# Article Title: Complementary and Alternative Medicine Status in Ovarian Cancer Guidelines: A Systematic Review

**Jeremy Y. Ng [1]§ and Stephanie Ka Ching Lau [1]**

[1] Department of Health Research Methods, Evidence, and Impact, Faculty of Health Sciences, McMaster University, Michael G. DeGroote Centre for Learning and Discovery, Room 2112, 1280 Main Street West, Hamilton, Ontario, L8S 4K1, Canada

§Corresponding Author's Email Address: ngjy2@mcmaster.ca

ORCiDs:
JYN: http://orcid.org/0000-0003-0031-5873

# Abstract

**Introduction:** Given the often-advanced stage of ovarian cancer upon diagnosis, many patients may seek complementary and alternative medicine (CAM), however, when improperly used, such therapies can be detrimental. Healthcare providers rely on clinical practice guidelines to give evidence-based advice. The objective of this study was to identify the quantity and assess the quality of CAM recommendations in ovarian cancer treatment and/or management in clinical practice guidelines.

**Methods:** MEDLINE, EMBASE and CINAHL were systematically searched from 2009 to April 2020, in addition to the Guidelines International Network, the National Center for Complementary and Integrative Health, and Google websites. Had CAM recommendations been found, the guidelines would have been assessed with the Appraisal of Guidelines, Research and Evaluation II (AGREE II) instrument.

**Results:** Fifteen eligible ovarian cancer guidelines were identified from 432 unique search results. No eligible guidelines made mention or recommendations of CAM. The guidelines focused on treatment with conventional therapies including surgery, chemotherapy, and radiation therapy.

**Conclusion:** The quality of CAM recommendations in ovarian cancer treatment could not be assessed and compared with overall guideline recommendations. Given that a large proportion of ovarian cancer patients use CAM, this lack of therapy recommendations for the treatment and/or management of ovarian cancer reflects a major knowledge gap. Future guidelines should consider incorporating evidence-based CAM in their recommendations given that clinicians require this information in order to inform important shared-decision making discussions regarding safe and effective CAM use with their patients.

## Abbreviations

AGREE II: Appraisal of Guidelines for Research & Evaluation II

CAM: complementary and alternative medicine

CPG: clinical practice guideline

NCCIH: National Center for Complementary and Integrative Health

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

## 1. Background

Ovarian cancer remains the leading cause of mortality among gynecological cancers in developed countries [1,2]. Annually, there are 240,000 ovarian cancer diagnoses and 150,000 ovarian cancer deaths worldwide [3]. Ovarian cancer refers to a collection of malignancies that originate from the ovaries, a set of reproductive organs located in the pelvis. They are heterogenous and subtypes depend on the histology, namely the cell type of origin [1]. It is difficult to detect in its early stages as the symptoms are non-specific, resulting in 4 out of 5 diagnoses being with advanced cancer [4]. When confined to the ovaries, the cure rate is 90%, but when the cancer spreads beyond the pelvis, the long-term survival rate falls below 20% [5]. Due to the often poor prognosis of ovarian cancer even with the conventional therapies, patients may turn to complementary and alternative medicine (CAM). A study in Canada and the United Kingdom demonstrated that 44% of patients with ovarian cancer were CAM users [6]. According to the National Center for Complementary and Integrative Health (NCCIH), complementary therapy refers to the use of non-conventional therapy together with conventional therapy, while alternative therapy refers to the use of non-conventional therapy in place of conventional therapies [7].

Among the CAM users with ovarian cancer, 37% of them use multiple CAM therapies and among the most popular are medicinal herbs, spiritual therapy, omega 3/fish oil, vitamin C, soy products, and green tea [6], [8]. The major motivation for the use of CAM in ovarian cancer is the belief that CAM use will enhance the effects of conventional therapies, and boost the immune system and body's natural healing [6]. Likewise, 93.6% of CAM users indicated they were "satisfied" or "very satisfied" with the use and effects of CAM [8]. However, while 89% of CAM users with ovarian cancer believed their oncologist should know about their use of CAM, only 62% of the patients actually informed their oncologist [6]. The main reasons for such discrepancies include the lack of inquiry by oncologists, and patients' hesitancy to report CAM use to their oncologists believing that they would not be knowledgeable or approving [6]. However, improper use of CAM may be detrimental to individuals with ovarian cancer. The majority of patients are on chemotherapy treatment, which comprise of medications with narrow therapeutic windows, and the use of CAM may alter the pharmacodynamics of the chemotherapy and pose toxic effects to users [9]. Drug interactions aside, CAM use alone can also be associated with adverse health effects, such as varying degrees of hepatotoxicity [10].

