Kalya Research: Complementary and Alternative Medicine (CAM) Virtual Research Assistant from Biomedical Literature

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Abstract

Complementary and alternative medicines (CAM) become an emerging subject of interest both for users and health professionals. Rigorous studies identify efficient and safe methods for human health, frequently called by researchers, non-pharmacological interventions. The challenge is to determine relevant articles in a large and increasing volume of publications and journals. To meet this challenge, we created Kalya Research (KR), a medical assistant tool based on artificial intelligence that selects and characterizes CAM literature and bring support to medical researchers. Based on rule models and ontologies, KR can suggest relevant and recent CAM publications. It presents key indicators through analytical visualizations. KR has been compared to Medline by searching CAM literature concerning alopecia in breast cancer patients. It proves to be a relevant and time saver tool. Thus, KR is constantly evolving with the extensions to other health topics and the addition of new features such as text annotations.

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Introduction

Complementary and alternative medicines and non-pharmacological interventions increased extensively in biomedical literature toward an integrative approach of medicine and health. Patient demands and practitioner preference motivated researchers to intensify studies on this topic. An Australian survey evaluated the practice of complementary medicine (CM) by general practitioners (GP) and concluded that there is a real need for evidence-based CM[1]. In parallel, a Chinese review evaluated the quality of reporting Randomized Clinical Trials (RCTs) on traditional Chinese medicine treatments[2]. The review also concluded a real need for improving the standards of RCTs reports. A more recent study performed a bibliometric analysis of apitherapy from the scientific literature covering a 36-year period[3]. This study revealed that although there is a growing interest in apitherapy, an imbalance in research on this subject is observed in the literature which could be explained by the lack of resources. These different examples illustrate the point and show the diversity of therapies used in CM. Knowledge in the biomedical field is advancing every day, reaching millions of publications. For example, in cancer, representing one of the leading causes of death in the world after cardiovascular disease[4], there are approximately 6.6 million publications (GoogleScholar November 2023). Among them, Kalya assessed that about 600,000 (10%) studies focus on complementary and alternative medicines (CAM). Besides, this volume increased to 58% during the last decade. Thus, the problem is how to identify these publications when there is no repository.

With the quickly increasing volume of the biomedical literature, any biomedical researcher finds himself confronted with obstacles, well known to scientists, namely the extraction of relevant information, the sorting of documents, and their exploration. To overcome these obstacles, there are already various tools like text exploration by visual analytics that allow filtering query results[5]. The functionalities differ according to the tools. Some of them allow to query directly using keywords and to obtain a list of publications with the annotated abstract on Named Entity Recognition (NER). It's the case for BioIE (based on a rule model)[6], LitSense (specialized in sentence retrieval)[7], and GeneView (targeted biological entities) which also annotates the full text if it is avalaible[8]. Other tools provide additional functionalities, as in Thalia which displays the frequencies of an entity in the corpus of texts resulting from the query[9], BioTextQuest+ that suggests various methods to cluster the abstracts[10]. Some tools provide other functionalities such as BEST[11] which is a biomedical entity search tool that provides visual analytics on frequent terms and interaction network for each identified entity. There is also FACTA+[12] which furnishes the biomedical associated concepts with some text analysis pipeline. There are some tools dedicated to a specific task like Quertle[13] that performs a semantic search in multiple biomedical databases (PubMed included) and runs a query via relationships between concepts. BioReader[14] is a binary text clustering tool enabling filtering relevant articles from query results. Then, in a general context, we notice that text mining techniques are becoming essential tools for finding and sorting relevant articles.

Digital bibliographic tools dedicated to CAMs are also available[15]. CAM-QUEST®[16], MOTRIAL[17], LIVIVO[18], AMED[19], and CAMbase[20] are bibliographic databases covering a wide spectrum of CAM therapies. Only CAM-QUEST has a pre-defined request system by disease, therapy, and study design categories. CAMbase has not been kept up-to-date since 2005 and AMED groups mainly European journals. Moreover, there are many specialized bibliographic databases, for example, PEDro for physiotherapy[21], HOMEOINDEX for homeopathy[22], ABIM for phytotherapy and Indian medicine[23], NAPRALERT for natural products[24], OTseeker for occupational therapy[25], Arthedata for art therapy[26], CAIRSS for music therapy[27], and CARDS for dietary supplements[28]. Furthermore, the enthusiasm of patients for natural medicines such as Chinese medicine questions "evidence-based medicine" and the number of websites dedicated to it is significant compared to other disciplines. The tendency to evaluate these practices is also growing and the bibliographic databases are flourishing. Many examples including -but not limited to- AcuTrials[29], MANTIS[30], CNKI[31], Societas Medicinae Sinensis[32], Wanfang[33] and Qigong and Energy Medicine Database[34]. Thus, by targeting these bibliographic tools, it is possible to query the different databases and extract relevant information in several languages on a specific subject. Then, the next task would be to collect all the query results from the same search on different search engines to sort. That will not be an easy task, to the best of our knowledge, there is not any automatic tool to perform this task. In addition, tasks such as identifying the most influential authors on a subject, cross-checking information (e.g., a disease with specific therapy and a given outcome), NER, relationship extraction, or topic modelling are less obvious. Therefore, we observe a lack in this area to make an easy search with just a few clicks.

To fill this gap, we created a virtual research assistant based on text mining techniques and specific ontologies to find, sort, and analyze worldwide CAMs scientific publications. Currently, we have essentially elaborated this tool for the topic of cancer, but extensions to other health topics are planned and still under development. In this article, we present Kalya Research (KR) cancer prevention and care as a real-time digital system dedicated to evidence-based CAMs. It references all CAM that are evaluated from clinical trials, reviews, systematic reviews meta-analysis which also are published in peer-reviewed scientific journals. As we mentioned in the preceding paragraphs, one of the difficulties which the researchers are facing is the exploitation of a vast volume of information resulting from a given request. Convert this mass of information into a structured form is a major challenge that constitutes the starting point for the development and the fine-tuning of a suitable query and automatic processing tool. To meet these needs, KR identifies all the elements contained in a publication, characterizes these elements by creating mastered metadata and ontologies. One of KR's strengths is its ability to characterize the trio: outcomes, diseases, and CAMs. With KR, researchers can refine their results with original filters and thus better target the desired corpus of articles. Not only that they can also visualize correlations, trends but also themes allowing to nourish their reflection. In addition, it can also visualize the strongholds of its research. Furthermore, KR has been designed to stay as close as possible to the needs of its users. With this in mind, we compared our tool with a Medline search for CAM publications addressing alopecia issues in women with breast cancer.

In the following, we introduce KR tool, the functionality and use of the tool in section 2. Then, we present the application architecture, and implementation in the section 3. In addition, we explained the experimental comparison between KR and Medline in a concrete example of bibliographic research. In the section 4, we present the results of this experiment. The section 5 is dedicated to summarize the current approach, discuss the learned lessons, and suggest future directions to meet the researchers' expectations. Finally, we conclude the paper in the section 6.

1. Tool Description

Currently KR reference 350,088 publications, 2,220 NPIs, and 2,050 outcomes related to cancer. These results continue to grow as the tool integrates new publications daily. In this section, we present the usage of the tool through its search engine version and its visualization capabilities.

After login, users access the KR interface. The user interface is divided into three main parts (Figure 6): a search box, the left-side panel to select criteria, and the right-side panel for displaying the results.

