

# Using Common Table Expressions to Build a Scalable Boolean Query Generator for Clinical Data Warehouses

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**Abstract**—We present a custom, Boolean query generator utilizing common-table expressions (CTEs) that is capable of scaling with big datasets. The generator maps user-defined Boolean queries, such as those interactively created in clinical-research and general-purpose healthcare tools, into SQL. We demonstrate the effectiveness of this generator by integrating our study into the Informatics for Integrating Biology and the Bedside (i2b2) query tool and show that it is capable of scaling. Our custom generator replaces and outperforms the default query generator found within the Clinical Research Chart cell of i2b2. In our experiments, 16 different types of i2b2 queries were identified by varying four constraints: date, frequency, exclusion criteria, and whether selected concepts occurred in the same encounter. We generated nontrivial, random Boolean queries based on these 16 types; the corresponding SQL queries produced by both generators were compared by execution times. The CTE-based solution significantly outperformed the default query generator and provided a much more consistent response time across all query types ( $M = 2.03$ ,  $SD = 6.64$  versus  $M = 75.82$ ,  $SD = 238.88$  s). Without costly hardware upgrades, we provide a scalable solution based on CTEs with very promising empirical results centered on performance gains. The evaluation methodology used for this provides a means of profiling clinical data warehouse performance.

**Index Terms**—Biomedical computing, biomedical informatics, data systems, data warehouses, health information management, large-scale systems.

## I. INTRODUCTION

**C**LINICAL data warehouses (CDWs) are a necessary component to any healthcare institution for operational and re-

search purposes [1]. Informatics for Integrating Biology and the Bedside (i2b2) is an initiative sponsored by the NIH Roadmap National Centers for Biomedical Computing [2]. One of the initiative's main products is the i2b2 Web Client—a query tool that is capable of supplying aggregate counts and basic analyses of patient populations from CDWs. i2b2 has been shown to be effective in estimating cohort sizes [2]–[4] and serves as a potential cost-effective back end for performing genome-wide association studies [3], [5]. It is reported to be used by over half of all sites awarded a Clinical and Translational Science Award (CTSA), over 60 academic medical centers, and 10 international medical centers [3].

In the age of Google, users expect instantaneous query results. This client-side consumer assumption is often difficult to satisfy for informatics software due to open challenges with big data and the complexity of queries upon clinical data warehouses. For instance, i2b2's performance is reasonable with our single hospital clinical dataset containing approximately 540 000 patients across 4 million encounters. However, significant performance degradation was experienced with our larger state-wide Medicaid dataset containing approximately 1.8 million patients across 160 million encounters. The poorest performing queries were those requiring concepts to occur in the same encounter, especially when additional constraints such as exclusion criteria or occurrences (frequency) were used.

Some institutions have been able to achieve reasonable performance on large datasets with significant investments in hardware upgrades. Because not every medical center can afford extensive and elaborate hardware environments and because the growth of biomedical data is outpacing Moore's law for the growth of computational power [6], elegant software solutions that are capable of scaling are needed. The goal of this study is to provide a scalable query generator that greatly decreases the end-user's wait time for obtaining aggregate counts. In addition, our experimental design provides a methodology for profiling and comparing the performance of clinical data warehouse query tools.

## II. BACKGROUND

Clinical data warehouses naturally expand as time elapses. An increased emphasis on adopting electronic health records and other clinical information systems has led to the expansion of CDWs in both volume and breadth [1]. Additionally, the inclusion of genomic data is increasingly important for translational science [5], which suggests that the scale of the modern CDW

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will continue to increase. In addition to scale, the use of the data is evolving; the Shared Health Research Information Network (SHRINE) is a federated query tool that was motivated by the CTSA to produce a tool to enable collaboration across multiple sites [7]. SHRINE is an i2b2-based solution, where queries are distributed to multiple i2b2 warehouses within the SHRINE and result sets are aggregated for the end user. The expansion of data in terms of raw size and scope of usage is further evidence that scalability is pivotal to the success of the individual informatics software solutions and consequently to the much larger goals of clinical and translational science.

