

Complementary and Alternative Medicine (CAM) Use in Patients Undergoing Radiotherapy: Sex-specific Prevalence and Associations of Use Based on the S3 Guideline Complementary Medicine in Oncology Questionnaire

LUKAS KÄSMANN^{1,2}, RALPH GURTNER¹, ROBERT RENNOLLET¹, JUDITH BÜNTZEL³, OLIVER MICKE⁴, CLAUD BELKA^{1,2,5}, MONTSERRAT PAZOS¹, RALPH MÜCKE⁶, JOSEFINE RAUCH¹ and JUTTA HÜBNER⁷

¹Department of Radiation Oncology, University Hospital, LMU Munich, Munich, Germany;

²German Cancer Consortium (DKTK), Partner Site Munich, Munich, Germany;

³University Medical Center Goettingen, Goettingen, Germany;

⁴Department of Radiotherapy and Radiation Oncology, Franziskus Hospital Bielefeld, Bielefeld, Germany;

⁵Bavarian Cancer Research Center (BZKF), Munich, Germany;

⁶Strahlentherapie RheinMainNahe GmbH, Bad Kreuznach, Germany;

⁷University Hospital Jena, Jena, Germany

Abstract

Background/Aim: This study aimed to assess the sex-specific prevalence and patterns of complementary and alternative medicine (CAM) use in patients undergoing radiotherapy, using the standardized questionnaire developed as part of the S3 Guideline on Complementary Medicine in Oncology.

Patients and Methods: Between August and December 2022, 112 out of 697 eligible cancer patients receiving radiotherapy were prospectively enrolled and completed a structured questionnaire assessing CAM use. The questionnaire included 38 CAM methods classified according to their potential for interactions.

Results: Female participants generally used more CAM methods than male participants (median methods: 3 vs. 1, $p < 0.001$). The most frequently used CAM methods were vitamin D (46.4%), sports/exercise (33%) and vitamin A/C/E or beta-carotene (25%). At least one of the listed CAM methods was used by 79.5%. At least three of the listed CAM methods were used by 52 (46.4%) patients. Thirty-six (32.1%) and 54 (48.2%) patients used CAM methods with known or potential interactions, while 76 (67.9%) used methods with no known interactions. In addition, a higher number of female patients used uncertain methods or medications compared to males ($p = 0.022$). The desire for counseling was very similar between both sexes, with no significant difference ($p = 0.973$).

continued



Lukas Käsmann, Department of Radiation Oncology, University Hospital, LMU Munich, 81377 Munich, Germany. Tel: +49 89440057561, e-mail: Lukas.Kaesmann@med.uni-muenchen.de

Received March 15, 2024 | Revised May 17, 2025 | Accepted May 23, 2025



This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

©2025 The Author(s). Anticancer Research is published by the International Institute of Anticancer Research.

Conclusion: The high rate of CAM utility before radiotherapy, especially among females, and the use of uncertain methods, highlights the need for standardized questionnaires to identify potential interactions. This would help enhance patient safety through structured screening and counseling.

Keywords: Complementary and alternative medicine, interactions, patient-physician communication, cancer care.

Introduction

The use of complementary and alternative medicine (CAM) among patients with cancer has significantly increased over the past decades (1, 2). Many patients seek CAM methods to enhance their well-being and alleviate treatment-related side effects, often without sufficient knowledge of potential risks and interactions (3-5). To provide evidence-based guidance for both patients and physicians, the S3 Guideline Complementary Medicine in the Treatment of Oncological Patients systematically evaluates the most commonly used CAM methods in Germany (6).

As part of this initiative, a concise patient questionnaire was developed to assess CAM use, ensuring a standardized approach to identifying potential risks, including interactions with oncological treatments (7). Integrating this tool into routine clinical practice aims to improve patient safety, foster informed decision-making, and enhance the quality of supportive care.

Given the observed sex differences in CAM use, a deeper understanding of sex-specific patterns is essential for optimizing counseling and risk assessment (8). This study aimed to evaluate the prevalence and associations of CAM use among patients undergoing radiotherapy, with a specific focus on sex differences, using the questionnaire of the S3 Guideline Complementary Medicine in the Treatment of Oncological Patients.

Patients and Methods

In this prospective study, all cancer patients (n=697) treated with radiotherapy at our department between August 2022 and December 2022 were asked for participation.