In the search box, the user can enter keywords and by clicking on the “advanced” button below, users can add and/or exclude disease(s), NPI(s), outcome(s), or other terms. In addition, by clicking on the “Save” button, users can save and name their queries and choose to send the results to their mailboxes. In the following, we will describe the tool through a case study research example: what are the NPIs that prevent alopecia following chemotherapy? To answer this question, we enter the term chemotherapy in the search box and click on the advance button to enter the terms alopecia in the outcome research criterion (Figure 1 and Figure 2). We save our query by clicking on the green “save” button (Figure 2) so that we will be notified about new studies on this subject. The number of articles concerned with chemotherapy-induced alopecia (CIA) contained in the KR database is displayed below on the results panel. At the top left of the right-side panel, there are two tabs: “View by analytics” and “View by list”. The first offers an analytical visualization of the results while keeping the filters panel available. The second offers a raw view of the list of articles as presented above. Thus, the first display shows the graphical analysis of the results and we can see the list of NPIs studied and used to remedy this problem. On the right of the banner, a logout button, allows the users to leave the search area.

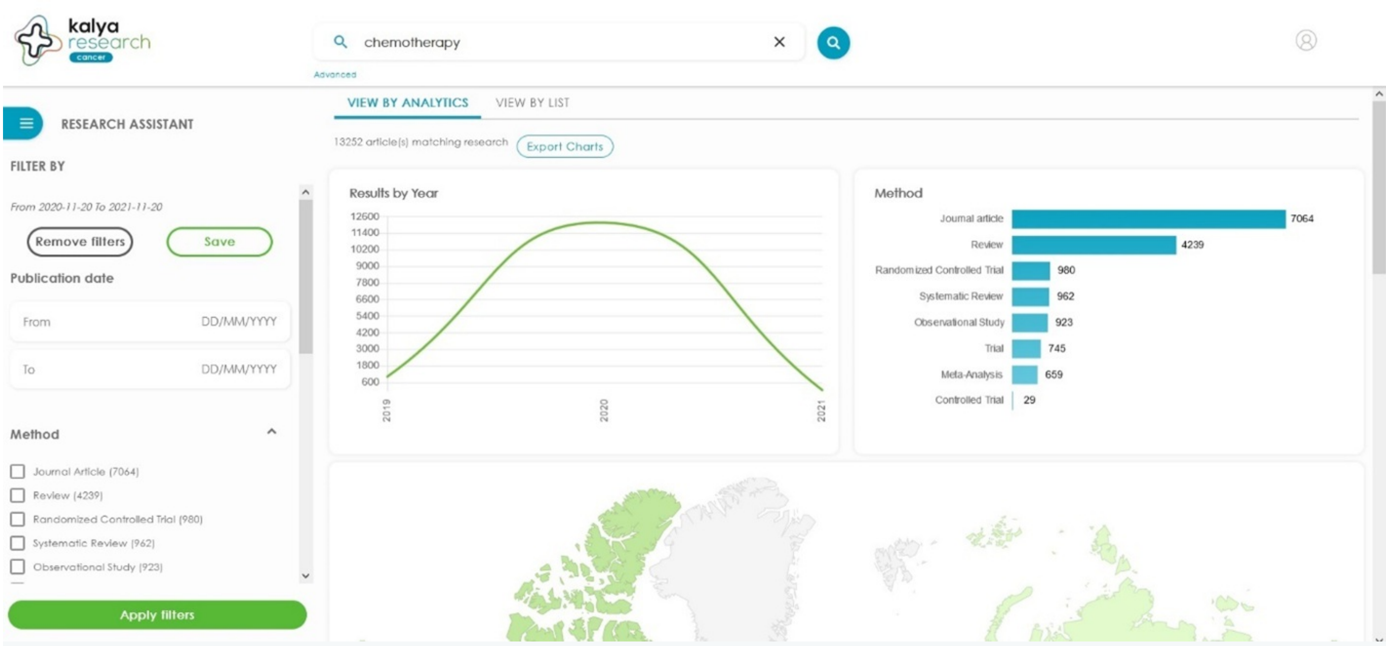

Figure 1. *Screen shot of a research example in Kalya Research tool – enter query*

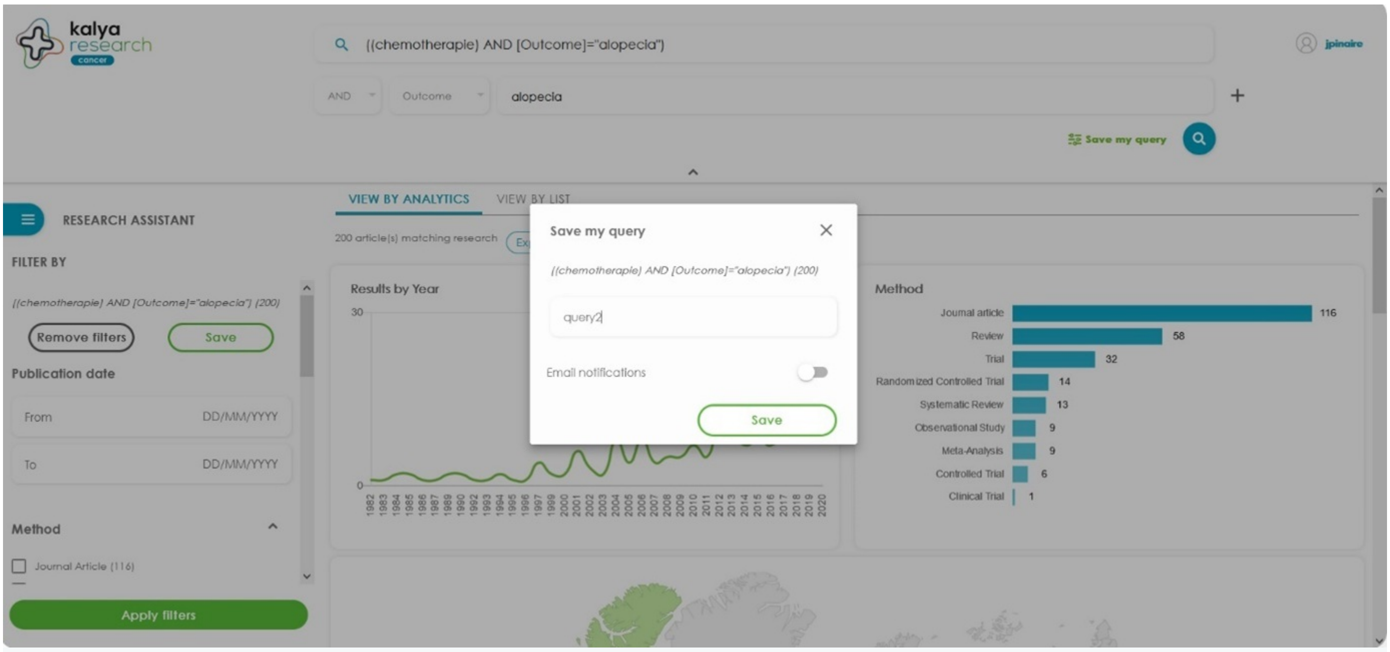

Figure 2. *Screen shot of a research example in Kalya Research tool – save query.*

Graph-based visualization

The users can navigate through the selection of articles via different graphics. KR offers an original visualization of the different key indicators such as the number of publications by year or by methods (Figure 1) and the countries interested in these research issues (Figure 3). Figure 4, represents the most cited NPIs, in our previous mentioned example, the most studied is ergonomic tools. There are also the most targeted outcomes, the cancer localization, and the most frequent journals. The graphics are interactive. Indeed, users can also apply filters or refine their results by clicking on the bars of the histograms. For example, a user can choose to focus only on one NPI, the scalp cooling. To do so, users should click on the scalp cooling bar of the NPIs histogram at the top left (Figure 4) that will automatically reduce the selection (Figure 5).