Other query tools exist for performing clinical research, including BTRIS [8], DEDUCE [9], FURTHeR [10], STRIDE [11], and VISAGE [12]. Note that these are tools created with specific goals in mind, while i2b2 is essentially an extendable platform for open-source development. Regardless of the specific design, a tool must somehow allow the user to construct a query that pinpoints the data being requested. Boolean queries are important in clinical data warehousing because they provide the natural mapping for inclusion and exclusion criteria when selecting sets of patients, cohorts, and encounters. Additionally, this selection stage is critical for clinical research [1], [4].

Each of the listed tools has an interface that allows the user to actively construct a query, either visually or with the help of pull-down menus; the tool must somehow translate this construction into valid SQL so that the CDW can be interactively explored. We call this translation component the *query generator*, which plays a crucial role by allowing nontechnical users to build queries without writing complex statements in a language such as SQL. Our query generator works by receiving an XML message from the tool and translates it into an SQL query that can be run against the CDW. FURTHeR uses i2b2 as a front-end and could use our query generator, since its queries are composed in an identical interface. The other tools would need to package their query requests in a similar XML message in order to receive a query from our generator.

The most commonly published enhancements or extensions of i2b2 have been in the form of project forks and plug-ins that provide novel functionality [13]–[15] or in-depth examinations of i2b2's use cases [4], [16], [17]. In this paper, we present our research in developing a scalable query generator and present our results on associated performance gains when it is used as an alternative to the internal generator of i2b2. We note that there exists related work [18] directed toward enhancing the performance of i2b2, which focuses on precomputing aggregate values and obtaining inexact counts via simulation. This related work could also be layered on top of our solution, which, in contrast, focuses on improvements in query generation.

i2b2 consists of a web client and desktop client that increasingly share similar functionality. In both clients, the user interface consists of a series of panels (also called groups). Users select concepts from an ontology and drag them into the panels to form basic Boolean queries; concepts within a panel represent a logical OR, while concepts across panels represent a logical AND (see details in the METHODS section). Additionally, panels can be negated and constrained by time, frequency, and whether the concepts occurred in the same encounter—that

```
WITH common_table_1 AS (
    <select statement>
),
common_table_2 AS (
    <select statement, can additionally
    reference common_table_1
    as if it were a table>
), ... ,
common_table_N AS (
    <select statement, can reference
    any previously defined common
    table as if it were a table>
)
SELECT <columns of common_table_N>
FROM common_table_N
WHERE <condition>
```

Fig. 1. General framework of a CTE containing  $N$  common tables that join  $N$  select statements. In each common table, a select statement determines the result set and previous common tables can be referenced in subsequent ones. The last SELECT statement dictates what the final result set will be.

is, a single billable visit to a provider or inpatient stay at a hospital. The basic internal structure of i2b2 is that of a modular hive, where each hive cell is designed to provide a certain function [19]. Our contribution concerns the Clinical Research Chart (CRC) cell, which acts as the core data repository handler. When the user submits a query, the CRC cell converts the panels that the user has composed through the interface into an SQL statement that is executed against the local data repository. Our work replaces the query generation logic found within the CRC cell, so that more elegant SQL statements are produced and are followed by performance gains.

The default query generator that is packaged with i2b2 generates queries that use a procedural, multiple transaction approach. The panels assembled by the user are converted into multiple SQL statements. This approach takes patient records that match the concepts in the first panel and inserts them into a temporary table. The process continues and the records that also match the second panel's concepts are updated in the temporary table. This process continues for all panels where the subsequent set of patients in the temporary table to be updated is never larger than the previous and the resulting temporary table will hold only those patient records that match the query the user constructed. The major issue is that this technique is heavily dependent on hard disk access- and write-speeds coupled with the large amounts of temporary storage on the database required for storing and logging these temporary result sets.

### III. METHODS

As an alternative to the procedural approach, we developed a query generator that produces a single relational query using Common Table Expressions (CTEs), which were first introduced in Microsoft SQL Server 2005 [20] and later integrated into Oracle and other database management systems. Fig. 1 shows the general framework for a CTE.