Despite the high prevalence of CAM use and the demand for more knowledge about the implications associated with CAM use, there is little emphasis on CAM in the medical training of healthcare providers [11]. With the ever-evolving nature of medicine, health care professionals often depend on evidence-based clinical practice guidelines (CPG) to inform their decisions when providing patient-centered care. To our knowledge, there have been no studies looking at the mention and recommendations of CAM in CPGs for ovarian cancer. Therefore, the purpose of this study was to conduct a systematic review to determine

mentions of CAM in ovarian cancer CPGs, and to assess the quality of the development of CAM recommendations.

# 2. Methods

## 2.1. Approach

A systematic review was conducted to identify ovarian cancer CPGs using standard methods [12] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [13]. A protocol was registered with PROSPERO, registration number CRD42020182238. Had eligible CPGs with CAM recommendations been found, they would have been assessed with the widely used and validated Appraisal of Guidelines, Research and Evaluation II (AGREE II) instrument [14]. The AGREE II instrument consists of 23 items grouped in six domains: scope and purpose, stakeholder involvement, rigor of development, clarity and presentation, applicability, and editorial independence.

## 2.2. Eligibility criteria

Eligibility criteria for ovarian cancer CPGs were based on the Population, Intervention, Comparison and Outcomes framework. Eligible populations were adults aged 19 years and older with ovarian cancer. With respect to interventions, only CPGs that included treatment or management of ovarian cancer were included, so that we could determine if CAM therapies were included. The consideration of therapies as CAM was based on the Cochrane Complementary Medicine operational definition: https://cam.cochrane.org/operational-definition-complementary-medicine. The comparison was to be assessed on the quality of CAM recommendations compared to the overall CPG recommendations in ovarian cancer CPGs. Outcomes would were AGREE II scores which reflect CPG quality. The following conditions were also applied to define eligible CPGs: developed by non-profit organizations

including academic institutions, government agencies, disease-specific foundations, or professional associations or societies; published in 2009 or later; English language; and either publicly available or could be ordered through our library system. The following study designs were not eligible: publications in the form of consensus statements, protocols, abstracts, conference proceedings, letters or editorials; based on primary studies that evaluated ovarian cancer management or treatment; or focused on ovarian cancer curriculum, education, training, research, professional certification or performance. It should be noted that only eligible CPGs that contained CAM therapy recommendations were to be assessed using the AGREE II tool, in order to determine the difference in AGREE II scores between the CAM-specific recommendations and the overall CPG; only demographic information was reported for eligible CPGs that did not contain CAM therapy recommendations.

## 2.3. Searching and screening

MEDLINE, EMBASE and CINAHL were searched on April 17, 2020 from 2009 to April 16, 2020 inclusive. The search strategy (Supplementary File 1) included indexed headings and keywords that reflect terms commonly used in the literature to refer to ovarian cancer. We also searched the Guidelines International Network, a repository of guidelines [https://www.g-i-n.net/] using keyword searches restricted based on the eligibility criteria including "ovarian cancer" and "ovarian neoplasms". Next, we searched the NCCIH web site which contained a single list of CAM CPGs [https://www.nccih.nih.gov/health/providers/clinicalpractice]. Finally, we conducted a gray literature search of the first three pages of search results on Google [www.google.com] on September 30, 2020 using the search terms "ovarian cancer clinical practice guidelines", "ovarian cancer practice guidelines", and "ovarian cancer guidelines". SKCL and another research assistant screened titles and abstracts from all other sources. SKCL and the other

research assistant screened full-text items to confirm eligibility. JYN reviewed the screened titles and abstracts and full-text items to standardize screening, and helped to discuss and resolve selection differences between the two screeners.

### 2.4. Data extraction and analysis

The data extraction was performed by SKCL and another research assistant independently but in duplicate, and then JYN reviewed their work. The following information was obtained for each CPG and summarized: date of publication, country of first author; type of organization that published the CPG (such as academic institutions, government agencies, disease-specific foundations, or professional associations or societies); and whether there was any mention of CAMs in the CPG. If CAMs were mentioned in a CPG, the following data was to be extracted: types of CAM mentioned, specific CAM recommendations, CAM funding sources, and whether any CAM providers participated in the CPG development. Afterwards, the quality of the CPGs with CAM recommendations were to be assessed with the AGREE II instrument.

# 3. Results

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

Searches retrieved 522 articles, 432 were unique, and 340 titles and abstracts were eliminated, leaving 92 full text articles that were considered. Of those, 77 were determined to be ineligible after full-text screening because they were either not a CPG (n = 52), not available in English (n = 9), or did not meet other eligibility criteria (n = 16), leaving 15 CPGs eligible for review. Of these 15 CPGs, none mentioned CAM or made any CAM recommendations (Fig. 1)

### 3.2. Guideline characteristics (Table 1)

Eligible CPGs were published from 2011 to 2019 in Europe (n = 7), Canada (n = 3), USA (n = 2), Australia (n = 1), Japan (n = 1), and Singapore (n = 1) [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30]. The CPGs were funded and/or developed by professional associations or societies. None of the CPGs made mention of CAMs. Table 1 provides a summary of more information regarding the aforementioned CPGs.