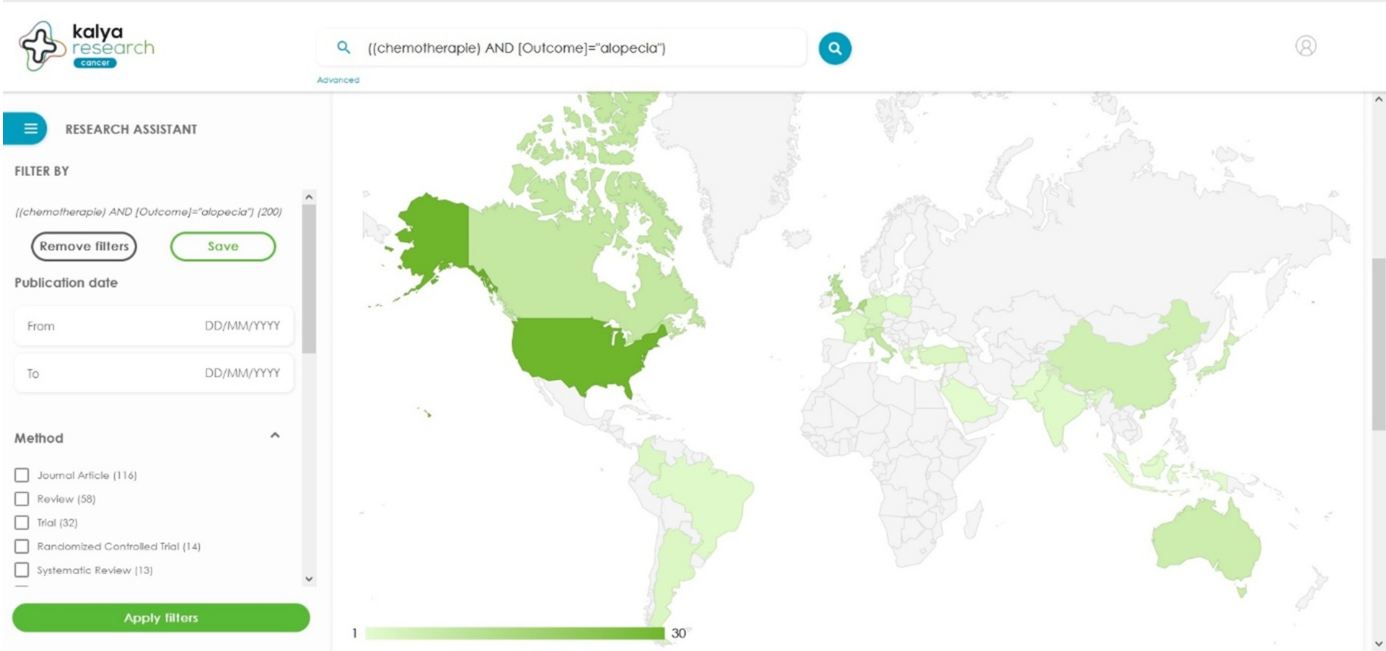

Figure 3. *World map of articles related to chemotherapy-induced alopecia.*

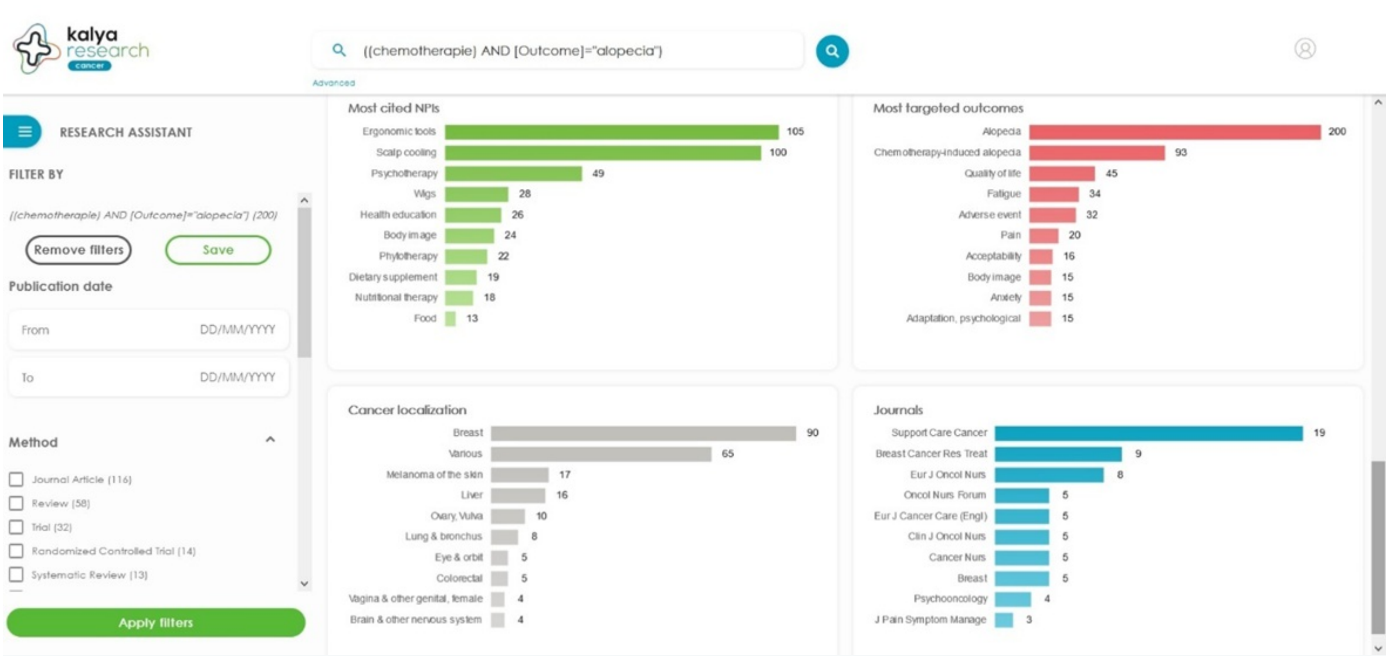

Figure 4. *Visualizations of key indicators summarizing results of the query related to chemotherapy-induced alopecia.*