CTEs are temporary, named result sets that reside in memory as complex derived views of the underlying data and can be referenced multiple times within a single SQL statement (including self-reference); additionally, they can be chained together

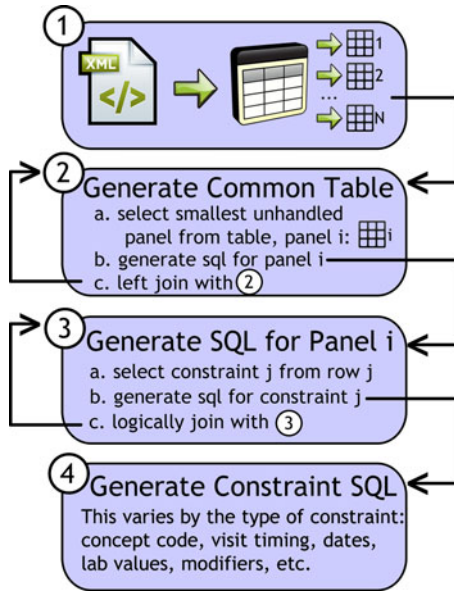


Fig. 2. Overview of the CTE-generation process. In stage 1, the incoming XML message containing the query definition is placed inside a table where groups of rows represent panels. Joined common tables are generated (stage 2) from generating SQL for panels (stage 3) by generating logically joined SQL for constraints (stage 4).

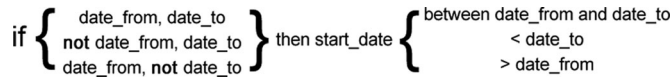


Fig. 3. Example of stage 4 from Fig. 2 showing the logic needed to generate the SQL for a date constraint. This is conditionally based on the query definition's values for the "to" and "from" of the date constraint received from the user interface; for example, if both values are present, a between clause is needed. This returns an SQL clause comparing "start\_date," which is found in the source database table.

to create a more complex final query. Due to the derived nature of CTEs, there is no need to write these temporary result sets to disk, thus reducing I/O requirements to complete each transaction.

Suppose we have multiple tables that contain different complementary pieces of information about a patient such as their personal information, physician visits, and prescriptions. Often, researchers need to correlate information in these different tables to select a set of patient records that satisfy certain criteria. This correlation is generally accomplished using database table joins performed on fields common across all tables. A straightforward approach to join multiple tables is to form a sequence of joins, where the result of a join between two tables is used in turn to perform a join with the next table. As such, the result set of a join can also be treated as a table consisting of fields from multiple tables that are selected in the join. Instead of storing these intermediate results as explicit temporary tables, CTEs enable us to use named result sets or common tables that provide the same functionality.

#### A. Transformation of i2b2 Queries to CTE-Based Queries

A high-level overview of the translation process can be found in Fig. 2, and Fig. 3 represents an example of the inner-most

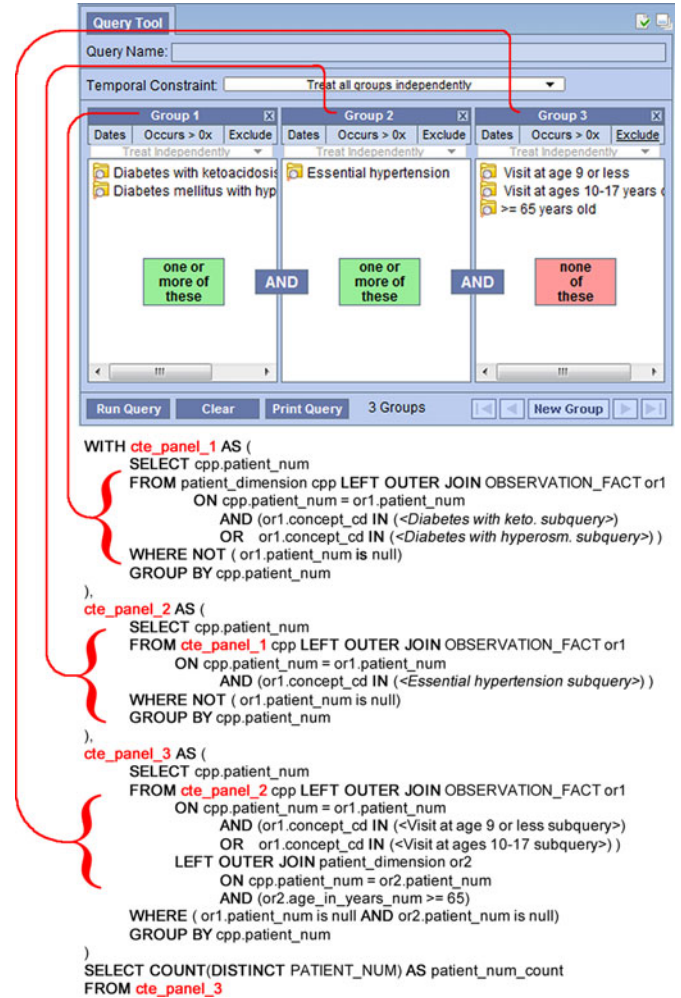


Fig. 4. Example of a patient-count query translated into common table expression.

