

# **Article Title: Evaluation of the Canadian Natural Health Product Regulatory Framework in Academic Research: A Scoping Review**

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## **Abstract**

**Introduction:** Traditional, complementary and alternative therapies, many of which incorporate natural health products (NHPs), are widely used and relied upon globally. In Canada, NHPs were first regulated in 2004; prior to this, they were regulated as either food or drugs. The objective of this study was to summarize the peer-reviewed literature on the evaluation of the NHP regulatory framework in Canada.

**Methods:** We conducted a scoping review of academic research evaluating the NHP regulatory framework in Canada. Only peer-reviewed research studies were eligible for review. Our approach followed the five-stage methodological framework proposed by Arksey and O'Malley.

**Results:** One article was eligible for review, which highlighted perceived challenges by industry and government regarding NHP regulations. These included significant delays in authorization for sale on the market, industry perception that the provision of research evidence to support their health claims was overly demanding, and understanding how NHPs were now defined as part of this new category separate to food and drugs.

**Conclusions:** Studies evaluating the Canadian NHP regulatory framework are extremely limited; further research is needed to inform and optimize the regulatory process. Academic research in this area should be supported, especially in conjunction with consultations with stakeholders, so that an awareness of past research is present and can identify both positive and negative aspects of the current framework, and inform areas for improved regulation of NHPs in Canada.

## Abbreviations

DHS: dietary and herbal supplement

NHP: natural health product

NNHPD: Natural and Non-prescription Health Products Directorate

## 1. Introduction

Dietary and herbal supplements (DHSs) are commonly used around the world, typically in an effort to maintain health, and prevent or treat illness, with approximately 80 % of the population using them globally [1]. In many cases, DHSs are used concurrently with pharmaceutical therapies, which may result in adverse DHS-drug interactions [2]. In spite of this, not all countries have traditional medicine policies or regulate herbal medicines, including DHSs [3]. In 2013, the World Health Organization reported that 69 out of 129 member states had traditional medicine policies and 119 out of 129 member states regulated herbal medicines [3]. Even in countries that do regulate the sale of DHSs, there is often considerably lesser research or requirements of evidence supporting their safety, efficacy, and quality prior to them being brought to market [[4], [5], [6], [7], [8]], which may place consumers at risk [9].

In Canada, the Natural and Non-prescription Health Products Directorate (NNHPD) is the Canadian regulating authority for DHSs, and specifically refers to them as “natural health products” (NHPs) [10]. The NNHPD is a directorate of the Health Products and Food Branch of Health Canada [11]. The Natural Health Products Regulations came into force in 2004, which created a regulatory framework for NHPs separate to food or drugs, and categorized into 6 categories inclusive of: 1) vitamins and minerals; 2) herbal remedies; 3) homeopathic

medicines; 4) traditional medicines such as traditional Chinese medicines; 5) probiotics; and 6) other products, such as amino acids and essential fatty acids [12].

These NHPs are licensed by Health Canada based on two pathways, including: 1) NHPs making modern health claims [13] and 2) NHPs used as traditional medicines [14]. In short, while the former pathway is more analogous to the pathway in which scientific evidence for pharmaceutical drugs are generated (i.e. trials) [13], the latter pathway requires the demonstration of an NHP's long history of use without necessarily relying on scientific evidence [14].

Given that NHPs have been regulated in Canada for over 15 years, the present study sought to identify and summarize what academic research has been conducted to evaluate the NHP regulatory framework since 2004. We felt that this would be of value given that a number of revisions have been made to the Natural Health Products Regulations over this period of time. More recently, Health Canada has held a series of public consultations regarding improving the NHP regulatory framework since 2016 [16], which has resulted in the development of a new regulatory framework to be carried out from 2019 to 2021 [17]. In addition to government-lead stakeholder consultations, academic researchers are well-positioned to support an improved regulatory framework by conducting health policy analyses in the context of NHP stakeholder perceptions or how research on NHPs is conducted, as examples. Such research, if conducted rigorously and at arms-length, can be used to successfully inform future consultations surrounding the NHP regulatory framework. To our knowledge, no study has systematically identified and summarized this research, thus the purpose of this review is to identify what academic research has been conducted on the evaluation of the NHP regulatory framework in Canada.