Ethics approval was given by the Ethics Committee of the University of Munich (Ludwig-Maximilians-University, Faculty of Medicine) (file number=2022-509). Patients completed the questionnaire anonymously between the outpatient/inpatient consultation and the first day of radiotherapy, with no possibility of linking their responses to other patient data.

The questionnaire, developed by the German Program for Guidelines in Oncology and published alongside the S3 Guideline Complementary Medicine in the Treatment of Oncological Patients was used to assess CAM use. It includes a table listing 38 CAM methods, each categorized using a color-coded system (green vs. yellow vs. red) to indicate potential interactions with oncological treatments. Red and yellow symbols highlight methods that warrant discussion with a physician due to possible interactions, while green indicates no known interactions. The questionnaire features nine red-labeled and fifteen yellow-labeled items. Participants were asked to indicate which CAM methods they were using by selecting the corresponding items.

Statistical analyses were performed using R (version 4.2.0, R Foundation for Statistical Computing, Vienna, Austria). The R packages readxl (version 1.4.1), dplyr (version 1.0.10) and tidyr (version 1.2.1) were employed for data processing. For data visualization, ggplot2 (version 3.4.0) and networkD3 (version 0.4) were employed.

Statistical analyses included Chi-square tests to assess the impact of sex on the usage of CAM methods with possible interactions. When sample sizes were insufficient, Fisher's exact test was used as an alternative. A significance level of $\alpha=0.05$ was set for all tests.

Results

A total of 112 patients participated in the prospective study (response rate: 16,1%). Median age was 63 years (range=34-89 years), and 69 (61.6%) patients were female. Table I presents an overview of the CAM methods used by patients, categorized by overall usage and sex.

Vitamin D was the most commonly used method for both sexes, but with a significant difference (62.3% among women vs. 23.8% among men, Table I). Sports/exercise was the second most common method among women (39.1%) and the third most common among men (21.4%). The vitamin B complex is frequently used by both sexes (23.2% among women vs. 21.4% in male patients) (Figure 1). Zinc appears in the top 5 only among men (11.9%). Female participants generally use more CAM methods than male participants (median methods: 3 vs. 1, $p<0.001$) (Figure 2).

The distribution of CAM usage among patients was as follows: 23 patients (20.5%) did not use any CAM methods, 23 (20.5%) used one, 14 (12.5%) used two, 29 (25.9%) used three to four, and 23 (20.5%) used five or more. Figure 3 illustrates the sex-specific utilization of CAM methods, highlighting differences in usage patterns between male and female patients.

79.5% used at least one of the listed CAM methods. Among patients using CAM methods, 76 (67.9%) used methods without known interactions, while 54 (48.2%) engaged in methods with potential interactions with oncological therapy, as defined by the S3 Guideline on Complementary Medicine (6). Notably, 36 patients (32.1%) utilized CAM methods with known interactions (Figure 4). The number of used CAM methods was correlated with interaction type (possible interactions: $p=0.022$; known interactions: $p=0.03$). In addition, more female than male patients used CAM methods/medications with possible or known interactions ($p=0.022$). However, the desire for counseling was very similar between both sexes, with no significant difference ($p=0.973$).

Table I. Utilization of CAM among all patients and by sex.

