KnowledgeButton: An Evidence Adaptive Tool for CDSS and Clinical Research

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***Abstract*—Healthcare domain is continuously growing with new knowledge emerged at different levels of clinical interest. At the same time, there is an increasing interest in the use of clinical decision support systems (CDSSs) to increase the healthcare quality and efficiency. Majorly the existing CDSSs are not designed to adapt scientific research in a well-established and automatic manner. Clinicians and researchers access the online resources on frequent basis for unmet questions during the course of patient care. They usually follow a dis-integrated approach to search for their required information from resources of their interest. Additionally, there is lack of defined mechanism to integrate the relevant knowledge for future use. To overcome the disintegrated and non-automatic approach, we introduce the concept of KnowledgeButton; a comprehensive model for evidence adaption from online credible knowledge sources in a well-defined and established manner. It saves the time of clinicians spend unnecessary in searching research evidence using disintegrated and manual mechanism. In this paper, we provide architecture design, workflows, and scenarios complemented with primary results. It covers walk-through from search query generation to evaluation of search results.**

Keywords—KnowledgeButton; CDSS; Research Evidence; Query Generation; Knowledge Base Maintenance

I. INTRODUCTION

Good doctors use individual clinical expertise and the best available external evidence in combination, and neither alone is enough [1]. Without clinical expertise, an even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Similarly, without current best evidence, only clinical expertise cannot provide the ultimate confidence over clinical decision. The research evidence persuades the doctors to pursue the care plan and decision with higher level of confidence.

Contemporary CDSSs are majorly based on clinical expertise and already available evidences which keep them off from recent research advancements in the domain. The full promise of CDSSs for facilitating evidence based medicine will occur only when CDSSs can "keep up" with the literature [2]. It is not surprising that most clinicians consider the research literature to be unmanageable [1] and of limited applicability to their own clinical practices [3]. A sheer amount of literature is available online in the medical domain. Only MEDLINE/PubMed Baseline yearly citations totals 22,376,811 from 2014 reported in statistical reports on MEDLINE/PubMed Baseline data by U.S. National Library of Medicine [4].

Searching for literature base evidence using ad hoc approaches results in issues of unnecessary time consumption, context losing and integration of evidence to knowledge base of CDSS. Manual query generation to search for up-to-date scientific literature required a lot of doctors' time. Using third-party search engines in a non-integrated environment results in context gone astray. Moreover, without an established infrastructure it is very hard to integrate the relevant research evidence to the local knowledge base of CDSS. There is need of automated tool that keep the CDSS knowledge base up-to-date with research literature-based evidence keeping the practice-based evidence in place.

We propose a comprehensive model called KnowledgeButton that exhibits the properties of evidence adaption from credible knowledge sources. This covers both input request manipulation (query generation) and output response handling ranging from information retrieval to knowledge creation. The ultimate goal of this approach is to evolve the knowledge base of a CDSS system with new research emerged in the domain.

One of the projects utilizes the services of KnowledgeButton is Smart CDSS [5] which consists of three major components; knowledge authoring, knowledge base, and research evidence support. **Knowledge authoring** component is covered in our previous work [6] that provides the environment for physicians to create their clinical knowledge in the form of knowledge rules. The knowledge rules are created using domain ontology derived from SNOMED CT. It has Verification and Compilation subcomponents for verifying and compiling the rules. **Knowledge base** maintains the knowledge rules in the form of Medical Logic Module (MLM). MLM encapsulates knowledge as software module that triggers an action based on data event generated at healthcare system [7]. The third part is **research evidence support** which is the focus of this paper where initial idea of this approach is covered in publication [8]. Smart CDSS system has been realized for cancer domain more specifically for head and neck cancer (H&N cancer).

KnowledgeButton model realizations posture several research challenges regarding context manipulation, search query generation, related information retrieval, information presentation and finally the knowledge rule generation. This paper focuses on the solution space for these challenges. The concept not only enhance the capabilities of CDSSs by supplementing the knowledge base with new evidences, but also provides a learning environment for medical researcher to conduct clinical research.