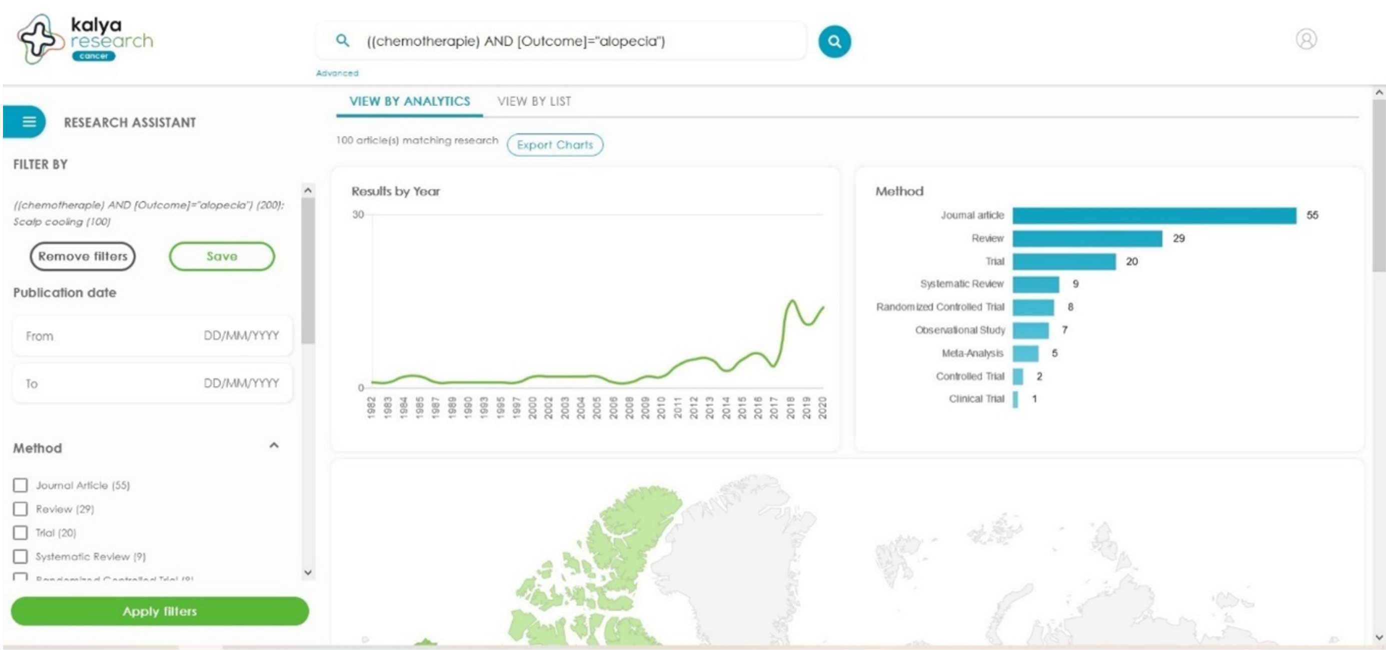

Figure 5. *Refine the query from chemotherapy-induced alopecia to scalp cooling NPI by clicking directly on the graphs.*

Text information

In the “View by List” panel, the list of articles is displayed under the search box in the right-side panel, in chronological order - the most recent to the oldest. For each article, KR displays its title, its journal name, its date of publication, and the name of the first author. By clicking on the black arrow, the first lines of the abstract appear as well as the health goal, the disease, the outcomes, and NPI terms related to this article. In our example (Figure 7), for the first article, the health goal is Care and the disease is Various cancer (it means all cancers) whereas the outcomes are alopecia and fatigue while the NPI terms related to the article are the physical activity. The hand display, allowing users to click and access the article reference page. It is activated by hovering over the article information.

The left side panel allows the user to add filters to the initial search (Figure 6 and Figure 7). The publication period can be defined by filling in the fields under Publication date. Then, the study design of the article sought can be defined by checking the corresponding boxes in the “Methods” field. For example, it is easy to quickly know the number of trials (Figure 3). The choice is made by checking among the following methods: journal article, review, trial, observational study, randomized controlled trial (RCT), controlled trial, a meta-analysis (MA), and systematic review (SR). In the same way, the symptoms sought can be selected in the “Outcomes” field located just below. The list includes all outcomes related to the list of articles resulting from the initial research (made using the search box). It is the same for the “Disease” field. The health goal criterion includes the following choices: Care, Cure and Prevent. Indeed, Care is related to supportive or treatment care, Cure is related to healing or recovery, and Prevent is related to health troubles that require to be prevented. The different types of the population studied are Adult, Child and Elderly. The minimum number of participants is chosen by filling the ad hoc input field. Next, a selection can be made on the country using the checkbox. Finally, the last criterion concerns the Research design of the study with the following choices: Mechanistic, Interventional, Observational, Implementation, and Prototypal. In details, a mechanistic study uses various experiments to find causal models (e.g., in vitro experiments), an interventional study compares benefits and risks of NPIs on several outcomes, an observational study describes the natural use and response of NPIs, an implementation study is a monitoring study, and a prototypal study is a design study to evaluate the feasibility of a study.

All filters apply when the user clicks on the "Apply filter" button. These filters can be either deleted or saved for a future search, by clicking on the relevant buttons (“Remove filters” or “Save”) at the top of the panel. In addition, at the top left of the filter panel, a blue button displays a contextual menu offering the user access to the saved queries, as well as to the personal lists of the saved articles.

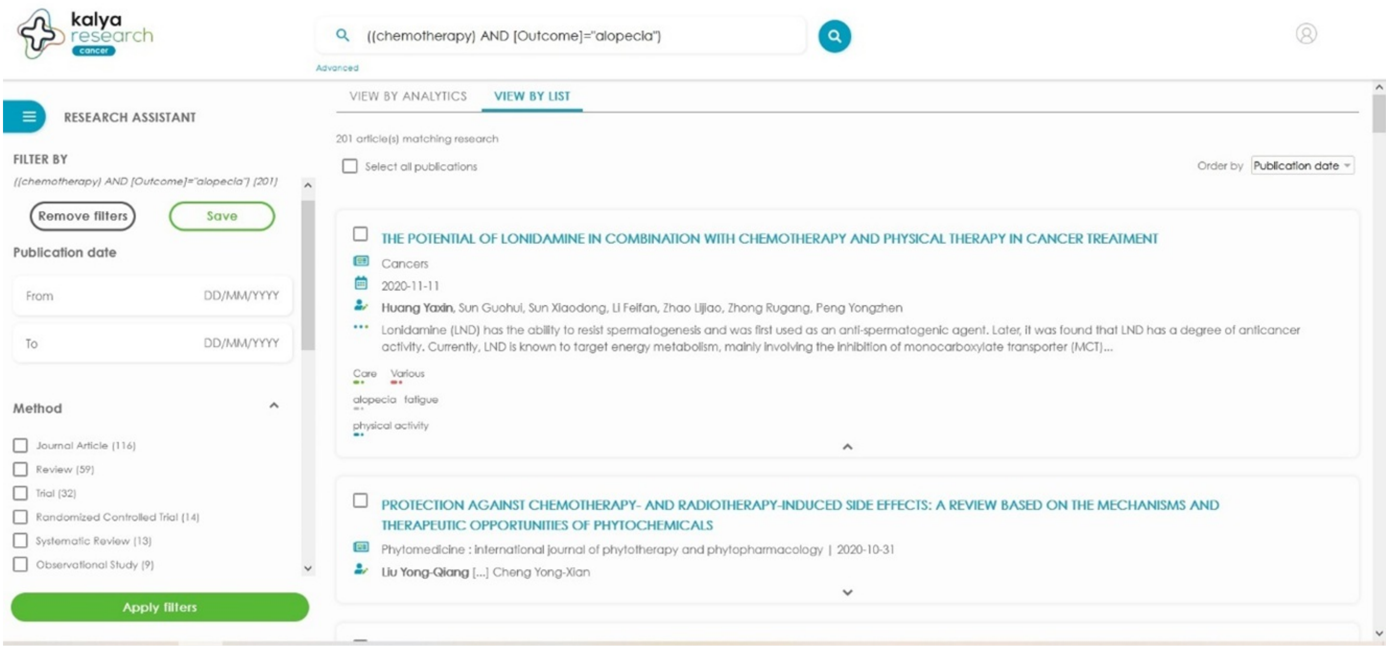

Figure 6. *Screen shot of a research example in Kalya Research tool – View by List - view 1.*