CAM method	Total users	Male users	Female users
Vitamin D	53 (47.3%)	10 (23.8%)	43 (62.3%)
Sports/Exercise	37 (33%)	9 (21.4%)	27 (39.1%)
Vitamin A/C/E or Beta-carotene	28 (25%)	6 (14.3%)	22 (31.9%)
Vitamin B1/B2/B6/B12 or Folic acid	25 (22.3%)	9 (21.4%)	16 (23.2%)
Selenium	21 (18.8%)	4 (9.5%)	17 (24.6%)
Zinc	16 (14.3%)	5 (11.9%)	11 (15.9%)
Homeopathy, Schüssler Salts, Bach Flower Remedies	13 (11.6%)	0 (0%)	13 (18.8%)
Green tea	12 (10.7%)	4 (9.5%)	8 (11.6%)
Chamomile	12 (10.7%)	4 (9.5%)	8 (11.6%)
Salvia	11 (9.8%)	4 (9.5%)	7 (10.1%)
Relaxation techniques	11 (9.8%)	1 (2.4%)	10 (14.5%)
Lavender	9 (8%)	2 (4.8%)	7 (10.1%)
Yoga/Tai Chi/Qi Gong	9 (8%)	1 (2.4%)	8 (11.6%)
Classical complementary medicine	8 (7.1%)	1 (2.4%)	7 (10.1%)
Ketogenic diets	8 (7.1%)	3 (7.1%)	5 (7.2%)
Curcumin	6 (5.4%)	0 (0%)	6 (8.7%)
Mistletoe	5 (4.5%)	0 (0%)	5 (7.2%)
Vegan nutrition	4 (3.6%)	0 (0%)	4 (5.8%)
Aromatherapy	4 (3.6%)	0 (0%)	4 (5.8%)
Acupuncture/Acupressure	3 (2.7%)	1 (2.4%)	2 (2.9%)
Carnitine	2 (1.8%)	0 (0%)	2 (2.9%)
Enzymes	2 (1.8%)	0 (0%)	2 (2.9%)
Phytotherapeutics	2 (1.8%)	0 (0%)	1 (1.4%)
Chinese herbs/Teas	2 (1.8%)	0 (0%)	2 (2.9%)
Detoxification methods	2 (1.8%)	0 (0%)	2 (2.9%)
Chiropractic/Osteopathy	2 (1.8%)	0 (0%)	2 (2.9%)
Laying on of hands	2 (1.8%)	0 (0%)	2 (2.9%)
Probiotics	1 (0.9%)	0 (0%)	1 (1.4%)
Ayurvedic medicinal plants	1 (0.9%)	0 (0%)	1 (1.4%)
Fasting	1 (0.9%)	0 (0%)	1 (1.4%)
Massages	1 (0.9%)	1 (2.4%)	0 (0%)
Vitamin B17/Amygdalin	0 (0%)	0 (0%)	0 (0%)
Isoflavone	0 (0%)	0 (0%)	0 (0%)
Lycopene	0 (0%)	0 (0%)	0 (0%)
Resveratrol	0 (0%)	0 (0%)	0 (0%)
Anthroposophic medicine	0 (0%)	0 (0%)	0 (0%)
Hyperthermia	0 (0%)	0 (0%)	0 (0%)

CAM: Complementary and alternative medicine.

Discussion

Our study confirms the high prevalence of CAM use among patients with cancer undergoing radiotherapy, with nearly 80% of participants reporting the use of at least one CAM method/medication. This aligns with previous reports