The rest of the paper is organized as; section II discusses the related work, section III presents the methodology of the system and section IV discusses the push and pull models. Section V presents the case study and initial results of the system followed by section VI on discussion. Section VII concludes the work.

II. Realted Work

Evidence based systems have long been used in clinical domain for clinical efficacy. The efficacy studies of clinical practice that form the basis for evidence-based medicine constitutes only a small fraction of the total research literature [9]. It is not surprising that most clinicians consider the research literature to be unmanageable [1] and of limited applicability to their own clinical practices [3]. Sim, Ida, et al. [2] provided the idea of evidence-adaptive CDSS; a subclass of CDSSs that are evidence-adaptive, in which the clinical knowledge base of the CDSS is derived and continually reflects the most up-to-date evidence from the research literature and practice-based sources. Evidence-adaptive CDSS is different from conventional evidence-based CDSS that alerts clinicians to a known drug–drug interaction and its clinical knowledge base is derived from scientific evidence, but no mechanisms are in place to incorporate new research findings.

Many CDSS systems are developed for clinical decision assistance specifically in cancer domain such as MATE [13] and TADS [14]. MATE (Multi-disciplinary meeting Assistant and Treatment sElector) is a tool designed to assist breast clinicians in making management decisions for their patients in Multi-disciplinary Meeting (MDM) [13]. TADS (Triple Assessment Decision Support) is designed to support clinician in decisions for breast cancer patient cases at three decision points; family history and genetic risk assessment, selection of imaging and biopsy modalities, and final management decision [14, 15].

For any evidence based system to efficiently work in a domain, the context of that domain plays a critical role. Context provide the features for query generation in order to approach for relevant information. The source and format of data are crucial to consider for automatic or semi-automatic query generation.

Cimino, James J. presented the idea of "Infobuttons" [10] and "Infobutton Manager" (IM) that attempts to determine the information need based on the context of what the user is doing. Infobuttons are mainly topic specific with a question facility for the users to tune the query more towards the context. The main focus of Infobuttons approach is to establish context-specific links to health information resources. It is based on simple topic based linkage to the resource from within the context of EMR/EHR and is not suitable to develop complex queries.

CDAPubMed [11] is a browser extension aiming to provide a tool to semi-automatically build complex quires. It provides additional information to the contents of EHR for improving and personalizing biomedical literature searches. HL7 Clinical Document Architecture (CDA) is used as a main source to extract clinical terms for query generation. It loads the patient clinical documents (CDA documents), identifies relevant terms for scientific search, and generates and launch literature search queries to a major search engine i.e. PubMed, to retrieve citations related to the EHR under examination.

MCRDR (Multiple Classification Ripple-Down Rules) [Kang, 1995] knowledge base is used to generate queries to fetch information from MSN web search service [Kim, 2008]. MCRDR is a document classification system which employed knowledge acquisition method. The knowledge base of MCRDR document classification consists of rule tree, category tree, and cornerstone cases. Its automatically generate query in multiple ways including category based, rule based, category-rule combined and case based. The claim is to replace domain expert with simulated expert in order to avoid knowledge engineering work. However, information credibility and