# 4. Discussion

The purpose of this study was to conduct a systematic review to determine and assess the quality of the recommendations regarding CAM in CPGs for the treatment and/or management of ovarian cancer. Although a good proportion of patients with ovarian cancer are CAM users, many of them do not have discussions surrounding their CAM usage with their physicians. Therefore, we wanted to identify credible and knowledge-based resources upon which both patients and healthcare professionals could draw upon to assist in their decision-making process surrounding CAM use in ovarian cancer. This study found 15 CPGs that were published between 2011 and 2019 and that discussed the treatment and/or management of ovarian cancer, but none made any mention of CAM therapy recommendations. Consequently, no articles were assessed with AGREE II. This study reveals a major knowledge gap in the existing literature as healthcare providers do not have access to evidence-based CPGs to use when consulting with their ovarian cancer patients about CAM use.

To the best of our knowledge, this is the first systematic review conducted to identify and assess the quality and quantity of CAM recommendations in ovarian cancer CPGs. Thus, this

is the first study to demonstrate the lack of credible recommendations surrounding the use of CAM therapy in ovarian cancer CPGs. The findings from this study are similar to a systematic review published in 2020 that aimed to identify and assess CAM recommendations in colon cancer CPGs [31]. Eight CPGs on the treatment or management of colon cancer were found but none of them made CAM recommendations [31]. The authors concluded that despite literature showing 82.8% of patients with colon cancer are CAM users, there was a major knowledge gap regarding the evidence-based recommendations on CAM use in colon cancer [31]. Furthermore, another systematic review was conducted to assess the quality and quantity of CAM recommendations in lung cancer CPGs and the results were limited; only three out of 26 eligible CPGs made CAM recommendations and within that, only one included a comprehensive list of CAM therapies [32]. However, in recently published systematic reviews that sought to assess CAM therapy recommendations in other health conditions, namely lower back pain and arthritis (both osteoarthritis and rheumatoid arthritis), it was found that the majority and half of eligible CPGs had made CAM recommendations, respectively [33,34]. Therefore, rather than an overall knowledge gap in CAM recommendations in medicine, there seems to be a slower uptake of CAM recommendations in cancer CPGs specifically.

Although the lack of CAM recommendations in ovarian cancer CPGs precluded us from assessing them, a study published in 2007 used AGREE to assess systemic therapy recommendations in recurrent ovarian cancer guidelines [35]. There were four guidelines assessed and there was great variability in the domain scores between guidelines. Overall, the Clarity of Presentation domain scored the highest among the guidelines and the Applicability domain scored the lowest among the guidelines. Moreover, another study published in 2016 used AGREE II to assess recommendations on herbal medicines, acupuncture, and spinal

manipulation in CAM guidelines [36]. There were 17 eligible guidelines which ranged in terms of their clinical topic, including breast cancer and lung cancer. Among the eligible guidelines, the Clarity of Presentation domain scored the highest with a scaled domain percentage of 85.3%, and the Applicability domain scored the lowest with a scaled domain percentage of 20.7%. This study included and assessed five CAM guidelines that focused on oncology specifically, and of these, one study was recommended as 'Yes with Modifications' by both appraisers; two studies were recommended as 'Yes with Modifications' and 'No'; and the remaining wo studies were recommended as 'No' by both appraisers. Overall, these authors came to a similar conclusion in terms of the lack of CAM guidelines available to assist healthcare providers in making informed decisions surrounding such therapies.

As shown by our systematic review, the underrepresentation of CAM in guidelines is especially true in ovarian cancer CPGs. In general, CPGs are typically supported by primary research and the strength of the recommendations are correlated with the level of evidence. However, the poor funding of CAM research is one of the major reasons as to why there is limited high-quality CAM research conducted, which can limit its inclusion in guidelines [37]. Moreover, a search for primary studies on CAM therapies in ovarian cancer yielded limited results. However, there has been primary research conducted on the efficacy of one of the most popular CAM therapies, ascorbate or vitamin C in ovarian cancer. In 2014, Ma and colleagues [38] looked at the effects of intravenous ascorbate-induced ovarian cancer cell death. When assessing the susceptibility of human ovarian cancer cell lines to ascorbate, there was a concentration-dependent cytotoxicity observed. Additionally, when combined with the conventional chemotherapy treatments carboplatin or paclitaxel, there was synergistic action of cancer cell death seen in certain human cell lines. Furthermore, in a pilot clinical trial with patients with stage III or IV ovarian cancer, chemotherapy-associated

toxicity was reduced with the addition of high dose intravenous ascorbate (statistically nonsignificant). It was postulated that with a greater statistical power (i.e., larger sample size) and a higher ascorbate dose (i.e., possible dose-response relationship), statistical significance regarding the efficacy of ascorbate may be achieved. Therefore, there is great potential in the use of CAM therapies to treat ovarian cancer but more research is needed.

