A Report on Programming a Clinical Decision Support Algorithm to Capture Inappropriate Complete Blood Count and Basic Metabolic Panel Lab Orders Using Arden Syntax, a Formalism for Medical Logic Modules

A THESIS
SUBMITTED TO THE FACULTY OF THE
UNIVERSITY OF MINNESOTA

BY

DIVYA RUPINI GUNASHEKAR

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
MASTER OF SCIENCE

Adviser: Dr. Terrence Adam, RPh, PhD, MD

October 2019

ProQuest Number: 22624605

ProQuest 22624605

COPYRIGHT PAGE

Divya Rupini Gunashekar

2019

ACKNOWLEDGEMENT

Firstly, I would like to express my sincere gratitude to my advisor Dr. Terrence Adam, for giving me an opportunity to work under him and for his continuous support related to my master's project, for his patience, motivation, and immense knowledge.

I would like to extend my sincere gratitude to Dr. David Pieczkiewicz, a great teacher and who I have always looked up to. His kindness, encouragement and continuous support has helped me come a long way both in my grad school and in my career.

I would also like to extend my heartfelt thanks to Dr. Sripriya Rajamani, who gave me a chance to prove my mettle. Thank you for believing in me and guiding me through the right path in my grad school.

Finally, my heartfelt thanks to Dr. Caleb Murphy for providing me an opportunity to work in this project. And, my family for all your sacrifices, unconditional love, support, guidance and many more. You are the best family and a Shout Out to you all.

DEDICATION

To Daddy, M K Gunashekar, who I miss immensely. Without your love, prayers, constant support and encouragement my master's would have been only a dream.

Contents

PROJECT BACKGROUND

This project is the second phase of research on Minnesota Laboratory Appropriateness (MLAB) Criteria that focuses on developing medical logic for the clinical decision support system that can be adapted to a wide variety of electronic health record (EHR) systems. Of all the wasteful spending on healthcare in the United States one third of the wasteful spending and overtreatment includes laboratory test utilization. Research findings indicate that up to four billion labs of the seven to ten billion lab tests ordered annually are inappropriate[3,4]. To address this area of overutilization, guidelines for laboratory tests to identify appropriate and inappropriate utilization for complete blood count (CBC) and Basic Metabolic Panel (BMP) lab orders in an inpatient setting were developed by Dr. Caleb Murphy and his research team in phase one of this study. The recommendations for MLAB criteria were based on Choosing Wisely initiative[22,23]. Though there are many studies reported on lab overutilization, to our knowledge, no prior studies have developed or programmed a clinical decision support system (CDSS) embedded into the EHR to monitor and correct the rates of inappropriate CBC and BMP screening in an inpatient setting [1]. To facilitate the detection of imprudent lab orders for the aforementioned tests, the Arden Syntax, a formalism for representation of procedural medical knowledge, is used to facilitate knowledge transfer [2] . The unit of representation in the Arden Syntax is the Medical Logic Module (MLM), which contains enough data and logic to make a single medical decision.

1

INTRODUCTION

An electronic health record (EHR) stores health care information about an individual's lifetime with the purpose of supporting continuity of care, education and research. In recent years, the expansion and transition of health record systems from paper-based records to computerized, digital formats has opened a vast range of opportunities in health care to facilitate continuity of care, along with an opportunity to analyze health data to enhance the quality of care and cost efficiency in healthcare. The influx of enormous silos of health data from EHRs has enabled clinicians, researchers, health informaticians and stakeholders to use information technology more frequently than ever to transform knowledge into executable actions and deliver value based care with the help of Clinical Decision Support Systems (CDSS) embedded in the EHR[5]. With rapid advancement in technology, measuring low value health services, improving quality and eliminating waste has become a major goal of healthcare delivery systems. Clinical decision support tools embedded in electronic health records have substantial potential to help with real-time monitoring and can help to avoid unnecessary medical procedures and tests thereby cutting costs. The Choose Wisely campaign by American Board of Internal Medicine Foundation has established many initiatives to reduce waste in the healthcare system. One of them is the American Society for Clinical Pathology, which continuously strives to enhance and develop pathology advocacy to improve patient care. Many studies that adapted Choose Wisely have demonstrated reductions in overutilization in many areas of healthcare in diverse settings[14] .

2

Two of the most overutilized diagnostic tests in the healthcare setting are the Complete Blood Count (CBC) and the Basic Metabolic Panel (BMP). These tests are the two most common tests done when a patient is hospitalized for an overnight observation or for a longer duration due to a medical condition[6]. These blood tests such as red blood cell (RBC), white blood cells (WBC), platelets, hemoglobin and hematocrit of CBC help the care providers to diagnose a medical condition or a disease that affects the blood cells like anemia, inflammation, infection, bleeding disorder or cancer[29]. The BMP test, which includes eight tests, i.e., glucose, calcium, sodium, potassium, chloride, CO2, BUN and creatinine, helps to identify the presence of any metabolic disorder, as well as gauge renal function and acid/base balance and electrolytes. A combination of abnormal results in CBC/BMP will suggest presence of an abnormality that would require immediate medical attention. Besides identifying an underlying condition, they also indicate if the treatment plan is working or not. Many a time, these tests are ordered daily or even repeatedly on the same day by busy physicians out of habit or in a hurry[7]. This mere over sightedness has led to high volume of blood tests, raising the risk of iatrogenic anemia and transfusion in hospitalized patients, along with increased burden of healthcare costs both on the patient and the payor.

