Dissertation

Complementary and alternative medicine in supportive cancer care: patient perspectives and possible ways for its integration

submitted by

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Declaration

I hereby declare that this thesis is my own original work and that I have fully acknowledged by name all those individuals and organizations that have contributed to the research for this thesis. Due acknowledgement has been made in the text to all other material used. Throughout this thesis and in all related publications I followed the Guidelines of the Medical University of Graz on Good Scientific Practice.

Graz, January 2024 *Matthias Huemer eh*

Disclosures

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Symptom clusters associated with complementary and alternative medicine use by cancer patients: A cross-sectional study

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Mapping the clinical practice of traditional, complementary, and integrative medicine in oncology in Western countries: A multinational cross-sectional survey

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List of abbreviations

AIC *Akaike information criterion*

AIDS *acquired immunodeficiency syndrome*

AIIA *aromatase inhibitor induced arthralgia*

ASCO *American Society of Clinical Oncology*

AWMF *Association of the Scientific Medical Societies in Germangy*

BFI *Brief Fatigue Inventory*

BIC *Bayesian information criterion*

BPI *Brief Pain Inventory*

CAM complementary and alternative medicine

CI *confidence interval*

CINV *chemotherapy induced nausea and vomiting*

CIPN *chemotherapy induced polyneuropathy*

COVID-19 *coronavirus disease 2019*

CRF *cancer-related faituge*

CYP450 *cytochrome P450*

ESAS *Edmonton Symptom Assessment Scale*

HCAMQ *Holisitic Complementary and Alternative Medicine Questionnaire*

HH *holistic health*

HIV *human immunodeficiency virus*

HR *hazard ratio*

IQR *interquartile range*

KM *Komplementärmedizin*

LPA *latent profile analysis*

MBSR *mindfulness-based stress reduction*

MD *mean difference*

mg *milligram*

NCCN *National Comprehensive Cancer Network*

NCI *National Cancer Institute*

NRS *numerical rating scale*

OR *odds ratio*

PhD *doctor of philosophy*

QoL *Quality of Life*

REDCap *Research Electronic Data Capture*

RINV *radiotherapy induced nausea and vomiting*

RR *risk ratio*

SD *standard deviation*

SMD *standardized mean difference*

USA *United States of America*

WHO *World Health Organization*

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Abstract

Background:

Cancer patients commonly turn to complementary and alternative medicine (CAM) once they have been diagnosed with cancer. Various factors have been described to contribute to a higher willingness to use CAM during the disease trajectory. However, to date, no thorough assessment of patterns of CAM use has been performed among Austrian cancer patients. This study explored factors influencing CAM use in Austrian cancer patients, focusing on symptom clusters and demographical characteristics as predictors. Additionally, the study assessed the evidence-informed practices and research literacy among CAM practitioners involved in cancer patient care. Gaining a deeper understanding of their clinical practice and the role of research in it will facilitate better interdisciplinary collaboration between oncologists and CAM practitioners to benefit cancer patients.

Methods:

We designed two comprehensive cross-sectional studies involving Austrian cancer patients and CAM practitioners from Austria, Germany, the United States of America, Australia, and New Zealand. Patient data encompassed socio-demographic details, clinical characteristics, patterns of CAM use, and symptom assessment. To identify distinct symptom clusters, we performed a latent profile analysis. We then used bivariate and multivariate analysis to identify predictive factors for CAM use. CAM practitioners provided insights into their demographics, clinical practices, information sources, and the role of research in their clinical practice through an international online survey. We used descriptive statistics and qualitative analysis to describe differences between the participating countries.

Results:

Among the 171 cancer patients, 63.7% utilized CAM, with prevalent therapies including homeopathy, supplements, herbs, massage, and acupuncture. However, only 42.2% of CAM users disclosed their utilization to their treating oncologist. Symptom cluster analysis identified four distinct clusters, with the drowsiness-depression-anxiety cluster showing a 3.83-fold higher likelihood of CAM use. Multivariate analysis revealed no additional predictors beyond socio-demographic factors. Of the 404 CAM practitioners, 62.9% treated cancer patients, predominantly utilizing acupuncture and herbal treatments. Effective management of pain, depression, nausea, and fatigue was perceivably best achieved with acupuncture, while herbal medicine was preferred for addressing constipation, according to our study respondents. CAM practitioners commonly used acupuncture and herbs concurrently with biomedicine for

supportive care, aiming to alleviate treatment side effects. However, only 28.0% maintained contact with treating oncologists. Among all respondents, 87.4% were interested in research, and 62.6% stated that research influenced their practice of acupuncture. In general, CAM practitioners rated the importance of research in their daily practice as moderate. However, they still rated experts' opinions as the most reliable information source. We further found country-specific differences concerning the educational background of CAM practitioners, with the most significant proportion of medical doctors performing acupuncture in Austria.

Conclusion:

Our study found symptom clusters representing valuable predictors for CAM use among cancer patients. The development of the drowsiness-depression-anxiety cluster may serve as an indicator to reassess the CAM use of patients by oncologists, suggesting continuous monitoring of the symptom burden during the patient’s disease trajectory. However, we also identified a communication gap between oncologists and patients. Promoting proactive patient-centered communication into clinical practice may identify potentially harmful CAM practices and offer the chance to guide patients in their choice of CAM treatments, further strengthening the physician-patient relationship. Austrian acupuncturists and herbalists commonly treat cancer patients in their clinics. They are aware of the risks and concerns associated with this vulnerable patient cohort, which is why they gain general clinical experience before starting to treat cancer patients. However, they predominantly rely on experts' opinions rather than research papers to inform their clinical practice. Emphasizing basic research skills during the education of CAM practitioners may improve their research literacy and foster better interdisciplinary collaboration with oncologists.

Zusammenfassung

Hintergrund:

Tumorpatient*innen greifen häufig auf Komplementärmedizin (KM) zurück, sobald sie mit einer malignen Grunderkrankung diagnostiziert werden. In vergangenen Studien wurden unterschiedliche Faktoren beschrieben, die die Bereitschaft KM während des Krankheitsverlaufs zu nutzen erhöhen. Bisher wurde jedoch keine gründliche Erhebung zur KM-Nutzung unter österreichischen Tumorpatient*innen durchgeführt. Diese Studie untersuchte Faktoren, die die Anwendung von KM in österreichischen Tumorpatient*innen beeinflussen, wobei der Schwerpunkt auf Symptomclustern und demografischen Merkmalen als Prädiktoren lag. Zusätzlich erhob die Studie die evidenzbasierte Praxis und Forschungskompetenz von Komplementärmediziner*innen, welche Tumorpatient*innen betreuen. Ein tieferes Verständnis ihrer klinischen Praxis und der darin spielenden Rolle von wissenschaftlichen Erkenntnissen wird die interdisziplinäre Zusammenarbeit zwischen Onkolog*innen und Komplementärmediziner*innen zum Nutzen der Tumorpatient*innen verbessern.

Methoden:

Wir führten zwei umfassende Querschnittsstudien durch, an denen österreichische Tumorpatient*innen und Komplementärmediziner*innen aus Österreich, Deutschland, den Vereinigten Staaten, Australien und Neuseeland teilnahmen. Die Patient*innendaten umfassten soziodemografische Charakteristika, klinische Merkmale, Nutzung von KM und eine umfassende Erhebung der klinischen Symptome. Um unterschiedliche Symptomcluster zu identifizieren, führten wir eine latente Profilanalyse durch. Mittels bivariater und multivariater Analysen, wurden prädiktive Faktoren für die Nutzung von KM identifiziert. Komplementärmediziner*innen gaben Einblicke in ihre demografischen Daten, klinischen Praktiken, Informationsquellen und die Rolle von Forschung in ihrer klinischen Praxis. Unter Verwendung von deskriptiver Statistik und qualitativer Analysen wurden Unterschiede zwischen den teilnehmenden Ländern beschrieben.

Ergebnisse:

Von den 171 Tumorpatient*innen nutzten 63,7% KM, wobei vorwiegend Homöopathie, Nahrungsergänzungsmittel, Kräuter, Massage und Akupunktur angewendet wurden. Allerdings teilten nur 42,2% der Patient*innen ihren Gebrauch von KM dem*der behandelnden Onkolog*in mit. Die Cluster-Analyse ergab vier unterschiedliche Symptomgruppen, wobei der Cluster „Müdigkeit-Depression-Angst“ mit einer um das 3,83-fache höherer Wahrscheinlichkeit

für einen Gebrauch von KM assoziiert war. Unsere multivariate Analyse zeigte keine zusätzlichen Prädiktoren. Von den 404 Komplementärmediziner*innen behandelten 62,9% Tumorpatient*innen und nutzten dafür hauptsächlich Akupunktur und Kräutertherapien. Eine effektive Behandlung von Schmerzen, Depression, Übelkeit und Müdigkeit wurde laut unseren Studienteilnehmer*innen am besten mit Akupunktur erreicht, während Kräutermedizin für die Behandlung von Obstipation bevorzugt wird. Komplementärmediziner*innen verwendeten Akupunktur und Kräuter oft parallel zur konventionellen Medizin als supportive Therapie um die Nebenwirkungen der tumorspezifischen Therapien zu lindern. Allerdings standen nur 28,0% in Kontakt zu den behandelnden Onkolog*innen. Unter allen Befragten zeigten 87,4% Interesse an Forschung und 62,6% gaben an, dass Forschung die Anwendung ihrer Akupunktur beeinflusste. Im Allgemeinen bewerteten Komplementärmediziner*innen die Bedeutung von Forschung in ihrer täglichen Praxis als moderat. Allerdings stuften sie Expert*innenmeinungen weiterhin als zuverlässigste Informationsquelle ein. Wir fanden länderspezifische Unterschiede hinsichtlich der Ausbildung von Komplementärmediziner*innen, wobei der höchste Anteil an Ärzt*innen unter den Akupunkteur*innen in Österreich praktizierte.

Schlussfolgerung:

Unsere Studie ergab, dass Symptomcluster nützliche Prädiktoren für die Anwendung von KM bei Tumorpatient*innen sind. Die Entwicklung des „Müdigkeit-Depression-Angst“-Clusters könnte als Indikator dienen, um den Gebrauch von KM im Krankheitsverlauf von Tumorpatient*innen durch Onkolog*innen neu zu bewerten. Hierfür sollte die Symptomlast der Patient*innen kontinuierlich überwacht werden. Jedoch zeigte sich eine unzureichende Kommunikation zwischen Onkolog*innen und Patient*innen bezüglich des Gebrauchs von KM. Eine proaktive, patientenzentrierte Kommunikation könnte potenziell schädliche Therapien identifizieren und die Möglichkeit bieten, Patient*innen bei der Wahl von KM zu unterstützen, wodurch weiters die Arzt-Patienten-Beziehung gestärkt werden könnte. Österreichische Akupunkteur*innen und Kräutertherapeut*innen behandeln häufig Tumorpatient*innen in ihren privaten Kliniken und sind sich der damit verbundenen Risiken und Herausforderungen bewusst. Daher sammeln sie zuerst allgemeine klinische Erfahrung, bevor sie beginnen Tumorpatient*innen zu begleiten. Allerdings verlassen sie sich hauptsächlich auf Expert*innenmeinungen anstelle von Forschungsarbeiten, um sich zu informieren. Die Vermittlung grundlegender Forschungsfähigkeiten während der Ausbildung von Komplementärmediziner*innen könnte ihre Forschungskompetenz verbessern und eine bessere interdisziplinäre Zusammenarbeit mit Onkolog*innen fördern.

1 Introduction

1.1 Supportive Cancer Care

Cancer is one of the leading causes of death worldwide and is associated with a significant disease burden, limiting the quality of life of the patients (1). A cancer diagnosis affects various dimensions, exerting profound impacts on physical, psychological, social, and spiritual levels. As a result, an effective cancer treatment approach necessitates a comprehensive, multidisciplinary strategy. This approach not only targets the cancer itself but also addresses the diverse needs of the patient throughout the course of the illness and post-disease (2). Supportive cancer care focuses on the support of cancer patients in addition to cancer-specific treatment and includes symptom management, psycho-oncological support and rehabilitation. Originating within the medical oncology domain, supportive cancer care is not confined to a specific discipline but involves multiple disciplines. Consequently, the responsibility for providing comprehensive support to cancer patients falls upon multiple health disciplines, recognizing the holistic nature of the challenges posed by the disease (3).