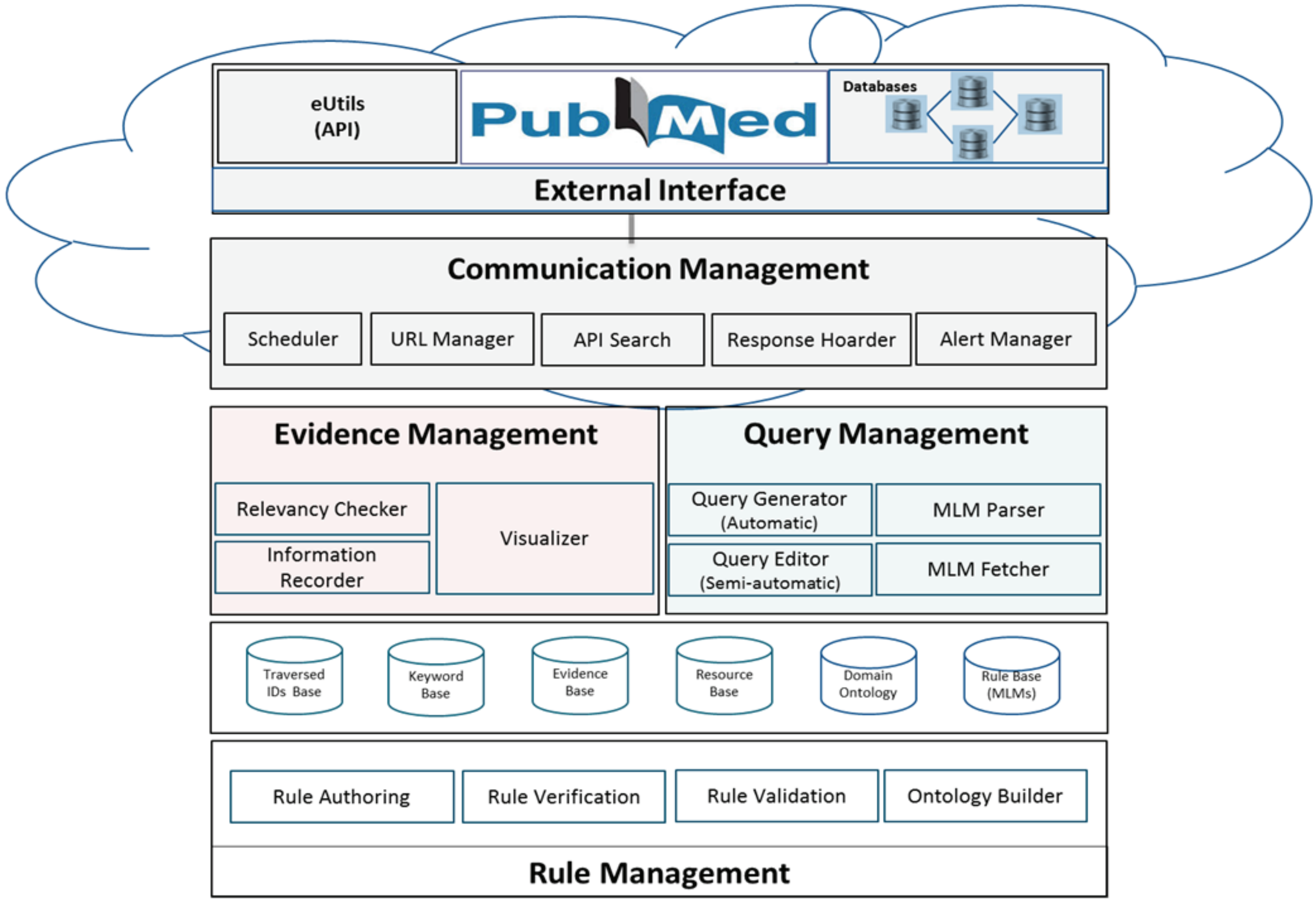

Fig 1: KnowledgeButton Architecture diagram consisting four major modules: Query Management, Communication Management, Evidence Management and Rule Management

verification need to be sorted out before it can be used for any purpose.

Unlike MATE and TADS, our proposed KnowledgeButton model is based on automatic adaption of new research evidence incorporation to the knowledge base of a CDSS system. It automatically fetches the current evidence from online credible journals available through PubMed service. For maximization of relevancy and keeping the search results in the context, it uses automatic and semi-automatic approaches for query generation. It also covers the presentation part of relevant research documents in order to approve the research article as an evidence by the domain expert. New knowledge rules can also be culminated from these newly approved articles.

III. METHODOLOGY

Investigating the CDSS requirements led us to the conclusion of physicians and oncologists' continuous dependency on online medical resources for decision making. The objective is to find new evidences emerged in the domain. Sometimes, they connect to the online resources to gain more confidence before proceeding to the final clinical decision. Realizing the need for more information by the physicians we analyzed the domain and design a detailed architecture for KnowledgeButton as shown in Fig 1. The architecture works for both push and pull models. We discuss these two models in section IV. First we discuss the major components of KnowledgeButton. The architecture in Fig. 1 is composed of four major components that are further divided into sub-components. These four components are Query Management, Communication Management, Evidence Management and Rule Management.