workings. To make things less abstract, we use an example to demonstrate how queries from the i2b2 interface are transformed into the corresponding CTE-based SQL queries. As mentioned earlier, the i2b2 interface provides panels to formulate Boolean queries on patient records involving certain concepts. In our approach, each panel in the i2b2 user-interface is mapped to a common table where the joins between CTEs facilitate logical ANDs and the inner-expression within each CTE facilitates logical ORs and NOTs by using nested left-joins. Left-join predicates capture additional constraints such as dates, frequency, concept modifiers, and can be used to support additional query features such as lab value constraints, provider details, and text searches.

Fig. 4 shows a query that has three panels, where the first panel is a logical OR upon two different diabetes-related concepts and the second panel simply selects the hypertension concept. The last panel is slightly more complicated; it is the logical OR between those patients who had a visit at an age of less than 9 years, or between 10–17 years, or older than 65 years today. This panel is also negated, so only those patients who are outside of those age ranges will be selected. We show the corresponding



CTE-based SQL query below the panel diagram. To conserve space, sub-queries for concept children in the ontology have been replaced by placeholders. We use a special table of inter-concept hierarchical relationships to help manage our ontology so that child concepts can be returned quickly. In short, this mapping generates a single SQL statement that can be completed in one transaction with minimal need for temporary disk space or logging.

The CTE-based approach described above is in stark contrast to the procedural approach, which generates multiple SQL statements. In turn these statements invoke costly inserts, updates, and hard-disk temporary table commits which require disk space and are limited by disk-access speeds. Additionally, the multiple statement procedural approach prevents the SQL optimizer from generating an optimal join strategy due to its limited knowledge of the overall query sequence. In contrast, our relational approach presents the optimizer with a single query that can be optimized effectively.

The left outer-join provides an elegant method for performing both the logical OR and NOT operations by using a compound WHERE predicate with the help of the NOT operand. For example, when a panel contains two or more concepts from different tables, a new alias *or1*, *or2*, ..., *orN* is added to each table in subsequent joins. The final WHERE predicate for a panel then looks like *WHERE not (or1.patient\_num is NULL AND or2.patient\_num is NULL ... AND orN.patient\_num is NULL)*.

Note that this will return patients where at least one of the concepts in the OR panel returns true. The logical NOT of a panel is found simply by removing the NOT keyword before the compound WHERE predicate. That is, the left join will then only return those patient records that fail to return null for all of the concepts in the OR list. The records that match at least one of the concepts will be excluded. The modified query generator also combines all exclusion panels into one CTE, where it is logically consistent to do so.

For any query that can be logically composed in the i2b2 user interface, the query generator can construct a corresponding CTE-based query. Although lab values were not present in our CDW at the time of this testing, the current version of the software supports searching for explicitly entered values such as *glucose >126 mg/dL*. We also support the use of patient sets or previous queries as a panel concept. Additionally, it is feasible to expand functionality to support queries with temporal relationships between panels such as before, after, or within a certain number of days, by retrieving the encounter date to further refine the joins between common tables.

## B. Experiments

We created a random query generator to generate randomized XML request messages that the CRC cell would have normally received from the user interface. The query generators processed these XML messages so that they could translate the user supplied i2b2 query into actual SQL queries that can be run on the warehouse. We chose to generate random queries because our i2b2 user-base is small and may not accurately represent the usage at other institutions. For example, the occurrence