Supportive cancer care aims to preserve the patients physical, psychological and social state to lower the diseases impact on their health-related quality of life. Recent systematic reviews have yielded conclusive findings that supportive cancer care significantly enhances cancer-specific treatment tolerance and adherence (4). This underscores the pivotal role of supportive cancer care in not only improving the overall well-being of patients but also ensuring the effective delivery and continuity of cancer-specific treatments. Consequently, this contributes to an increased likelihood of positive treatment outcomes, including prolonged survival or cure. The relationship between supportive cancer care and cancer-specific treatment underscores their equal importance in delivering a comprehensive and multidimensional approach to cancer treatment (3). Recognizing supportive cancer care as an integral part of oncology is crucial for optimizing the overall therapeutic strategy and maximizing the potential for favorable patient outcomes.

In addition to active interventions aimed at enhancing health-related quality of life, supportive cancer care encompasses counseling patients in various aspects of life, often referred to as patient navigation (5). Patient navigation involves guiding individuals through their entire disease trajectory, addressing questions related to diagnosis, treatment plans, and supportive measures. The overall goal is to formulate an individualized treatment plan that spans from the moment of diagnosis onward (5). Within the counseling process, patients are encouraged to express their concerns, wishes, and needs, with the expectation of receiving evidence-based

guidance on how to address these aspects comprehensively. This approach aims to facilitate multidimensional cancer care tailored to the specific circumstances and preferences of each patient.

1.2 Palliative Care

Similar to supportive cancer care, palliative care aims to preserve and enhance the health-related quality of life for patients facing advanced, incurable diseases, including cancer. However, palliative care's emphasis is not on prolonging life, and certainly not on curing the underlying disease (6). When it becomes evident that a cancer-specific treatment no longer benefits the patient and is discontinued, the disease will inevitably progress until death (7). Accepting death as a natural and unavoidable process, palliative care aims to alleviate and address the accompanying symptoms of disease progression, offering guidance in psychological, social, and spiritual aspects for both the patient and their caregivers (8).

The initiation of palliative care is not solely bound to the termination of cancer-specific treatment. Given the ongoing advancements and increased efficacy of cancer therapies, cancer is evolving into a chronic condition necessitating a continuous provision of both supportive and palliative care (7). Consequently, the concept of integrated early palliative care has been increasingly recognized within medical oncology. Current clinical guidelines recommend referring patients diagnosed with advanced cancer to palliative care teams at the time of diagnosis (7).

Unlike supportive cancer care, palliative care is typically administered by a specialized multidisciplinary team including physicians, nurses, psychologists, physiotherapists, and social workers. Another distinctive feature of palliative care in Austria is the widespread availability of mobile palliative care teams that conduct home visits for patients and their families (6). A Cochrane systematic review and meta-analysis demonstrated that mobile palliative care services could reduce hospital admission rates for patients with advanced diseases, including cancer, chronic obstructive pulmonary disease, congestive heart disease, multiple sclerosis, and human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) (9). Consequently, providing home palliative care has the potential to prevent serious medical issues in advanced diseases and reduce the amount of patient visits to emergency clinics.

Comparing supportive cancer care and palliative care directly, they share many similarities in terms of the interventions they perform. However, the fundamental difference lies in their respective goals. While both care models aim to strengthen and preserve the patients' physical

state and quality of life, the objective of supportive care is to ensure and continue cancer-specific treatment with the ultimate goal of prolonging life or curing cancer. In contrast, the goal of palliative care is to alleviate the process of progressive disease up until death (10).

1.3 Complementary and Alternative Medicine

The definition of complementary and alternative medicine (CAM) remains a subject of ongoing debate, with various attempts made to establish frameworks for classifying health resources and therapies as either CAM or "conventional medicine." One of the most prevalent and straightforward definitions characterizes any health practice not fully integrated into a public healthcare system, performed either adjunctively or instead of conventional medicine, as CAM (11).

The National Cancer Institute (NCI) published detailed definitions and classifications of CAM, which are widely adopted in research (12). This classification framework categorizes health practices based on their intervention type and theoretical background into five distinct categories, as detailed in Table 1 (12).

Table 1: Classification framework of the National Cancer Institute (12).

Category	**Description**
Mind-body therapies	Practices combining mental focus and body movements aiming to relax the body and mind.
Biologically-based practices	Therapies using natural products or dietary supplements to promote health or treat health issues.
Manipulative and body-based practices	Physical therapies manipulating specific body parts.
Energy healing	Therapies that are based on concepts of balancing a vital energy or energy field of the body.
Whole medical systems	Complete healing systems based on different philosophical, traditional, and cultural believes.

It is crucial to recognize that certain CAM therapies are rooted in traditional medical practices originating from the unique cultural background of a country. While these traditional practices

may sometimes differ significantly from modern scientific principles, it is necessary to differentiate them from pseudoscientific and esoteric belief systems, which typically lack this cultural background and historical context. Traditional medical practices constitute an integral part of a country's culture and may even serve as the primary source of healthcare for individuals in some rural areas (13).

The global practice of traditional and complementary medicine is on the rise, gaining popularity among patients, particularly in Western countries. This trend poses challenges for policymakers, health professionals, and public healthcare systems, necessitating attention to issues related to safety, regulation, quality control, and the effectiveness of CAM therapies (13). In response to these challenges, the World Health Organization (WHO) published the strategy paper "World Health Organization traditional medicine strategy: 2014-2023" in 2013. The objective of this paper is to provide a comprehensive overview of the current state of CAM therapies worldwide, identify common issues on global and regional levels, and offer guidance on facilitating the integration of CAM therapies into national healthcare systems (13).

A central component of this strategy involves reinforcing the research and regulation of CAM therapies within individual countries. This encompasses assessing the actual prevalence of CAM use within the country's population, analyzing reasons and usage patterns, and monitoring the education and training of CAM practitioners (13).

1.4 Integrative Oncology

The term “complementary and alternative medicine” faced persistent criticism, as it combines the contradictory words “complementary” and “alternative”, each having a distinct meaning (14). Most patients choose to incorporate complementary therapies alongside conventional treatments rather than replacing them. This tendency towards a combined approach shows the inadequacy of the term "complementary and alternative medicine" in accurately reflecting the preference of cancer patients to utilize complementary therapies in addition to conventional cancer treatment. In response to this criticism, Deng et al. proposed the adoption of the term "integrative medicine" or "integrative oncology" as an alternative to "CAM” (15). This term aims to better describe the collaborative nature of patient choices, emphasizing the integration of conventional and complementary therapies within the overall treatment framework.

Witt et al. further elaborated the definition of integrative oncology and presented a comprehensive framework defining its components (16). Accordingly, integrative oncology is an evidence-informed and patient-centered practice incorporating mind-body therapies,

natural products, and lifestyle modifications that are not fully implemented in public health care alongside conventional tumor-specific treatments and supportive cancer care. Witt et al. defined the aims of integrative oncology as promoting the quality of life, optimize health and clinical outcomes of cancer patients (16).

The practice of integrative oncology requires a comprehensive knowledge of the available scientific evidence concerning complementary therapies. The overall aim is to provide safe and effective treatments that were proven to benefit cancer patients. Many leading cancer centers in North America including the Memorial Sloan Kettering Cancer Center and MD Anderson implemented integrative oncology and established clinical departments focusing on the provision and research of evidence-based complementary therapies in order to meet the responsibility of assuring a patient-centered and safe medical care (16-18).

1.5 Practice of complementary and alternative medicine in Austria

In Austria, the prescription of CAM for health purposes requires a medical degree and is regulated by the “Ärztegesetz” (19). The Austrian Medical Chamber plays a pivotal role in regulating the education of medical doctors in CAM, offering specific certification programs for a range of modalities, including acupuncture, traditional Chinese medicine, homeopathy, anthroposophical medicine, Kneipp medicine, manual therapy, neural therapy, orthomolecular medicine, phytotherapy, and therapy by Dr. Franz Xaver Mayr (20). Additionally, various Austrian medical universities offer elective courses about certain CAM modalities or the use of CAM in general (21, 22).

Despite these regulations, some biologically based CAM therapies are marketed as dietary supplements over the counter and remain inadequately regulated. Furthermore, practices of energy healing are legally conducted, provided their health claims are confined to the "wellbeing" of clients, with no treatment of physical issues (23). This low regulation of esoteric and pseudoscientific practices has been repeatedly criticized in Austria after Dr. Ryke Geerd Hamer treated an estimated 20,000 cancer patients in Austria and other European countries using his self-established “new German medicine.” Several of his patients died, highlighting the potential risks associated with insufficient regulation in the field of alternative therapies (24).

In Austria, the general populations trust in CAM practitioners is significantly improved if they are medical doctors and hold a license certified by an institution like the Austrian Medical Chamber (25). Hence, limiting the practice of CAM to medical doctors seems to be a

meaningful way to protect patients from dubious CAM providers who could mislead them in medical decisions. However, the case of Dr. Ryke Geerd Hamer also shows that even CAM practitioners that hold a medical doctor's degree may fall for pseudoscientific and esoteric practices which may cause tremendous harm to individuals and the general public (24). Furthermore, Austrian medical doctors with a background in CAM disciplines exhibit a tendency toward greater skepticism regarding contemporary research methodologies, as indicated by findings from a small-scale qualitative study surveying 11 Austrian CAM practitioners, mostly homeopaths (26). Additional studies found that this general distrust among CAM practitioners towards scientific methodology is, in part, attributed to a distinct emphasis on the generation of evidence and a low level of research literacy. The rigorous methodology of evidence-based medicine is frequently perceived as insufficient in capturing the effects of certain CAM modalities. Consequently, the assessment of efficacy tends to focus on the personal experiences of CAM practitioners and anecdotes from colleagues (27, 28).

1.5.1 Role of research literacy in evidence-based medicine

Research literacy among health practitioners including medical doctors and CAM practitioners is the fundamental principle of evidence-based medical practice, providing them with the skills and knowledge to critically evaluate and incorporate the latest research findings into their clinical decision-making (29). A high level of research literacy ensures medical doctors to stay informed about advancements in medical science, allowing them to offer patients the most current and effective treatments. Furthermore, it motivates them for continuous learning and professional development within the medical community (30). Practitioners with a higher level of research literacy are better positioned to engage in scholarly activities, contribute to medical literature, and participate in clinical trials, fostering a dynamic and progressive healthcare environment (31). Ultimately, enhancing research literacy among medical doctors and CAM practitioners not only improves patient care by ensuring the application of evidence-based approaches but also contributes to the advancement of medical knowledge and the evolution of healthcare standards (32). Concerning CAM in particular, research literacy plays a crucial role for both oncologists and CAM practitioners (15). Oncologists must stay well-informed about the efficacy and safety profiles of various CAM modalities to provide insightful guidance to their patients (33). Simultaneously, CAM practitioners bear the responsibility of delivering their therapies in a manner that aligns with evidence-based practices, ensuring the current highest standards of care. The relationship between research literacy and effective practice supports the need for a collaborative and informed approach between oncologists and CAM

practitioners in the sense of integrative oncology, where the expertise of both disciplines overlap for the optimal benefit of the patient (15).

1.6 CAM use in oncology

1.6.1 Prevalence and demographical factors

Research across various global healthcare settings consistently reveals a substantial prevalence of CAM utilization among oncology patients. Recent systematic reviews from cross-sectional studies indicate that a significant proportion of cancer patients, ranging from 22% to 80%, integrate CAM into their overall cancer care. This prevalence is influenced by factors such as cultural norms, individual beliefs, and the availability of CAM services within healthcare systems(11, 34-36).

Keene et al. conducted a systematic review to examine the prevalence and demographic predictors of CAM utilization among cancer patients undergoing active cancer treatment. The study analyzed data from 61 studies from 27 countries published between 2009 and 2019 and found a mean prevalence of 51% (11). This finding highlights a significant increase in CAM utilization compared to earlier reviews that focused on studies published between 1970 and 1998 (37). Specifically, there has been a 20% rise in the use of CAM among cancer patients, showing the increasing popularity of complementary approaches within this patient group (11). In their study, Keene et al. further identified a correlation between CAM utilization and specific demographic characteristics, noting that young females with higher education and income levels were more likely to use CAM. The authors suggested potential mechanisms to explain this relationship. One consideration is that CAM is typically not integrated into public healthcare systems in most countries, and therefore, it may not be covered by standard insurance plans. Patients with higher education are more likely to have a better paid profession allowing them to privately invest in CAM therapies (11).