### 4.1. Strengths and limitations

One notable strength is the use of a comprehensive systematic review across multiple academic databases with two research assistants performing each step independently to ensure accuracy. However, we may have missed guidelines that are only available on specific society websites (i.e. government generated publications) and not available in the academic databases and websites that we searched. To minimize this potential of missing CPGs, we hand-searched www.google.com to find CPGs not captured by our academic database searches. Furthermore, another limitation included the fact that we only included English-language CPGs. This criterion may have excluded ovarian cancer CPGs with CAM therapy recommendations since CAM use is common in countries where English is not widely-spoken. Lastly, recommendations for CAM use in ovarian cancer or CAM use for general cancer management may have been published in general oncology guidelines, which were not searched for in our study, but may have been applicable to ovarian cancer patients (e.g. the use of CAM to treat chemotherapy induced nausea and vomiting).

## 5. Conclusions

This study identified 15 CPGs on the treatment and/or management of ovarian cancer published since 2011. None of the eligible CPGs made any mention or recommendations on the use of CAM for ovarian cancer, thus no quality assessment was conducted using the

AGREE II instrument. However, studies have shown that nearly half of patients with ovarian cancer use some sort of CAM therapy [6]. Patients often rely on their healthcare providers to inform them about their treatment regimen, and healthcare providers often rely on CPGs to guide their decision-making process. With the lack of evidence-based recommendations on CAM use during ovarian cancer, clinicians may be relying on less reliable and lower quality studies to guide their patient-centered care. This poses a risk to the patient as CAM therapies can be dangerous when improperly used, especially in the case of chemotherapy, a conventional treatment with a narrow therapeutic index, resulting in serious adverse drug-CAM interactions. When patients fail to respond to or cannot tolerate conventional treatments, they may turn to CAM without any professional guidance, especially if the attending healthcare provider is unknowledgeable about the evidence surrounding CAM use. Therefore, this study's findings justify the need for a greater emphasis on CAM therapy recommendation development in ovarian cancer CPGs. Future research should focus on evidence-based CAM recommendations so that there will be credible resources for healthcare providers to use when caring for their patients, with the safety and effectiveness of these therapies in mind.

## Ethics approval and consent to participate

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

## Data availability

All relevant data are included in this manuscript.

# Author contributions

JYN: made substantial contributions to the design of the study, collected and analysed data, drafted the manuscript, and gave final approval of the version to be published.

SKCL: assisted with the collection and analysis of data, drafted the manuscript, and gave final approval of the version to be published.

# Funding

# Declaration of Competing Interest

The authors declare that they have no competing interests.

# Acknowledgements

# Supplementary materials

Supplementary File 1: MEDLINE Search Strategy for Ovarian Cancer Clinical Practice Guidelines Executed April 17, 2020

# References

[1] M. Kossaï, A. Leary, J.Y. Scoazec, C Genestie. Ovarian Cancer: a heterogeneous disease. Pathobiology, 85 (1–2) (2018), pp. 41-49, 10.1159/000479006. Available from https://pubmed.ncbi.nlm.nih.gov/29020678.

[2] C.A. Doubeni, A.R. Doubeni, A.E Myers. Diagnosis and management of ovarian cancer Am. Fam. Physician, 93 (11) (2016), pp. 937-944. Available from https://pubmed.ncbi.nlm.nih.gov/27281838.

[3] P.M. Webb, S.J. Jordan. Epidemiology of epithelial ovarian cancer. Best Pract. Res. Clin. Obstet. Gynaecol., 41 (2017), pp. 3-14, 10.1016/j.bpobgyn.2016.08.006. Available from https://pubmed.ncbi.nlm.nih.gov/27743768.

[4] L.A. Torre, B. Trabert, C.E. DeSantis, K.D. Miller, G. Samimi, C.D. Runowicz, et al. Ovarian cancer statistics, 2018. CA. Cancer J Clin, 68 (4) (2018), pp. 284-296, 10.3322/caac.21456. Available from https://pubmed.ncbi.nlm.nih.gov/29809280.

[5] K.M. Elias, J. Guo, R.C Bast. Early detection of ovarian cancer. Hematol. Oncol. Clin. North Am., 32 (6) (2018), pp. 903-914, 10.1016/j.hoc.2018.07.003. Available from https://pubmed.ncbi.nlm.nih.gov/30390764.