For example, a study conducted by the Society for the Advancement of Blood Management (SABM) published that up to 90% of patients become anemic by day 3 in the intensive care unit. Although laboratory testing aids in diagnosis, prognosis and treatment of disease, a significant number of tests are inappropriate or unnecessary. To avoid increased length of

stay and mortality due to anemia caused by iatrogenic blood loss, SABM recommends that the blood testing should not be performed in the absence of clinical indications and encourages judicious use of laboratory testing[8]. In another study conducted at UF Health Shands Hospital, Dr. Bejjanki found that the hospital's lab annual costs were over the national average and noticed that some of the blood tests, such as CBC and hemoglobin A1C, were performed multiple times on the same patient in a span of two to three days. To address this excess utilization, the researchers developed a computerized alert system following the recommendations of Choosing Wisely. The study focused on monitoring and controlling excessive lab orders for 17 clinical lab tests, including complete blood count (CBC with diff), B12, HbA1C and for prostate specific antigen. The alert system developed by the researchers helped the care team to track the most recently ordered test by displaying the test ordering time, collecting time, resulting time and the most recent results, thereby decreasing the duplicate orders. Results from this study indicated that, at the end of the 17 months trial the hospital's cost for duplicate labs declined by roughly by $70,000 over the study period. This change came from a 58.7 percent decrease in duplicate Vitamin D and a 6.9 percent decrease in duplicate PSA tests. Overall, this study's intervention was effective in reducing the total number of inpatient duplicate orders, as well as the percentage of duplicate orders among the total number of inpatient lab orders. The researchers of this study attributed success to the EHR-based intervention strategy[9]. At Vanderbilt University, the medical center's Choosing Wisely steering committee led by Wade Iams and his team conducted research to minimize the unnecessary lab orders for CBC and BMP in inpatient general medicine and surgical services. The committee

4

approached this issue by conducting a several months long competition between teams of physicians by peer review and monitoring lab orders. The team that avoided the most unnecessary lab orders were declared winners at the end of each month. At the end of one of the month's studies, the Choose Wisely committee of the VUMC reported the following outcomes: about 308 unnecessary labs were eliminated, 77 misleading lab results were avoided, \$38,222.78 in billable costs were saved by patients and about 1,541 ml of blood was not drawn[11]. This initiative improved the meaningful use of healthcare resources and patient experience.

In different scenarios such as lab tests, and other tests such as ECG in patients undergoing low-risk surgery, it is estimated that about \$18 billion is spent annually on preoperative testing in the US alone. It is not known how much wasteful testing is done in preoperative cases. To understand the services of questionable value in low value services, researchers at general internal medicine division at Dartmouth-Hitchcock Medical Center analyzed their patient data following the standard guidelines established by choosing wisely initiative, to measure the number and rates of unnecessary tests performed. Results from the baseline study indicated that approximately 36% of the tests were unnecessary. At the end of the intervention of minimising the wasteful preoperative tests, the researchers noticed a 5-fold reduction in unnecessary testing[17].

In most of the above studies the researchers have used the EHR system in some way to capture, analyze and deploy strategies that helped reduce the ordering of unwanted lab tests. In order to facilitate the computer-based detection of excess or repetitive lab orders

5

in any hospital settings, the use of CDSS could serve as an effective tool[1]. Many evidence based CDSS components such as checking on drug-drug interactions, duplicate therapy, drug-allergy interactions, generalized drug dosing, checking on contraindications (diseases and drugs), individualized dosing support during renal impairment, and guidance for medication-related laboratory testing have proven that their relatively low cost to implement along with demonstrably positive outcomes make them useful for clinical implementation and regular use. In addition, the option of customizing the CDSS allows the care provider to look only at the necessary data needed to direct actions and/or track data over a period of time. EHR-based clinical decision tools are simple, relatively inexpensive tools to achieve consistent and sustainable change in healthcare practice.

6

CLINICAL DECISION SUPPORT SYSTEMS: FUNCTION AND DEFINITION

Clinical decision support tools are learning health system tools designed to help sift through enormous amounts of digital data to suggest next steps for treatments, alert providers about available information they may not have seen, or catch potential problems, such as dangerous medication interactions, etc. A clinical decision support system derives its definition from its prefix clinical decision support, which is a process for enhancing health-related decisions and actions with appropriate, organized clinical knowledge and patient information to improve health and healthcare delivery. Information recipients can include patients, clinicians, and others involved in patient care delivery; Information delivered can include general clinical knowledge and guidance, intelligently processed patient data, or a mixture of both; and information delivery formats can be drawn from a rich palette of options that includes data and order entry facilitators, filtered data displays, reference information, alerts, and others[15].

Historically, the first known CDSS was called the Leeds Abdominal Pain System and was developed at the University of Leeds using Bayesian probability theory. This system used sensitivity, specificity and disease-prevalence data for various signs, symptoms, and lab test results to calculate the probability of seven possible explanations for acute abdominal pain due to appendicitis, diverticulitis, perforated ulcer, cholecystitis, small-bowel obstruction, pancreatitis, and nonspecific abdominal pain. This system required manual entry of data to predict cause of pain by Bayes rule and the diagnosis prediction was made assuming that each patient had one of the seven conditions for pain and selected the most

likely one based on the recorded observations. This system was built to predict the diagnosis within five minutes after the data form was completed. During the system evaluation the Leeds system was 91.8% accurate and predominantly used for appendicitis diagnosis.