A. Query Management

This component is modeled to generate queries both automatically and semi-automatically. Automatic way of query generation is related to Push Model while semi-automatic is related to pull model . Query Management component consists of following sub-components.

1) MLM Fetcher

MLM Fetcher component fetches all the MLMs required for a query set. The MLMs reside in knowledge base of CDSS in the form of parent-child hierarchies classified in different categories. During fetching, the categories of the MLMs are identified.

Step 1: Select the method to create the query

Step 2: Select the MLM set to be used in query from large set of MLMs in KB

Step 3: Load the MLMs to Memory with identification of Parent MLM and Child MLM

Step 4: Extract the term set from both Parent and Child MLMs

Step 5: Identify the clinical terms in the extracted term set using SNOMED CT

Step 6: Add connectors (AND, OR, NOT) at appropriate places to connect the clinical terms

Step 7: Create the query

Step 8: Add the query to Entrez basic URL and set the Entrez database to form final URL

Step 9: Pass the URL to Entrez eSearch service call

Step 10: Get the UIDs of returned articles in results set

Step 11: Evaluate the results by matching the bench mark data set using formula

$$R = \frac{MA_{BM} \cap TA_{BM}}{TA_{RS}} \quad \text{where}$$

$\boldsymbol{MA_{BM}}$ *is showing number of articles that are matched in Bench Mark Data Set*
$\boldsymbol{TA_{BM}}$ *is the total number of articles in Bench Mark Data Set*
$\boldsymbol{TA_{RS}}$ *is the total numbar of articles in Result Set*

Step 12: Check the R value, if it fulfils the threshold value then store it as Methodi evaluation.

Step 13: Repeat Step 1 to Step 13 for all the methods

Step 14: Choose the method with highest R value

Fig 2: Selection of Best Automatic Query Generation Method

2) MLM Parser

The fetched MLMs need to be parsed individually for information extraction. Each MLM has several slots where one of them is "knowledge". The knowledge part has sub-slots to further specify the knowledge. Among these sub-slots, one is known as "logic" where the knowledge is represented by IF-THEN structure. In IF part of the structure we have patient's health condition, staging and diagnosis. While the THEN part lead towards the treatment modality option. Every single term of parent or child MLM is not necessary to be used in query. This component extracts the terms that are meaningful for use in query formation, called keywords. We check each term with SNOMED CT terminology concepts/value set; if matched, it is considered as keyword and is extracted.

3) Query Generator

Query generator accumulates the extracted keywords, connect them with logical and priority operators and generate the final query set in automatic manner. The connector between the keywords as well as between parent and child MLMs impact greatly the results of queries. At this stage, the synonym terms are added to each keyword using synonym dictionary. We created synonym dictionary for commonly used terms in head and neck cancer domain. Different strategies can work to generate queries and the objective is to select the best strategy. Fig 2 shows the algorithm steps followed for selection best automatic query generation method.

4) Query Editor

Query Editor is designed for the user to customize the query options with the support of Editor's added tips and tools support. It is very common of users to change their mind especially when they are interested in specific kind of research outcomes. Query Editor provides the environment for the guidance of user to create their customized search queries. Domain concepts are opened in the context and the previous queries are loaded from the query bank for reuse option. When user write something, a controlled vocabulary option populates the required concepts/values from the SNOMED CT repository.

B. Communication Management

Communication Management is designed to communicate with external world that includes the search engines and their services. This component has five sub-components to fulfill its objective.

1) Scheduler

Scheduler component takes care of managing query set with respect to time and event. Instead of running all the queries at once, rather schedule them category wise. Some query run on regular basis and other run in a specific time period. In case of journals, the Scheduler keeps track of the publishing period.

2) URL Manager

URL Manager transform the query according to the format of target search engine. We consider the PubMed as search engine for KnowledgeButton due to medical knowledge richness and credibility of the contents. Most of the credible medical journals are accessible through PubMed interface. PubMed requires user query to be appended with basic URL in a specified format.