[6] L. Helpman, S.E. Ferguson, M. Mackean, A. Rana, L. Le, M.A. Atkinson, et al. Complementary and alternative medicine use among women receiving chemotherapy for ovarian cancer in 2 patient populations. Int. J. Gynecol. Cancer, 21 (3) (2011), pp. 587-593, 10.1097/IGC.0b013e31820fa24a. Available from https://pubmed.ncbi.nlm.nih.gov/21436708

[7] Complementary, Alternative, or Integrative Health: What's In a Name?: National Center for Complementary and Integrative Health; 2020. Available from: https://www.nccih.nih.gov/health/complementary-alternative-or-integrative-health-whats-in-a-name

[8] M Bahall. Prevalence, patterns, and perceived value of complementary and alternative medicine among cancer patients: a cross-sectional, descriptive study. BMC Complement Altern. Med., 17 (1) (2017), p. 345, 10.1186/s12906-017-1853-6. Available from https://pubmed.ncbi.nlm.nih.gov/28666435.

[9] E.S. Sweet, L.J. Standish, B.A. Goff, M.R Andersen. Adverse events associated with complementary and alternative medicine use in ovarian cancer patients. Integr. Cancer Ther., 12 (6) (2013), pp. 508-516, 10.1177/1534735413485815. Available from https://pubmed.ncbi.nlm.nih.gov/23625025.

[10] Teo D.C., Ng P.S., Tan S.H., Lim A.T., Toh D.S., Chan S.Y., et al. Drug-induced liver injury associated with complementary and alternative medicine: a review of adverse event reports in an Asian community from 2009 to 2014. BMC Complement Altern Med. 2016;16:192. Available from: https://pubmed.ncbi.nlm.nih.gov/27389194 DOI: 10.1186/s12906-016-1168-z.

[11] S.J. Patel, K.J. Kemper, J.P Kitzmiller. Physician perspectives on education, training, and implementation of complementary and alternative medicine. Adv. Med. Educ. Pract., 8 (2017), pp. 499-503, 10.2147/AMEP.S138572. Available from https://pubmed.ncbi.nlm.nih.gov/28794663.

[12] Cochrane. J Higgins, S Green (Eds.), The Cochrane Collaboration (2011).

[13] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, P Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement Ann. Intern. Med., 151 (4) (2009), pp. 264-269, 10.7326/0003-4819-151-4-200908180-00135. Available from https://pubmed.ncbi.nlm.nih.gov/19622511.

[14] M.C. Brouwers, M.E. Kho, G.P. Browman, J.S. Burgers, F. Cluzeau, G. Feder, et al. AGREE II: advancing guideline development, reporting and evaluation in health care

CMAJ, 182 (18) (2010), pp. E839-E842, 10.1503/cmaj.090449. Available from

https://pubmed.ncbi.nlm.nih.gov/20603348.

[15] V. Lavoue, C. Huchon, C. Akladios, P. Alfonsi, N. Bakrin, M. Ballester, et al.

Management of epithelial cancer of the ovary, fallopian tube, and primary peritoneum. Long

text of the joint French clinical practice guidelines issued by FRANCOGYN, CNGOF,

SFOG, and GINECO-ARCAGY, and endorsed by INCa. Part 1: diagnostic exploration and

staging, surgery, perioperative care, and pathology. J. Gynecol. Obstet. Hum. Reprod., 48 (6)

(2019), pp. 369-378, 10.1016/j.jogoh.2019.03.017. Available from

https://pubmed.ncbi.nlm.nih.gov/30936027.

[16] V. Lavoue, C. Huchon, C. Akladios, P. Alfonsi, N. Bakrin, M. Ballester, et al.

Management of epithelial cancer of the ovary, fallopian tube, primary peritoneum. Long text

of the joint French clinical practice guidelines issued by FRANCOGYN, CNGOF, SFOG,

GINECO-ARCAGY, endorsed by INCa. (Part 2: systemic, intraperitoneal treatment, elderly

patients, fertility preservation, follow-up). J. Gynecol. Obstet. Hum. Reprod., 48 (6) (2019),

pp. 379-386, 10.1016/j.jogoh.2019.03.018. Available from

https://pubmed.ncbi.nlm.nih.gov/30936025.

[17] I. Ray-Coquard, P. Morice, D. Lorusso, J. Prat, A. Oaknin, P. Pautier, et al.

Non-epithelial ovarian cancer: ESMO clinical practice guidelines for diagnosis, treatment and

follow-up. Ann. Oncol., 29 (2018), 10.1093/annonc/mdy001. Suppl 4:iv1-iv18. Available

from https://pubmed.ncbi.nlm.nih.gov/32169220.