In 1976, Shortliffe and et. al, took a different approach to build a clinical decision support system to manage patients who had infections. The system was built with the help of *artificial intelligence* (AI), that focused on manipulation of abstract symbols rather than on numerical calculations. This system was called as MYCIN. The knowledge of infectious diseases in MYCIN was represented as production rules, such as conditional statements that relates observations to associated inferences for diagnosis prediction. The developers of MYCIN system examined its performance in a pilot study on patients with blood-borne bacterial infections and meningitis. MYCIN, performed well in the latter case with appropriate and favorable advice which was better over the advice offered by the experts in infectious diseases. However, this system was never used clinically, but it paved the way for CDSS research and development in the following years[24].

Prior to the development of the above two systems, in 1967, a complete knowledge base hospital management system called as HELP was developed at LDS Hospital in Salt Lake City, Utah. The primary use of this system was to support heart catheterization laboratory and post open heart surgery intensive care unit. Since then the system has been expanded to become an integrated hospital information system providing services with sophisticated clinical decision-support. This system was originally created with created a specialized

8

language named PAL for writing medical knowledge in logic modules. Later in 1990's the system developers for HELP adopted a standard formalism for encoding decision rules known as the Arden Syntax. More details about the Arden Syntax is discussed in the next section[24].

Over the years HELP system has served as an exemplary example of an integrated decision support system with multiple functions such as an alert and warning system and as an CDSS embedded with EHR. Though all the afore mentioned systems were used with lot of skepticism, the subsequent evolution of EHR has changed the perception over time and the CDSS are now an integral part of healthcare team, patient and disease management.

ARDEN SYNTAX: DEFINITION & STRUCTURE

The Arden Syntax is a widely and commonly used standard for representing clinical and scientific knowledge in an executable format through CDSS to generate alerts, interpretations and to screen and send messages to clinicians. It was first introduced in 1989 at the **Arden** Homestead Conference in Harriman, New York, hence the name 'Arden Syntax'[17]. It has two versions, i.e., Version 1.0 that was adopted by the ASTM in 1992, and Version 2.0 was adopted by HL7 and ANSI in August 1999. It is currently maintained by the Health Level 7 (HL7) organization. The syntax used in this project is based on Version 2.

This syntax uses rule sets called Medical Logic Modules (MLM), that comprise enough logic to make a single medical decision[18]. An MLM is an independent unit in a health knowledge base and a hybrid between a production rule (i.e., an "if-then" rule) and a procedural formalism that makes it simpler to read and comprehend when compared to other types of computer enabled coding structures. Each MLM is invoked as if it were a single-step "if-then" rule, and then is executed serially as a sequence of instructions, including queries, calculations, logic statements and write statements. Sequencing tasks are modelled by chaining a sequence of MLMs. MLMs, when integrated into computer programs, are run automatically, generating advice as needed[17]. In this project, the MLM is coded to warn physicians when a patient's blood test for CBC and BMP are inappropriate.

Structure

An MLM is composed of slots grouped into three categories, namely, *maintenance, library, and knowledge*. A category is indicated by a category name and immediately followed by a colon. The categories must appear in the order they appear in this standard.

1. Maintenance Category

The maintenance category contains the slots that specify information unrelated to the health knowledge in the MLM. These slots are used for MLM knowledge base maintenance and change control. The maintenance category also contains information about the version of the Arden Syntax that is being used.

A sample of the maintenance category with its slots is described below.

```
Maintenance:

        title: /* write your project title here*/;;
        arden: Version 2.0;;
        version: 1.00;; /* current version of MLM*/
        institution: University of Minnesota;;
        author: /*type the author name- first name, middle
name or initial, last name, comma, suffixes, comma, and
degrees preceded by email in parenthesis*/ ;;
        specialist:/*type specialist name in the following
order - first name, middle name or initial, last name, comma,
suffixes, comma, and degrees*/  ;;
        date: 1989-01-02;;
        validation: testing;; /* Use one of the following
terms:
a) production—approved for use in the clinical system,
```

```
b) research—approved for use in a research study,

c) testing—for debugging (when an MLM is written, this should
be the initial value), or

d) expired—out of date, no longer in clinical use.*/
```

2. Library Category

The library category contains the slots relevant to knowledge base maintenance that are related to the MLM's knowledge. These slots provide health personnel with predefined explanatory information and links to the health literature. They also facilitate searching through a knowledge base of MLMs.

A sample of the library category with its slots is described below.

```
Library:
    purpose: /* type purpose for building the syntax*/ ;;
    explanation: /* Brief description of the purpose*/ ;;
    keywords: example, CBC; lab tests;;
    citations: Examples,
            1. SUPPORT Steiner RW. Interpreting the
        fractional excretion of sodium. Am J Med
        1984;77:699-702.

            2. Goldman L, Cook EF, Brand DA, Lee TH, Rouan
        GW, Weisberg MC, et al. A computer protocol to
        predict myocardial infarction in emergency
        department patients with chest pain. N Engl J Med
        1988;318(13):797-803.

     ;;
    links: Examples,
        OTHER_LINK 'CTIM .34.56.78';
```

```
        MESH               'agranulocytosis/ci              and
    sulfamethoxazole/ae';

        URL "NLM Web Page", 'http://www.nlm.nih.gov/';

        ;;

    /*Note: Each institution should test for expired links
    when receiving shared MLMs*/
```

3. Knowledge Category:

This category contains the slots that actually specify what the MLM does. These slots are four types and define the terms used in the MLM (data slot), the context in which the MLM should be evoked (evoke slot), the condition to be tested (logic slot), and the action to take if the condition be true (action slot).