## **2. Methods**

### **2.1. Approach**

We conducted a scoping review based on the five-stage methodological framework proposed by Arksey and O'Malley [18] which included: (1) identifying the research question, (2) identifying relevant studies, (3) selecting the studies, (4) charting the data, and (5) collating, summarizing, and reporting the results [18]. This scoping review method was chosen based on preliminary searches which indicated that the literature on this topic may be sparse, which involved searching for and assessing the available literature on a given topic in order to identify the characteristics of eligible articles, summarize their contents and highlight knowledge gaps, making it more appropriate than a systematic review. We did not register a protocol.

### **2.2. Step 1: identifying the research question**

The research question was as follows: “What academic research has been conducted on the evaluation of the Canadian NHP regulatory framework?”. The term “natural health product” is largely a Canadian one; in this review, we adopt Health Canada’s definition whereby NHPs “are naturally occurring substances that are used to restore or maintain good health. They are often made from plants, but can also be made from animals, microorganisms and marine sources. They come in a wide variety of forms like tablets, capsules, tinctures, solutions, creams, ointments and drops.” The term “regulation” can be defined as “a rule or order issued by an executive authority or regulatory agency of a government and having the force of law”, and specifically refers to Natural Health Products Regulations in this review, which came into force on January 1, 2004 [15].

### **2.3. Step 2: finding relevant studies**

Following a preliminary scan of the literature, a search strategy was devised for MEDLINE, EMBASE, AMED, and PsycINFO databases, for English-language articles, from January 2004 to May 13, 2020, as well as reference lists of eligible studies. The search strategy is provided in Table 1. JYN designed and conducted the searches; both authors independently screened a subset of the search results, in order to standardize screening by discussing selection differences, before screening the remainder of titles and abstracts. Both authors reviewed full-text articles for eligibility.

### **2.4. Step 3: selecting the studies**

Preliminary searches indicated that literature on this subject area is largely absent. As a result, any type of primary research article, as well as review articles with an evaluation component, were included. Publications eligible for our review included any study design that provided an evaluation of the Canadian regulatory framework for NHPs. Articles that focused on the regulation of a single NHP (i.e. just vitamins) were excluded, as these would have been discussed more so in the context of general health as opposed to the NHP regulatory framework. Articles were excluded if they were: strictly aimed at capturing stakeholder perceptions of the NHP regulatory framework without providing any evaluation of the actual framework; based on the regulation of complementary and alternative medicine/integrative medicine (i.e. regulation of professions) in general without any mention of NHP regulation; literature related to the regulation medical cannabis (which are regulated separately to NHPs in Canada); policy/regulation articles about vitamins or minerals as dietary supplements, recommended daily intake, etc.; or news reports published in peer-reviewed journals. Opinion pieces, commentaries, and editorials were also excluded. For all potentially eligible titles/abstracts, the full-text article was retrieved, however, only articles that evaluated NHP

regulation in Canada were included. Both authors pilot-screened a subset of all titles and abstracts independently and met to verify their agreement in applying the inclusion criteria prior to screening all items, including the full-texts of potentially eligible articles, independently in duplicate. Disagreement was solved by discussion.

#### **2.5. Step 4: charting the data**

Articles meeting the inclusion criteria were critically reviewed using Arksey and O'Malley's descriptive-analytical narrative method [18]. Data extraction on this article described authors, year of publication, study location, aims of the study, and important results in significant detail. Analysing data involved summarizing abstracted data and discussing existing gaps in knowledge surrounding the evaluation of the NHP regulatory framework. Both authors independently extracted data from all eligible articles, then met to discuss and resolve discrepancies.

#### **2.6. Step 5: collating, summarizing, and reporting the results**

It was originally planned that charted data would be summarized in the format of tables, however, only one article was found to be eligible. Descriptive data were analysed using content analysis. Both authors reviewed the descriptive data and identified codes relative to the findings, organized codes into thematic groups, and presented a narrative relating to the research question as well as highlighted knowledge gaps in the currently existing literature. Both authors then met to discuss and resolve discrepancies.