[18] J. Francis, N. Coakley, L. Elit, H. Mackay, G.C.D.S Group. Systemic therapy for

recurrent epithelial ovarian cancer: a clinical practice guideline. Curr. Oncol., 24 (6) (2017),

pp. e540-e5e6, 10.3747/co.24.3824. Available from
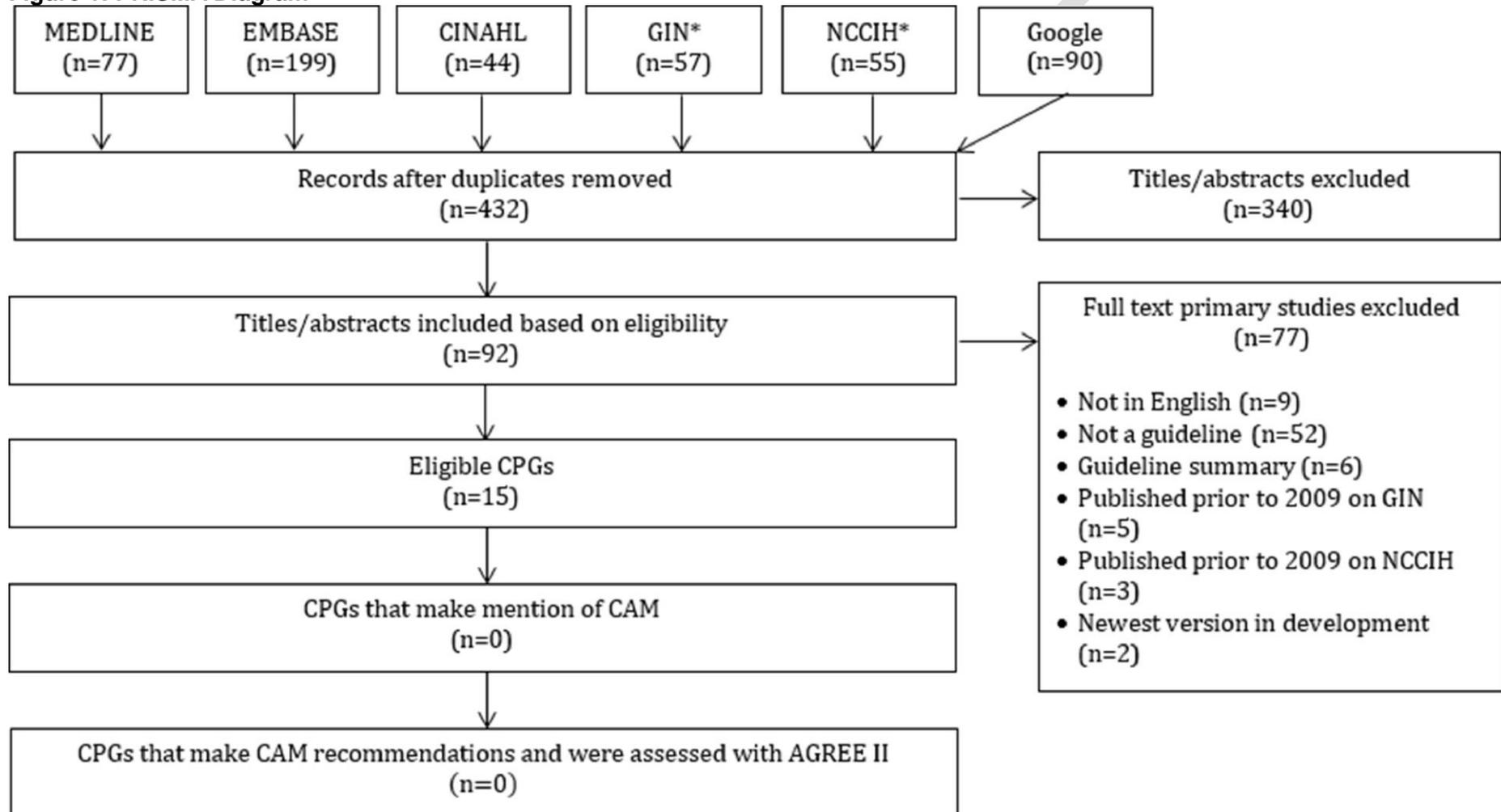
https://pubmed.ncbi.nlm.nih.gov/29270064.

[19] C. Fotopoulou, M. Hall, D. Cruickshank, H. Gabra, R. Ganesan, C. Hughes, et al. British Gynaecological cancer society (BGCS) epithelial ovarian/fallopian tube/primary peritoneal cancer guidelines: recommendations for practice. Eur. J. Obstet. Gynecol. Reprod. Biol., 213 (2017), pp. 123-139, 10.1016/j.ejogrb.2017.04.016. Epub 2017/04/18PubMed PMID: 28457647.

[20] A. Santaballa, P. Barretina, A. Casado, Y. García, A. González-Martín, E. Guerra, et al. SEOM clinical guideline in ovarian cancer (2016). Clin. Transl. Oncol., 18 (12) (2016), pp. 1206-1212, 10.1007/s12094-016-1588-8. Available from https://pubmed.ncbi.nlm.nih.gov/27905052.