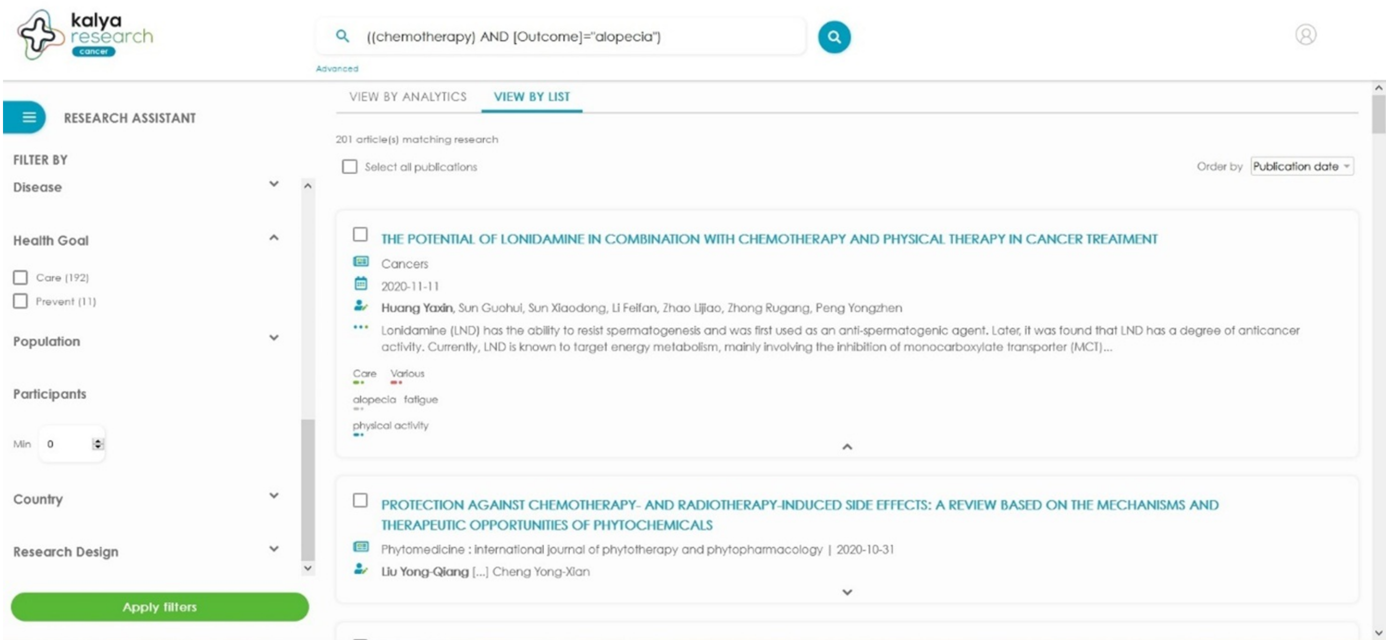

Figure 7. *Screen shot of a research example in Kalya Research tool - View by List – view 2.*

Back to our CIA research example, we had selected the NPIs of scalp cooling, to have the best levels of proof, we check RCT, SR and MA in the Method filter (Figure 8) and if we focus on the most recent publication i.e. the most recent, we can see by reading the conclusion of the abstract that the scalp cooling would be the most effective method to prevent CIA.

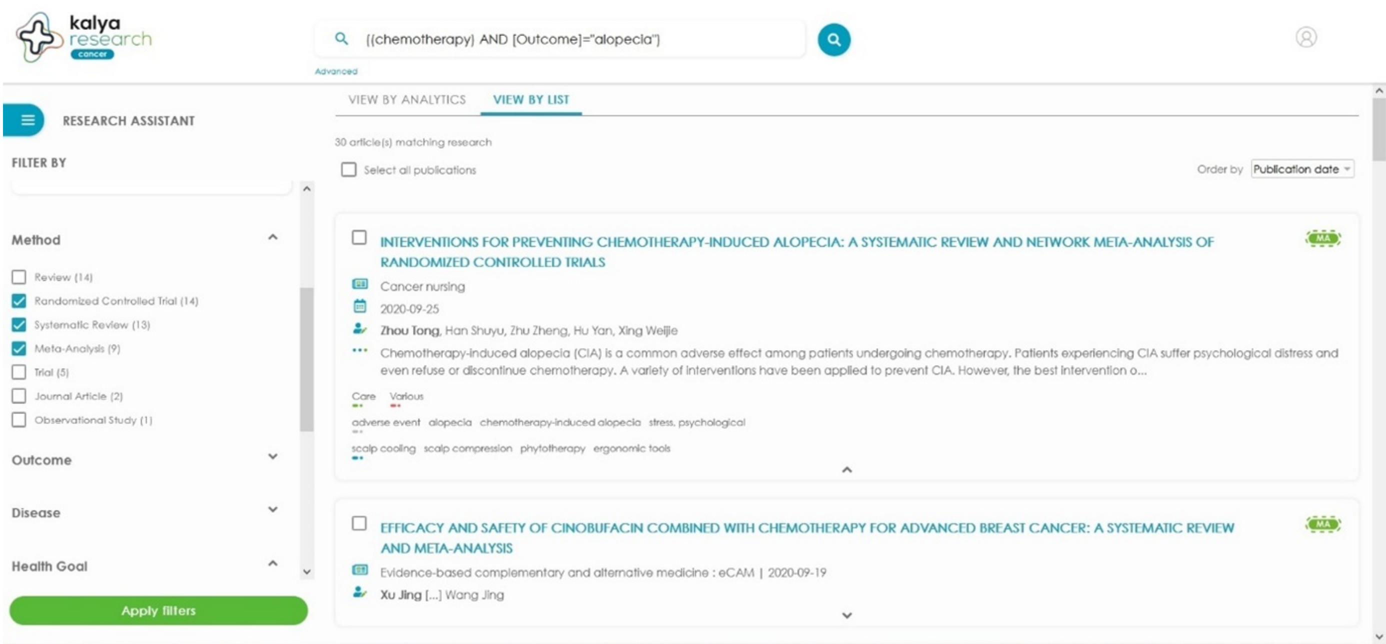

Figure 8. *Kalya research tool: refine a query with Method filter to have the best level of proof.*

When there are new results of my saved query it appears in the contextual menu under My Queries as shown in the left part of Figure 9. Then by clicking on new results, we see the list of saved queries and by clicking again on the request that you want to view, the new articles are displayed on a gray background.

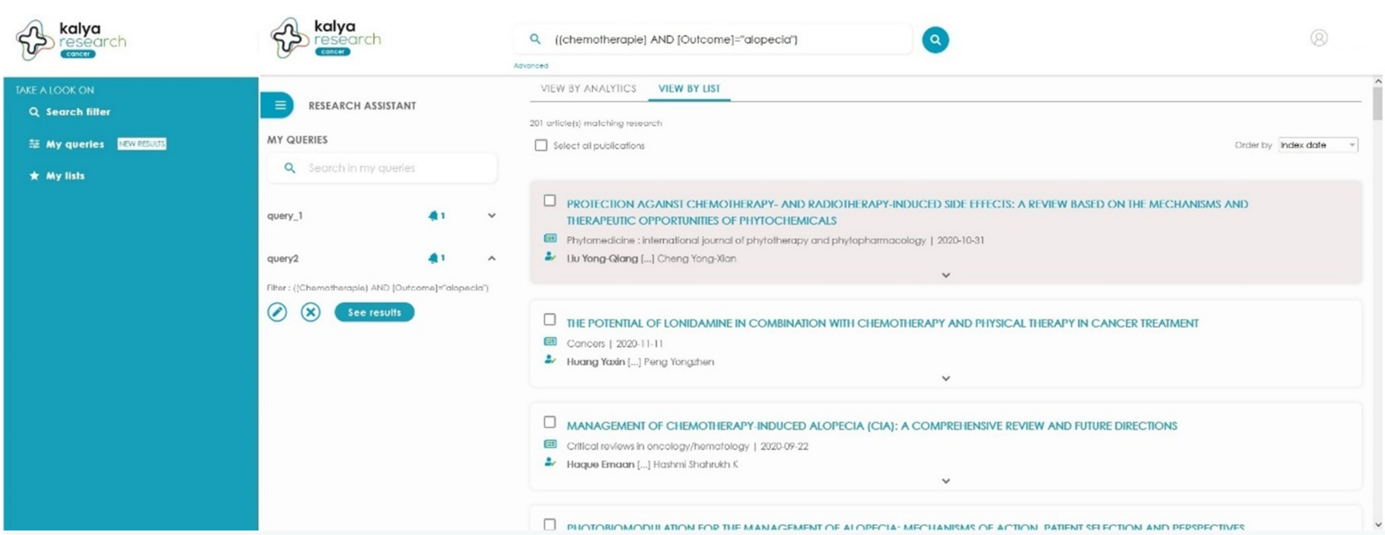

Figure 9. *Kalya research tool display new results for saved queries. By clicking in the contextual menu in the left banner, New Results is displayed*

in front of My queries (left part of the Figure, blue background). By clicking on the query concerned, the new articles appear on a gray background (right part of the Figure).