## 3. Results

### 3.1. Search results (Fig. 1)

Searches retrieved 1968 items following deduplication, of which 1897 titles and abstracts were eliminated, leaving 71 full-text articles that were considered. Of those, 70 were not eligible for the following reasons: commentary, letter, correspondence or editorial (n = 22); exclusively review (n = 15); evaluation of NHP regulation outside of Canada (n = 11); abstract (n = 9); news article (n = 7); not in English (n = 3); and irretrievable (n = 2). This left 1 article eligible for inclusion in this review.

The one eligible article included a 2013 study by Walji & Wiktorowicz [19], in which authors reviewed the NHP regulations enforced by Health Canada in 2004 to understand why they were implemented and evaluate how the regulations were perceived by government and stakeholders, including industries that manufactured NHPs and consumers. NHP regulations were created in 2003 and enforced in 2004. Their objectives were to help consumers engage in informed decision making by knowing their true benefits and risks. This would aim to ensure that the information provided on NHPs is accurate and as a result, products on the market would be of a higher quality. This new regulation placed NHPs in a unique category of their own, as prior to 2004, they were either categorized as food or drugs under the Food and Drugs Act, subjecting them to different rules and regulations in authorization. As a result of this change, industries were required to provide Health Canada with information relating to definitions, product licensing, site licensing, adverse reactions, evidence of claims, and identification numbers on each of their products as well as to comply with labeling standards.

The opinions regarding the 2004 NHP regulations were collected from 5 government, 1 consumer, and 8 industry representatives, as well as 1 company representative that aided



manufacturers with the new regulations. Walji & Wiktorowicz conducted a document analysis, semi-structured key informant interviews with government representatives, industry and consumer groups, and observed a government consultation meeting with industry members between December 2009 and May 2010. Data collected was then organised by emerging themes, which included: regulatory approach and criteria; application and review process; and industry adjustments.

### **3.2. Findings from Thematic Analysis**

#### **3.2.1. Theme 1: regulatory approach and criteria**

Regarding Health Canada's regulatory approach and criteria, defining NHPs as their own distinct classification, separate from food or pharmaceutical drugs, was difficult. This created a steep learning curve for industries and government as the definition of "natural health product" kept changing. This was significant as prior to the 2004 regulation, NHPs were either classified (and regulated) as food or drugs regarding their authorization and sale. As of 2004, NHPs were approved if they had research to support their modern health claims or if they had a history of being traditionally and safely used for at least 2 generations (50 years). Additionally, these regulations meant that many unauthorized NHPs were taken off the market at the time and all NHPs required a product license to be sold. This caused an influx of applications creating a backlog and burdened Health Canada in efficiently authorizing these products. Industries were required to abide by a 5-year deadline of submitting their applications based on their potential harm, but if there was a risk to health, immediate submission of their product license application was mandatory. As a result, the quality of information of NHPs' applications has since increased. By 2012, there were 2.5 times more NHPs product licenses authorized in comparison to drugs. Furthermore, stakeholder groups had varying perceptions of the enforcement of these regulations. Consumers strongly

approved, as it would allow for safety, quality, and transparency of industry claims. Industries approved of the regulations in agreements to standardizing NHPs for safety purposes and how it leveled the playing field, eliminating competitors that did not meet the new standards. Importers and distributors, however, experienced frustration in the beginning due to a difference in the standards of evidence and testing procedures between NHPs from other countries and Canada. The situation has improved since, however, as importing has been made more efficient through increased direct collaboration with Health Canada. Additionally, regular communication between the Natural Health Products Directorate (previous name of the NNHPD) Program Advisory Committee and industries, health care professionals, and consumers allowed for clarification of regulations.