[21] A.A. Wright, K. Bohlke, D.K. Armstrong, M.A. Bookman, W.A. Cliby, R.L. Coleman, et al. Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer: society of gynecologic oncology and American society of clinical oncology clinical practice guideline J. Clin. Oncol., 34 (28) (2016), pp. 3460-3473, 10.1200/JCO.2016.68.6907. Available from https://pubmed.ncbi.nlm.nih.gov/27502591.

[22] S. Komiyama, H. Katabuchi, M. Mikami, S. Nagase, A. Okamoto, K. Ito, et al. Japan society of gynecologic oncology guidelines 2015 for the treatment of ovarian cancer including primary peritoneal cancer and fallopian tube cancer. Int. J. Clin. Oncol., 21 (3) (2016), pp. 435-446, 10.1007/s10147-016-0985-x. Available from https://pubmed.ncbi.nlm.nih.gov/27142770.

[23] L. Elit, A. Chambers, A. Fyles, A. Covens, M. Carey, M Fung Kee Fung. Management of stage I ovarian cancer. Cancer Care Ontario (2016).

[24] S.L L, J.W.K C, S.E L, Y.W L, L N, H.T S, et al. Singapore cancer network (SCAN) guidelines for front-line systemic therapy of newly diagnosed advanced epithelial ovarian cancer. Ann. Acad. Med. Singapore, 44 (2015), pp. 421-433.

[25] C. Steer, K. Cox, J. Got, S. Jordan, E. Koussidis, Y. Leung, et al. First-line chemotherapy for the treatment of women with epithelial ovarian cancer. Cancer Australia (2014).

[26] J.A. Ledermann, F.A. Raja, C. Fotopoulou, A. Gonzalez-Martin, N. Colombo, C. Sessa, et al. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann. Oncol., 24 (2013), 10.1093/annonc/mdt333. Suppl 6:vi24-32. Available from https://pubmed.ncbi.nlm.nih.gov/24078660.

[27] N. Siddiqui, S. Bredin, EHFegan BChoi, M SFerguson. Management of epithelial ovarian cancer (SIGN CPG 135). Healthcare Improve. Scotland (2013).

[28] Alberta Health Services. Epithelial ovarian, fallopian tube, and primary peritoneal cancer Alberta Health Services (2013).

[29] R.J. Morgan, R.D. Alvarez, D.K. Armstrong, B. Boston, R.A. Burger, L.M. Chen, et al. Epithelial ovarian cancer. J. Natl. Compr. Canc. Netw, 9 (1) (2011), pp. 82-113, 10.6004/jnccn.2011.0008. Available from https://pubmed.ncbi.nlm.nih.gov/21233246.

[30]
(UK) NCCfC. Ovarian Cancer: the Recognition and initial management of ovarian cancer. 2011. Available from: https://pubmed.ncbi.nlm.nih.gov/22479719.

[31] J.Y. Ng, H. Thakar. Complementary and alternative medicine mention and recommendations are lacking in colon cancer clinical practice guidelines: a systematic review Adv. Integr. Med. (2020), 10.1016/j.aimed.2020.06.002.

[32] J.Y. Ng, H. Nault, Z Nazir. Complementary and integrative medicine mention and recommendations: a systematic review and quality assessment of lung cancer clinical practice guidelines. Integr. Med. Res. (2020), 10.1016/j.imr.2020.100452.

[33] J.Y. Ng, U. Mohiuddin. Quality of complementary and alternative medicine recommendations in low back pain guidelines: a systematic review. Eur. Spine J. (2020), 10.1007/s00586-020-06393-9. Available from https://pubmed.ncbi.nlm.nih.gov/32236685.

[34] J.Y. Ng, A.M Azizudin. Rheumatoid arthritis and osteoarthritis clinical practice guidelines provide few complementary and alternative medicine therapy recommendations: a systematic review. Clin. Rheumatol. (2020), 10.1007/s10067-020-05054-y. Available from https://pubmed.ncbi.nlm.nih.gov/32385761.

[35] L. Elit, L. Zitzelsberger, M. Fung-Kee-Fung, M. Brouwers, I.D. Graham, G. Browman, et al. Use of systemic therapy in women with recurrent ovarian cancer–development of a national clinical practice guideline. Gynecol. Oncol., 106 (1) (2007), pp. 181-192, 10.1016/j.ygyno.2007.03.025. Available from https://pubmed.ncbi.nlm.nih.gov/17498781.