A sample of the Knowledge category with its slots is described below.

```
Knowledge:
    type: data_driven;;
    or
    type: data-driven;;
    Data: /*in this slot, the institution-specific portions
are placed in mapping clauses and defined using {xyxz} and
ASCII 123 and 125 respectively. It also includes database
queries*/
    priority: example, between 1 to 90;;
/*The priority is a number from 1 (low) to 99 (high) that
specifies the relative order in which MLMs should be evoked
should  several  of  them  satisfy  their  evoke  criteria
simultaneously. An institution may choose whether or not to
use a priority.*/
```

```
    Evoke: /*this slot defines how an MLM may be triggered,
such as,

      1. during an occurrence of Some Event,
      2. A Time Delay After an Event and
      3. Periodically After an Event */ ;


    Logic: /* this slot contains the actual logic of the MLM
such as True/ false, if-then, if-then-else, etc. */


      Example,
      IF <expr1> THEN
      <block1>
      ENDIF;
    action: /* sends texts or coded messages*/
      Example,
      WRITE <expr>;
      WRITE <expr> AT <destination>;
      ;;
    Urgency:  /*urgency  of  the  action  or  message  is
represented as a number from 1 (low) to 99 (high). (this is
different from priority- executes MLM in certain order) */
      Example,
      urgency: 50;;
      urgency: urg_var;;
/* 50 is neutral to take an action, may vary from institution
to institution*/
    End: /* end of logic*/
```

Resource Category: (Optional)

This category is optional and allows for defining localized and different language messages. It Specify the textual resources from which the localized messages are taken.

A sample of Resource Category with different slots is given below.

```
    Example,
    default: en;; /*Default language*/
```

14

```
language: en /* varies for different languages*/
'SIRS': "alert for SIRS";
```

*Note: More details to write MLM can be found on "Arden Syntax for Medical Logic Systems"[19].

Although, MLMs are easier to write and read, it takes more than MLMs to make a logic unit work in real time. Besides MLMs, the Arden Syntax includes database queries, constructs for time, and lists, availability of data and compliance to the HIPAA standards to conciliate concerns surrounding data privacy and patient confidentiality. Each of these elements that are required to make a clinical decision tool work are discussed below in brief.

Many decision-support systems are able to collect data from a computerized patient database to support the triggering of an MLM without a specific request for assistance or human intervention. Unfortunately, all MLMs cannot handle every contingency for every query by connecting to different databases without the intervening of human support to filter data and queries. For each feature in the Arden Syntax queries, two factors are important: whether the feature is useful to medical rules and whether the feature can be implemented on patient and other databases such as laboratory, imaging, pharmacy and other databases in the existing clinical information systems. Since some of these silos of data are not always present in the same institutional data warehouse, additional efforts at mapping and matching of data to patient information may be needed prior to returning the information to the logic for MLM operation.

15

The diversity in vocabularies and database structures in different institutes and databases may not always match the definition of a single syntax for querying diverse databases. However, The Unified Medical Language System (UMLS), a compendium of many controlled vocabularies, provides mappings between many of the available standard vocabularies, and can facilitate the translation of queries to accommodate different databases and map terms to a local clinically descriptive vocabulary.

With regard to data availability, an MLM will not function if the data is not available in an institution's database. In such cases, the MLM has to be modified to capture the full rule set. Sometimes a missing data element can be derived from other data that are stored in different data marts or databases. Based on the intended purpose of a CDSS and the data types, Arden Syntax may have to use different operators such as logical operators, comparison operators, string operators, arithmetic operators, temporal operators, aggregation operators, and time and object operators to handle the situation of unavailable data. For instance, Arden Syntax will have to be coded to perform calculations on the results obtained from database queries. Then the result of the calculation can be assigned to the local variable name used in the logic of the MLMs. Also, the aggregation operations have to be coded separately from the decision-making query and logics[24]. A lot of research and work needs to be done to address the issues that can be encountered during the testing and implementation phases.

In case of issues concerning data safety for interoperability, the fact that Arden Syntax is maintained and sponsored by the Health Level 7 standards, provides several logistical

16

advantages. HL7 International specifies a number of flexible standards, guidelines, and methodologies by which various healthcare systems can communicate with each other. Such guidelines and data standards allow information to be shared and processed in a uniform and consistent manner. These data standards are meant to allow healthcare organizations to easily share and use clinical information that meets HIPAA standards and facilitates system interoperability.

Some of the most commonly used and implemented standards are:

- Version 2.x and Version 3 Messaging Standard – an interoperability specification for health and medical transactions

- Clinical Document Architecture (CDA) – an exchange model for clinical documents, based on HL7 Version 3.

- Continuity of Care Document (CCD) – a US specification for the exchange of medical summaries, based on CDA.

- Structured Product Labeling (SPL) – the published information that accompanies a medicine, based on HL7 Version 3.

- Clinical Context Object Workgroup (CCOW) – an interoperability specification for the visual integration of user applications[27].

- Other HL7 standards include:

- Fast Healthcare Interoperability Resources (FHIR) – a standard for the exchange of resources.

17

- Claims Attachments – a Standard Healthcare Attachment to augment another healthcare transaction.

- Functional Specification of EHR / PHR systems – a standardized description of health and medical functions available in such software applications.

- GELLO – a standard expression language used for clinical decision support.

Some of these standards can be researched further and applied in the intervention phase to implement the syntax that involves the integration of diverse data resources at the institute where the software will be tested.

TESTING AND IMPLEMENTATION

Though this project was mainly focused on developing an algorithm to monitor appropriate and inappropriate CBC and BMP lab orders, for an overview about Arden Syntax's System Development and Life Cycle, a brief review of testing and implementation is discussed here.