In another systematic review, Hill et al. reported a prevalence of CAM utilization among cancer patients in low-income countries across Asia, Africa, and South America, reaching a substantial percentage of 54.5%. Only 26.7% of these individuals reported a combination of CAM and modern cancer treatments (34). This finding differs to the outcomes observed by Keene et al., whose systematic review predominantly included studies from Western countries (11). The observed higher prevalence of CAM use in low-income countries might be attributed to factors such as the limited accessibility or high cost of modern biomedical therapies compared to traditional and complementary medicine (34). In regions where conventional cancer treatments

may be scarce or too expensive, CAM appears to be a viable and often more accessible option. Additionally, the cultural background and belief systems prevalent in these areas may play an important role. Traditional therapies, deeply rooted in cultural practices, may reach a higher level of trust among individuals, particularly those in rural settings, contributing to the widespread utilization of CAM in low-income countries (34).

In Europe, the prevalence of CAM utilization is reported as 35.9% according to a comparative study conducted by Molassiotis et al. (38). This percentage considerably varied across the 14 participating countries, ranging from 14.8% to 73.1%. In contrast to the findings from Keene et al.'s systematic review, the pooled prevalence in European countries was comparatively lower (11). It is also important to note that the European survey by Molassiotis et al. was published over a decade ago in 2005 and may not compare to the current prevalence of CAM utilization (38). On the other hand, the differences to Keene et al.'s results could suggest an increasing popularity of CAM over time (11). However, an important limitation of this survey is that it did not include Austria and other European countries, thereby limiting its generalizability over the entire European context. The absence of Austrian data highlights the need for more comprehensive and up-to-date research to provide a more accurate representation of CAM utilization patterns.

1.6.2 Patient-reported reasons for CAM use

The factors influencing why patients choose to utilize CAM alongside conventional cancer treatments are complex and not fully understood. The motivations behind range from fighting cancer to spiritual reasons. Keene et al. performed a topic analysis of patient reported reasons across 61 studies in their systematic review (11). Their analysis identified seven distinct themes that varied in prevalence among cancer patients. The most common theme was the desire to influence cancer itself, followed by the intention to address cancer-related complications (whether linked to the disease or its treatment). Additionally, patients expressed a wish for a holistic treatment approach, a motivation to improved general health, a desire to take control of their therapy and treatment related decisions, recommendations from others, and a strong belief in CAM, often coupled with dissatisfaction with conventional cancer treatment (11).

With the diagnosis of cancer, patients are suddenly confronted with a life-threatening and debilitating illness. This circumstance has led to the hypothesis that the utilization of CAM is associated with an existential distress, urging patients to explore and experiment with every available option that might contribute the fight against cancer (39). Interestingly, Söllner et al.'s

research did not find a direct association between CAM utilization and the perceived distress of cancer patients. Instead, they identified a link between CAM use and active coping behavior. It appears that patients turn to CAM as a possibility of taking self-directed action and managing the emotional challenges associated with feelings of hopelessness (40). In alignment with this perspective and the patient reported reasons summarized by Keene et al. (11), van Dongen et al. proposed that the use of CAM represents a form of self-management behavior, correlating with higher levels of patients' perceived self-efficacy in their systematic review (41). This heightened self-efficacy, in turn, is directly related to improved symptom management and a higher quality of life for cancer patients. This positive correlation is attributed to an increased engagement in active self-care practices and the adoption of a mindful lifestyle (42).

1.6.3 Physical disease burden and CAM use

It was repeatedly suggested that certain symptoms, such as pain, anxiety, or depression, may be linked to a greater willingness of cancer patients to turn to CAM. This is also supported by the reasons reported by patients, as mentioned earlier (11). However, when studies specifically analyzed the relationship between individual symptoms and CAM utilization in cancer patients and survivors, they did not find a clear positive correlation between the severity of symptoms and the use of CAM (43, 44). Interestingly, instead of symptom severity, studies revealed that the interference of symptoms with daily life was strongly associated with a higher likelihood of CAM utilization (44). This implies that it is not just the intensity of symptoms that drives patients towards CAM, but rather how these symptoms impact their day-to-day functioning. However, measuring single symptoms does not take interactions between symptoms into account. A recent advancement in symptom research is the concept of symptom clusters, recognizing that symptoms in cancer patients often appear in interdependent groups (45). In these clusters, each symptom within a group can significantly impact the others, creating a self-perpetuating cycle that enhances the overall perceived symptom burden for the patient. In contrast to single symptoms, these clusters have a greater interference with the patient's quality of life (46, 47). The relationship between the utilization of CAM and symptom clusters has not been addressed in research to date.

1.6.4 Spirituality and CAM use

Another notable phenomenon observed in cancer patients is spiritual distress caused by the diagnosis of cancer or with the progression of the disease. Patients start reflecting on their

meaning and purpose in life, question their destiny, and may struggle with past decisions and choices (48). This existential distress, in turn, profoundly impacts their overall quality of life (49). Interestingly, religious people are less likely to experience a negative impact of spiritual issues on their quality of life than individuals without religious beliefs (50). However, non-religious people may still identify as spiritual and find guidance in non-theistic, mystical, or esoteric traditions eliciting similar preventive effects on their quality of life as people believing in traditional religious practices. In general, it does not matter which source of spiritual guidance patients choose; the positive effects rely on the strength they have in their individual belief system (51). Trinkhaus et al. studied the relationship between CAM and spirituality and found that spiritual cancer patients often turn to CAM to fulfill their spiritual needs (52). Complementary therapies often root in traditional philosophical and epistemological systems providing resources for the apparent explanation of principally unsolvable questions of life (53). Despite the limitations in providing definitive solutions or cures for their circumstances, patients may find a sense of reassurance in these explanations. Recognizing the potential role of CAM in fulfilling spiritual needs, Steinhorn et al. proposed considering CAM as a means of spiritual care, particularly for patients who are drawn to it. Moreover, when healthcare practitioners assess the use of CAM in cancer patients during routine care, it is important to acknowledge that its utilization may carry a profound spiritual meaning for the patients. This spiritual dimension should be respected in patients without a confession equally to religious beliefs, emphasizing the importance of a holistic and culturally sensitive approach to patient care (54).

1.7 Clinical efficacy of CAM in oncology

The effectiveness of complementary therapies used alongside conventional medical treatments for cancer has been the subject of increasing research over the past decades, leading to the establishment of a developing clinical and scientific research field. The growing evidence related to CAM during oncological, supportive and palliative treatment has recently been summarized in a clinical guideline published by the Association of the Scientific Medical Societies in Germany (AWMF) in 2021 (55). It's important to note that, despite the efforts to create this guideline, the authors acknowledge the challenges associated to summarizing the evidence for CAM. The vast amount of possible current and evolving therapy modalities and the somewhat unclear definition of CAM make a comprehensive summary challenging (55). As a result, the guideline represents an initial effort toward providing an overview of various common CAM treatments. Its primary aim is to serve as a reference work for clinicians across all medical fields involved in cancer care to meaningfully discuss this diverse topic with their

patients. However, the guideline remains a valuable resource, offering insights concerning the effectiveness for some CAM modalities and providing recommendations for specific therapies in selected indications. The treatment modalities with a positive recommendation include: acupressure, acupuncture, anthroposophical complex therapy, some herbal therapies, physical activity and sport, homeopathy, meditation, mindfulness-based stress reduction, selene, Tai Chi/Qigong, and yoga (55). The respective indications are summarized in Table 2.

Table 2: Indications with positive recommendation by the AWMF for the use of CAM modalities in cancer patients (55).
CRF: cancer-related fatigue; CINV: chemotherapy-induced nausea and vomiting, RINV: radiotherapy-induced nausea and vomiting; AIIA: aromatase inhibitor-induced arthralgia; QoL: quality of life; CIPN: chemotherapy-induced polyneuropathy

Intervention	**Indications**
Acupressure	CRF, cancer pain, CINV, RINV
Acupuncture	AIIA, cancer pain, CRF, anxiety, depression, sleep disorders, constipation after surgery, cognitive impairment during chemotherapy, QoL, menopausal flush, CIPN, CINV, xerostomia
Anthroposophical complex therapy	Sleep disorders, CRF
Cimicifuga racemose	Menopausal symptoms
Ginseng	CRF
Ginger	CINV
Mistletoe	QoL
Physical activity and sport	CRF, QoL
Homeopathy	QoL
Meditation	Anxiety, depression, QoL, stress
Mindfulness-based stress reduction	Anxiety, depression, sleep disorders, CRF, cognitive impairment during chemotherapy, QoL, menopausal symptoms
Selene (Natrium selenite)	Diarrhea during radiotherapy, oral mucositis
Tai Chi/Qigong	Sleep disorders, CRF, depression, QoL
Yoga	CRF, anxiety, depression, sleep disorders, cognitive impairment during chemotherapy, QoL, menopausal symptoms

Within their guideline, the AWMF lists the most recommendations for acupuncture, mindfulness-based stress reduction (MBSR) and yoga. Therefore, these three interventions will be further discussed in detail. It's noteworthy that recommendations for biologically based practices are relatively scarce, indicating a potential lack of sufficient scientific evidence supporting their effectiveness or safety in the context of cancer patients (55).

1.7.1 Acupuncture

Acupuncture is one of the most globally utilized complementary therapies, experiencing a growing trend in recommendation and usage for addressing cancer-related symptoms (56). Its primary application is notably in the management of painful conditions associated with cancer, including general cancer pain (57, 58), aromatase inhibitor induced arthralgia (AIIA) (59, 60) and chemotherapy-induced polyneuropathy (CIPN) (61, 62). A recent meta-analysis conducted by He et al. found a clinical meaningful average pain reduction of -1.38 (95% confidence interval [CI] -2.13 to -0.64) points on the numerical rating scale (NRS) compared to sham acupuncture (57). Moreover, the analysis indicated a significant reduction in the mean daily morphine dosage by -30 milligram (mg) (95% CI -37.5mg to -22.5mg), providing additional support for the efficacy of acupuncture as a complementary approach to conventional medicine (57). Similar results were found in other cancer-related painful conditions, reducing the pain intensity significantly by -1.14 (95% CI 1.87 to −0.42) on the NRS in patients with CIPN (62) and by -3.81 (95% CI -5.15 to -2.47) on the Brief Pain Inventory (BPI) worst pain scale for AIIA in breast cancer (59). Moreover, breast cancer patients on anti-hormonal therapy were less likely to experience menopausal symptoms including hot flushes, fatigue, headache, and xerostomia when treated complementarily with acupuncture compared with non-hormonal medication such as venlafaxine and gabapentin (odds ratio [OR] 1.75; 95% CI 1.09 to 2.75) (63). Based on the findings across 11 systematic reviews and meta-analyses, Zhang et al. found that manual acupuncture was the most investigated form of acupuncture when treating cancer pain followed by auricular acupuncture and electroacupuncture. However, it's worth noting that other types of acupuncture such as acupoint injections, transcutaneous electrical acupoint stimulation, wrist-ankle acupuncture, and moxibustion are underrepresented in the context of treating cancer pain, emphasizing the need for further research to comprehensively understand and establish the efficacy of diverse acupuncture modalities in this specific domain (58).