TABLE I  
AVERAGE QUERY RESPONSE TIME (IN SECONDS) PER QUERY TYPE

Query Type				Modified		Stock	
Timing	Neg.	Date	Freq.	Mean	s.d.	Mean	s.d.
Any	F	F	F	0.73	<b>0.34</b>	<b>0.47</b>	0.78
Any	T	F	F	<b>1.36</b>	<b>0.84</b>	8.44	3.75
Any	F	T	F	0.59	<b>0.37</b>	<b>0.50</b>	0.55
Any	F	F	T	1.22	<b>0.97</b>	<b>1.11</b>	1.25
Any	T	T	F	<b>1.27</b>	<b>0.96</b>	7.00	5.63
Any	T	F	T	<b>6.01</b>	17.56	7.87	<b>7.13</b>
Any	F	T	T	<b>1.21</b>	<b>0.63</b>	1.50	1.12
Any	T	T	T	<b>1.68</b>	<b>4.55</b>	5.76	6.00
Same	F	F	F	<b>1.31</b>	<b>2.43</b>	2.49	4.97
Same	T	F	F	<b>2.03</b>	<b>2.23</b>	376.82	365.96
Same	F	T	F	<b>0.61</b>	<b>0.50</b>	1.12	1.47
Same	F	F	T	1.00	<b>0.53</b>	<b>0.75</b>	0.75
Same	T	T	F	<b>2.50</b>	<b>6.38</b>	332.04	293.49
Same	T	F	T	<b>5.52</b>	<b>13.41</b>	304.55	426.57
Same	F	T	T	1.28	1.35	<b>1.12</b>	<b>1.19</b>
Same	T	T	T	<b>4.44</b>	<b>10.82</b>	236.37	516.81

constraint might be used more at institutions with large longitudinal datasets as opposed to institutions with smaller datasets with transient populations. The goal was to stress test i2b2 by capturing every possible type of query that users might design; we determined that there were 16 types of queries possible by having binary choices on the four user interface constraints (date, frequency, negation/exclusion, and whether the concepts occurred in the same encounter) (See Table I). For each of the 16 types of queries, 40 queries were randomly selected. Each of these 40 random queries had between one and four panels, each of which had randomized constraints and contained between one and three randomly chosen concepts. Concepts that did not appear in the dataset were not considered to prevent trivial empty set calculations. Here concepts are arbitrary placeholders that represent sets of patients, allowing us to focus on how each query generator interprets the logical constraints to construct a resulting aggregate patient set. This approach to test query formulation might not represent clinical reality, but does represent faithfully the effort it would take to logically combine sets of these sizes for each generator. In all our queries, each of the four possible constraints of query timing, exclusion, date, and occurrence (frequency) need only apply to at least one panel in the query to be considered that query type. Date ranges were randomly assigned. The start date and end date of a date range were restricted to exist between the minimum and maximum date of our dataset, and the end date was required to be after the start date. Of these 640 queries, a small number were unable to be correctly processed due to erroneous SQL being generated by the stock query generator.

The requested result type was restricted to a simple patient count. The dataset used for this testing contains 10 years of Kentucky State Medicaid claims data, covering 1.8 million patients across 160 million encounters with 660 million facts. The Medicaid data contains only demographics, diagnosis billing codes (excluding procedures), and visit details such as age at visit,

TABLE II  
AVERAGE, MAXIMUM, AND STANDARD DEVIATION OF ALL QUERY RESPONSE  
TIMES (IN SECONDS)

	Modified Query Gen.	Stock Query Gen.
Avg. Time to Complete	2.03	75.82
Max. Time to Complete	89.48	2407.64
Standard Deviation	6.64	238.88

length of stay, and visit type. For comparison purposes, the i2b2 environment at the University of Kentucky is housed on SQL Server 2008 R2 on a Dell PowerEdge M910 blade server with 32 processor cores and 128GB RAM; storage is provided by a EMC CX3-40 SAN housing four 7.2K RPM hard drives with 4Gbps transfer capacity. Version 1.6.04 of i2b2 was used during the testing process. Both generators had access to the precalculated frequency of each concept. This allows the panels to be ordered starting with the smallest first, since an intersection is no larger than its smallest member.

#### IV. RESULTS AND DISCUSSION

Because i2b2 users' queries are placed into a processing queue, we note that the stress test results based on our query types are especially important in a multiple-client setting. Excessive delays incurred by poorly formed queries from novice users can affect the usability of i2b2 for other more experienced users. With the development and launch of SHRINE [7], query response times should be consistent and have as little impact on the server's resources as possible, which also improves the local user's experience.

Table I shows the mean and standard deviation of time in seconds for each of the 16 query types discussed in the previous section. Bolded values indicate the approach that provided the best performance in either average query response time or standard deviation. Table II shows the global average response time if all executed queries are considered. This gives an indication of the resources both techniques might use when deployed. In addition to these summary statistics, we chose to plot our testing results in a box plot to illustrate the variance in performance within and across all 16 query types. Fig. 5 shows the 16 query types by the four variables discussed in the last section: query encounter timing, exclusion, date, and occurrence (frequency) constraints.