Lex, or Lexical Analyzer, and Yacc, also known as 'parsers,' are the tools used to test the syntax for reliability and imprecision. When these two tools are used together, they create a compiler or interpreter. Lex splits the source file into tokens and Yacc finds the hierarchical structure of the program and also verifies that the input is syntactically sound. These tools help reduce ambiguities in the syntax[20].

The only true test of the syntax for implementation is to use it in an actual healthcare setting. Both its ability to represent medical knowledge within an institution and its amenability to sharing must be judged during testing. For implementation, different institutes use different compilers and translator tools to translate the MLM into an intermediate form for execution. Some of these tools are Yacc, Prolog and Arden2ByteCode (using Java ByteCode). In the future, during the intervention phase of this syntax for testing and implementation, more work in these lines would be carried out.

19

HIGHLIGHTS OF MLAB CRITERIA

The Minnesota Lab Appropriateness (MLAB) guidelines were developed by the primary authors at the University of Minnesota, following the guidelines described in the Society of Hospital Medicine's Choosing Wisely recommendations[16]. The purpose of MLAB guidelines is to help care providers identify inappropriate complete blood count (CBC) and serum electrolyte panel (SEP) lab orders in a timely & reliable manner in an inpatient setting. Developing the MLAB criteria was the first step in this project. A final version of the MLAB guidelines were used for the pilot study in phase one of this research, following a review of the MLAB criteria by the Alliance for Academic Internal Medicine's High Value Care Workgroup. These same guidelines were used to develop the CDSS algorithm.

MLAB Criteria for Complete Blood Count

A full CBC is appropriate: if it is within 2 days of admission, has been 2 days since the last CBC, or if vitals are unstable, if there are high or low WBCs, if Hgb is below baseline or there is a bleeding problem under management, if there are high or low platelet levels relative to baseline, if there was a procedure the previous day (last 24 hours), or if the physician thinks there is a lab error. Conditions that make a CBC inappropriate are: if the labs or vitals have been stable for 2 days, if high or low white blood cells resolved the prior day, if hemoglobin or platelets are normal for 2 days, if a procedure was more than a day prior, or if a CBC is ordered only because there was a blood or platelet transfusion.

20

MLAB Criteria for Basic Metabolic Panel (BMP)

A BMP is appropriate if it is within 2 days of admission, has been 2 days since the last BMP, or vitals are unstable; if more than 2 components of the BMP are needed; if there is a new-onset acidosis, alkalosis, or hyper- or hypo-natremia; if the patient is being actively diuresed or is on a nephrotoxic medication, if there was contrast imaging or a procedure the day before, if it is the day of dialysis, or if a lab error is being confirmed. A BMP is inappropriate if labs and vitals are stable for 2 days, if a component could have been ordered in isolation, if acidosis, alkalosis, or sodium are at baseline, or if it is more than 2 days after contrast imaging or 1 day after the procedure. For both CBCs and BMPs, the criteria cover most of the scenarios for which a lab might be ordered. Also, it is important to note that at the UMN medical institution, it is cheaper to order an individual blood component or electrolyte, such as hemoglobin or potassium, than it is to order the whole panel. This might vary by institution, and if this is not the case, it would require a slight alteration of the criteria with regard to the cost components of the project.

STUDY PURPOSE AND OBJECTIVE

Reducing clinical variation, reducing duplicative testing, ensuring patient safety and avoiding complications that may result in expensive hospital readmissions are the primary goals of enhancing value-based care over volume in the modern healthcare system. Many studies including the pilot study of this project has indicated that unwarranted wasteful lab tests may lead to further tests, prolonged hospital stays, unnecessary referrals and procedures, patient discomfort, and iatrogenic anemia, resulting in significant economic and clinical effects.

To combat this issue, the researchers and his team in the first phase of this study at the University of Minnesota, Medical School initiated a *Choosing Wisely* recommendation against ordering unnecessary daily labs as a starting point to develop the Minnesota Lab Appropriateness (MLAB) Criteria, which define the conditions for when it is appropriate to order daily labs in hospitalized patients. Based on the outcome in the first phase of the MLAB criteria study, a first attempt to automate the process of applying the criteria through CDSS, to ensure efficient utilization of the resources in medical practice is outlined in this project work.

Objective:

The goal in this project phase was to capture high-quality knowledge about appropriate MLAB Criteria (knowledge synthesis), transform it into a standard format that facilitates computer execution (knowledge formalization), and make it available to embed the formalized knowledge in systems that actually influence care (knowledge localization) in the future.

- The primary objective of this study was to build the clinical decision support system's logical algorithm using Arden Syntax & Medical Logical Module.
- The secondary and final objective of this study is to identify recommendations for future use.

METHODOLOGY

MLAB criteria developed by the primary researchers in the phase one of this study were used to develop the Clinical Decision Support System's algorithm. This algorithm which outlines the indications for complete blood count (CBC) and the basic metabolic profile (BMP) was developed using Arden syntax as the knowledge base of the clinical decision support system encoded as MLMs, an HL7 Standard. The algorithm will be tested in the intervention phase of this study in the future.

