3 Time to Achieve Target

5.5.5.4 Measurement Contraindicating Therapy

5.5.6 The Graphical User Interface

5.5.7 Criteria Processing with SQL or Sequential Implementation and Verification of Results

6.0 FRAMEWORK TESTING

6.1 An Overview of Software Testing Concepts

6.1.1 A Basic Introduction

6.1.2 Types of Functional Testing

6.1.2.1 Boundary Value Analysis

6.1.2.2 Equivalence Class Testing

6.1.2.3 All-Pairs Testing

6.2 Methods

6.3 Identification of Test Cases

6.3.1 Test Cases for Persistence of Medication and Timely Measurement Recording

6.3.2 Test Cases for Measurement Contraindicating Therapy

6.3.3 Test Cases for Time to Achieve Target

6.4 Random Testing to Ensure Software Reliability

6.5 Errors Detected

6.6 Limitations of Framework Testing

7.0 APPLICATIONS USING CHRONOMEDIT

7.1 Data Extract

7.2 Identifying patients satisfying the eight audit criteria

7.3 Investigating ACEi/ARB adherence issues and the relationship to BP control in patients with hypertension and diabetes

7.4 Antihypertensive adherence and impact on BP control

7.5 Interval Based Measures as Quality Indicators in Blood Pressure Management

7.5.1 Analysis Protocol
Lists of Tables

Table 3.1: Therapeutic state variables and their respective ATC codes ......................................................... 53
Table 3.2: Prescription durations, their therapeutic state variables and corresponding state transitions for a hypothetical patient ............................................................................................. 55
Table 3.3: Examples of types of quality audit report statistics for patients classified with hypertension .......................................................................................................................... 58
Table 3.4: The eight quality improvement criteria agreed with practice panel ........................................... 66
Table 3.5: Accuracy of automated queries as assessed against final review by the practice panel .......... 69
Table 3.6: Criteria and practice panel assessments for six-month evaluation period .............................. 69
Table 3.7: Cases where panel initially disagreed with classification by automated queries (False Positives); and final classification after review ................................................................. 70
Table 3.8: False Negatives ......................................................................................................................... 70

Table 5.1: Definitions of PDC uncapped and PDC capped ........................................................................ 103
Table 5.2: Different adherence calculations ............................................................................................ 104
Table 5.3: Using elements from the Criteria Model to formulate criteria in Table 3.4 ............................ 108

Table 6.1: Test cases for weak-robust equivalence class testing for medication lapse with diagnosis prior to evaluation period ........................................................................................................... 145
Table 6.2: All-pairs test cases for medication lapses with diagnosis prior to evaluation period .......... 146
Table 6.3: Test cases for weak-robust equivalence class testing for medication lapse with diagnosis during the evaluation period .................................................................................................. 148
Table 6.4: All-pairs test cases for medication lapses with diagnosis during the evaluation period ....... 149
Table 6.5: Test cases for special value testing .......................................................................................... 151
Table 6.6: Test cases when diagnosis date is just before, equal to or just after the beginning of the evaluation period ...................................................................................................................... 151
Table 6.7: BVA test cases for the interaction between the lapse period and the diagnosis date or beginning of the evaluation period ................................................................. 153
Table 6.8: Test cases for BVA on lapse duration ...................................................................................... 155
Table 6.9: Weak-robust equivalence class test cases for the management of compelling indications .................................................................................................................................. 157
Table 6.10: Test cases for BVA for the management of compelling indications ...................................... 158
Table 6.11: Test cases for weak-robust equivalence class testing for time to achieve target .............. 162
Table 6.12: BVA on location of uncontrolled measurements for time to achieve target ..................... 163
Table 6.13: BVA around the minimum required number of days over which consecutively uncontrolled measurements should occur ....................................................................................... 164
Table 6.14: BVA around the minimum number of measurements required to satisfy criterion ........... 164
Table 6.15: Operational profile for various parameters in the input space ........................................... 168
Table 6.16: Details of the populated test database ................................................................................ 170
Table 6.17: Audit criteria with parameters for random testing ............................................................... 171

Table 7.1: Summary of the two practice datasets for funded and enrolled patients .............................. 177
Table 7.2: Number of patients classified with hypertension satisfying the eight audit criteria ........... 178
Table 7.3: Number of patients classified with hypertension and diabetes satisfying different adherence criteria......................................................................................................................... 179
Table 7.4: ACEi/ARB adherence vs. BP in patients with hypertension and diabetes .............................. 180
Table 7.5: Antihypertensive adherence vs. BP in patients with hypertension ........................................ 180
Table 7.6: PPVs of quality indicators based on past performance on same indicator ......................... 185
Table 7.7: PPVs between different indicators for Practice-1 ............................................................. 186
Table 7.8: PPVs between different indicators for Practice-2 ............................................................ 186
Table 7.9: Patients with hypertension satisfying different quality indicators .................................. 189
Table 7.10: Patients with diabetes satisfying different quality indicators ....................................... 189
Table 7.11: Patients satisfying a QOF indicator (BP5/DM12), but failing any one of the three indicators of interest ............................................................................................................ 189
Table 7.12: Prescribing and dispensing frequencies for selected drugs ............................................ 194
Table 7.13: Adherence levels for selected long-term medications ...................................................... 194
Table 7.14: Association of individual MPR_Pr and MPR ................................................................. 195
Table 7.15: Frequencies with which patients are prescribed and dispensed multiple of the six selected drugs during the evaluation period, or with supply extending into the evaluation period ............................................................................................................. 196
Table 7.16: Prescriptions with associated first dispensing within 7 days after being prescribed ......... 197
Table 7.17: Characteristics of the patients on one or more of the six long-term medications .......... 198
Table 7.18: Association of prescribing based non-adherence and dispensing based non-adherence ........................................................................................................................................ 202
Table 7.19: Characteristics of patients prescribed antidepressant medication ................................. 203
Lists of Figures

