IMM/Serve: A Rule-Based Program for Childhood Immunization

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A rule-based program, IMM/Serve, is being developed to help guide childhood immunization for initial use within Oregon. The program is designed primarily for automated use with an online immunization registry, but can also be used interactively by a single user. The paper describes IMM/Serve and discusses 1) the sources of complexity in immunization logic, 2) the potential advantages of a rule-based approach for representing that logic, and 3) the potential advantage of such a program evolving to become the standard of care. Related projects include 1) a computer-based tool to help verify the completeness of the logic, 2) a tool that allows a central part of the logic to be generated automatically, and 3) an approach that allows visualization of the logic graphically.

INTRODUCTION

We are currently testing and refining a rule-based program, IMM/Serve, to help guide six childhood immunizations: *Haemophilus influenzae* type b (Hib), Hepatitis B (HB), Varicella (Var), Measles Mumps Rubella (MMR), Diphtheria Tetanus Pertussis (DTP), and Polio (OPV/IPV). IMM/Serve is being developed for initial use within Oregon, where it is planned to replace an existing table-driven system. The program is designed primarily for use with an online registry containing patients' immunization histories [1]. It can also be used interactively by typing patient information directly to the program. IMM/Serve may be accessed via the Web (http://ycmi.med.yale.edu/immserve/) for demonstration purposes.

Immunization authorities want their recommendations to be in a form that clinics can unambiguously apply to patients when no contraindications exist. Consensus recommendations for childhood immunization are developed by the American Academy of Pediatrics (AAP) and the CDC's Advisory Committee on Immunization Practices (ACIP) [2-4].

Until recently, immunization recommendations were more straightforward and were typically represented in tabular format, both for clinical use and for use internally within a computer program. In the past several years, however, the underlying logic has become increasingly complex, and subject to frequent changes. Tables are valuable for storing many of the parameters so that they can be viewed and modified easily. We are exploring the utility of a rule-based approach for representing the underlying logic, i.e., the logic which controls which parameters should be used in a given case. A rule-based approach to representing this logic has a number of potential advantages.

1. It allows the development of computer-based tools that operate on the rules to help verify, refine, update, and maintain the logic as it evolves over time.
2. It helps identify all the different combinations of conditions that must be anticipated in a set of comprehensive recommendations.
3. It may facilitate organized maintenance of different versions of the rules, customized for specific states or health organizations.
4. It may help let the recommendations become more complex to capture additional nuances of the clinical domain.

This paper discusses 1) the current implementation of IMM/Serve, 2) the sources of complexity in immunization logic, and 3) the potential advantage of a rule-based program evolving to become the standard of care for childhood immunization.

AN EXAMPLE

IMM/Serve is designed for use by clinicians. This section shows IMM/Serve in operation. As illustrated in Figure 1, IMM/Serve takes as input a description of a patient's immunization history, plus a small amount of other clinical data. This input includes:

1. The patient's birth date.
2. The forecast base date. (In clinical practice, this is usually the current date or the date when the patient is expected in a clinic. For retrospective analysis and for program testing, some other date may be used.)
3. For each vaccine series, the date (and optionally the brand) for each dose which the patient has received.
4. A list of any vaccines for which the patient has a contraindication.
5. Additional clinical information, such as the HBsAg status of the patient's mother, if known.

Date today: 7/1/95
Date of birth: 4/1/94
HB: 4/1/94, 6/2/94, 10/2/94
DTP: 6/2/94, 8/2/94, 10/2/94
Hib: PRP-OMP 6/2/94, PRP-OMP 8/2/94
OPV: 6/2/94 , 8/2/94
MMR: 4/1/95

Figure 1. Sample input to IMM/Serve.

The following immunization(s) are due today:
DTaP 4
Hib 3
OPV 3
VAR 1

The following immunization(s) will be due:
DTP Series dose 5 - on or after 4/1/1998 but before 4/1/2000 (if DTaP 4 is given today)
OPV 4 - on or after 4/1/1998 but before 4/1/2000 (if OPV 3 is given today)
MMR 2 or Me 2 - on 4/1/1999

The following vaccine series are either complete or no longer relevant for this case:
HB

Figure 2. IMM/Serve's current output in forecasting mode for the input seen in Figure 1.

When the data is derived from an online immunization registry, this input will be passed to IMM/Serve automatically. The data may also be input directly to the program interactively. In the future, we also plan for IMM/Serve to accept input and produce output in HL7 format.

IMM/Serve will ultimately be used in three modes: 1) forecasting, 2) reminder, and 3) compliance assessment. We are currently developing the forecasting mode. In this mode, IMM/Serve indicates which immunizations are due now or past due, and which should be scheduled next, as shown in Figure 2.

IMM/Serve's reminder mode will be designed to help target postcards or phone calls when a patient is late for an immunization. The compliance assessment mode will help measure the level of compliance with the recommendations for a population of patients.