3) API Search

PubMed provides API service support called Entrez Programming Utilities (eUtils) to build custom queries from within user programs. The eUtils are a set of seven server-side programs that provide a stable interface into the Entrez query and database system at the National Center for Biotechnology Information (NCBI) [4]. Entrez currently includes 23 databases covering a variety of biomedical data. To access these data, a piece of software first posts an eUtils URL to NCBI, then retrieves the results of this posting, after which it processes the data as required. The seven programs are EInfo, EGQuery, ESearch, EFetch, ESummary, EPost and ELink. Each of these programs has its own objective to fulfill. However, most of them performed action in a pipeline fashion. One program output is utilized by the other and so on. In current work we implemented three of the programs including ESearch, EFetch and ESummary with their internal methods and properties.

4) Response Hoarder

Response Handler takes care of the returned result set. The query result set contains data of research articles including ID, title, authors, abstract, journal, date and the link to actual source. This component prepare the data according to the user requirement.

5) Alert Manager

Alert Manager notify the users of new research evidences if found. In automation scenario since users have no interaction with the system (push model) so alert mechanism is required to notify the subscribed users.

C. Evidence Management

The documents returned are not necessary to be considered as evidences. The only articles approved by domain experts are considered as evidences. Evidence Manager performs all the necessary activities to rank the articles according to the relevancy criteria and present them to the physicians. If physicians approves an article it becomes an evidence. It has three sub-components.

- *Relevancy Checker*

According to physicians stand point; most of the credible journals publish research articles in a defined format. Title, Abstract and Conclusion are considered the key parts of any article able to provide evidence of the whole document relevancy to the context. This component ranks the document based on their relevancy level. We have criteria calculations at multiple levels to find a relevant document.

Criteria 1(Commonality Criteria): Finding documents that are common in all queries for a particular category.

Criteria 2 (Similarity Criteria): Finding documents that are similar to documents in training set for a particular category.

- *Knowledge Visualizer*

Knowledge Visualizer makes the knowledge explicit by presenting the concepts with relationships in visual format. Readability is always being the main concern for the users to benefit from online research results. It presents the MLMs as well as relevant research articles together at one place. The communal presentation of information helps the domain experts to create knowledge rule using Rule Management component.

- *Information Recorder*

Upon approval, the system records all necessary information about the article for future use. Moreover, we also record the ranking information about the article. Next time when we perform the search operation, we populate the information of existing articles from local repository and bring only new articles from online resources to avoid duplications.

D. Rule Management

Rule Manager provides the editor for the physicians to create knowledge rules from the available information as well as their wisdom and experience. After formation, the rule needs to be validated against standard syntax. The validated rules are compiled and saved to the knowledge base of CDSS. More details can be seen in one of our publications [6]. Physicians have problem to create rules of their own unless we have an easy to use graphical user interface enriched with intelligent capabilities. The automatic selection of concepts during rule formation as per the context is much helpful option compared to static approaches. Once rule is formed, validated and compiled, it is saved to the knowledge base of CDSS. The rules created by the rule management component are persisted in a specific format. We are using Arden Syntax to construct rules in Medical Logic Module (MLM) format.

IV. Push Model vs Pull Model

Push model is different from pull model in respect of system behavior. In push model the process is majorly automated while pull model involves human to start the process. The difference between the two models is described in Table 1 and the workflow diagram is provided to explain the interaction process of push and pull.

In Push model (Fig 3), the process is activated automatically based on two options: time and event. In Time based activation the system search for articles from specified online sources at particular time while for event based activation, the system is activated when specified event occur such as clinical decision. The steps followed in push model are as follows;

TABLE 1: PUSH MODEL VS PULL MODEL

Push	Pull
Search by system	Search manually
Automatic Query	Semi-automatic/Manual Query
Alerts mechanism required to notify users	No need of alerts mechanism
Asynchronous communication	Synchronous communication