2. Methods

In this section, we present the tool's design, architecture, and implementation. Finally, we describe how our tool compares with a Medline search in a concrete example of bibliographic research.

Material

KR focuses on CAM techniques also called Non-Pharmacological Interventions (NPI). “NPIs are non-invasive methods of care (programs, products or services) whose efficacy in improving the health and quality of life (QOL) of human beings has been proven. Their effects on health and QOL markers are observable (with measured risks and benefits beyond mere user opinions) and can be linked to identified biological and/or psychosocial processes. They can also have a positive impact on health behaviors and socio-economic indicators.”[35][36] According to the French Platform CEPS (*Collaborative d’Evaluation des programmes de Prévention et de Soins de support*) platform, NPIs can be divided into 5 categories of intervention: nutritional; digital; physical; psychological and elemental interventions.

To identify CAM or NPI publications, we have created a lexicon of NPI terms, classified according to the 5 categories specified above. The classification is based on various sources such as the CEPS platform (https://plateformeceps.www.univ-montp3.fr/fr/english-0), the lexical resources from the National Center for Complementary and Integrative Health (NCCIH) [37], and many others. This list cannot be exhaustive because of the daily monitoring of the different resources.

PubMed is considered as the most commonly used search engine by the medical researchers as it identifies much of the biomedical literature. Therefore, we are detecting CAM publications from this resource. At the beginning of 2020, PubMed references more than 30 million citations for biomedical literature from MEDLINE, life science journals, and online books. We supplement this resource with other journals specialized in CAM but not referenced in PubMed such as Journal of Client-Centered Nursing Care.

Kalya Research Implementation

KR architecture is based on 5 components: frontend, backend, data science, medical and scientific expertise, and user evaluations (Figure 10). The operating principle is as follows. The backend manages data recovery via APIs and integration into data warehouses. The data science component is decomposed of many modules that make it possible to extract the information of interest and transform this data into valuable information. The frontend provides the web interface that will be accessible by the researchers. The medical expertise ensures the integrity, the enrichment of the data, and makes it possible to decide in the event of litigation. Finally, user assessment allows KR to provide a service that meets the real needs of the end-user.

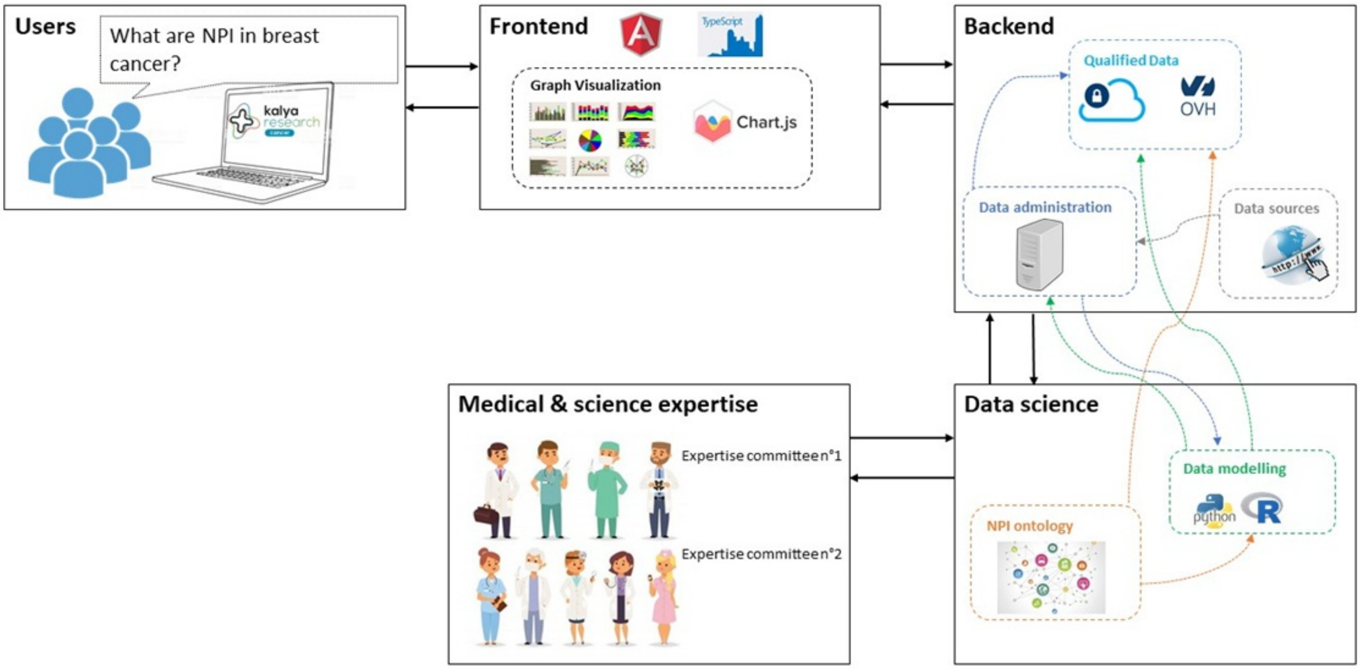

Figure 10. *Kalya Research architecture.*

The backend component extracts data from biomedical literature with import script by using APIs. Then, data with web micro-services architecture which provide API in.NetCore, to be integrated in a NoSQL database. This database remains accessible by the data science and frontend components.

The data science component identifies CAM articles with a complex rule-based model briefly explained in the following section.

The frontend component is developed with the IONIC and Angular TypeScript-based open-source front-end web application frameworks for high-performance application combined with chartJS and Ng2GoogleChartsModule for interactive visualization developments.

The security of the entire architecture is ensured by a strong authentication via an Open-Id SSO (Single Sign-On).

Detecting NPI in Natural language

KR uses a rule-based model to identify CAM articles among the thousands of biomedical literature publications. To optimize retrieval effectiveness, we define three rules:

i. The first rule focuses on relevant publications containing NPI terms. Specifically, we define a score based on the term frequency and inverse document frequency (TF-IDF) ranking function to find the most appropriate documents[38]. The score is calculated for a predetermined list of terms: the lexicon of NPI terms, mentioned in the Material section, on a preprocessed text. This text is the result of the concatenation of the title, abstract, and keywords. We use pure text with natural language processing frameworks without lemmatization[39].

ii. The second rule focuses on the rejected articles to check false negatives from the first rule. We define a score based on the occurrences of words combining both the interest terms in addition to the exclusion terms. According to the definition of an NPI, we have created a lexicon of exclusion terms linked, most often, to the administration mode. For example, vitamin C is an NPI but if the administration mode is by injection then, this method will be rejected, and the article concerned will not be listed in our search engine. The score is applied for the NPI lexicon combined with the exclusion terms lexicon to the same text as for the previous rule but this time with a lemmatization step.

iii. The third rule manages the false positives from the previous two rules. We define a score base on journal relevance and citation occurrences of CAM articles. This score is defined in such a way that it will favor articles published in dedicated journals (with a high CAM score, such as, the Integrative Cancer Therapies journal (https://journals.sagepub.com/home/ict). Besides, articles with many CAM publications in their references. This information is not always available. Indeed, it is possible that a journal has not yet been listed in our model (but listed in our database) or that we do not have access to the reference list of the publication analyzed. In this case, the decision of the last rule takes precedence.