The modified queries perform fairly consistently across all 16 query types and only show a large variance within a population of queries in three cases: (1) a query with both an exclusion and frequency constraint where the concepts must occur in the same encounter; (2) a query with both an exclusion and frequency constraint where the concepts do not have to occur in the same encounter; and (3) a query with exclusion, date, and frequency constraints, where the concepts must occur in the same encounter. In all three cases, the CTE queries performed better on average. The variation seen in these queries is relatively small (10–20 s) when compared to the stock query generator's largest variation (293–516 s).

As Fig. 5 shows, the stock queries performed very inconsistently with highly varying minima, medians, and maxima. Fur-

thermore, the interquartile range for the stock queries is much higher (almost twice the size) than those for CTE-based queries in 15 of the 16 types of queries. A nonparametric binomial test of proportions shows that significantly more than half (59%,  $p < 0.0001$ ) of the queries required less computing time for our modified approach; for these queries, the mean difference between stock and modified execution times was 125.66 s (s.d. 297.61), which indicates a significant, positive change in user experience. For the queries where stock outperformed our modified generator, the mean difference of execution times was only 1.21 s (s.d. 5.54).

The testing also reveals several use cases in which the stock procedural approach performs much more poorly than to be expected, such as a query with same encounter timing paired with an exclusion constraint. We feel this is a typical use case that many users are interested in. For example, this could be a query that is looking for patients who have diabetes but are not recorded to have hypertension in the same encounter. This test case and a few others in the same encounter timing query types present a great deal of variance and represent an unpredictable impact on server resources and the user's experience.

There are query types in which the stock approach outperformed the modified CTEs, such as the simplest case where no constraints are chosen at all. In these cases, both methods produced queries that finished in less than one or two seconds on average, likely resulting in no substantial difference in the user's experience. Additionally, all of the modified CTEs performed well under the 180 s timeout feature of the web-client user-interface, which would provide each user with a better experience in either concurrent-user systems or in systems that support i2b2 SHRINE.

Our solutions were implemented for Microsoft SQL Server, but i2b2 is released for both Microsoft and Oracle systems. Publishing an Oracle-compatible package is left as future work; common-table expressions and all other tuning features can be leveraged in an Oracle environment. We are confident we would see performance gains in a similar Oracle environment because there are principal differences in our query techniques. We generate relational queries that require only a single database transaction and thus are more friendly to the internal optimizer; this is partly why we see a high degree of parallelism. The stock technique generates procedural queries that require multiple transactions, which paralyzes the optimizer and inhibits parallelism. These philosophical differences in techniques are expected to carry performance differences regardless of architecture. We also acknowledge that testing across varying hardware configurations may provide insight into the relationship between memory and disk usage for these approaches. We currently use our approach in our production i2b2 environment and provide this as an open-source [21] proof of concept for SQL Server.

The key benefit of this study is that it can improve the users' experience by reducing response times and ensuring consistent performance regardless of the logical constraints of their queries. In i2b2, this is demonstrated by our queries returning far more quickly than the default 180 s that queries are allowed to run in the user interface. Because a queue for queries submitted by the users is used to delegate resources, returning result