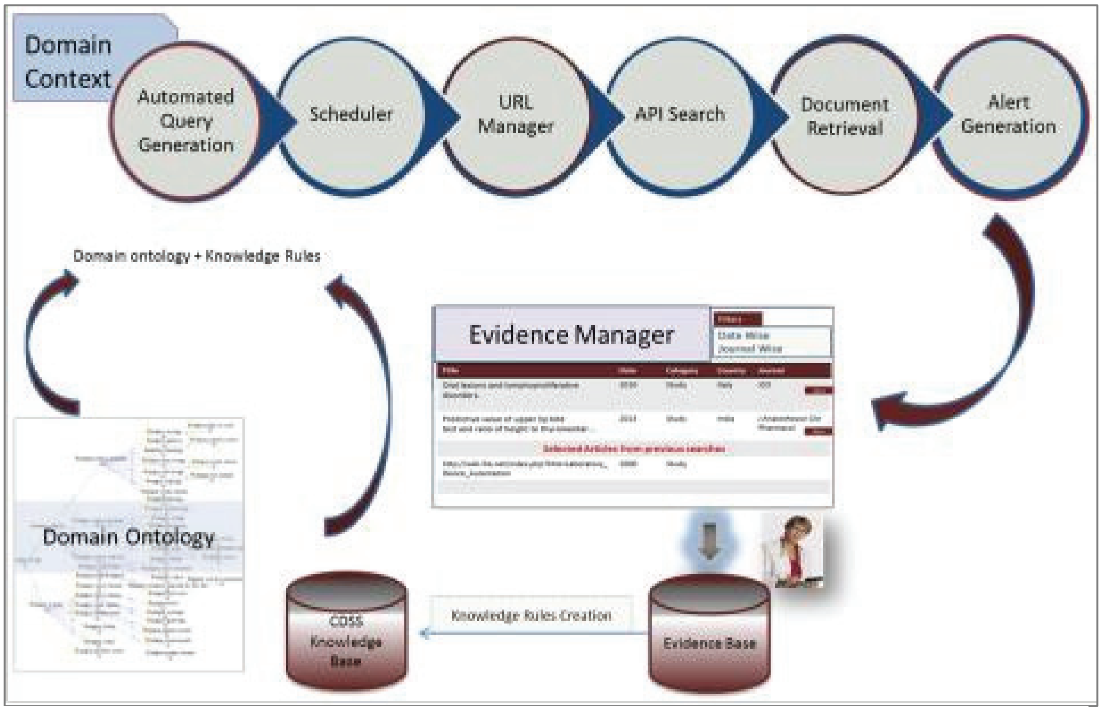

Fig 3: Push Model Flow Diagram

Extract keywords from MLMs (knowledge rules) and parent-child concepts from domain ontology for the extracted keywords.

- Associate the domain context and generate query set automatically.
- Schedule the query based on either time or event
- Transform the scheduled query into URLs required by target search engine such as PubMed
- Perform the search operation using API provided by target search engine
- Receive the retrieved document set
- Create alerts and notify the subscribed users
- Check the relevancy and present the documents to the user (domain expert) in combination with MLMs order by relevancy
- Let the user approve a document as an evidence
- Record information about the evidence such as ranking, title, date of publication etc. for future use
- Let the user to create new knowledge rule from the evidence using knowledge authoring tool (if any)

In Pull model, the process is activated manually by the medical researcher. It is independent of time or event. The steps followed are majorly same at that of Push model except three distinctive steps. Unlike Push model, here the query is generated manually rather automatically with the help of query editor. Query editor implements domain ontology to provide domain concepts to the user. It also take care of the previous queries made by the same or different users. It does not require scheduler component to schedule the queries. Also it does not need to acquire alert mechanism. The steps are performed in following order.