### **3.2.2. Theme 2: application and review process**

Although industry stakeholders supported the regulations, they were frustrated with the application and authorization approval process required to bring an NHP to market. With the application, the creation of new regulations created a steep learning curve for both industries and government. For the government, assessing a surplus of applications with limited staff created a backlog, particularly when each of the ingredients in NHPs had to be assessed, combined with the fact that there were a number of incomplete or inadequately detailed applications. In addition, industries found paper applications confusing because of a lack of specific instructions on how to properly complete them. Since then, Health Canada has clarified and digitized the application process, making it more comprehensive. The authorization approval process also caused industries to be frustrated as it affected business due to the amount of time it took, resulting in them feeling as though they were falling behind their international competitors. This process later became more efficient as applications were

prioritized by category and as similar products, also known as “me-too” products, which received approval in less than 60 days.

### **3.2.3. Theme 3: industry adjustments**

As a result of the 2004 regulations, manufacturers were required to list warnings and change recommended dosages according to levels of risk associated with an NHP on product labels. Depending on the type of health claim made and the risk level of the NHP, this dictated the requirements for safety and efficacy. From published and unpublished sources, all evidence of risks and benefits had to be provided in order for an NHP to be assessed for sale on the market. These requirements were seen as necessary by consumers, but burdensome by industries as they were perceived as too stringent. To assess the compliance of industries with regulations, Adverse Reaction Report (ARR) data, and annual summary reports were made mandatory. This enforcement was based on complaints received from assessments of agencies in Health Canada of unsafe or adulterated products. Despite this, due to a lack of resources on the part of the government, site inspections were not conducted unless there was a complaint of an identified risk. Furthermore, if a product was unlicensed, even if its application was awaiting authorization, it could not be sold. This burdened industries, causing Health Canada to process applications more efficiently and introduce the NHP-UPLAR (Unprocessed Product Licence Applications) on August 4, 2010 to allow a temporary permit to sell NHPs that were awaiting authorization after submission of their application if this permit was applied for within 180 days of applying for a product license. This temporary license was valid until their application assessment was complete or until it was repealed. Since February 2013, however, the NHP-UPLAR was repealed as the government created a new approach that allowed for applications to be processed faster (i.e. in 180 days or less).

## 4. Discussion

Our scoping review identified what academic research has been conducted on the evaluation of the Canadian NHP regulatory framework. Our study's inclusion criteria only included articles published in 2004 or after to reflect literature published on or after the year NHPs were regulated in Canada. As we only found one eligible article, this study highlights a major lack of research surrounding the NHP regulation framework in Canada. Further research is warranted as this may help identify the strengths and limitations of current policies, and inform areas for improved regulation of NHPs in Canada. The authors hypothesize that this research gap can be explained based on a number of reasons, including a lack of academic research funding to study this topic area, prioritization of pharmaceutical or medical device regulations, or even the complexity of studying the regulation of NHPs, which are comprised of thousands of unique products for which little may be known about their safety and effectiveness in the scientific and medical literature.

Although Walji & Wiktorowicz's study is far from recent, lessons learned from their study included the need to streamline authorization of NHP applications, properly differentiate NHPs from food or drugs, increase knowledge surrounding the potential adverse effects of NHPs, and ensure that industries comply with regulations. Ultimately, the authors argued that Canada still needs to improve on monitoring manufacturers' compliance with regulations by performing tasks such as overseeing quality control or conducting audits.

The 2004 regulations focused on authorizing NHPs by having industries provide information about the following: definitions; labeling and packaging; research regarding each ingredient in an NHP that included its benefits and risks such as adverse reactions; manufacturing practices; and product and site licensing. Some of these prove to be a challenge even today,

and an area to be addressed is increasing communication between industries and government [19]. While Health Canada's efforts have been primarily focussed on the manufacturing process up until an NHP is approved for sale on the market, it has relatively lesser measures in place to encourage post-market surveillance and address product complaints regarding adverse reactions.

Canada continues to face challenges in the face of the general public calling for the increased safety of NHPs [16], as Health Canada aims to maintain the balance between ensuring that a diverse range of products are available and that there is respect for consumer choice, while the public is still protected from NHPs that may pose risk of harm. To help industries encourage and overcome the financial burden and time-consuming process of conducting clinical trials, incentives such as data protection or funding could be offered as a potential remedy [22,23]. What can also be of further benefit, and especially in the context of this review, is increased academic research on stakeholder perceptions of NHPs. Academic research on stakeholder perceptions can also be used to compare the 2004 regulations with proposed changes to the framework, such as those planned by Health Canada in 2019–2021 [17]. In the paucity of other more recent studies evaluating the Canadian NHP regulatory framework, the themes identified in the present scoping review can be used to inform further research on this topic.