Evaluation of the tool on a practical case

We have evaluated the tool in a practical case, that of alopecia in breast cancer. The aim is to compare the results, their relevance and the time taken to sort the results.

We used the criteria of the PICO (Patient Intervention Comparison and Outcomes) method. The bibliographic search was carried out using 2 different methods: Medline (see Table 1) and the KR tool (see Table 1). Given the search theme, the criteria are as follows:

- Patient: patients with breast cancer, whatever age and stage of cancer.
- Intervention: any NPI
- Comparison: standard care or any NPI
- Outcome: alopecia.

Table 1. *Research algorithms for Kalya Research and Medline for alopecia in breast cancer.*

	Patient	Intervention	Comparison	Outcome
Kalya Research	Breast cancer			alopecia
Medline	("breast cancer"[Title/Abstract] OR "Breast Carcinoma"[Title/Abstract] OR "Mammary Carcinoma" [Title/Abstract] OR "Breast Tumor" [Title/Abstract] OR "Mammary Tumor"[Title/Abstract] OR "Malignant Breast Neoplasm"[Title/Abstract] OR "Invasive Ductal Carcinoma" [Title/Abstract] OR "Invasive Lobular Carcinoma"[Title/Abstract] OR "Ductal Carcinoma in Situ (DCIS)" [Title/Abstract] OR "Lobular Carcinoma in Situ (LCIS)" [Title/Abstract] OR "Triple-Negative Breast Cancer"[Title/Abstract] OR "HER2-Positive Breast Cancer" [Title/Abstract] OR "Estrogen Receptor-Positive Breast Cancer" [Title/Abstract] OR "Progesterone Receptor-Positive Breast Cancer" [Title/Abstract] OR "Metastatic Breast Cancer"[Title/Abstract] OR "Early-Stage Breast Cancer"[Title/Abstract])	(Integrative medicine[MeSH Terms] OR Complementary Therapies[MeSH Terms] OR Alternative Medicine[MeSH Terms] OR Traditional Medicine Mind-Body Therapies[MeSH Terms] OR Dietary Supplements[MeSH Terms] OR Therapeutics[MeSH Terms] OR Physical Therapy Modalities[MeSH Terms] OR Psychotherapy[MeSH Terms] OR Rehabilitation[MeSH Terms]) NOT Tamoxifen NOT "Aromatase inhibitors " NOT Anastrozole NOT Letrozole NOT Exemestane NOT Fulvestrant NOT Palbociclib NOT Ribociclib NOT Adriamycin NOT Doxorubicin NOT Cyclophosphamide NOT Paclitaxel NOT Docetaxel NOT Epirubicin NOT Gemcitabine NOT "5-Fluorouracil 5-FU" NOT Methotrexate NOT Vinorelbine NOT Trastuzumab NOT Herceptin NOT Pertuzumab NOT Perjeta NOT Lapatinib NOT Tykerb NOT T-DM1 NOT "Ado-Trastuzumab Emtansine" NOT Everolimus NOT Afinitor NOT Palbociclib NOT Ibrance NOT Ribociclib NOT Kisqali NOT Abemaciclib NOT Verzenio NOT Atezolizumab NOT Tecentriq NOT Pembrolizumab NOT Keytruda NOT Nivolumab NOT Opdivo NOT Bisphosphonates NOT Denosumab NOT "Zoledronic acid" NOT Zometa NOT Pamidronate NOT Aredia NOT Denosumab NOT Xgeva NOT "PARP Inhibitors" NOT Olaparib NOT Lynparza NOT Talazoparib NOT Talzenna NOT "Cytotoxic Antibiotics" NOT Eribulin NOT Halaven NOT Bevacizumab NOT Avastin		(alopecia[Title/Abstract] or "hair loss" [Title/Abstract])

The literature search identified several publications whose quality had yet to be determined. It was therefore necessary to carry out a second selection of the publications thus obtained, so as to optimize the quality of the results and identify the studies answering the research question.

This selection was made based on the title and the abstract. The criteria used to include the article were the same as those used to define the search strategy.

Rejected studies met one of the following criteria:

- Population: studies not assessing the population concerned, lack of population data
- Intervention: not involving an NMI
- Type of study: pharmacological studies, in vitro or in vivo animal studies, study protocols.

3. Results

In this section, we present the results of our literature search for non-drug interventions for alopecia in breast cancer patients, summarized in the flow chart in Figure 11.

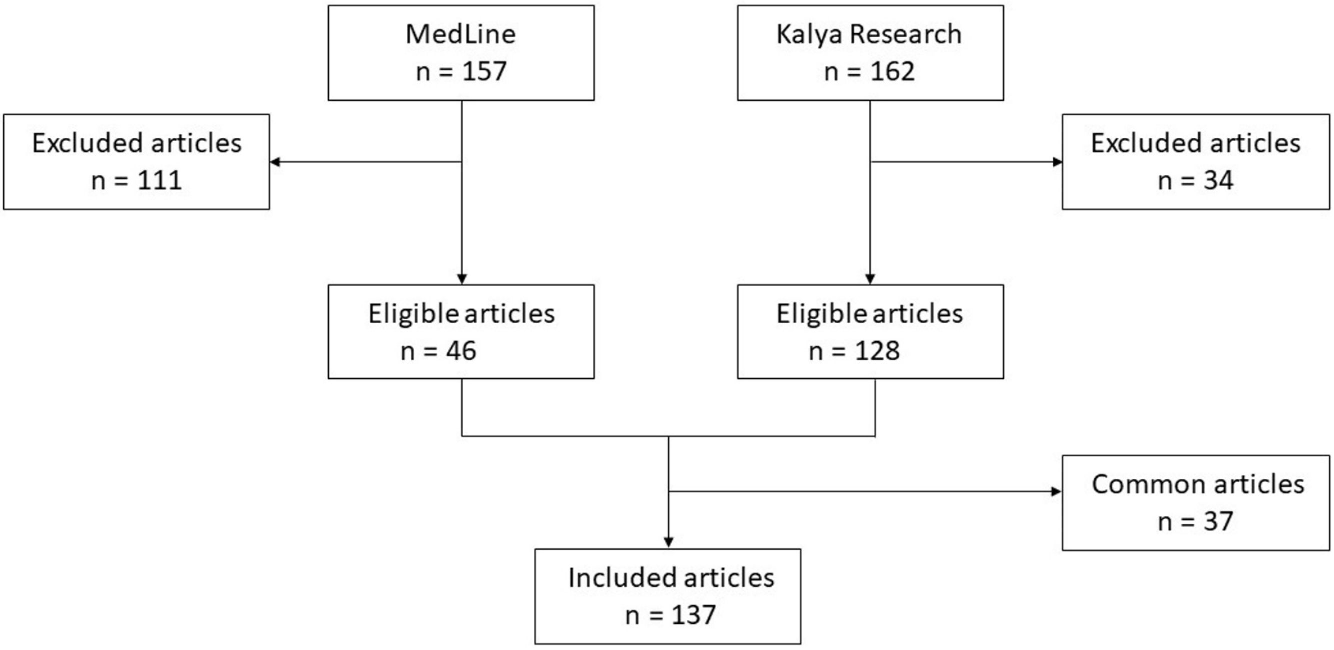

Figure 11. *Flow Chart.*

We used KR, as described in section 2, filling the search bar with the word 'breast' and the outcome field with 'alopecia' to specify that we wanted publications concerning alopecia in breast cancer. We obtained 162 publications.