- Build query manually using easy to use query editor
- Transform the query into URL required by target search engine such as PubMed
- Perform the search operation using API provided by target search engine
- Receive the retrieved document set
- Present the documents to the user (domain expert)
- Let the user to approve a document as an evidence

TABLE 2: QUERIES GENERATED FOR ORAL CAVITY SITE AT DIFFERENT HIERARCHICAL LEVEL

Root MLM	*"cancer and oral cavity"*
Chile 1 MLM	*"cancer and oral cavity and chemotherapy induction"*
Child 2 MLM	*"cancer and oral cavity and chemotherapy induction and radiotherapy"*
Child 3 MLM	*"cancer and oral cavity and chemotherapy induction and surgery"*
Child 4 MLM	*"cancer and oral cavity and chemotherapy induction and surgery and radiotherapy"*

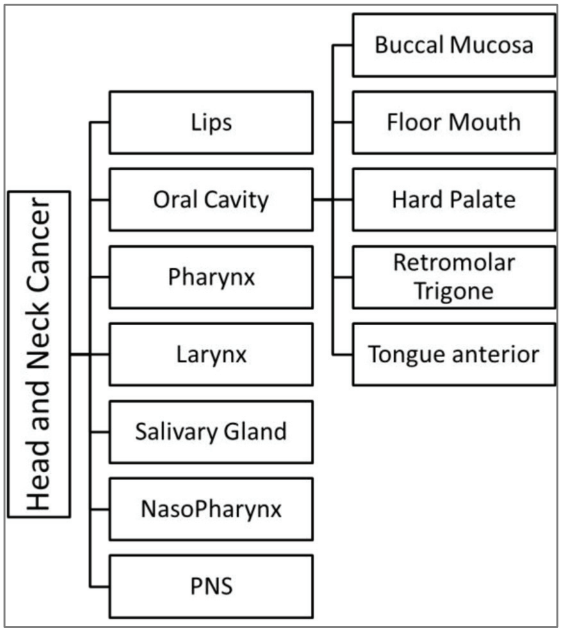

Fig 4: Head and NeckAnatomical sites and sub-sites for oral cavity

- Classify the evidence according to existing knowledge rules in knowledge base (if any)
- Record information about the evidence such as ranking, title, date of publication etc. for future use
- Let the user to create new knowledge rule from the evidence using knowledge authoring tool (if any)

V. CASE STUDY AND RESULTS

KnowledgeButton model is realized for the domain of cancer more specifically H&N cancer. The KB of Smart CDSS system is inspired from National Cancer Comprehensive Network (NCCN) guidelines [12]. NCCN has structured the guidelines for H&N cancer based on anatomical sites. The main sites include lip, oral cavity, pharynx, salivary glands and few others which are further categorized in sub-sites. Fig 4 shows the main anatomical sites with sub-sites for oral cavity. MLMs in Smart CDSS KB are also organized based on anatomical sites. Every site has one or more than one MLMs encoded in Arden syntax. In Push model, we generate one query set for each site. A query set contains one or more queries. Considering the site **oral cavity**, we generate a number of queries. The variations in queries are due to terms they possess. We consider root MLM first and generate a query in its scope. Child MLM is added to root MLM and generate second query and so on. The query generated from root MLM is more generic compared to child MLMs queries. Table 2 shows the sample queries generated for oral cavity site. These queries are transformed to PubMed URLs. After generating URLs against each query, the search function provided by Entrez is activated. Result sets are compiled at two levels; commonality factor and similarity check. Commonality factor finds the documents that are common in all queries of a query set. Taking the same oral cavity example, we run all the queries as shown in Table 2 and find the common documents in between as shown in Fig 5 using equation;

$$C= R_1 \cap R_2 R \ldots \cap R \qquad \text{Eq (1)}$$

Where C shows the list of common documents in all query results. R_1 represents the results of query1, R_2 represents results of query 2 and so on. The common documents are checked for similarity with bench mark data set of 320 evidences that are classified with the help of domain experts for different sites. For similarity check we use formula;

$$S=\frac{C_m}{C_t} \qquad \text{Eq (2)}$$

Where C_m showing the number of research articles from common document list C Eq (1) that are matched with bench mark data set in a specified category and C_t represents the total of research articles in common document list C Eq (1). Only articles that pass the criteria for selection are chosen as a final