#### **4.1. Strengths and limitations**

Notable strengths of this study included the use of a comprehensive systematic search strategy to identify eligible articles. Interpretation of these findings was strengthened by the fact that both authors independently screened, data extracted, and summarized the findings. Limitations include the fact that we did not include non-English language articles, despite the

fact that the vast majority of academic literature is published in English. Additionally, we did not include a search of the grey literature and acknowledge that this review may not necessarily capture industry researchers' evaluations of the Canadian NHP regulatory framework, however, we justify this decision given the parameters of our research question, which was specifically to identify only academic research in the peer-reviewed literature.

## **5. Conclusions**

Our scoping review involved a systematic search of the literature to identify academic research evaluating the Canadian NHP regulatory framework. We only found one article that met our eligibility criteria. The implementation of the Natural Health Products Regulations in 2004 which categorized NHPs as distinct from food or pharmaceutical drugs impacted government, industries, and consumers both negatively and positively. For consumers, these regulations enabled them to make better decisions as they could better understand the health claims associated with NHPs and decreased their risk of experiencing adverse effects. While NHP manufacturers generally supported the regulations from the perspective that only those products meeting the necessary safety standards levelled the playing field, they also felt burdened by the application process and the research required to verify their NHP's health claims. These regulations made it mandatory for manufacturers to obtain a product license for their NHPs, which created a significant backlog in processing NHP applications and caused frustration among manufacturers. This resulted in the need for Health Canada to address these issues and improve the way in which they processed applications. This study has identified a major gap in the academic research surrounding the evaluation of the Canadian NHP regulatory framework, despite Health Canada's ongoing plans to change the regulatory framework. Academic research in this area should be supported, especially in conjunction with consultations with stakeholders, so that efforts to improve the NHP regulatory

framework is informed by an awareness of past research that has identified both positive and negative aspects of the current framework.

## **Author contributions**

JYN: designed the study, collected, interpreted and analysed data, drafted the manuscript, and gave final approval of the version to be published.

ML: collected, interpreted and analysed data, revised the manuscript critically, and gave final approval of the version to be published.

## **Declaration of Competing Interests**

The authors declare that they have no conflicts of interest.

## **Funding**

This study was unfunded.

## **Data availability**

All data associated with this study is included within this manuscript.

## **Ethical statement**

This study involved a systematic search of the literature only; it did not require ethics approval or consent to participate.