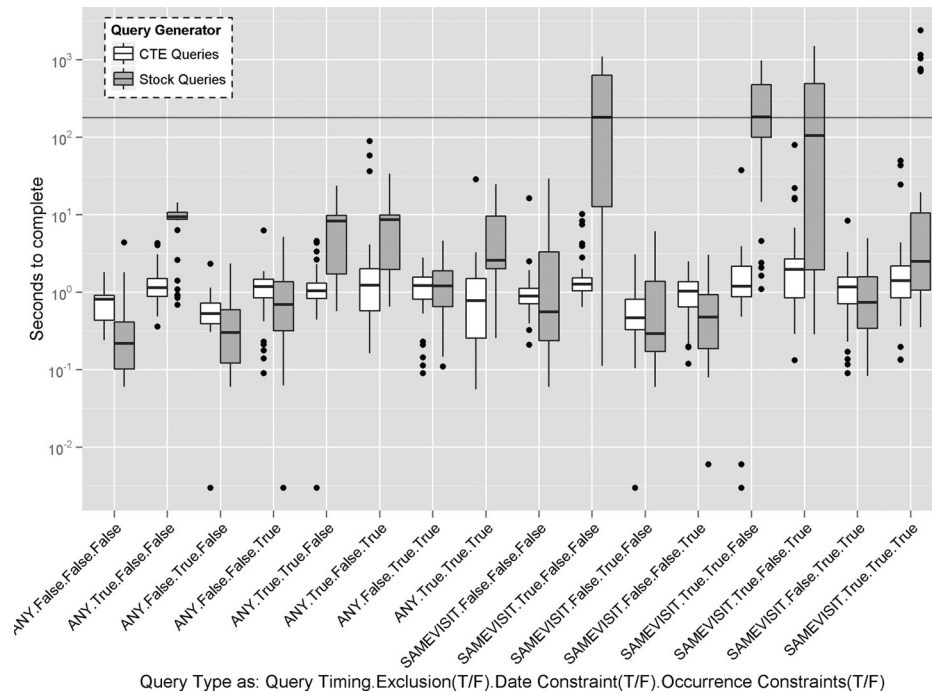


Fig. 5. Logarithmic-scale plot of the execution times of the randomly generated queries across the 16 query combinations that were tested. The gray horizontal line represents the default amount of time (180 seconds) that the user interface allows queries to run before timing out.

sets quickly is crucial. Otherwise, queries that take far too long to complete can block activity from other users, which would be especially critical to address in a federated query network such as SHRINE.

## V. CONCLUSION

We have shown that stable and scalable Boolean queries can be constructed using common table expressions. This improvement is purely algorithmic and the result of elegant relational programming. Hardware improvements can also provide performance gains but require a costly investment. The improvements we have presented can be installed and integrated into an i2b2 system in a short amount of time and can provide performance gains with no investment of additional financial resources. Because of their low cost, these types of graceful programming solutions are crucial. Furthermore, without scalable algorithms, clinical and translational science cannot be performed at a national level. Translational work must ultimately bridge and transcend across individual institutions, which is only possible with truly scalable architecture. Our contribution enables efficient local querying, which in turn, enables efficient federated querying.

Our experiments also describe an evaluation methodology that provides a means of profiling and comparing CDW performance using one or more algorithmic approaches across a range of query types, and for tuning CDWs for the types of queries that are most common to local user needs. The process of enumerating the possible query types and randomly generating queries per type gives a good indication of the global performance profile and may help avoid local institutional biases.

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## REFERENCES

- [1] K. Marsolo, "Research patient data warehousing," in *Pediatric Biomedical Informatics*. New York, NY, USA: Springer-Verlag, 2012, pp. 93–108.
- [2] S. N. Murphy, G. Weber, M. Mendis, V. Gainer, H. C. Chueh, S. Churchill, and I. Kohane, "Serving the enterprise and beyond with informatics for integrating biology and the bedside (i2b2)," *J. Amer. Med. Inform. Assoc.*, vol. 17, no. 2, pp. 124–130, 2010.
- [3] I. S. Kohane, S. E. Churchill, and S. N. Murphy, "A translational engine at the national scale: Informatics for integrating biology and the bedside," *J. Amer. Med. Inform. Assoc.*, vol. 19, no. 2, pp. 181–185, 2012.
- [4] V. Deshmukh, S. Meystre, and J. Mitchell, "Evaluating the informatics for integrating biology and the bedside system for clinical research," *BMC Med. Res. Methodol.*, vol. 9, no. 1, pp. 70–82, 2009.
- [5] S. Murphy, S. Churchill, L. Bry, H. Chueh, S. Weiss, R. Lazarus, Q. Zeng, A. Dubey, V. Gainer, M. Mendis, J. Glaser, and I. Kohane, "Instrumenting the health care enterprise for discovery research in the genomic era," *Genome Res.*, vol. 19, no. 9, pp. 1675–1681, 2009.
- [6] National Human Genome Research Institute. (2012). DNA sequencing costs. [Online]. Available: <http://www.genome.gov/sequencingcosts/>
- [7] G. M. Weber, S. N. Murphy, A. J. McMurry, D. MacFadden, D. J. Nigrin, S. Churchill, and I. S. Kohane, "The shared health research information network (shrine): A prototype federated query tool for clinical data repositories," *J. Amer. Med. Inform. Assoc.*, vol. 16, no. 5, pp. 624–630, 2009.
- [8] J. J. Cimino, "The biomedical translational research information system: Clinical data integration at the national institutes of health," in *Data Integration in the Life Sciences*. New York, NY, USA: Springer-Verlag, 2012, pp. 92–92.
- [9] M. M. Horvath, S. Winfield, S. Evans, S. Slopek, H. Shang, and J. Ferranti, "The deduce guided query tool: Providing simplified access to clinical data for research and quality improvement," *J. Biomed. Inform.*, vol. 44, no. 2, pp. 266–276, 2011.