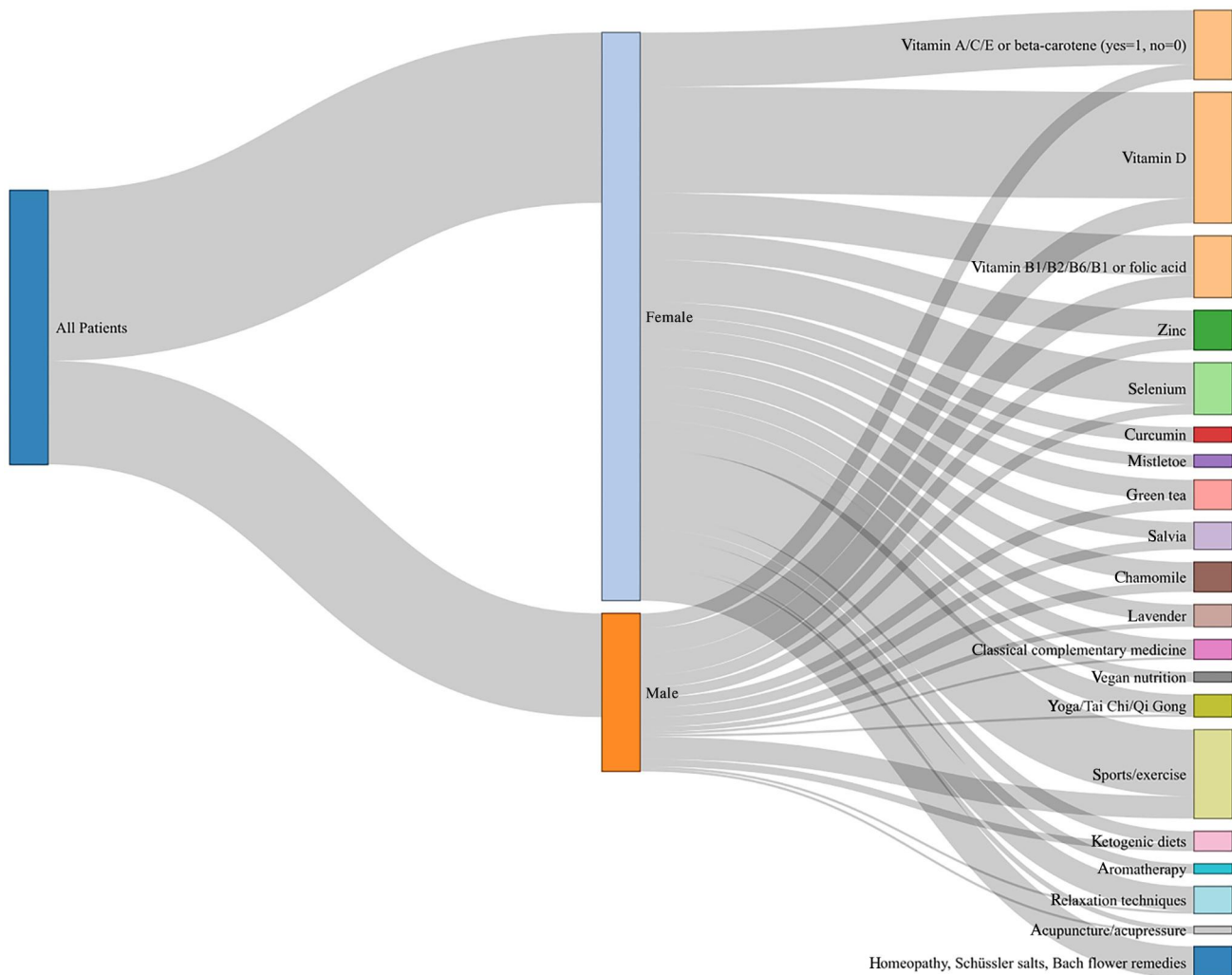


Figure 1. Sankey diagram of used complementary and alternative medicine (CAM) methods according to sex.

ranging between 11-95% suggesting that a majority of cancer patients integrate CAM into their treatment regimen (9-11). However, a significant sex disparity was observed, with female patients not only using CAM methods more frequently but also being more likely to engage in methods associated with potential or known interactions. These findings emphasize the need for selected counseling strategies to ensure patient safety. In addition, many patients do not inform their radiation oncologist or any physician about their CAM practice (3, 12). Several studies have explored the reasons why

patients choose not to disclose their use of CAM methods. Common factors include the lack of inquiry from physicians, patients' concerns about potential disapproval, perceived disinterest or limited support from healthcare providers, and the belief that CAM use is irrelevant to their conventional treatment (7, 9). It is important to raise physicians' awareness on these topics and actively ask patients regarding CAM usage (13).

The S3 guideline and its questionnaire offer a valuable tool for the early assessment and follow-up of CAM use, providing an easy and structured way to

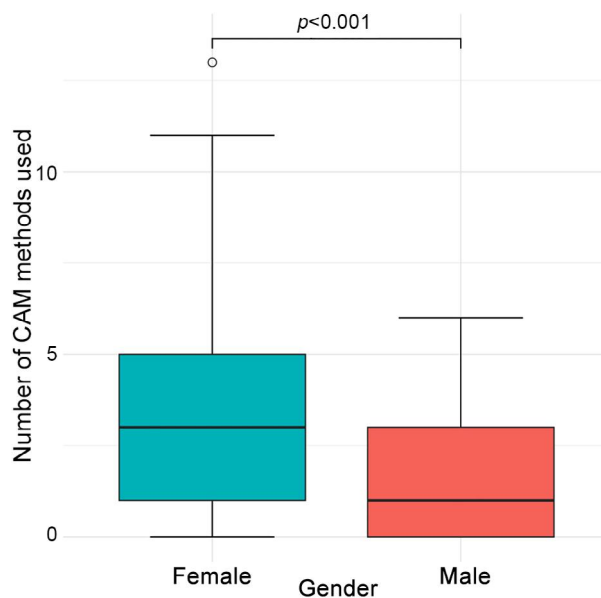


Figure 2. Number of complementary and alternative medicine (CAM) methods used by sex.