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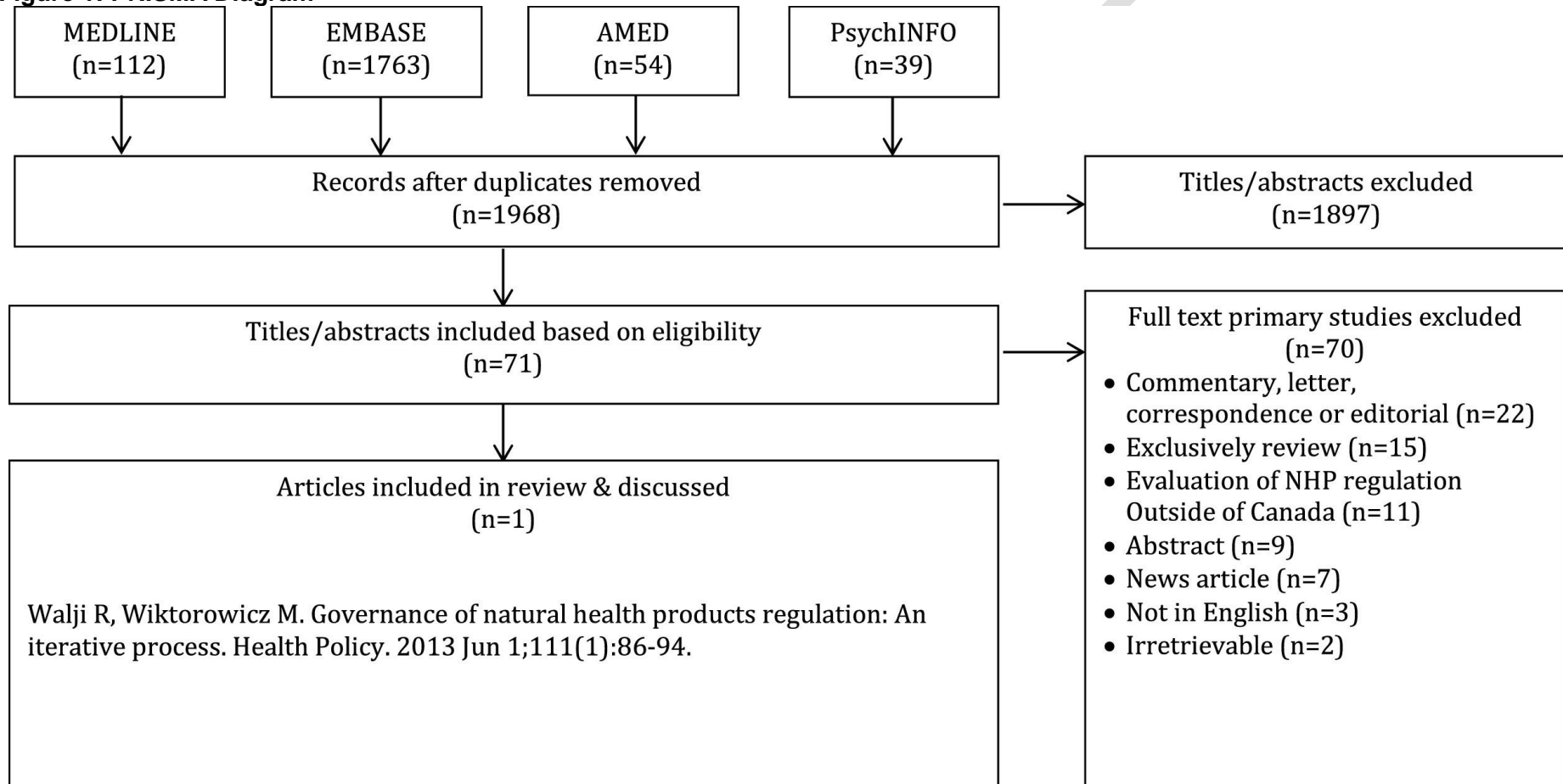
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## Figures

Figure 1: PRISMA Diagram



## Tables

**Table 1: Search Strategy for Studies Evaluating the Canadian Natural Health Product Regulatory Framework, Executed May 15, 2020**

Database: AMED (Allied and Complementary Medicine) <1985 to May 2020>, Embase <1974 to 2020 May 14>, APA PsycInfo <1806 to May Week 2 2020>, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to May 14, 2020>

Search Strategy:

- 
- 1 natural health product\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (1106)
  - 2 complementary medicine\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (14430)
  - 3 complementary therap\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (32224)
  - 4 alternative medicine\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (64874)
  - 5 alternative therap\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (35189)
  - 6 integrat\* medicine\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (10861)
  - 7 integrat\* therap\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (3559)
  - 8 traditional medicine\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (63025)
  - 9 traditional therap\*.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kw, fx, dq, tc, id, tm, mh, nm, kf, ox, px, rx, ui, sy] (7839)
  - 10 (vitamin\* or mineral\* or herb\* or homeopathic\* or probiotic\*).m\_titl. (421846)
  - 11 or/1-10 (610421)
  - 12 (regulation\* or polic\* or legislation\* or law\* or framework\*).m\_titl. (873032)
  - 13 11 and 12 (5383)
  - 14 remove duplicates from 13 (3338)
  - 15 limit 14 to english language (2953)
  - 16 limit 15 to yr="2004 -Current" (1968)

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