Acupuncture can also effectively treat gastrointestinal symptoms, most importantly CINV (64, 65), constipation after abdominal surgery (66) and xerostomia (67, 68). When applied during

and in the immediate days after the application of emetogenic chemotherapies, acupuncture reduces the duration and frequency of CINV (64). Additionally, it enhances the chance of complete-control of acute (risk ratio [RR] 1.13; 95% CI 1.02 to 1.25) and delayed vomiting (RR 1.47; 95% CI 1.07 to 2.00) compared with usual care (65). After surgery, manual acupuncture showed the greatest reduction of the time to first defecation (standardized mean difference [SMD] -1.70; 95% CI -3.33 to -0.05) but electroacupuncture was associated with a better pain control of abdominal pain caused by constipation (SMD -0.50; 95% CI -0.79 to -0.21) compared to manual acupuncture and usual care (66). The choice between manual and electroacupuncture, in combination with usual care, should be informed by the predominant symptom, whether constipation or pain. Similar positive outcomes were observed in a recent meta-analysis for opioid-induced constipation, with a remission rate of 86.8% for acupuncture plus usual care (RR 1.10; 95% CI 1.03 to 1.18) (69). However, acupuncture for opioid-induce constipation is currently not supported by the AWMF guideline mentioned above (55). Another debilitating gastrointestinal symptom is xerostomia after radiotherapy. Acupuncture can alleviate the perceived symptoms of dry mouth. However, it is important to note that acupuncture does not increase salivary production to a clinically relevant extent (67, 68).

Favorable results for acupuncture were also reported for psychological symptoms including cancer-related fatigue (CRF) (70, 71), insomnia (72, 73), anxiety, and depressive symptoms (74). CRF is one of the most prevalent symptoms among cancer patients and compromises significantly their quality of life (QoL). Currently, treatment options for CRF are limited, contributing to an elevated risk of developing additional psychological symptoms such as anxiety and depression. Acupuncture can reduce the burden of CRF by 2.12 (95% CI -3.21 to -1.04) points on the Brief Fatigue Inventory (BFI) compared to usual care (71). Moreover, acupuncture promotes a better sleep quality (73) and cancer-related anxiety and depression (74) when combined with usual care.

The complementary integration of acupuncture with established treatments has demonstrated the most significant benefits for cancer patients, emphasizing the importance of incorporating this integrative approach into clinical practice provided acupuncture is carried out by trained practitioners. Numerous studies have consistently shown that this combined strategy contributes to an improvement in the health-related QoL among cancer patients. The various applications of acupuncture underscore its potential as a valuable adjunctive therapy, providing a holistic and supportive framework for enhancing the overall well-being of individuals undergoing cancer treatment (75).

1.7.2 Mindfulness-based stress reduction

MBSR constitutes a holistic approach combining mindfulness meditation, body awareness, exploration of behavioral and thinking patterns, and elements of yoga. Originating in 1970 at the University of Massachusetts Medical Center by Jon Kabat-Zinn, MBSR was initially developed for stress, anxiety, depression, and pain management (76). Its primary application among cancer patients lies in addressing psychological symptoms, including anxiety, depression, insomnia, CRF, and cognitive impairment during chemotherapy (77, 78). Notably, MBSR has demonstrated the potential to enhance mood and endocrine-related QoL in breast cancer patients (79, 80).

While MBSR has shown promising short-term results in the reduction of psychological symptoms, the clinical significance of these effects remains unclear and necessitates further research (77). Despite these uncertainties, the AWMF guideline supports the recommendation of MBSR, acknowledging its ability to enhance resilience against distressing symptoms and since it offers a complementary psychoeducational support for cancer patients. MBSR is recommended as a valuable intervention for managing the psychological challenges associated with cancer, offering a holistic and supportive approach to improve the overall well-being of individuals undergoing cancer treatment (55).

1.7.3 Yoga

Like MBSR, yoga promotes the psychological health of cancer patients and offers a valuable complementary treatment option for CRF, anxiety, depression, insomnia, menopausal symptoms, the promotion of cognitive function during chemotherapy, and a better QoL during and after cancer treatment (81-87). Yoga significantly reduces CRF (SMD -0.90; 95% CI -0.52 to -0.19), anxiety (SMD -2.21; 95% CI -3.90 to -0.61), depression (SMD -2.29; 95% CI -3.97 to -0.61) and sleep disturbances (SMD -0.25; 95% CI -0.40 to -0.09) when compared to psychosocial or educational interventions (81, 82). Comparable results were found for the promotion of cognitive function, mood and menopausal symptoms in breast cancer patients (84-87). However, yoga, as a form of physical exercise, requires a higher level of performance scale to be utilized by patients, limiting its use in compromised patients.

1.8 Challenges of CAM use in oncology

1.8.1 Adverse events

Like conventional medical interventions, CAM modalities may induce adverse events that impact the safety profile of specific treatments. Contrary to the common belief that "natural

medicine" is in principle safe and well-tolerated, evidence suggests that especially biologically based practices like herbal medicine are potentially harmful in some cases (88). Nevertheless, certain CAM therapies are regarded as safe when employed alongside conventional cancer treatments.

Mind-body therapies, such as yoga and Tai Chi/Qigong, are generally considered safe in terms of direct adverse events associated with the interventions (81, 82). However, it is important to highlight that patients undergoing cancer treatment should be in good physical condition to engage in such practices. Furthermore, the guidance of an experienced therapist is recommended to minimize the risk of physical injuries during these interventions (81, 82).

Comparably, manipulative, and body-based practices are safe when performed by an experienced practitioner with a profound knowledge of anatomy. Common adverse events of such therapies are limited to physical injuries including local pain, bruising, and, if invasive procedures like setting acupuncture needles are performed, local infections (89-92). Usually, these are mild and do not require further medical treatment. However, severe adverse events including organ damage, fractures and death were reported in some rare cases (91-93). The occurrence of adverse events by manipulative and body-based practices are directly associated to the experience, anatomical knowledge, adherence to hygienic standards, and consideration of patients' individual risk factors such as bone metastases by the treating CAM practitioner (89-92).

Biologically based practices carry a higher risk of direct adverse effects and toxic side effects, in addition to potential interactions with conventional cancer-specific therapies. Mild adverse effects may include gastrointestinal issues such as nausea, vomiting, diarrhea, and mild abdominal pain, comparable to those seen with conventional pharmacological treatments (94). However, more severe, and toxic side effects are also possible (88, 95). An often underestimated concern is the anti-platelet effects associated with seemingly harmless herbs like tea (*Camellia sinensis*), ginger (*Zingiber officinale*), garlic (*Allium sativum*), turmeric (*Curcuma longa*), ginkgo (*Ginko biloba*), ginseng (*Panax ginseng*), thyme (*Thymus vulgaris*), fennel (*Trifolium partense*), sea-buckthorn (*Hippophae rhamnoides*), black cumin (*Nigella sativa*), olives (*Olea europaea*), or fenugreek (*Trigonella foenum-graecum*), potentially increasing the risk of bleeding (88). Furthermore, herbal remedies can rarely induce hepatotoxic or nephrotoxic effects, leading to acute liver or kidney failure (96, 97). Despite these potential risks, the prevalence of severe adverse effects and the individual risk associated with most herbal compounds remain unknown to date requiring more rigorous

research and a tentative appraisal by medical and CAM practitioners when prescribing herbal products (88).

1.8.2 Pharmacological interactions

Herbal and supplementary therapies are known to interact with pharmacological therapies. The previously mentioned potential of some common herbs and foods to inhibit platelet function may enhance the effect of anticoagulant therapies, increasing the risk of severe bleeding substantially (88). However, various herbal remedies and supplements sold over the counter may increase the risk for therapy failure or adverse effects of conventional cancer-specific therapies by affecting the Cytochrome P450 (CYP450) enzymes (95). CYP450 induction can reduce the bioavailability and subsequently the effectiveness of pharmacological anticancer therapies, while an inhibition may increase the potential of toxic side effects (88). Known biologically based CAM agents to induce CYP450 enzymes are St. John's wort (*Hypericum perforatum*), Aloe vera, turmeric (*Curcuma longa*), garlic (*Allium sativum*), ginger (*Zingiber officinale*), green tea extracts, hawthorn (*Crataegus rhipidophylla*), medical mushrooms, black cumin (Nigella sativa), and spirulina (*Arthrospira*) (95). Moreover, antioxidative effects of many supplements including vitamins, coenzyme Q10, and minerals are able to reduce the cytotoxic effects of chemo- and radiotherapy (95, 98). Mistle therapy may reduce the effect of paclitaxel by inhibiting the ribosomal protein synthesis and may induce allergic reactions and interactions with immunotherapy by an unspecific activation of the immune system (98, 99). However, since biologically based therapies often include multiple biologically active components, it is hardly ever possible for medical doctors to estimate the risk for interactions with pharmacological substances (95). It is therefore generally advised to avoid using biologically based practices during ongoing anticancer treatment (55).

Contrarily to biologically based practices, mind-body therapies and manipulative body-based practices are not known to have potential pharmacological interactions and should be favored during active anticancer treatment (55).

1.8.3 Interference with therapy adherence and therapy refusal

Another significant challenge associated with CAM in the context of cancer is its potential to interfere with therapy adherence and contribute to the refusal of conventional medical practices. This challenge arises from varying perspectives on the efficacy and safety of CAM modalities, which may lead individuals to refuse established medical treatments. Non-

adherence to conventional therapies can compromise treatment outcomes and potentially affect the overall prognosis (100). In a retrospective observational study conducted by Johnson et al., no difference between users and non-users of CAM was observed in the delay to the initiation of conventional cancer treatment. However, a significantly higher refusal rate among CAM users was identified for chemotherapy (34.1% versus 3.2%), surgery (7.0% versus 0.1%), radiotherapy (53.0% versus 2.3%), and anti-hormonal treatment (33.7% versus 2.8%) compared to non-users (101). The elevated rate of therapy refusal may contribute to the suboptimal outcomes observed in the group of CAM users, including a lower 5-year overall survival (82.2% versus 86.6%) and a greater risk of death (hazard ratio [HR] 2.08; 95% CI 1.50 to 2.90) among CAM users (101).

1.9 Discussing CAM with cancer patients

Despite the increasing prevalence of CAM usage among cancer patients and the associated risks of adverse events, pharmacological interactions, and therapy refusal, there is a notable lack of effective discussion about CAM in the clinical setting (102). The communication gap regarding CAM may be associated to various factors, including limited awareness among healthcare providers, time constraints during clinical consultations, or a lack of standardized guidelines for integrating discussions about CAM into routine cancer care (103).

However, research has demonstrated that effectively discussing CAM with patients can have positive outcomes, including strengthening the relationship between physicians and patients. Such discussions contribute to increased patient satisfaction with the provided cancer care and improvements in patients' QoL and overall well-being (104). Engaging in an open dialogue about CAM during and after cancer treatment further enhances patients' understanding of the scientific knowledge and preferences related to CAM, guiding them toward evidence-based and safe complementary treatment modalities (104). Establishing a robust relationship with cancer patients, acknowledging their reasons for choosing CAM, and providing support in their decision-making process can also play a role in preventing treatment refusal (100). Addressing CAM openly within the healthcare setting is essential for fostering patient-centered care and promoting informed decision-making (105).

1.10 Delineating the study questions and aims

Complementary therapies are increasingly used worldwide, with some of these therapies even receiving recommendations from current clinical guidelines (55). While certain CAM modalities

can effectively and safely manage cancer- or therapy-related symptoms in specific cases, other complementary therapies pose a potential threat to the health and clinical outcomes of cancer patients (101). The ambivalent nature of CAM, offering both potential benefits and risks, emphasizes the importance of evidence-informed decision-making and comprehensive discussions between medical practitioners and patients. Openly discussing CAM can further enhance the patient physician relationship and increase the quality of cancer care in general (105).

The WHO encourages the meaningful implementation of CAM into clinical practice and research (13). Following these guidelines, the emerging field of integrative oncology has complemented the established domains of supportive and palliative care. However, for the successful integration of CAM into clinical practice at the regional level in Austria, it is necessary to collect demographic data, understand the reasons behind CAM utilization, and identify patterns of CAM use among Austrian cancer patients. This information is crucial for informing medical practitioners and facilitating evidence-based decision-making in the implementation of CAM strategies tailored to the unique needs and preferences of the Austrian population. Another aspect contributing to a justified implementation of CAM is the reliability of practitioners delivering these complementary therapies. Similar to any medical intervention, an evidence-informed practice of their respective CAM modality is the fundamental principle for ensuring safe administration. Healthcare professionals must have confidence that CAM practitioners are reliable and adhere to scientifically valid recommendations when referring their patients to these practitioners (30).

Thus, the aim of this dissertation project was to conduct two cross-sectional studies to investigate the following questions.