SYSTEM DESIGN

Figure 3 outlines IMM/Serve's system design, which consists of 4 main components: 1) KnowledgeCraft, a shell program used to build the knowledge base (KB), 2) the immunization KB itself, 3) the IMM/Serve server which executes the KB logic, and 4) the IMM/Serve client which provides program's user interface.

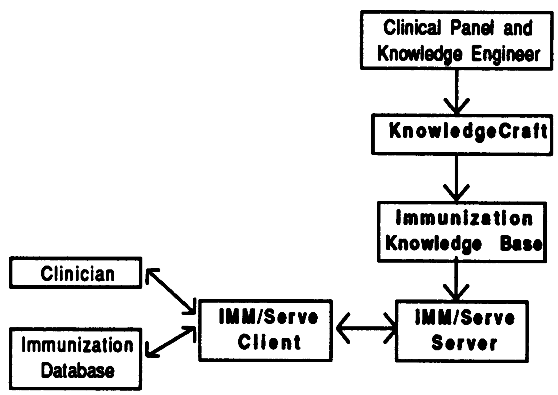

Figure 3. An overview of IMM/Serve's design.

The KnowledgeCraft Shell Program

KnowledgeCraft (KC) is a rule-based system-building shell designed to facilitate the creation of rule-based programs. KC is designed for use by expert clinicians, assisted by a knowledge engineer, to build a clinical knowledge base. KC runs on a PC/Windows machine and allows the immunization KB to be created and partially tested using a graphical user interface. For further testing and for operational use, KC outputs the KB in a structured form which is then linked to the IMM/Serve server.

The Immunization Knowledge Base

The immunization KB consists of a set of *if-then* rules which define the immunization logic. These rules test facts which are derived from the input. The rules assert intermediate facts and produce textual output. Figure 4 shows three of the rules for varicella, which is the simplest of the 6 vaccine series. The first rule says: "If there are no prior varicella vaccinations and varicella vaccine is not contraindicated and the patient is at least 1 year old and there has been no live vaccine given in the past 30 days, then the first varicella dose is due now." For all 6 vaccine series, IMM/Serve contains roughly 150 rules.

```
if    VAR.prior = 0 and
      not VAR_contraindicated and
      age_in_years >= 1 and
      not live_vaccine_in_past_30_days
then due.VAR1

if    due.VAR1 and
      age_in_years >= 13
then next.VAR2

if    VAR.prior = 0 and
      not VAR_contraindicated and
      (age_in_years < 1 OR
      live_vaccine_in_past_30_days)
then next.VAR1
```

Figure 4. This figure shows part of the rule-based logic for varicella, which is the simplest of the 6 vaccine series.

The IMM/Serve Client

The IMM/Serve client is written in C and resides on the user's machine. It accepts input and performs certain rudimentary error checks. In client-server mode, the client transmits data to the IMM/Serve server. In stand-alone mode, the client passes the data to the IMM/Serve server running on the same machine. Finally, it displays the recommendations to the user.

The IMM/Serve Server

The IMM/Serve server is written in C and therefore runs on a range of machines. It accepts its input from the IMM/Serve client, executes the immunization KB in the form produced by KC to process a case, and then passes its output back to the client. The IMM/Serve server performs several additional functions.

1. Converting input to facts It preprocesses the input, transforming it into a set of facts that can be tested by the KB rules.

2. Filtering out "invalid" vaccinations At the same time, it filters the input data to identify any past immunizations that were given too early and which therefore must be ignored in formulating the immunization recommendations. If it finds any of these, it produces a error message and adjusts the internal set of facts to reflect only those vaccinations that are valid.

3. Postprocessing Finally the server program postprocesses the output of the KB. The main form of postprocessing involves converting the recommendations of the KB which are expressed in terms of ages and time intervals involving days, weeks, months, and/or years into specific dates. This logic is more easily expressed in a C program, rather than using rules. This design allows the KB rules themselves to be much cleaner, since they can produce output indicating ages and intervals, without worrying about how those values actually get translated into specific dates.

IMMUNIZATION KNOWLEDGE MANAGEMENT TOOLS

In addition to IMM/Serve, we are developing several knowledge management tools designed to help in testing, maintaining, and updating the rule-based logic as it evolves over time.

Commander: Verifying KB Completeness

Commander is a computer-based tool designed to help verify the completeness of the logic.

IMM/Def: Using "Definition Logic"

IMM/Def is a computer-based tool which allows a central part of the immunization logic to be represented in a declarative form ("definition logic") from which the actual rules ("implementation logic") can be generated automatically to handle the three different temporal contexts in which the logic applies.

Graphical Visualization of the Logic

We have developed an approach that allows visualization of the logic graphically in a way that can potentially help a) a clinician panel develop and maintain the logic and b) a knowledge engineering team understand and discuss the logic [5]. This project does not currently involve computer-generated graphics, but might in the future.

Generating Test Cases (Planned)

A future project will build a computer-based tool to automatically generate test cases which can help in validating the accuracy of the immunization recommendations produced.