In Medline we used a complex query (see Table 1) with synonyms or related terms to breast cancer, with alopecia and synonyms combined with MeSH terms related to CAM and excluded a list of drugs approved for the treatment of breast cancer. We obtained 157 publications.

We examined the various publication lists to check that we had publications related to non-drug therapies. The flow chart (see Figure 11) shows that we find more CAM publications with KR than with Medline.

Next, we compare the results and find 37 CAM publications common to both queries. We also note that 91 publications were in the KR results but not in the Medline results. Conversely, 9 CAM publications were in the Medline results but not in the KR results.

4. Discussion

KR is a new medical research assistant focused on CAM, referencing scientific publications. The originality of KR is to make the data quickly intelligible through visualizations. Regarding the implementation, our choice of tools and methods is simple, classic, and at the same time, it has proven to be very effective [40][41]. This strategy constitutes a solid base to evolve in order to improve our system both in terms of the flexibility of the system to manage the vast increasing amounts of data, as well as the capacity to detect CAM documents. KR provides an even more user-friendly interface for end-users.

The example query presented in this paper shows that KR is more efficient in terms of time, query design and results obtained. Indeed, while the query can be formulated quickly and obtained in a few clicks, KR delivers results in a matter of seconds. We have shown that the number of CAM publications is much higher via KR than via Medline. The loss is very small (9 publications found in Medline but not in KR). On the other hand, the development of the query via Medline required a great deal of preliminary thought, necessitating tests (not detailed in this paper). Despite this, the number of CAM articles was lower, and we obtained many off-topic publications. This suggests that the query should certainly be reworked beforehand. However, it appears difficult to compete with a selection made by a learning model process.

KR also competed with Medline, in another context. One study presented a systematic literature review of NPIs offered to hormone-suppressed prostate cancer patients according to PRISMA rules, comparing the Medline and KR databases [42]. The authors showed that all publications (n=37) were found by the KR search algorithm, and that the Medline database was able to find 70% of the articles (n=26), but did not uncover any CAM articles different from KR. They concluded that the KR search method was a relevant method for accessing CAM publications.

In the light of these application examples, further improvements are possible. To manage the high volume of data, we planned to strengthen our architecture with Elastic Search for indexing data[43], Redis for the in-memory data structured storage[44], RabbitMQ to streamline communication between micro-services[45]. Likewise, the NPI detection model is based on methods that have been tested in many natural language processing models[46]. Since we have built a substantial knowledge database, we planned to assess the performance of models via text similarity analysis to detect CAM publications[47]. The challenge is to determine the most appropriate method, in terms of performance in our context, among the different existing approaches. We also plan to refine the annotation of the texts to enrich our metadata system. In the literature, there are many biomedical NER systems linked to the surge of biomedical data[48][49][50]. However, the task of identifying named entities in biomedicine still a complex task[51]. Another future challenge will be to assess the annotation system that best meets our needs or even combines several ones.

The development of computational linguistics and identification methods in data mining shows promising opportunities to guide the extraction and optimization of the sequestered CAM knowledge. These may be contained within the continuously growing biomedical literature. However, automatic approaches cannot completely replace the in-depth analysis required by a conservative expert. In addition, the diversity of both studies and evaluations challenges the implementation of a robust automatic system. It should also be noted that the construction of the KR database is based on the validation of our experts to reinforce the automatic detection system. Nonetheless, automated systems taken in combination with the expert knowledge is much opportunity to leverage new CAM knowledge.

Such a tool as KR is useful for any biomedical researcher in his process of scientific discovery in order to identify work plan before the start of a scientific study, discuss the results at the end of a study, define the scientific validity of an NPI in prevention or treatment of several pathologies and health issues (e.g., Nordic walking to combat cancer, meditation to limit stress...), and/or conduct systematic review higher covered. Besides, KR is useful for clinicians looking for new and proven results to support clinical decisions, for instance, to identify which NPIs are the most effective in preventing certain pathologies (Cancer, Diabetes...). The usefulness of KR is even more important as it allows to link the diseases with the

NPIs and their outcomes. Moreover, we have created and structured our metadata, such a way for KR to make it possible to cross queries like “the set of studies on breast cancer and nutritional therapies with an economic evaluation”, by using words "breast" and "nutritional therapies" and check "eco" in the Outcome field. The user can select the publications based on other outcomes evaluated by the study. We identify several outcomes such as clinical, psychological, social, behavioral, and economical. CAM-QUEST and LIVIVO allow crossing information. However, in CAM-QUEST the user can filter by study design no more else whereas in LIVIVO there are more criteria, but the proposed metadata does not contain the outcomes. So, to the best of our knowledge, this type of search does not exist on any other search engine and accords the uniqueness and the novelty of KR.

KR is constantly being updated and enriched with the extension to other medical themes, such as, healthy aging and physical activity which are scheduled for the next version. Currently, KR is mainly based on PubMed, but access to other data sources, with crawled-web techniques like Google Scholar, is under development. In addition, NPIs’ ontologies are under building[35]. This aims to facilitate the detection of articles, the management of synonyms and make it possible to propose categories for classifying articles. This can be combined with other sources, for example, iDISK (for dietary supplements)[52], ethnopharmacological knowledge[53], Customary Medicinal Knowledgebase (aboriginal plants)[54], TCMGeneDIT (a database for associated traditional Chinese medicine, gene and disease information using text mining)[55], TM-MC (constituent compounds of medicinal materials in Northeast Asia traditional medicine)[56], and many others. In our perspectives, this ontology will be accessible via KR in which the user can navigate. In addition, technologies are constantly developing to offer an even more efficient and relevant application to meet the needs of our end-users.

5. Conclusion

In this article, we present KR as a novel virtual research assistant tool for biomedical literature. KR is mainly dedicated to CAM. The originality of KR is to offer a double interface allowing the end-users to display the list of the results of their queries (as in a conventional search engine), perform an analytic visualization of these results, and notify the users with their saved queries’ results. The biomedical researchers could easily navigate through these different displays and extract both the publications of interest meanwhile scrutinize key indicators from which they could establish initial findings or orient their research. In the context of enthusiasm for CAM prompted by an awakening of interest in mainstream medicine, an anthology of small tools has emerged[15]. Thus, documentary research on CAM has hitherto been possible using these different search engines but was a real challenge because most of these tools are very specialized for a specific set of therapies, some of which are no longer kept up-to-date [57][58]. KR is therefore prompt and time saver.

We compared literature searches via KR and Medline to find NPI solutions for breast cancer patients with alopecia. This simple example highlighted KR's advantage over Medline in terms of ease of use, speed and relevance of results. These initial results are encouraging and open up the prospect of modifications to offer users future improvements.

In the future, we plan to improve KR on technical points to streamline data management with the implementation of

Elastic Search[43] and RabbitMQ[45] or the implementation of text similarity to detect CAM publications more easily[47]. Besides, we propose to increase KR coverage by adding other biomedical literature sources like Google Scholar and Scopus and by expanding to other health topics. Furthermore, we are working on a new evaluation indicator for scientific publications to measure their scientific relevance and consequently the benefit of a CAM for a given context. In addition, we work on new functionalities such as NER to highlight diseases, NPIs, and outcomes at a glance.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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