1. Characterization of CAM utilization of Austrian cancer patients
    - Characterize the demographical factors, patterns and reasons for CAM use
    - Symptom clusters associated to CAM use
2. Assessing the research literacy and evidence-informed practice of CAM practitioners
    - Characterize the educational background, clinical experience with cancer patients, evidence-informed practice patterns, and role of research in the clinical practice of CAM practitioners in Austria in an international context

The results of this project are published separately in *PLOSE ONE (Huemer et al., 2023)* (106) and the *Journal of Integrative Medicine (Huemer et al., 2023) (107)*.

2 Methods

2.1 Preamble

This section includes parts of the content that has been previously published in *PLOSE ONE (Huemer et al., 2023)* (106) and the *Journal of Integrative Medicine (Huemer et al., 2023)* (107) as part of my dissertation thesis, and certain portions are presented identically.

The thesis incorporates two surveys, one among cancer patients and one among CAM practitioners, investigating the research questions outlined in section 1.10.

2.2 Patient survey

Parts of this section were reproduced from or similarly published in Huemer et al. (106).

2.2.1 Study design

This pan-cancer cross-sectional study was carried out at the Division of Oncology, Department of Internal Medicine, Medical University of Graz and the University Palliative Care Unit, Division of Oncology, Department of Internal Medicine, Medical University of Graz. Patients with the diagnosis of solid cancers in any stage were included in the study to assess the prevalence and characteristics of CAM utilization during and after oncological care. Additionally, the study aimed to assess the association between symptom clusters and CAM use among cancer patients.

2.2.2 Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. The local ethics committee approved the study (Ethics Committee of the Medical University of Graz, Austria; document number 32-665 ex 19/20). Written informed consent was obtained from each patient prior to completing the survey questionnaire.

2.2.3 Eligibility criteria and recruitment

Eligible patients were recruited between October 2020 and March 2021 in the clinics of the Division of Oncology and its associated Palliative Care Unit at the Department of Internal

Medicine, Medical University of Graz, Austria according to predefined inclusion and exclusion criteria.

Inclusion criteria

- Histologically confirmed solid tumor
- ≥18 years of age
- Ability to read and complete the provided questionnaires

Exclusion criteria

- Significant language barrier
- Physically or mentally unable to consent

After obtaining the written informed consent of each participant, we handed out the paper-based questionnaire, which the participants completed on their own without further assistance by members of the study staff during their stay at the clinic. The completed questionnaires were returned to the study staff on the same day of participation (106).

2.2.4 Questionnaire design

We developed a paper-based self-administered questionnaire gathering the following information from patients incorporating CAM alongside their oncological care (106):

1. Patients' demographics and patterns of CAM use
2. Attitudes towards CAM and holistic health
3. Assessment of symptom burden and symptom clusters

The first section of the questionnaire included demographical questions to characterize the diversity of participants. This section encompassed questions about gender, age, living arrangements, educational level, and annual income. Additionally, information regarding the histologically confirmed cancer diagnosis, the presence of metastasis, and the current tumor-specific treatment was extracted from the patients' medical records (106). Furthermore, a list of 24 therapies, employed in prior studies, was incorporated to assess the prevalence of CAM

therapies (38). We added supplementary questions regarding the source of information, about personal motivations for employing CAM, the perceived positive and negative effects of CAM, and whether its use had been discussed with the attending oncologist (106). The list of different CAM therapies participants could choose included practices such as:

- Homeopathy
- traditional Chinese medicine
- ayurveda
- anthroposophical medicine
- yoga
- hypnosis
- herbal remedies
- medical teas
- vitamin/mineral supplements
- massages
- osteopathy
- chiropractic
- acupuncture/acupressure
- qi gong/tai chi
- meditation
- prayers
- dietary changes
- spiritual healing
- shamanism
- reiki/healing touch
- healing stones/crystals
- mistletoe therapy
- shiatsu
- kinesiology

The subsequent two sections encompassed validated questionnaires aiming to explore attitudes towards CAM and holistic health, as well as assessing the symptom burden. Initially, we employed the Holistic Complementary and Alternative Medicine Questionnaire (HCAMQ) to capture attitudes toward CAM (108, 109) followed by the Edmonton Symptom Assessment Scale (ESAS), a widely used tool to assess the symptom burden and its severity in cancer patients (110).

The HCAMQ is a two-factor patient-reported outcome measurement tool comprising eight items. The two latent factors are measured by two subscales: the holistic health (HH) subscale and the CAM subscale, compromising four of the eight items each (108). The HH factor measures a mental model consistent with the desire to avoid iatrogenic effects of conventional medicine and the belief that various lifestyle factors impact health. The HH items specifically explore the belief in how factors like mood, stress, and conflicts impact health. Simultaneously, the CAM subscale evaluates the general attitude toward complementary therapies, considering factors such as the lack of scientific evidence, potential dangers of CAM, appropriate circumstances for its use, mechanisms of action, and suitable health conditions

for CAM application (108). The range per score is 4 to 24, whereas a higher score on each subscale indicates a more positive belief in HH and CAM. Both scores demonstrate acceptable psychometric properties with Cronbach's alphas of 0.75 and 0.83, respectively (109).

For the evaluation of the symptom burden and to model symptom clusters, we employed the ESAS, a widely utilized tool for assessing the severity of individual symptoms in cancer patients (110). This scale encompasses 12 individual symptoms, including pain, fatigue, drowsiness, nausea, anorexia, breathlessness, depression, anxiety, well-being, sleep, constipation, and emesis. Participants rate each symptom on a numerical scale ranging from 0 to 10, where higher scores indicate greater symptom severity. The ESAS total score is obtained by summing the individual scores of all 12 symptoms, resulting in a range of 0 to 120 (111).

2.2.5 Data analysis

Sample size

The prevalence of CAM users among Austrian oncological patients was previously documented at 27% (112). To obtain a representative sample with a similar incidence and a margin of error set at 6%, the required sample size was determined to be 171 patients. The calculation of the sample size was performed using G*Power (Version 3.1.9.6, 2020) (113).

Analysis plan

The survey data were manually entered into a Microsoft Excel spreadsheet (Microsoft Corporation, 2019, version 2306, 64-bit) (114). For subsequent analysis and data visualization, we used the statistical program R (RStudio, 2020, version 4.0.3) (115). Differences in socio-demographic data between CAM users and non-users were assessed using the Chi²-test or Fisher’s exact test for categorical variables and the Wilcoxon-rank-sum-test for continuous variables. Additionally, logistic regression was employed for multivariable analysis, incorporating symptom clusters and the predictors for CAM use, such as sex, age, and education, as covariates which were identified in previous studies (38, 106).

Modeling symptom clusters

For modeling symptom clusters, we conducted a latent profile analysis (LPA) using the tidyLPA package in R (116). LPA, a form of exploratory factor analysis, identifies latent groups within a study sample based on a specific set of variables (116). This approach was repeatedly used in previous studies to identify hidden groups of patients with distinct clinical signs and

symptoms (117, 118). In our study, LPA was employed to identify patient groups with similar response patterns on the ESAS symptom list. LPA provides mean severity scores for each item per group, facilitating clear patient allocation to clusters. The choice of the best LPA model was guided by the Akaike information criterion (AIC), Bayesian information criterion (BIC), entropy, and clinical interpretability, aiming for a parsimonious solution for the number of clusters (46, 106).

Due to LPA's restriction on variables of different lengths, missing ESAS values had to be imputed to conduct the analysis without list-wise deletion and loss of statistical power (46). We examined the pattern of missing ESAS values, revealing 30 incomplete cases where participants reported only one or more symptoms with scores >0. These missing values were treated as structurally missing, assuming that patients not reporting a value for an ESAS symptom were not experiencing that specific symptom. Thus, missing ESAS values were replaced with 0. All other variables with missing data were analyzed with the available data (106).

2.3 Practitioner survey

Parts of this section were reproduced from or similarly published in Huemer et al. (107).

2.3.1 Study design

To assess the research literacy and evidence-informed practice of CAM practitioners, we designed a bilingual multinational online-survey among acupuncturists and herbalists in Austria, Germany, the United States of America (USA), Australia, and New Zealand. The study host was the Division of Oncology, Department of Internal Medicine, University of Graz, Graz, Austria (107).

2.3.2 Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. The local ethics committee approved the study (Ethics Committee of the Medical University of Graz, Austria; document number 34-432 ex 21/22). Electronical informed consent was obtained from each participant prior to completing the survey questionnaire.

2.3.3 Eligibility criteria, recruitment and data collection

Invitations were disseminated through social media and emails from October 2022 to January 2022, with the help of professional organizations representing acupuncture and Chinese medicine. The participating organizations are listed in Table 3. Practitioners with the following inclusion criteria were eligible to participate (107).

Inclusion criteria

- ≥18 years of age
- valid license to perform acupuncture, herbal medicine, or both
- ability to read and speak English or German
- currently living and practicing in Austria, Germany, USA, Australia, or New Zealand

Table 3: Participating organizations, country, and platform of dissemination (107)

Organizations name	Country	Dissemination
Österreichische Gesellschaft für kontrollierte Akupunktur (OGKA)	Austria	Email, social Media
Wiener Schule für Traditionelle Chinesische Medizin (WSTCM)	Austria	Email
Societas Medicinae Sinesis (SMS)	Germany	Email
Arbeitsgemeinschaft für Klassische Akupunktur und Traditionelle Chinesische Medizin (AGTCM)	Germany	Email
American Society of Acupuncturists (ASA)	USA	Social Media
Hospital Handbook Project (HHP)	USA	Email
National Certification Commission for Acupuncture and Oriental Medicine (NCCAOM)	USA	Social Media
Australian Acupuncture and Chinese Medicine Association (AACMA)	Australia	Email
Acupuncture New Zealand (Acupuncture NZ)	New Zealand	Email

The invitations included an online survey-link leading to the electronical consent form questionnaire. After giving consent to participate, the survey data was collected in anonymous form and managed using the Research Electronic Data Capture (REDCap) online survey and

distribution tool hosted by the Medical University of Graz, Austria (119, 120). The survey-link was open for data acquisition from October 1st, 2022 to January 15th, 2023.

2.3.4 Questionnaire design

We developed an anonymous self-administered questionnaire to gather data on the demographics and clinical practices of participating practitioners in integrative oncology. The questionnaire incorporated both open and closed questions, utilizing single-choice or free-text response formats. The main topics of the questions asked were demographical data of the practitioner, educational background and clinical experience, details concerning their practice, and research literacy. Finally, participants who did not treat or ceased treating cancer patients were asked to provide reasons for their decision. A summary of the item categories within each topic are presented in Table 4. The questionnaire was initially developed in English and then translated into German using the forward-backward-translation process involving three native speakers. Following a review of the two final versions, both language versions underwent piloting by 10 CAM practitioners speaking either German or English. Minor formatting and editing adjustments were implemented based on the feedback received during the pilot phase (107).

Table 4: Summary of topics and item categories of the online-questionnaire (107)
NRS: Numerical rating scale

Topic	**Item categories**
Demographics	• Occupation • Age • Place of living
Education/Experience	• Highest completed education • Education in acupuncture/herbal medicine • Specialization in oncology • Years of practice • Experience in treating oncology patients
Practice details	• Estimated number of patients treated per week • Patient characteristics seeking the practitioners help • Communication with medical oncologist
Research literacy	• Interest and participation in research • Source of information for treatment guidance • Importance of research for daily practice (NRS 0 to 100) • Challenges in understanding research

2.3.5 Data analysis

The survey data was transferred from the REDCap system to RStudio (“Ghost Orchid” Release, R version 4.0.3) (115). Questionnaires failing to meet the inclusion criteria and those with more than 30% missing data were excluded from subsequent analysis. Missing data were acknowledged and not subjected to imputation. Descriptive statistics, encompassing mean ± SD or numbers and percentages, were presented. Where appropriate, 95% CIs were employed. Bivariate analysis involved parametric or non-parametric statistical tests as deemed suitable, using a significance level of $p < 0.05$. R version 4.0.3 ("Ghost Orchid" Release) was used for all analytical procedures and graphical representations (115).

To qualitatively analyze responses to open-ended questions regarding reasons for not treating cancer patients, a qualitative descriptive approach was adopted. Initial condensation of meaning units into codes preceded the grouping of codes into categories based on shared patterns. This analytical process underwent discussion and review by all authors (107).