- [10] O. E. Livne, N. D. Schultz, and S. P. Narus, "Federated querying architecture with clinical & translational health it application," *J. Med. Syst.*, vol. 35, no. 5, pp. 1211–1224, 2011.
- [11] H. J. Lowe, T. A. Ferris, P. M. Hernandez, and S. C. Weber, "Stride—An integrated standards-based translational research informatics platform," in *Proc. Amer. Med. Inform. Assoc. Annual Symp.*, 2009, vol. 2009, pp. 391–395.
- [12] G.-Q. Zhang, T. Siegler, P. Saxman, N. Sandberg, R. Mueller, N. Johnson, D. Hunscher, and S. Arabandi, "Visage: A query interface for clinical research," *AMIA Summits Translat. Sci. Proc.*, vol. 2010, pp. 76–80, 2010.
- [13] D. Segagni, F. Ferrazzi, C. Larizza, V. Tibollo, C. Napolitano, S. G. Priori, and R. Bellazzi, "R engine cell: Integrating r into the i2b2 software infrastructure," *J. Amer. Med. Inform. Assoc.*, vol. 18, no. 3, pp. 314–317, 2011.
- [14] D. Segagni, M. Gabetta, V. Tibollo, A. Zambelli, S. G. Priori, and R. Bellazzi, "Onco-i2b2: Improve patients selection through case-based information retrieval techniques," in *Data Integration in the Life Sciences*. New York, NY, USA: Springer-Verlag, 2012, pp. 93–99.
- [15] N. Wattanasin, A. Porter, S. Ubaha, M. Mendis, L. Phillips, J. Mandel, R. Ramoni, K. Mandl, I. Kohane, and S. N. Murphy, "Apps to display patient data, making smart available in the i2b2 platform," in *Proc. Amer. Med. Inform. Assoc. Annual Symp.*, 2012, vol. 2012, pp. 960–969.
- [16] T. Ganslandt, S. Mate, K. Helbing, U. Sax, and H. Prokosch, "Unlocking data for clinical research—The german i2b2 experience," *Methods Inf. Med.*, vol. 47, no. 2, pp. 117–123, 2008.
- [17] V. Gainer, K. Hackett, M. Mendis, R. Kuttan, W. Pan, L. C. Phillips, H. C. Chueh, and S. Murphy, "Using the i2b2 hive for clinical discovery: An example," in *Proc. Amer. Med. Inform. Assoc. Annu. Symp.*, 2007, vol. 959.
- [18] G. M. Weber, "Supercharging i2b2," in *Proc. Amer. Med. Inform. Assoc. Summit on Translational Bioinformatics*, 2012, vol. 2012, p. 182.
- [19] S. N. Murphy, M. Mendis, K. Hackett, R. Kuttan, W. Pan, L. C. Phillips, V. Gainer, D. Berkowicz, J. P. Glaser, I. Kohane, and H. Chueh, "Architecture of the open-source clinical research chart from informatics for integrating biology and the bedside," in *Proc. Amer. Med. Inform. Assoc. Annu. Symp.*, 2007, vol. 2007, pp. 548–552.
- [20] Microsoft. (2004). "SQL server 2005 beta 2 transact-SQL enhancements," [Online]. Available: [http://msdn.microsoft.com/en-us/library/ms345144.aspx#sql05b2tsqlen\\_r\\_ecquercte](http://msdn.microsoft.com/en-us/library/ms345144.aspx#sql05b2tsqlen_r_ecquercte)
- [21] Division of Biomedical Informatics, University of Kentucky. (2012). "i2b2 common-table expression query generator," [Online]. Available: <https://code.google.com/p/i2b2-cte-query-generator-ukbmi/>



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