Inclusion Criteria:

1. All in-patients with age above 18 years

2. Hospitalization continuing beyond 1 day

3. Tests values included in CBC - RBC, WBC, Platelets, Hemoglobin and Hematocrit

4. Test values included in BMP- Sodium, Potassium, CO2 and Chloride.

Exclusion Criteria:

1. Patients in ICU (MICU, SICU, Neuro ICU, etc.)

2. Patients with Liver conditions (Diagnosis code: K74.60, K74.69, K70.30, K70.31)

3. Pediatric patients

4. Tests values excluded in CBC - Differential analysis

5. Test values excluded in BMP- Glucose, Calcium, BUN and Creatinine

RESULTS

The primary end point of this phase was to build the Arden Syntax for real-time implementation. Two Arden Syntax MLMs, one for CBC and another for BMP, were coded during this research phase as per the Minnesota Lab Appropriateness criteria with the help of the Arden Syntax reference manual[19]. The domain knowledge encoded in the MLM for both CBC and BMP, primarily consists of the criteria to check for appropriateness of these two tests based on certain clinical, patient and laboratory data. Two versions of MLMs were written during this phase of research, of which the later version is used for presenting in this report, attached under appendix. To capture all the criteria described in MLAB guidelines along with the ones described in the inclusion and exclusion rules in a single syntax for both CBC and BMP was a challenging task, and to mitigate this complexity, the syntax was first built with coding for only one logic at a time and then merged to capture most of the requirements.

Recommendation for Proposed Mode of CDSS Action

The Clinical Decision Support System will be programmed to examine each patient's lab data elements that are uploaded to the EHR repository comparing each report to a collection of triggers, each of which is linked to one or more MLMs. When a match, defined as exact class of occurrent events, the related MLMs will be triggered. These in turn retrieve patient data from the database and reach conclusions using the logic encoded in the MLM[24]. Depending on the result, the conclusions can be sent to an authorized recipient and recorded in the EHR for subsequent display and action.

DISCUSSION

Complete Blood Count and Basic Metabolic Panel are the two most commonly ordered lab tests that allow clinicians to diagnose, treat and monitor treatment prognosis in a patient. These tests are also the most over utilized tests in hospitals all over the globe. To differentiate appropriate CBC and BMP tests from inappropriate tests, an Arden Syntax with MLM formalism was built using MLAB criteria. Since Arden Syntax uses patient-specific information and organizes clinical knowledge to conduct an analysis using the information and the knowledge programmed instead of displaying or transmitting the information, it is a commonly used tool for clinical decision support. The syntax produces specific, targeted actionable recommendations for the diagnosis, treatment or management of a disease for a specific patient utilizing all the patient and health data that is available. The syntax's ability to be easily incorporated into an electronic health record, swift clinical workflow, along with its quick and easy interpretation makes it a viable tool for clinical decision-making development by health care professionals. In addition, the use of standard formalism in Arden syntax helps to reduce the barriers to inter-institutional knowledge transfer. The service-oriented architecture of Arden Syntax makes it possible to host the CDS system on different servers. However, all these factors can only be tested during its testing and implementation phase in real time.

Challenges and Recommendations:

Since the syntax is not physically tested in this project, it is difficult to determine the exact challenges that we would have encountered. So far, the greatest challenge was to compile several lines of logic into one syntax which makes it an advanced clinical decision support tool. Coding a 'Time' factor for a test and 'Days' for hospitalization and test routines may require some more research and revisions in the MLMs as the MLAB criteria covers guidelines that capture CBC and BMP blood tests appropriateness between first day of hospitalization until discharge. Lack of standardized vocabularies and patient data schemas and the lack of up to date tutorials and manuals may hinder revision of the syntax in the future. Further, since the biochemical tests, normal range change from lab to lab based on analytic methods and reference materials, a concern of over or under representation of test results may exist. Periodic review of codes and generic names for diagnosis, procedures and medications, is necessary since they will change over time which would require the researcher or the IT team to update the logic accordingly.

CONCLUSION

Clinical decision support (CDS) has the ability to significantly impact improvements in quality, safety, efficiency, and effectiveness of an intervention in health care. They incorporate a broad and complex array of activities, since the development of clinical guidelines and policy statements to the design, development, and deployment of machine-executable advice. It will be interesting to observe the outcome of the syntax written in this project in the scope of reducing inappropriate CBC and BMP lab order rates.

REFERENCES

1. Challenges in using the arden syntax for computer-based nosocomial infection surveillance; Robert A. Jenders, MD, MS and Anuj Shah, MA; J Am Med Inform Assoc: Vol 9, Nov-Dec 2002 PMC419.

2. Laboratory medicine: a national status report May 2008; Wolcott, J., Schwartz, A. & Goodman, C, The Lewin Group.

3. The landscape of inappropriate laboratory testing: A 15-Year Meta-Analysis; Zhi, M., Ding, E. L., Theisen-toupal, J., Whelan, J. & Arnaout, R. *PLoS One* **8,** 1–8 (2013).

4. Towards personal health record: Current situation, obstacles and trends in implementation of electronic healthcare record in Europe. Ilias Iakovidis European Commission, Telematics Applications for Health, Rue de la Loi 200, BU 29 3/50, 1049 Brussels, Belgium.

5. Blood tests when you are in the hospital, taking them every day may not be necessary. An initiative of the ABIM foundation, Choosing Wisely.

6. How Can Labs Tackle Utilization of High-Volume, Low-Cost Tests? Bill Malone, Sep.1.2013, Source**:** Clinical Laboratory News

7. Decrease in unnecessary vitamin D testing using clinical decision support tools: making it harder to do the wrong thing; Andrew H Felcher, Racchel Gold, David m Mosen, Ashley B Stoneburner. Journal of the American Medical Informatics Association, Volume 24, Issue 4, July 2017, Pages 776-780.