3 Results

This section includes parts of the content that has been previously published in *PLOSE ONE (Huemer et al., 2023)* (106) and the *Journal of Integrative Medicine (Huemer et al., 2023)* (107) as part of my dissertation thesis, and certain portions are presented identically.

3.1 Patient survey

Parts of this section were reproduced from or similarly published in Huemer et al. (106).

3.1.1 Patient characteristics

A total of 199 patients were invited to participate in the study. However, 28 participants did not adequately complete the questionnaire, resulting in 171 completed questionnaires eligible for further analysis. 63.7% (109/171) of the participants used some form of CAM. The gender distribution was relatively even, with 50.9% (87/171) identifying as females. Regarding age distribution, the majority (45.0%, 77/171) fell within the 51-65 age category. Education-wise, a significant portion had completed primary education and apprenticeship (36.3%, 62/171). In terms of income, 26.3% (45/171) reported an annual income between €10,001 and €20,000. Marital status indicated that a majority of participants were married (59.6%, 102/171).

Concerning cancer types, breast cancer emerged as the most prevalent among the study sample, accounting for 24.0% (41/171), followed by cancer of the lower gastrointestinal tract (23.4%, 40/171) and the pancreobiliary area (19.3%, 33/171). A substantial proportion of participants (87.7%, 150/171) had metastasized disease, and the majority (67.8%, 116/171) were undergoing palliative tumor-specific treatment. The overall symptom burden in our study sample was mild, with an average ESAS total score of 27.2 (SD 16.6). The total sample had a high believe in holistic health (HH subscale 21.3 SD 2.7) but were moderately convinced by CAM (CAM subscale 11.8 SD 4.4). A summary of sociodemographic and clinical characteristics is presented in Table 5 and Table 6.

Table 5: Symptom burden and attitude towards CAM and holistic health (106)

Variable	**Total (n=171)**		**Users (n=109)**		**Non-users (n=62)**	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
ESAS						
Total score (0 -120)	27.2	16.6	28.3	16.5	25.5	16.9
HCAMQ						
HH subscale	21.3	2.7	21.4	2.4	21.1	3.0
CAM subscale	11.8	4.4	12.2	4.4	10.8	4.3

Table 6: Sociodemographic and clinical characteristics (106)

Variable	**Total (n=171)**		**Users (n=109)**		**Non-users (n=62)**	
	N	%	N	%	N	%
Age (years)						
18-36	5	2.9	4	3.7	1	1.6
37-50	20	11.7	13	11.9	7	11.3
51-65	77	45.0	47	43.1	30	48.4
66-80	64	37.4	41	37.6	23	37.1
>80	5	2.9	4	3.7	1	1.6
Sex						
Male	84	49.1	58	53.2	26	41.9
Female	87	50.9	51	46.8	36	58.1
Other	0	0.0	0	0.0	0	0.0

Variable	Total (n=171)		Users (n=109)		Non-users (n=62)	
	N	**%**	**N**	**%**	**N**	**%**
Marital status						
Single	14	8.2	9	8.3	5	8.1
Married	102	59.6	70	64.2	32	51.6
Divorced	15	8.8	9	8.3	6	9.7
Widowed	7	4.1	6	5.5	1	1.6
Missing	33	19.3	15	13.8	18	29.0
Education						
None	3	1.8	2	1.8	1	1.6
Primary	12	7.0	6	5.5	6	9.7
Apprenticeship	62	36.3	35	32.1	27	43.5
Higher secondary	28	16.4	22	20.2	6	9.7
Technical college	29	17.0	17	15.6	12	19.4
University	28	16.4	20	18.3	8	12.9
Other	7	4.1	6	5.5	1	1.6
Missing	2	1.2	1	0.9	1	1.6
Income per year						
<10 000 €	21	12.3	15	13.8	6	9.7
10 001- 20 000 €	45	26.3	27	24.8	18	29.0
20 001- 30 000 €	34	19.9	24	22.0	10	16.1
30 001-40 000 €	30	17.5	16	14.7	14	22.6
>40 000 €	23	13.5	16	14.7	7	11.3
Missing	18	10.5	11	10.1	7	11.3
Diagnosis						
Breast	41	24.0	30	27.5	11	17.7
Gynecological	4	2.3	3	2.8	1	1.6
Lung	6	3.5	2	1.8	4	6.5
Pancreobiliary	33	19.3	22	20.2	11	17.7
Upper gastrointestinal	12	7.0	8	7.3	4	6.5
Lower gastrointestinal	40	23.4	23	21.1	17	27.4
Urological	12	7.0	8	7.3	4	6.5
Prostate	9	5.3	7	6.4	2	3.2
CUP	2	1.2	0	0.0	2	3.2

Other	12	7.0	6	5.5	6	9.7
Metastasis						
None	21	12.3	14	12.8	7	11.3
Yes	150	87.7	95	87.2	55	88.7
Therapy						
Neo-adjuvant	24	14.0	19	17.4	5	8.1
Adjuvant	19	11.1	12	11.0	7	11.3
Palliative	116	67.8	72	66.1	44	71.0
Observation	5	2.9	3	2.8	2	3.2
Best supportive care	7	4.1	3	2.8	4	6.5
Immunotherapy						
Yes	21	12.3	12	11.0	9	14.5
None	150	87.7	97	89.0	53	85.5

3.1.2 Use of Complementary and Alternative Medicine

CAM utilization was notably high in our study sample, with a proportion of 63.7% (109/171), of which 42.2% (46/109) discussed their CAM use with their oncologist (106). The most frequently employed therapies alongside conventional treatments included homeopathy (30.3%, 33/109), vitamin and mineral supplementation (28.4%, 31/109), herbs (26.6%, 29/109), massage (24.8%, 27/109), acupuncture (22.0%, 19/109), and medical teas (22.0%, 24/109). Patients reported using CAM primarily to strengthen their body (47.7%, 52/109) and enhance their quality of life (45.9%, 50/109). Additionally, they believed that CAM alleviated the side effects of their cancer treatment, contributing to improved physical well-being and overall quality of life. However, 15.6% (17/109) reported experiencing side effects caused by CAM therapies, with gastrointestinal symptoms like nausea being the most prevalent adverse reaction. Family members (37.6%, 41/109) and friends (45.0%, 49/109) emerged as the primary sources of information about CAM for patients. Among healthcare practitioners, family physicians most provided guidance (21.1%, 23/109), followed by CAM practitioners (11.9%, 13/109) and oncologists (9.2%, 10/109). Further details on reasons for CAM use, perceived effects, and sources of CAM information are presented in Table 7 (106).

Table 7: Characteristics reasons for CAM use, perceived effects, and sources of CAM information (106)

	Total (n=109)	**%**
Informed oncologist		
Yes	46	42.2
No	42	38.5
Missing	21	19.3
Reasons for CAM use (multiple choice)		
Fight cancer	26	23.9
Strengthen body	52	47.7
Symptom control	20	18.3
Enhance Quality of Life	50	45.9
Enhance emotional well-being	30	27.5
Enhance treatment effect	31	28.4
Lower treatment side effects	37	33.9
Take self-control	24	22.0
Try everything	34	31.2
Subjective effects of CAM (multiple choice)		
Total reports	83	76.1
Reduced pain	20	18.3
Stress reduction	15	13.8
Reduced fatigue	16	14.7
Improved physical well-being	37	33.9
Improved emotional well-being	24	22.0
Improved Quality of Life	28	25.7
Improved immune system	22	20.2
Improved hope	20	18.3
Fewer treatment side effects	38	34.9
Subjective side effects of CAM (multiple choice)		
Total reports	17	15.6
Abdominal pain	4	3.7
Nausea	5	4.6
Emesis	1	0.9
Headache	1	0.9

Diarrhea	1	0.9
Constipation	0	0.0
Other	8	7.3
Source of information (multiple choice)		
Family	41	37.6
Friends	49	45.0
Internet	18	16.5
Other media	20	18.3
Family physician	23	21.1
Psychologist	4	3.7
Oncologist	10	9.2
Radiologist	1	0.9
CAM practitioner	13	11.9
Religious contact	1	0.9
Other	11	10.1

3.1.3 Symptom cluster analysis

To determine an optimal and parsimonious solution for symptom clusters, we conducted exploratory LPA. Since we did not know the final number of clusters before conducting the analysis, we performed an iterative LPA with an incremental increase in the number of clusters (106). This analysis yielded one to eight potential clusters for further investigation (Table 8). The choice of the final number of clusters was mainly based on the model with the lowest BIC and AIC as well as clinical interpretability and usefulness of the cluster solutions (106).

Although the model with the lowest BIC suggested five clusters, it would generate two clusters that were remarkably similar in terms of included symptoms and their severity. Given the difficulty in distinguishing these clusters in a clinical context, we opted for a solution with four clusters, collapsing the two similar clusters within the five-cluster solution into one. This choice aimed to achieve a balanced model with favorable fit indices and clinical interpretability. Moreover, our model demonstrated sufficient entropy, surpassing 0.8, indicating accurate group assignments for individual cases (106).

Table 8: Model fit indices of LPA for an increasing number of clusters (106)

Cluster	AIC	BIC	Entropy
1	9293.89	9369.29	1.00
2	8907.35	9023.59	0.89
3	8830.37	8987.45	0.82
4	8718.56	8916.48	0.87
5	8661.76	8900.53	0.87
6	8644.38	8923.99	0.80
7	8643.38	8963.83	0.90
8	8653.54	9014.83	0.91

The outcomes of our model identified four well-defined symptom clusters (see Figure 1). Cluster 1 demonstrated elevated scores in drowsiness, depression, and anxiety, while Cluster 2 exhibited moderate scores in fatigue, drowsiness, and sleep (106). The subsequent cluster (Cluster 3) primarily featured high scores for gastrointestinal symptoms, encompassing anorexia, nausea, constipation, and emesis. The last cluster, Cluster 4, represented patients with consistently low symptom scores and was employed as a reference for subsequent analyses (106). Membership of patients varied across all clusters with Cluster 2 being the most prevalent (n=83), followed by Cluster 4 (n=48), Cluster 1 (n=23), and Cluster 3 (n=17) (106).

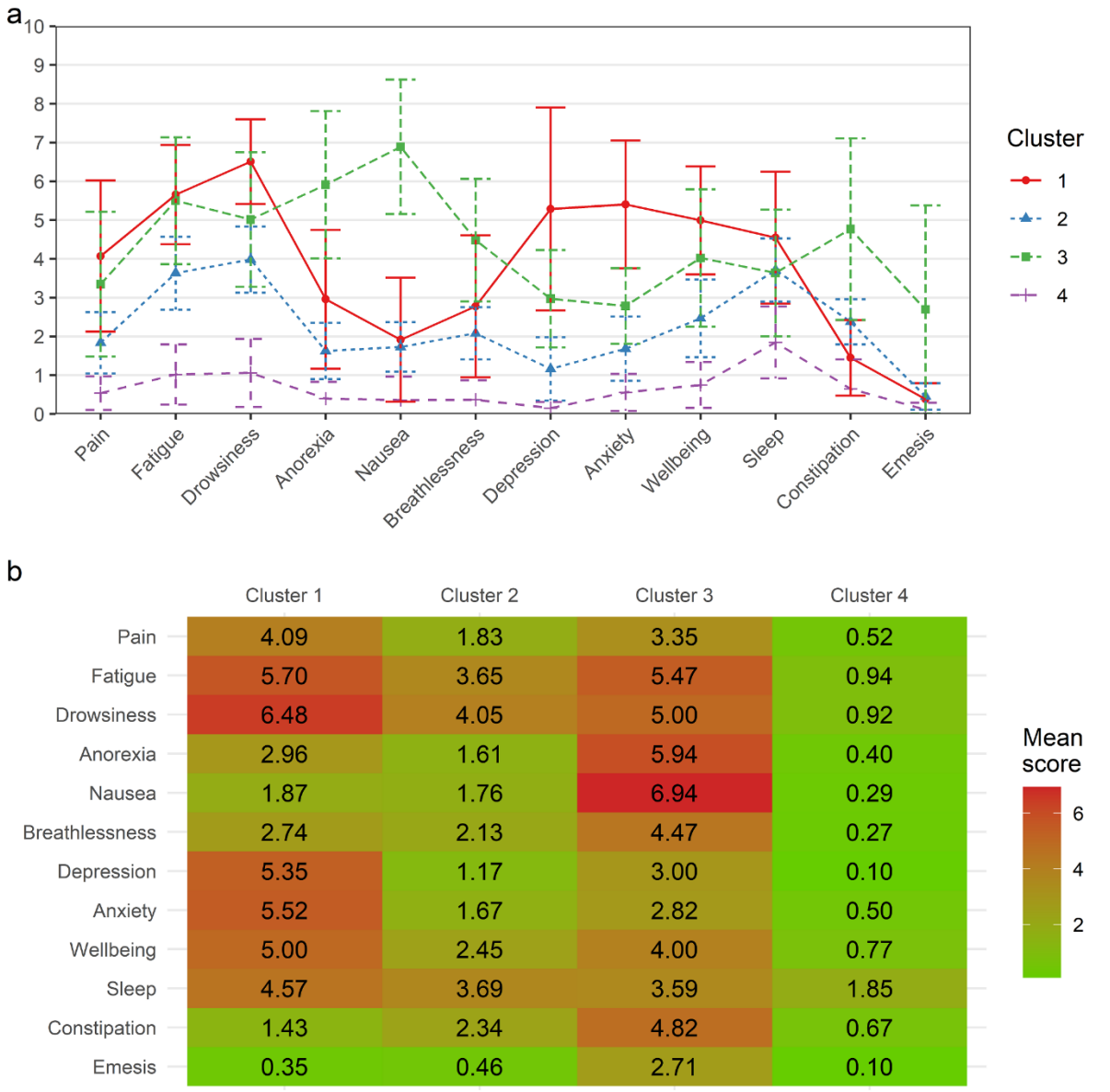

Figure 1: Symptom clusters resulting from latent profile analysis using a four-class solution (as published in (106))