Figure 2.1: A sample ATHENA advisory recommendation appearing as a popup window on top of the existing EMR system ................................................................. 20
Figure 2.2: A sample BP-Prescription graph produced by the ATHENA DSS ........................................ 21
Figure 2.3: The classes of objects in the PRODIGY III Virtual Medical Record ................................. 23
Figure 2.4: A high level view of a hypertension guideline .................................................................. 23
Figure 2.5: The thirteen possible relationships between time intervals. X and Y denote time intervals ............................................................................................................................... 28
Figure 2.6: Typical inputs to and outputs of RÉSUMÉ together with point and interval based abstractions ......................................................................................................................... 31
Figure 2.7: The EON architecture .......................................................................................................... 33
Figure 2.8: The components of the IDAN architecture ........................................................................... 35
Figure 2.9: Main interface of KNAVE-II ................................................................................................. 37
Figure 2.10: The VISITORS main interface ............................................................................................ 38
Figure 3.1: Therapeutic state-transitions for antihypertensive prescribing over a 20-month period for patients with hypertension and diabetes (for transitions with ≥3 occurrences) .... 54
Figure 3.2: An individual path diagram ................................................................................................ 55
Figure 3.3: The evaluation period specific to the quality audit report .................................................. 57
Figure 3.4: Some of the different ways of recording prescription durations within the PMS .............. 59
Figure 3.5: Multiple classifications of a single patient. PROV indicates the GP initials ....................... 62
Figure 3.6: The data preparation process ............................................................................................... 63
Figure 3.7: Overview of the QAR generation process ........................................................................... 64
Figure 3.8: Base cases to identify a lapse in medication during the evaluation period ....................... 65
Figure 3.9: Criteria and sampling for evaluation ................................................................................... 67
Figure 3.10: The three-question assessment instrument ....................................................................... 68
Figure 4.1: Temporal cases to be taken into account when formulating a query to determine “patients classified with diabetes not on ACEi/ARB any time during the evaluation period” ................................................................................................................................. 75
Figure 4.2: Stages of data pre-processing ............................................................................................. 80
Figure 4.3: Temporal cases when determining a lapse in therapy ....................................................... 81
Figure 4.4: Creation of the next_prescription links for various drug classes ........................................ 82
Figure 4.5: The Protégé-OWL classes tab showing knowledge base concepts created to represent patient diagnoses codes and the various antihypertensive drug classes ........................................... 84
Figure 4.6: Protégé-OWL instances tab showing the populated disease management ontology ...... 85
Figure 4.7: The patient data ontology and details for a selected patient ............................................ 87
Figure 4.8: The best-practice violation taxonomy ................................................................................ 88
Figure 4.9: SQWRL query to identify hypertensive patients with a lapse in their antihypertensive therapy for over 30 days with lapse extending into or occurring during the evaluation period ................................................................................................................................. 90
Figure 4.10: The rule/query authoring and executing environment ....................................................... 91
Figure 4.11: Visualisation of a prescription timeline for a selected patient ........................................ 93
Figure 5.1: Temporal relations to consider when calculating MPR .................................................... 101
Figure 5.2: Prescribing patterns for a hypothetical patient ................................................................. 104
Figure 5.3: Elements of ChronoMedIt’s Criteria Model (using UML notation) ................................. 105
### Glossary of Terms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEi</td>
<td>Angiotensin-converting enzyme inhibitor</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin receptor blocker</td>
</tr>
<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical</td>
</tr>
<tr>
<td>ATHENA</td>
<td>Assessment and Treatment of Hypertension: Evidence-Based Automation</td>
</tr>
<tr>
<td>CDSS</td>
<td>Clinical decision support system</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Intervals</td>
</tr>
<tr>
<td>CIG</td>
<td>Clinical interpretable guideline</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>CPG</td>
<td>Clinical practice guideline</td>
</tr>
<tr>
<td>CPT</td>
<td>Current Procedural Terminology</td>
</tr>
<tr>
<td>CSV</td>
<td>Comma-separated values</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>CVR</td>
<td>Cardiovascular risk</td>
</tr>
<tr>
<td>DHB</td>
<td>District Health Board</td>
</tr>
<tr>
<td>eGFR</td>
<td>Estimated glomerular filtration rate</td>
</tr>
<tr>
<td>EMR</td>
<td>Electronic medical record</td>
</tr>
<tr>
<td>EP</td>
<td>Evaluation period</td>
</tr>
<tr>
<td>GLEE</td>
<td>GLIF3 Guideline Execution Engine</td>
</tr>
<tr>
<td>GLIF</td>
<td>GuideLine Interchange Format</td>
</tr>
<tr>
<td>GP</td>
<td>General practitioner</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Haemoglobin A1c</td>
</tr>
<tr>
<td>HTML</td>
<td>HyperText Markup Language</td>
</tr>
<tr>
<td>HTTP</td>
<td>Hypertext Transfer Protocol</td>
</tr>
<tr>
<td>ICD</td>
<td>International Classification of Diseases</td>
</tr>
<tr>
<td>ICPC</td>
<td>International Classification of Primary Care</td>
</tr>
<tr>
<td>JDBC</td>
<td>Java Database Connectivity</td>
</tr>
<tr>
<td>JNC6</td>
<td>Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure</td>
</tr>
<tr>
<td>JNC7</td>
<td>Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>UTAR</td>
<td>Unexpected temporal association rule</td>
</tr>
<tr>
<td>VBA</td>
<td>Visual Basic for Applications</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>XML</td>
<td>Extensible Markup Language</td>
</tr>
</tbody>
</table>