[36] J.Y. Ng, L. Liang, A.R Gagliardi. The quantity and quality of complementary and alternative medicine clinical practice guidelines on herbal medicines, acupuncture and spinal manipulation: systematic review and assessment using AGREE II. BMC Complement Altern Med, 16 (1) (2016), p. 425, 10.1186/s12906-016-1410-8. Available from https://pubmed.ncbi.nlm.nih.gov/27793133.

[37] A. Bensoussan, G.T. Lewith. Complementary medicine research in Australia: a strategy for the future. Med. J. Aust., 181 (6) (2004), pp. 331-333. Available from https://pubmed.ncbi.nlm.nih.gov/15377248.

[38] Y. Ma, J. Chapman, M. Levine, K. Polireddy, J. Drisko, Q Chen. High-dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer and reduced toxicity of chemotherapy Sci. Transl. Med., 6 (222) (2014), 10.1126/scitranslmed.3007154. 222ra18. Available from https://pubmed.ncbi.nlm.nih.gov/24500406.

# Figures
**Figure 1: PRISMA Diagram**

| MEDLINE (n=77) | EMBASE (n=199) | CINAHL (n=44) | GIN* (n=57) | NCCIH* (n=55) | Google (n=90) |
|---|---|---|---|---|---|

Records after duplicates removed (n=432) → Titles/abstracts excluded (n=340)

Titles/abstracts included based on eligibility (n=92) → Full text primary studies excluded (n=77)

- Not in English (n=9)
- Not a guideline (n=52)
- Guideline summary (n=6)
- Published prior to 2009 on GIN (n=5)
- Published prior to 2009 on NCCIH (n=3)
- Newest version in development (n=2)

Eligible CPGs (n=15)

CPGs that make mention of CAM (n=0)

CPGs that make CAM recommendations and were assessed with AGREE II (n=0)

# Tables

**Table 1: Characteristics of Eligible Guidelines**

| Guideline | Country (First Author) | Developer | Guideline Topic | Endorsement |
|---|---|---|---|---|
| Lavoue 2019 [15, 16] | France | French research group for oncologic gynecologic surgery (FRANCOGYN), the French national college of gynecologists and obstetricians (CNGOF), the French society of gynecologic oncology (SFOG), and the national investigators' group for studies in ovarian and breast cancer (GINECO-ARCAGY) | Management of epithelial ovarian cancer, fallopian tube, and primary peritoneum | National Cancer Institute (INCa) |
| Ray-Coquard 2018 [17] | Switzerland | European Society for Medical Oncology | Management of non-epithelial ovarian cancer | N/A |
| Francis 2017 [18] | Canada | Gynecology Cancer Disease Site Group | Systemic therapy for recurrent epithelial ovarian cancer | N/A |
| Fotopoulou 2017 [19] | United Kingdom | British Gynaecological Cancer Society | Management of epithelial ovarian, fallopian tube, and primary peritoneal cancers | N/A |
| Santaballa 2016 [20] | Spain | Spanish Society of Medical Oncology | Management of ovarian cancer | N/A |
| Wright 2016 [21] | United States | American Society of Clinical Oncology and Society of Gynecologic Oncology | Neoadjuvant chemotherapy for newly diagnosed and advanced ovarian cancer | N/A |
| Komiyama 2016 [22] | Japan | Japan Society of Gynecologic Oncology | Treatment of ovarian cancer, primary peritoneal cancer, and fallopian tube cancer | N/A |
| Elit 2016 [23] | Canada | Gynecology Cancer Disease Site Group | Management of stage I ovarian cancer | N/A |
| Lim 2015 [24] | Singapore | Singapore Cancer Network | Systemic therapy of newly diagnosed advanced epithelial ovarian | N/A |

| Guideline | Country (First Author) | Developer | Guideline Topic | Endorsement |
|---|---|---|---|---|
| | | | cancer | |
| Steer 2014 [25] | Australia | Cancer Australia | Chemotherapy for epithelial ovarian cancer | Australia New Zealand Gynaecological Oncology Group, Australian Society of Gynaecological Oncologists, and Medical Oncology Group of Australia |
| Ledermann 2013 [26] | England | European Society for Medical Oncology | Management of newly diagnosed and relapsed epithelial ovarian cancer | Japanese Society of Medical Oncology |
| Siddiqui 2013 [27] | Scotland | Scottish Intercollegiate Guidelines Network | Management of epithelial ovarian cancer | N/A |
| Alberta Health Services 2013 [28] | Canada | Alberta Provincial Gynecologic Oncology Tumour Team | Management of epithelial ovarian, fallopian tube, and primary peritoneal cancers | Alberta Provincial Gynecologic Oncology Tumour Team |
| Morgan 2011 [29] | United States | National Comprehensive Cancer Network | Epithelial ovarian cancer | N/A |
| National Collaborating centre for Cancer (UK) 2011 [30] | United Kingdom | National Institute for Health and Care Excellence | Recognition and initial management of ovarian cancer | N/A |