a Cluster 1: drowsiness-depression-anxiety-cluster, Cluster 2: moderate fatigue-drowsiness-sleep-cluster, Cluster 3: anorexia-nausea-breathlessness-constipation-emesis-cluster, Cluster 4: all-low-cluster; **b** Mean symptom scores of each cluster.

3.1.4 Bivariate analysis

We observed no significant difference in symptom burden between CAM users and non-users (ESAS total score CAM 28.3±16.5 vs. non-CAM 25.5±16.9, t-test, p=0.23). Additionally, both groups reported a similar number of simultaneously experienced symptoms (CAM median 8 symptoms, interquartile range [IQR] 6, 10 vs. non-CAM median 7 symptoms, IQR 4.25, 9,

p=0.13). However, there was a robust and statistically significant association with cluster membership (Chi^2=10.07, df=3, p=0.018). Although the study cohort exhibited a strong belief in HH and a moderate belief in CAM, attitudes towards both beliefs did not significantly differ between CAM users and non-users (CAM subscale 12.2±4.4 versus 11.0±4.5, p=0.08; HH subscale 21.4±2.4 versus 21.1±3.2, p=0.65) (106).

Surprisingly, we did not identify any bivariate associations between CAM use and sociodemographic characteristics, including the previously described predictors sex (Chi^2=1.58, df=1, p=0.208), age (p=0.909 Fisher's exact test), and education (p=0.259 Fisher's exact test) (106). Furthermore, no statistically significant associations were found for marital status (p=0.699 Fisher's exact test), annual income (Chi^2=3.25, df=4, p=0.517), cancer type (p=0.362 Fisher's exact test), metastatic disease (Chi^2=0.003, df=1, p=0.956), therapy regime (p=0.396 Fisher's exact test), or if patients are undergoing immunotherapy (Chi^2=0.18, df=1, p=0.668) (106).

3.1.5 Multivariable analysis

To further investigate the statistical association between symptom cluster membership and CAM utilization, we fitted a multiple logistic regression model. We used cluster membership, sex, age, and education as predictive factors for CAM use (106).

Cluster 1 (drowsiness-depression-anxiety cluster) emerged as the only significant predictor for all variables included in CAM use. Patients belonging to this cluster exhibited a 3.83-fold higher likelihood of using CAM (95% CI 1.14 to 15.48; p=0.039) compared to cluster 4 (reference, all-low symptoms cluster). Conversely, Cluster 3 (anorexia-nausea-breathlessness-constipation-emesis cluster) indicated a 0.57-fold decreased likelihood of using CAM, although not statistically significant. Cluster 2 (moderate fatigue-drowsiness-sleep cluster) showed a slightly increased although not significant chance for using CAM alongside conventional cancer treatment (OR 2.09; 95% CI 0.96 to 4.59; p=0.062) (106).

Female sex, lower age, and higher education exhibited an insignificant tendency toward a higher likelihood of CAM use, as reported in Table 9 (106).

Table 9: Predictors of CAM use from multiple logistic regression (106)
Ref.: reference

Predictor	**CAM use (yes=1)**		
	OR	**95% CI**	**p-value**
Sex (Ref.=male)			
Female	1.52	0.76, 3.09	0.242
Symptom-cluster (Ref.= Cluster 4)			
1 = drowsiness-depression-anxiety	3.83	1.14, 15.48	0.039
2 = moderate fatigue-drowsiness-sleep	2.09	0.96, 4.59	0.062
3 = anorexia-nausea-breathlessness-constipation-emesis	0.57	0.17, 1.88	0.362
Age (Ref.= >80 years)			
18-36	0.44	0.01, 14.99	0.613
37-50	0.23	0.01, 2.24	0.251
51-65	0.26	0.01, 1.77	0.209
66-80	0.25	0.01, 2.02	0.250
Education (Ref.=none)			
Primary	0.81	0.03, 12.93	0.881
Apprenticeship	0.98	0.04, 12.62	0.989
Higher Secondary	2.77	0.11, 40.63	0.464
Technical college	0.99	0.04, 13.74	0.999
University	1.81	0.07, 25.22	0.667
Other	6.30	0.16, 266.26	0.290

3.2 Practitioner survey

Parts of this section were reproduced from or similarly published in Huemer et al. (107).

3.2.1 Practitioners' demographics

The survey was distributed to 43,695 email and social media contacts through the collaborating professional organizations. A total of 742 CAM practitioners responded to the questionnaire, resulting in a response rate of 1.7% (742/43,695). After screening, 404 (54.5%, 404/742) responses met the inclusion criteria for further analysis. Of the included responses, 254 practitioners (62.9%, 254/404) reported treating cancer patients (107). Among these, 145 (57.1%, 145/254) held licenses for both acupuncture and herbal medicine, 60 (23.6%, 60/254)

were medical doctors, 207 (81.5%, 207/254) had completed university-level education, and 92 (36.2%, 92/254) were in the age range of 46–55 years (107).

There were variations between countries regarding the proportion of medical doctors and the highest completed educational levels of CAM practitioners. Austria had the highest proportion of medical doctors among CAM practitioners (100%, 38/38), followed by Germany (18.6%, 13/70) (107). While the majority across all countries had completed education at the university level, Germany had the highest proportion of CAM practitioners with a high school diploma as their highest educational degree (107).

Regarding training, most respondents held a diploma with over 100 hours of training in acupuncture (48.8%, 124/254) or herbal medicine (25.6%, 65/254), and 35.0% (89/254) had completed oncology-focused training (107). Educational differences between countries were observed, with the highest proportion of CAM practitioners holding a master's degree or doctor of philosophy (PhD) in acupuncture (master’s degree 65.1%, 54/83, PhD 32.5%, 27/83) and herbal medicine (master’s degree 55.4%, 46/83, PhD 15.7%, 13/83) practicing in the USA. The majority of respondents (74.4%, 189/254) operated in their own solo clinics, while only 12.6% (32/254) worked in clinics focused on treating cancer patients. Again, there were differences among countries in terms of place of practice (107). In Germany, the vast majority of CAM practitioners work on their own in their private clinic (94.3%, 66/70), while CAM practitioners in Austria, the USA, and Australasia are more often located in multidisciplinary settings such as hospitals or multidisciplinary clinics (107). Complete demographic details are outlined in Table 10.

Table 10: Demographics of CAM practitioners per country (107)

	Austria (N=38)		**Germany (N=38)**		**United States (N=83)**		**Australasia (N=41)**		**Missing (N=22)**		**Total (N=254)**	
Profession												
Acupuncturist	23	60.5	30	42.9	21	25.3	23	56.1	12	54.5	109	42.9
Acupuncturist & Herbalist	15	39.5	40	57.1	62	74.7	18	43.9	10	45.5	145	57.1
Missing	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Medical Doctor												
Yes	38	100.0	13	18.6	1	1.2	1	2.4	7	31.8	60	23.6
No	0	0.0	55	78.6	81	97.6	38	92.7	15	68.2	189	74.4
Missing	0	0.0	2	2.9	1	1.2	2	4.9	0	0.0	5	2.0
Licensed Acupuncturist/Herbalist												
Yes	9	23.7	62	88.6	82	98.8	41	100.0	20	90.9	214	84.3
No	27	71.1	7	10.0	1	1.2	0	0.0	2	9.1	37	14.6
Missing	2	5.3	1	1.4	0	0.0	0	0.0	0	0.0	3	1.2
Age												
18-25	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
26-35	7	18.4	0	0.0	7	8.4	3	7.3	1	4.5	18	7.1
36-45	10	26.3	6	8.6	14	16.9	9	22.0	4	18.2	43	16.9
46-55	13	34.2	32	45.7	29	34.9	10	24.4	8	36.4	92	36.2
56-65	6	15.8	23	32.9	19	22.9	16	39.0	7	31.8	71	28.0
>65	2	5.3	9	12.9	14	16.9	3	7.3	2	9.1	30	11.8
Missing	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

	Austria (N=38)		Germany (N=38)		United States (N=83)		Australasia (N=41)		Missing (N=22)		Total (N=254)	
Highest completed education level												
High school	0	0.0	13	18.6	1	1.2	0	0.0	1	4.5	15	5.9
College	0	0.0	21	30.0	2	2.4	4	9.8	3	13.6	30	11.8
University	38	100.0	36	51.4	80	96.4	36	87.8	17	77.3	207	81.5
Missing	0	0.0	0	0.0	0	0.0	1	2.4	1	4.5	2	0.8
Highest qualification in acupuncture												
Short-term course (<100h)	4	10.5	1	1.4	0	0.0	0	0.0	1	4.5	6	2.4
Diploma or >100h	32	84.2	55	78.6	1	1.2	28	68.3	8	36.4	124	48.8
Masters' degree	1	2.6	13	18.6	54	65.1	13	31.7	11	50.0	92	36.2
PhD	0	0.0	1	1.4	27	32.5	0	0.0	1	4.5	29	11.4
Missing	1	2.6	0	0.0	1	1.2	0	0.0	1	4.5	3	1.2
Highest qualification in herbal medicine												
Short-term course (<100h)	3	7.9	1	1.4	0	0.0	0	0.0	1	4.5	5	2.0
Diploma or >100h	11	28.9	32	45.7	2	2.4	15	36.6	5	22.7	65	25.6
Masters' degree	1	2.6	7	10.0	46	55.4	3	7.3	3	13.6	60	23.6
PhD	0	0.0	0	0.0	13	15.7	0	0.0	1	4.5	14	5.5
Missing	23	60.5	30	42.9	22	26.5	23	56.1	12	54.5	110	43.3

	Austria (N=38)		Germany (N=38)		United States (N=83)		Australasia (N=41)		Missing (N=22)		Total (N=254)	
Focused training in oncology												
Yes	8	21.1	18	25.7	44	53.0	12	29.3	7	31.8	89	35.0
No	30	78.9	51	72.9	38	45.8	29	70.7	15	68.2	163	64.2
Missing	0	0.0	1	1.4	1	1.2	0	0.0	0	0.0	2	0.8
Place of practice												
Own solo clinic	26	68.4	66	94.3	53	63.9	29	70.7	15	68.2	189	74.4
Hospital	10	26.3	1	1.4	13	15.7	1	2.4	1	4.5	26	10.2
Multidisciplinary clinic	2	5.3	3	4.3	17	20.5	10	24.4	6	27.3	38	15.0
Missing	0	0.0	0	0.0	0	0.0	1	2.4	0	0.0	1	0.4
Clinic is focused on oncology												
Yes	8	21.1	4	5.7	16	19.3	4	9.8	0	0.0	32	12.6
No	28	73.7	62	88.6	67	80.7	36	87.8	21	95.5	214	84.3
Missing	2	5.3	4	5.7	0	0.0	1	2.4	1	4.5	8	3.1
Main sources of information												
Online literature	6	15.8	8	11.4	41	49.4	13	31.7	4	18.2	72	28.3
Conferences	2	5.3	9	12.9	4	4.8	4	9.8	1	4.5	20	7.9
Courses (CPD/CEU)	16	42.1	26	37.1	21	25.3	16	39.0	5	22.7	84	33.1
Print media	4	10.5	16	22.9	2	2.4	3	7.3	2	9.1	27	10.6
Webinars or seminars	6	15.8	8	11.4	7	8.4	3	7.3	6	27.3	30	11.8
Missing	4	10.5	3	4.3	8	9.6	2	4.9	4	18.2	21	8.3