SOURCES OF COMPLEXITY IN IMMUNIZATION LOGIC

In recent years, immunization recommendations have become increasingly complex. Certain of the complexity involves the clinical logic. Other complexity arises from temporal issues. Whereas the clinical complexity must be dealt with by the clinical experts developing the recommendations, the temporal complexity arises as a problem only when attempting to enter the logic explicitly into the computer.

Clinical Complexity

Not long ago, immunization logic was reasonably straightforward and could be readily expressed in tabular form, indicating when each of a series of vaccinations should be given, and how long one should wait between vaccinations. The current recommendations are considerably more complex. For example:

1. A major concern with Hib immunization is to protect the child during the early years of life. As a result, the number and schedule of vaccinations varies depending on whether the child has missed one or more of the early recommended vaccinations. In the extreme case, if the child is 60 months old with no prior vaccinations, none is required.
2. A further feature of the Hib series is that the recommended number of vaccinations depends on the brand used. The logic also must anticipate what to do if the brand of a previously given Hib vaccination is not known.
3. In the OPV/IPV series, one must anticipate what to do if a mixed history of OPV and IPV vaccinations is reported.
4. In several vaccine series, one must determine what to do if not all antigens have been given at some past vaccination. For example, in the MMR series, a past shot may have only involved measles vaccine.
5. Other clinical factors also influence the recommendations. For example, the recommendations for HB vary depending on whether the mother is HBsAg positive or not, and must also deal with the possibility that the mother's HBsAg status may not be known.
6. Another consideration is that certain live vaccines (e.g., OPV, MMR, Var) must either be given at the same time or at least 30 days apart. The exact set of vaccines to which this rule applies differs for different domain experts.

As a result of considerations such as these, there are many exceptions, special cases, and interacting factors that add complexity to the clinical logic.

Temporal Complexity

Time enters into the immunization recommendations in several ways. A particularly interesting feature is that time must be handled in several different formats.

1. Many recommendations involve the patient's age, which may be expressed in weeks, months, or years.
2. Many recommendations also involve time intervals, which may be expressed in days, weeks, months, or years.
3. In following a set of recommendations, the program must often combine several considerations involving age (possibly expressed in several different units) and intervals (possibly expressed in several different units) to produce a specific recommended date.

The problem of integrating different temporal units involves common sense knowledge about time, not clinical judgment about immunization. As a result, we handle these temporal issues in the preprocessing and postprocessing modules of IMM/Serve, independent of the KB.

This temporal complexity is compounded by the question of how to define a month. For scheduling immunizations in the *future*, it is most natural clinically to treat a month as a calendar month. On the other hand, when analyzing a set of *past* immunizations (e.g., when filtering a patient's history for "valid" vaccinations, or when performing compliance assessment), it makes most sense to use a fixed length such as 28 days as the definition of a month. (Otherwise, for example, if a vaccine series required a one month interval between vaccinations, a 29 day interval would be considered valid if the first vaccination had been given in February, but would be considered invalid if the first vaccination had been given in July.)

IMM/Serve currently uses calendar months when dealing with future immunizations and a 28 day month when analyzing past immunization intervals (but not when analyzing age). Here again, these issues are dealt with in IMM/Serve's preprocessing and postprocessing modules. The KB itself can be written without concern for the definition of a month.

Separating the Two Forms of Complexity
An important feature of IMM/Serve's design is its separation of clinical complexity from temporal complexity. Clinical complexity is dealt with primarily by the immunization logic in the KB. Temporal complexity is dealt with by preprocessing and postprocessing. The result is that the clinicians developing the logic in the KB need not deal with the temporal complexity in any detail.

LOOKING TO THE FUTURE: ADVANTAGES OF RULE-BASED LOGIC AS A STANDARD FOR CARE

The current standard of care for immunization consists of consensus recommendations produced in paper form by national panels. We believe that it is desirable and possible for a rule-based program itself to evolve to become a repository for the standard of care. To allow this, there would need to be very close coordination between the knowledge engineers maintaining the program and the clinical experts formulating the recommendations. Ideally, a medical informatician would work closely with the panel and would be responsible for the iterative process of:

1. translating the panel's recommendations into computer-based rules,
2. helping test the rules using test cases and computer-based tools,
3. conveying back to the panel any concerns and issues that need to be considered to make the recommendations complete and operational.

In fact, this process occurred during the development of IMM/Serve itself. The process of converting clinical recommendations into a concrete computer-based form exposed a host of considerations which the clinicians would not otherwise have confronted. When the recommendations were expressed only in paper form, it was virtually impossible to think through all the different combinations of conditions that needed be anticipated. Expressing the logic as computer-based rules, and then using the immunization knowledge management tools described above, helped explicitly expose all those combinations in a organized way.

In summary, we believe that the evolution of a rule-based program to be a standard of care for childhood immunization could potentially facilitate 1) the maintenance of the logic by an expert clinician panel, as well as 2) the automated delivery of the recommendations to clinical users. It could also potentially eliminate the need for many groups to develop redundantly their own computer programs for immunization logic. We hope that the current implementation of IMM/Serve can be one step towards this goal.

Acknowledgements

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