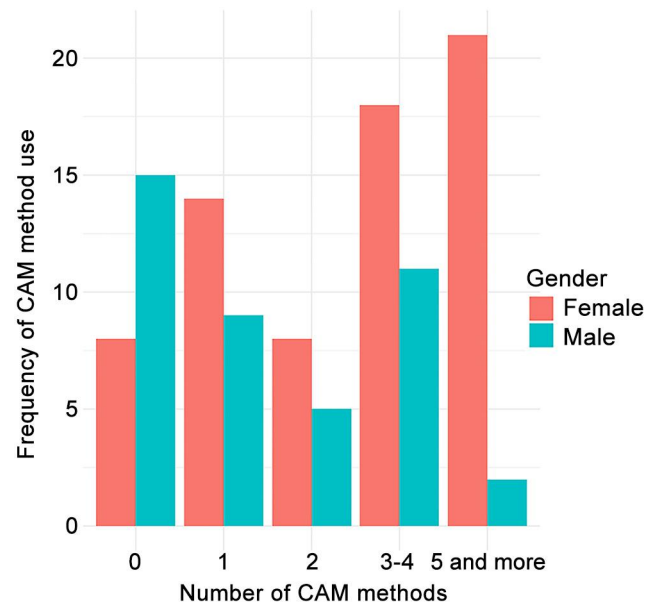


Figure 3. Frequency of complementary and alternative medicine (CAM) methods used by sex.

document and discuss these methods with patients. By integrating the questionnaire into routine clinical practice, healthcare providers can proactively identify CAM use, lowering the threshold for patient disclosure and fostering open communication (7). The color-coded system serves as a visual aid, offering immediate feedback on potential risks and interactions, thereby enhancing patient understanding.

The most commonly used CAM method was vitamin D, which was significantly more prevalent among women than men. This could be attributed to endocrine therapy for hormone receptor-positive breast cancer among female patients, as seen in previous studies (14, 15). Adequate blood level of 25-hydroxyvitamin D has been shown to have a positive impact on the prognosis of various solid tumors (16). Patients with breast cancer or prostate cancer experiencing musculoskeletal impairment under endocrine therapy may benefit from vitamin D supplementation if a deficiency is present (17, 18). In palliative care, vitamin D supplementation has been associated with improved quality of life, reduced pain, and lower opioid requirements (19).

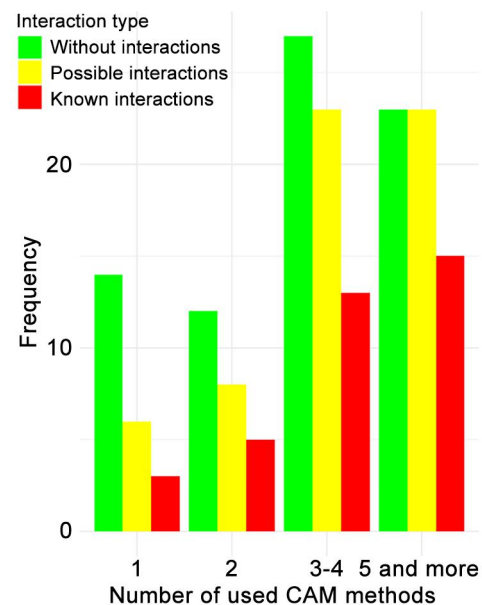


Figure 4. Number of complementary and alternative medicine (CAM) methods and possible interaction with oncological treatment.

In addition, sports and exercise were more commonly reported by female participants, reflecting a broader trend in health-conscious behavior. Interestingly, zinc was

among the top five CAM methods used by men but not women, which may suggest sex-specific preferences in supplementation choices.

Notably, a substantial proportion of patients (48.2%) used CAM methods with at least some possible interactions to oncological treatments, while 32.1% engaged in methods with known interactions. Given that the number of CAM methods used correlated with the likelihood of interactions, the implementation of structured screening tools, such as the S3 Guideline questionnaire, is crucial for identifying at-risk patients and preventing adverse effects (20).