8. Hospitalist Tackles Repetitive Labs; Jan 17 2019; https://www.choosingwisely.org/resources/updates-from-the-field/hospitalist-tackles-repetitive-labs/

9. Don't perform laboratory blood testing unless clinically indicated or necessary for diagnosis or management in order to avoid iatrogenic anemia; Society for the advancement of blood management; July 23, 2018, Choosing Wisely.

10. A multidisciplinary house staff-led initiative to safely reduce daily laboratory testing; Wade Iams, Josh Heck, Meghan Kapp, David Leverenz, Michael Vella, Eszter Szentirmai, Irene Valerio-Navarrete, Cecelia Theobald, Kathryn Goggins, Kevin Flemmons, Kelly Sponsler, Cody Penrod, Patricia Kleinholz, Donald Brady, Sunil Kripalani, Ovid - Academic Medicine. 1(6):813–820, JUNE 2016 DOI: 10.1097/ACM.0000000000001149; PMID: 27028031; Issn Print: 1040-2446; Publication Date: June 2016.

11. https://www.choosingwisely.org/resources/updates-from-the-field/hospitalist-tackles-repetitive-labs/

12. Decrease in unnecessary vitamin D testing using clinical decision support tools: making it harder to do the wrong thing; Andrew H Felcher, Rachel Gold, DavidM Mosen, Ashley B Stoneburner; Journal of the American Medical Informatics Association, Volume 24, Issue 4, July 2017, Pages 776–780.

13. https://www.choosingwisely.org/getting-started/resource-library/does-choosing-wisely-work/

14. Clinical Decision Support: a 25 Year Retrospective and a 25 Year Vision; B. Middleton, D.F. Sittig,and A.Wright; Yearb Med Inform. 2016; (Suppl 1): S103–S116. Published online 2016 May 20.

15. Choosing wisely in adult hospital medicine: Five opportunities for improved healthcare value; Bulger J, Nickel W, Messler J, *et al.* J Hosp Med. 2013;8(9):486-92.

16. Choosing Wisely: A Quality Improvement Initiative to Decrease Unnecessary Preoperative Testing; Matulis J Liu, S Mecchella J, North F Holmes; BMJ Qual Improv Rep. 2017 May 23;6(1).

17. http://www.openclinical.org/gmm_ardensyntax.html

18. https://en.wikipedia.org/wiki/Arden_syntax

19. Arden Syntax for medical logic systems;

http://www.hl7.org/documentcenter/public_temp_36917C7C-1C23-BA17-0CBF59B7BCB9F897/wg/dss/Arden.pdf .

20. The Arden Syntax for medical logic modules; Pryor, T.Allan, Hripcsak, George; International journal of Clinical Monitoring and Computing; Vol 10, Issue 4; doi:10.1007/BF01133012.

21. Health Level 7 International,

https://en.m.wikipedia.org/wiki/Health_Level_Seven_International

22. Choosing Wisely in Adult Hospital Medicine: Five Opportunities for Improved Healthcare Value. Bulger, J. *et al.* *J. Hosp. Med.* **8,** 486–492 (2013).

23. Choosing Wisely: An Initiative of the ABIM Foundation. (2013).

24. Biomedical Informatics; Computer Applications in Healthcare and Biomedicine.
Edward H. Shortliffe James J. Cimino. Chapter 20: Clinical Decision-Support
System; Springer, New York, NY, 978-0-387-36278-6.

Table 1: CBC MLAB Criteria

Appropriate	Inappropriate
If CBC performed within 48 hours of admission, 48 hours since last CBC or if vitals are unstable	When labs and vitals are stable for more than 48 hours
When leukocytosis/ - 'penia is present	Leukocytosis/ - 'penia was resolved on previous day
For patients with bleeding or hemoglobin is below baseline, CBC order once daily	If Hemoglobin is normal or at baseline for 2 days
Thrombocytopenia/ '-cytosis' relative to baseline	When platelets are normal and are trending towards normal for 2 days
On a day prior to any procedure	If done after 24 hours after a procedure
If potential lab errors are confirmed comments on test results / create new syntax	Full CBC after blood or platelet transfusion

Table 2: BMP MLAB Criteria

Appropriate criteria	Inappropriate criteria
If done within 48hrs of admission, 48hours since last BMP or when the vitals are unstable	If labs and vitals are stable for more than 48 hours
>2 components needed (Na,Cl,etc.)	If two or fewer components are needed
Acidosis /alkalosis present and not chronic	If acidosis /alkalosis is resolved or is at baseline
Presence of hypernatremia/ hyponatremia	If serum sodium is normal
If patients are on diuretics or nephrotoxic medicines	If patients are not on diuretics or nephrotic medicines
If imaging study was done with contrast, a day prior	If imaging study was done before 48 hours
If patient had a procedure, on a day prior	More than 24 hours after procedure
On the day of hemodialysis - Write in discussion*	If done after hemodialysis
If potential lab error was identified	

34

ARDEN SYNTAX FOR CBC

Maintenance:

title: Screen for inappropriate CBC orders;;

mlmname: inappropriate_complete_blood_count;;

arden: Version 2;; */*if missing default version is 1*/*

version: 1.0

institution: University of Minnesota - Institute for Health Informatics;;

author: Divya Rupini Gunashekar, M.Sc, (M.S) (gunas017@umn.edu);;

specialist: Dr. Terrence Adam,RPh,PhD,MD;;

date: 2018-07-21;;

validation: testing;; */*Change to appropriate validation during   implementation*/*

library:

purpose: screen for inappropriate Complete Blood Count orders since time of admission;;

explanation: A patient's lab order for CBC needs to be assessed for appropriateness ;;

keywords: CBC, appropriate ;

citations: https://www.mayoclinic.org/tests-procedures/complete-blood-count/about/pac-20384919 ;