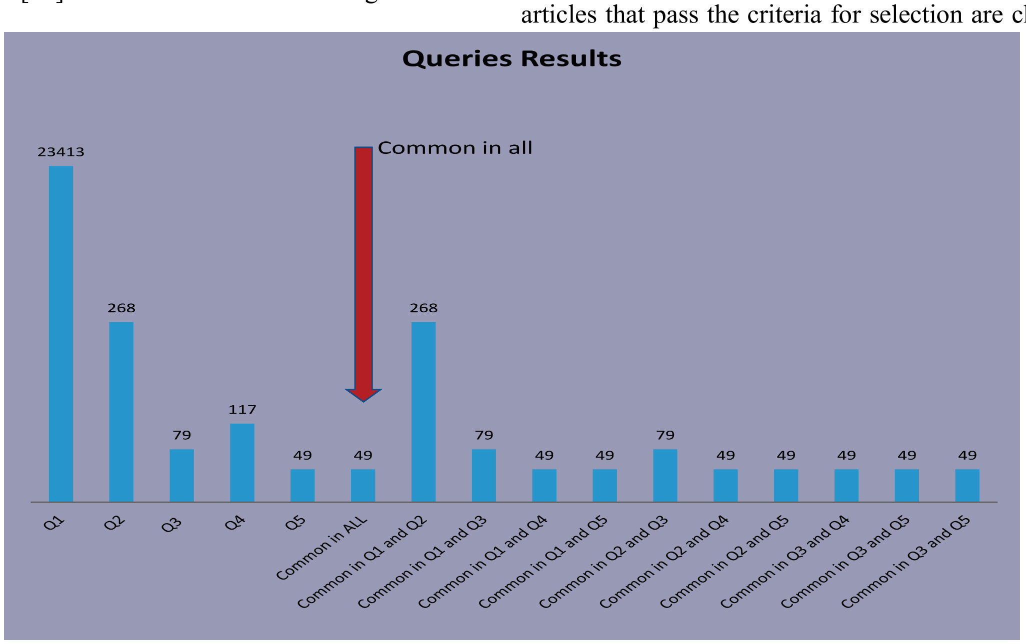

Fig 5: Common documents in the result sets of queries under oral cavity site

set. The final set is put for approval of the physicians. The common observations made upon the results by the physicians are related to the preciseness of the articles. The pointed out that most of the articles are related but there are many which are not that important to consider. They suggested to improve the precision and making the final set reduced so that physicians go through them in less amount of time.

VI. Discussion

For any evidence based system to efficiently work in a domain, the context of that domain plays a critical role. Context provide the features for query generation in order to approach for relevant information. The source and format of data are crucial to consider for automatic or semi-automatic query generation. KnowledgeButton is a promising approach towards automatic acquisition of knowledge from online resources in the context of clinical setup. It not only keeps the things in the context but also helps in automation of several important steps in the process of knowledge acquisition.

A number of research challenges need to be resolved in order to achieve the objective. Three obvious research challenges fall in the areas of context enrichment, relevant information retrieval and finding concepts and their relationships. Additional challenges include information presentation and bringing contextual intelligence to assist the clinicians in the process of rule generation. Despite these challenges, this work is of high significance according to the opinion of clinicians. We got overwhelming response from the physicians working in H&N cancer care setup regarding important and usefulness of KnowledgeButton.

So far we implemented the push model and pull model is yet to be realized. We found difficulties to sort out only relevant articles from large set of documents based on automatically generated queries. The query generation strategy and results evaluation strategy need to be matured.

VII. Conclusion

Online text sources such as biomedical literature are great resources for information to acquire for assistance in clinical decision making process. In current scenarios, clinicians spent a lot of their time on searching for required information from online biomedical resources using ad-hoc approaches. We introduced KnowledgeButton concept as a comprehensive model to clinical knowledge base of CDSS with research evidences. The model supports both push model, where the queries are generated automatically, and pull model for the users to interact with online sources by manual query generation. The work is undertaken with the support of two domain experts who verify the system at every logical step. The prototype system is deployed in a cancer hospital for the users to test different scenarios.

Acknowledgment

This research was supported by the MKE (Ministry of Knowledge Economy), Korea, under the ITRC (Information Technology Research Center) support program supervised by the NIPA (National IT Industry Promotion Agency) (NIPA-2009(C1090-0902-0002)).

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