Despite these findings, the desire for counseling on CAM use was similar between male and female patients, suggesting that both groups recognize the importance of professional guidance. However, several limitations need to be considered when interpreting our findings. In order to increase the response rate and enable low-threshold participation in the study, we collected the questionnaire anonymously before the start of radiotherapy, with no possibility of linking their responses to other patient data. As a result, potential bias factors such as socioeconomic status, education level, tumor stage and entity are not available. In fact, the response rate was still low (16.1%) in our study, which may limit generalizability, as patients with a pre-existing interest in CAM may have been more likely to participate.

Conclusion

The high prevalence of CAM use, particularly among female patients, highlights the importance of integrating standardized assessment tools into oncological care. The implementation of the questionnaire of the S3 Guideline Complementary Medicine in the Treatment of Oncological Patients can help mitigate risks, improve patient safety, and ensure that complementary treatments are aligned with evidence-based oncology practice. Notably, more female than male patients use CAM methods or medications with possible or known interactions, emphasizing the need for targeted counseling and risk assessment in this patient group.

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

Conceptualization: LK; Data curation: RG; Formal analysis: LK; Investigation: LK, RG, RR, MP, JR; Methodology: LK; Project administration: LK; Resources: CB; Software: Supervision: JH; Visualization: LK; Writing - original draft: LK; Writing - review & editing: all Authors. All Authors have read and agreed to the published version of the manuscript.

Acknowledgements

The Authors acknowledge the assistance of ChatGPT (Premium version, GPT-4o, March 2025 edition, accessed on 01-03-2025) for grammar correction and manuscript improvement.

Funding

No funding was received.

Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

References

- 1 Fjær EL, Landet ER, McNamara CL, Eikemo TA: The use of complementary and alternative medicine (CAM) in Europe. *BMC Complement Med Ther* 20(1): 108, 2020. DOI: 10.1186/s12906-020-02903-w
- 2 Horneber M, Bueschel G, Dennert G, Less D, Ritter E, Zwahlen M: How many cancer patients use complementary and alternative medicine. *Integr Cancer Ther* 11(3): 187-203, 2012. DOI: 10.1177/1534735411423920
- 3 Wortmann JK, Bremer A, Eich HT, Wortmann HP, Schuster A, Fühner J, Büntzel J, Muecke R, Prött FJ, Huebner J: Use of complementary and alternative medicine by patients with