;;

Knowledge:

type:data-driven;;

data:

/ get test results */*

inappropriate _CBC_count:= event

{Check appropriate CBC orders}; */* the value in braces is specific to runtime environment */*

```
/* If the test results are lower or higher than the
CBC_Threshold or ordered inappropriately then output a
message */

CBC := read last (select result from test_table where
test_code  = 'CBC');

CBC_threshold:= RBC = Male: 4.32-5.72 trillion cells/L

                      Female: 3.90-5.03 trillion cells/L;

WBC = 3.5-10.5 billion cells/L;

Hb = Male: 13.5-17.5 grams/dL

     Female: 12.0-15.5 grams/dL;

Hematocrit = Male:38.8-50.0 %

             Female:34.9-44.5 %;

Platelet count = 150-450 billion/L;


                 /*email for research log*/

Email_desti:= destination {'email', 'name' =
adamx004@umn.edu} ;

; ;

evoke: inappropriate CBC orders;

logic: (if RBC where Male = < 4.32 trillion cells/L or >
5.72 trillion cells/L OR

where female = < 3.90 trillion cells/L or > 5.03 trillion
cells/L) then

conclude true;

else conclude false;

end if;

if (WBC < 3.5 billion cells/L  or > 10.5 billion cells/L)
then

conclude true;

else conclude false;

end if;
```

```
if (Hb where Male < 13.5 grams/dL or > 17.5 grams/dL or
where female < 12.0 grams/dL   or > 15.5 grams/dL) then
conclude true;
else conclude false;
end if;
if (Hematocrit where Male < 38.8% or > 50.0 % grams/dL or
where female < 34.9 % or > 44.5 % grams/dL) then
conclude true;
else conclude false;
end if;
if (platelet count < 150 billion/L or > 450 billion
cells/L) then
conclude true;
else
conclude false;
end if;
if (Dx_code = Dxx / Thrombocytopenia/cytosis) then
conclude true;
else false;
end if;
if (age >= 19) then
conclude true
else conclude false;
end if;
if (n:time of inpatient_admission > 1 day) then
conclude true;
else conclude false;
end if;
```

```
if (Treatment = 'Any Procedure') then

conclude true;

else conclude false;

end if;

if (n:time of 'Any Procedure' < 1 day) then

conclude true;

else conclude false;

end if;

if (n:time of latest CBC_test is within 1 day for the first
3 days) then

conclude true;

else conclude false;

end if;

;;

Action:

write "the CBC blood test was inappropriate"

At email_dest;

;;

resources:

default:en ;;

language:en

'msg': "An appropriate order is done after 24hrs and if
needed"

Urgency: 50;; /* the scale is from 1(low) to 99(highest),
50 is neutral, it can be changed as per the priority
level*/

end:
```

ARDEN SYNTAX: BASIC METABOLIC PANEL

```
Maintenance:

title:  Screen for inappropriate BMP orders;;

mlmname: inappropriate_Basic_Metabolic_panel;;

arden: Version 2;; /*if missing default version is 1*/

version: 1.0

institution: University of Minnesota - Institute for Health
Informatics;;

author: Divya Rupini Gunashekar, M.Sc, (M.S)
(gunas017@umn.edu);;

specialist: Dr. Terrence Adam,RPh,PhD,MD;;

date: 2018-07-21;;

validation: testing;; /*Change to appropriate validation
during          implementation*/

library:

purpose:  screen for inappropriate Basic Metabolic Panel
orders since time of admission;;

explanation: A patient's lab order for BMP needs to be
assessed for appropriateness;;

keywords: BMP, appropriate;

citations:        https://www.mayoclinic.org/tests-
procedures/complete-blood-count/about/pac-20384919 ;

;;

Knowledge:

type:data-driven;;

data:

/* get test results */

inappropriate _BMP_count:= event

{Check appropriate BMP orders}; /* the value in braces is
specific to runtime environment */
```

```
/* If the test results are lower or higher than the
CBC_Threshold or ordered inappropriately then output a
message */

CBC:= read last (select result from test_table where
test_code  = 'BMP');

BMP_threshold:= Sodium 135-145 mmol/L;

                Potassium = 3.6-5.2 mmol/L;
                Chloride = 98-107 mmol/L;

                 /*email for research log*/

Email_desti:= destination {'email', 'name' =
adamx004@umn.edu} ;

; ;

evoke: inappropriate BMP orders;

logic: if (Sodium < 135 mmol/L or > 145 mmol/L) then

conclude true;

else conclude false;

end if;

if (Potassium < 3.6 mmol/L or > 5.2 mmol/L) then

conclude true;

else conclude false;

end if;

if (Chloride > 112 mmol/L) then

conclude true;

else conclude false;

end if;

if (if (age >= 19) then

conclude true

else conclude false;

end if;

if (n:time of inpatient_admission > 1 day) then
```

```
conclude true;

else conclude false;

end if;

if (n:time of latest BMP_test is within 1 day for the first
3 days) then

conclude true;

else conclude false;

end if;

;;

Action:

write "the BMP blood test was inappropriate"

At email_dest;

;;

resources:

default:en

;;

language:en

'msg': "An appropriate order is done after 24hrs and if
needed"

Urgency:50;; /* the scale is from 1(low) to 99(highest), 50
is neutral, it can be changed as per the priority level*/

end:
```