- cancer: a cross-sectional study at different points of cancer care. *Med Oncol* 33(7): 78, 2016. DOI: 10.1007/s12032-016-0790-4
- 4 Gras M, Vallard A, Brosse C, Beneton A, Sotton S, Guyotat D, Fournel P, Daguenet E, Magné N, Morisson S: Use of complementary and alternative medicines among cancer patients: a single-center study. *Oncology* 97(1): 18-25, 2019. DOI: 10.1159/000499629
 - 5 Huebner J, Muenstedt K, Prott FJ, Stoll C, Micke O, Buentzel J, Muecke R, Senf B: Online survey of patients with breast cancer on complementary and alternative medicine. *Breast Care (Basel)* 9(1): 60-63, 2014. DOI: 10.1159/000360381
 - 6 Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Komplementärmedizin in der Behandlung von onkologischen PatientInnen, Langversion 1.1 (AWMF Registernummer: 032/0550L), 2021. Available at: https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Komplement%C3%A4r/Vers_1/LL_Komplement%C3%A4r_Langversion_1.1.pdf [Last accessed on May 18, 2025]
 - 7 Shalgouny M, Bertz-Lepel J, Fischer V, Weikersthal L, Herbin J, Meier-Höfig M, Mücke R, Rohe U, Stauch T, Stoll C, Troeltzsch D, Wittmann S, Kurz O, Naumann R, Huebner J: Introducing a standardized assessment of patients' interest in and usage of CAM in routine cancer care: chances and risks from patients' and physicians' point of view. *J Cancer Res Clin Oncol* 149(18): 16575-16587, 2023. DOI: 10.1007/s00432-023-05182-3
 - 8 Dubois C, Eisfeld H, Bauer F, Schmidt T, Kastrati K, Hochhaus A, Hübner J: Not all cancer patients with an interest in CAM are the same. Differences between patients with a CAM interest prior to the cancer diagnosis and those with first-time interest since diagnosis. *Complement Ther Med* 45: 167-171, 2019. DOI: 10.1016/j.ctim.2019.06.009
 - 9 Davis EL, Oh B, Butow PN, Mullan BA, Clarke S: Cancer patient disclosure and patient-doctor communication of complementary and alternative medicine use: a systematic review. *Oncologist* 17(11): 1475-1481, 2012. DOI: 10.1634/theoncologist.2012-0223
 - 10 Alsharif F: Discovering the use of complementary and alternative medicine in oncology patients: a systematic literature review. *Evid Based Complement Alternat Med* 2021: 6619243, 2021. DOI: 10.1155/2021/6619243
 - 11 Valerio MR, Scandurra G, Greco M, Gebbia V, Piazza D, Sambataro D: A survey on the prescribing orientation towards complementary therapies among oncologists in Italy: symptoms and unmet patient needs. *In Vivo* 39(2): 1000-1008, 2025. DOI: 10.21873/invivo.13905
 - 12 Cramer H, Cohen L, Dobos G, Witt CM: Integrative oncology: best of both worlds-theoretical, practical, and research issues. *Evid Based Complement Alternat Med* 2013: 383142, 2013. DOI: 10.1155/2013/383142
 - 13 Hoppe C, Büntzel J, von Weikersthal LF, Junghans C, Zomorodbakhsch B, Stoll C, Prott FJ, Fuxius S, Micke O, Richter A, Sallmann D, Huebner J: Usage of complementary and alternative methods, lifestyle, and psychological variables in cancer care. *In Vivo* 37(1): 106-114, 2023. DOI: 10.21873/invivo.13059
 - 14 Rabenberg M, Mensink G: Vitamin-D-status in Deutschland. *J Health Monit* 1(2): 36-42, 2016. DOI: 10.17886/RKI-GBE-2016-036
 - 15 Huebner J, Micke O, Muecke R, Büntzel J, Prott FJ, Kleeberg U, Senf B, Muenstedt K: User rate of complementary and alternative medicine (CAM) of patients visiting a counseling facility for CAM of a German comprehensive cancer center. *Anticancer Res* 34(2): 943-948, 2014.
 - 16 Bersanelli M, Cortellini A, Leonetti A, Parisi A, Tiseo M, Bordi P, Michiara M, Bui S, Cosenza A, Ferri L, Giudice GC, Testi I, Rapacchi E, Camisa R, Vincenzi B, Caruso G, Rauti AN, Arturi F, Tucci M, Santo V, Ricozzi V, Burtet V, Sgargi P, Todeschini R, Zustovich F, Stucci LS, Santini D, Buti S: Systematic vitamin D supplementation is associated with improved outcomes and reduced thyroid adverse events in patients with cancer treated with immune checkpoint inhibitors: results from the prospective PROVIDENCE study. *Cancer Immunol Immunother* 72(11): 3707-3716, 2023. DOI: 10.1007/s00262-023-03522-3
 - 17 Arul Vijaya Vani S, Ananthanarayanan PH, Kadambari D, Harichandrakumar KT, Niranjana R, Nandeesh H: Effects of vitamin D and calcium supplementation on side effects profile in patients of breast cancer treated with letrozole. *Clin Chim Acta* 459: 53-56, 2016. DOI: 10.1016/j.cca.2016.05.020
 - 18 Rastelli AL, Taylor ME, Gao F, Armamento-Villareal R, Jamalabadi-Majidi S, Napoli N, Ellis MJ: Vitamin D and aromatase inhibitor-induced musculoskeletal symptoms (AIMSS): a phase II, double-blind, placebo-controlled, randomized trial. *Breast Cancer Res Treat* 129(1): 107-116, 2011. DOI: 10.1007/s10549-011-1644-6
 - 19 Helde-Frankling M, Höijer J, Bergqvist J, Björkhem-Bergman L: Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections-Results from a matched case-control study. *PLoS One* 12(8): e0184208, 2017. DOI: 10.1371/journal.pone.0184208
 - 20 Wolf CPJG, Rachow T, Ernst T, Hochhaus A, Zomorodbakhsch B, Foller S, Rengsberger M, Hartmann M, Huebner J: Complementary and alternative medicine (CAM) supplements in cancer outpatients: analyses of usage and of interaction risks with cancer treatment. *J Cancer Res Clin Oncol* 148(5): 1123-1135, 2022. DOI: 10.1007/s00432-021-03675-7