	Austria (N=38)		**Germany (N=38)**		**United States (N=83)**		**Australasia (N=41)**		**Missing (N=22)**		**Total (N=254)**	
Most reliable source of information												
Research papers	11	28.9	14	20.0	37	44.6	16	39.0	5	22.7	83	32.7
Experts	16	42.1	37	52.9	23	27.7	12	29.3	6	27.3	94	37.0
Books	1	2.6	4	5.7	5	6.0	6	14.6	5	22.7	21	8.3
Conferences	4	10.5	10	14.3	10	12.0	5	12.2	2	9.1	31	12.2
Missing	6	15.8	5	7.1	8	9.6	2	4.9	4	18.2	25	9.8
Mean years of practice ± SD	13.3	10.0	18.9	9.5	14.8	8.5	18.6	10.5	19.8	11.6	16.8	9.9
Median number of patients per week (range)	30	15, 55	21.5	15, 30	30	20, 43.8	30	20, 40	30	20, 40	25	15, 40
Mean years of treating cancer patients ± SD	12.5	9.6	12.3	8.6	11.4	8.1	14.5	10.1	13.9	10.8	12.5	9.1
Median number of cancer patients per week (range)	2	1, 10	2	1, 3	3	1, 7	2	1, 3	1.5	1, 3	2	1, 4

3.2.2 Clinical experience and practice

The number of years in practice significantly differed from the years of treating patients with cancer (mean difference [MD] = 4.19, 95% CI 3.40 to 4.98, $p < 0.001$) (107). Despite this, the median of 2 (1, 4) cancer patients seen per week suggests a relatively low frequency compared to the total weekly number of patients (median 25 [15, 40]). CAM practitioners are predominantly consulted by breast cancer patients (61.8%, 157/254), primarily at the start of (39.8%, 101/254) or in between cancer-specific treatment sessions (33.1%, 84/254). Patients with or without metastases are evenly distributed according to the responses (with metastases 39.0%, 99/254, without metastases 39.8%, 101/254) (107).

The most common reason for consultation, as reported by survey respondents, is "to alleviate side effects of cancer treatment" (52.4%, 133/254), followed by "to strengthen their body during cancer treatment" (28.7%, 73/254) (107). Only a small percentage (6.7%, 17/254) indicated that their patients' primary goal was "to cure their cancer." A majority of respondents (64.6%, 164/254) utilize a combination of CAM therapies and other modalities considered complementary medicine (107).

CAM practitioners identified the most common side effects of tumor-specific treatment as "fatigue/drowsiness" (21.7%, 55/254), "pain" (16.1%, 41/254), and "depression/anxiety" (7.5%, 19/254) (107). When asked about the most effectively treated symptoms using acupuncture, 34.3% (87/254) mentioned "pain," followed by "nausea/emesis" (21.3%, 54/254) and "depression/anxiety" (20.1%, 51/254). Herbal medicine was reported to be more effective for "fatigue/drowsiness" (22.4%, 57/254), "constipation" (7.1%, 18/254), "depression/anxiety" (6.7%, 17/254), and "sleep problems" (6.7%, 17/254) (107).

While it is uncommon (28.0%, 71/254) for respondents to be in contact with their patients' treating oncologists, those who are, often share information about their CAM treatment (64.8%, 46/71) using a combination of CAM and scientific terminology (46.5%, 33/71). Comprehensive information about respondents' clinical experience and practice can be found in Tables 10 and 11.

Table 11: Characteristics of clinical practice by country (107)

	Austria (N=38)		Germany (N=70)		USA (N=83)		Australasia (N=41)		Missing (N=22)		Total (N=254)	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Type of Cancer												
Breast	21	55.3	56	80.0	51	61.4	20	48.8	9	40.9	157	61.8
Gastrointestinal	7	18.4	1	1.4	5	6.0	2	4.9	3	13.6	18	7.1
Lung	2	5.3	3	4.3	3	3.6	6	14.6	0	0.0	14	5.5
Pancreas/Liver	0	0.0	0	0.0	2	2.4	2	4.9	0	0.0	4	1.6
Prostate	2	5.3	3	4.3	1	1.2	3	7.3	1	4.5	10	3.9
Other	4	10.5	6	8.6	21	25.3	8	19.5	7	31.8	46	18.1
Missing	2	5.3	1	1.4	0	0.0	0	0.0	2	9.1	5	2.0
Tumor stage												
With metastases	14	36.8	24	34.3	40	48.2	13	31.7	8	36.4	99	39.0
Without metastases	12	31.6	30	42.9	29	34.9	22	53.7	8	36.4	101	39.8
Remission/cured	10	26.3	14	20.0	11	13.3	6	14.6	4	18.2	45	17.7
Missing	2	5.3	2	2.9	3	3.6	0	0.0	2	9.1	9	3.5
First time consultation												
Shortly after cancer diagnosis	8	21.1	18	25.7	10	12.0	7	17.1	7	31.8	50	19.7
At the start of or during treatment	16	42.1	28	40.0	35	42.2	17	41.5	5	22.7	101	39.8
After or in between treatment	8	21.1	22	31.4	31	37.3	16	39.0	7	31.8	84	33.1
If they have been told that their cancer is incurable	4	10.5	2	2.9	5	6.0	1	2.4	1	4.5	13	5.1

Missing	2	5.3	0	0.0	2	2.4	0	0.0	2	9.1	6	2.4
	Austria (N=38)		**Germany (N=70)**		**USA (N=83)**		**Australasia (N=41)**		**Missing (N=22)**		**Total (N=254)**	
Main reason for consultation												
To cure their cancer	4	10.5	4	5.7	2	2.4	5	12.2	2	9.1	17	6.7
To strengthen their body during cancer treatment	15	39.5	27	38.6	12	14.5	15	36.6	4	18.2	73	28.7
To alleviate side effects of cancer treatment	12	31.6	34	48.6	56	67.5	20	48.8	11	50.0	133	52.4
To alleviate disease specific symptoms	6	15.8	4	5.7	11	13.3	1	2.4	4	18.2	26	10.2
Missing	1	2.6	1	1.4	2	2.4	0	0.0	1	4.5	5	2.0
Side effect of cancer specific treatment												
Pain	1	2.6	3	4.3	27	32.5	9	22.0	1	4.5	41	16.1
Fatigue/Drowsiness	9	23.7	18	25.7	12	14.5	10	24.4	6	27.3	55	21.7
Nausea/Emesis	0	0.0	3	4.3	8	9.6	0	0.0	3	13.6	14	5.5
Anorexia (loss of appetite)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Breathlessness	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Depression/Anxiety	1	2.6	8	11.4	9	10.8	0	0.0	1	4.5	19	7.5
Sleep problems	0	0.0	1	1.4	0	0.0	1	2.4	0	0.0	2	0.8
Constipation	1	2.6	0	0.0	0	0.0	0	0.0	0	0.0	1	0.4
Missing	26	68.4	37	52.9	27	32.5	21	51.2	11	50.0	122	48.0

	Austria (N=38)		Germany (N=70)		USA (N=83)		Australasia (N=41)		Missing (N=22)		Total (N=254)	
Acupuncture is most effective for												
Pain	18	47.4	14	20.0	32	38.6	18	43.9	5	22.7	87	34.3
Fatigue/Drowsiness	6	15.8	9	12.9	11	13.3	8	19.5	7	31.8	41	16.1
Nausea/Emesis	6	15.8	20	28.6	21	25.3	5	12.2	2	9.1	54	21.3
Anorexia (loss of appetite)	0	0.0	0	0.0	1	1.2	1	2.4	0	0.0	2	0.8
Breathlessness	0	0.0	1	1.4	0	0.0	0	0.0	0	0.0	1	0.4
Depression/Anxiety	3	7.9	23	32.9	14	16.9	4	9.8	7	31.8	51	20.1
Sleep problems	2	5.3	1	1.4	1	1.2	2	4.9	0	0.0	6	2.4
Constipation	1	2.6	0	0.0	1	1.2	1	2.4	1	4.5	4	1.6
Missing	2	5.3	2	2.9	2	2.4	2	4.9	0	0.0	8	3.1
Herbs are most effective for												
Pain	0	0.0	0	0.0	0	0.0	2	4.9	1	4.5	3	1.2
Fatigue/Drowsiness	8	21.1	17	24.3	19	22.9	10	24.4	3	13.6	57	22.4
Nausea/Emesis	1	2.6	4	5.7	6	7.2	3	7.3	3	13.6	17	6.7
Anorexia (loss of appetite)	0	0.0	2	2.9	3	3.6	0	0.0	0	0.0	5	2.0
Breathlessness	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Depression/Anxiety	2	5.3	7	10.0	6	7.2	0	0.0	2	9.1	17	6.7
Sleep problems	1	2.6	4	5.7	9	10.8	2	4.9	1	4.5	17	6.7
Constipation	1	2.6	4	5.7	13	15.7	0	0.0	0	0.0	18	7.1
Missing	25	65.8	32	45.7	27	32.5	24	58.5	12	54.5	120	47.2

	Austria (N=38)		Germany (N=70)		USA (N=83)		Australasia (N=41)		Missing (N=22)		Total (N=254)	
Combination with other CAM therapies												
Yes	21	55.3	47	67.1	55	66.3	27	65.9	14	63.6	164	64.6
No	17	44.7	23	32.9	27	32.5	14	34.1	8	36.4	89	35.0
Missing	0	0.0	0	0.0	1	1.2	0	0.0	0	0.0	1	0.4
Contact with oncologist												
Yes	18	47.4	13	18.6	33	39.8	5	12.2	2	9.1	71	28.0
No	19	50.0	57	81.4	49	59.0	36	87.8	20	90.9	181	71.3
Missing	1	2.6	0	0.0	1	1.2	0	0.0	0	0.0	2	0.8
Share information with oncologist												
Yes	13	34.2	5	7.1	24	28.9	2	4.9	2	9.1	46	18.1
No	5	13.2	8	11.4	9	10.8	3	7.3	0	0.0	25	9.8
Missing	20	52.6	57	81.4	50	60.2	36	87.8	20	90.9	183	72.0
How is information shared												
CAM terminology only	1	2.6	0	0.0	0	0.0	0	0.0	0	0.0	1	0.4
Biomedicine and scientific language only	4	10.5	1	1.4	5	6.0	1	2.4	0	0.0	11	4.3
A mixture of both	8	21.1	4	5.7	19	22.9	1	2.4	1	4.5	33	13.0
Missing	25	65.8	65	92.9	59	71.1	39	95.1	21	95.5	209	82.3

Once again, we observed country-specific differences in the clinical practice patterns of CAM practitioners. In the USA, practitioners tend to encounter cancer patients in later disease stages, with 48.2% (40/83) having metastatic disease (107). However, the time of the first consultation did not vary between countries. Another difference across countries was found in the perceived effectiveness of acupuncture. German CAM practitioners indicated that acupuncture is most effective for treating "depression and anxiety" (38.6%, 32/70) compared to practitioners in Austria (7.9%, 3/38), the USA (16.9%, 14/83), and Australasia (9.8%, 4/41) (107). Conversely, "pain" was identified as the symptom that benefited the most from acupuncture by practitioners from Austria (47.4%, 18/38), the USA (38.6%, 32/83), and Australasia (43.9%, 18/41) compared to Germany (20.0%, 14/70) (107).

German CAM practitioners also reported the lowest rate of contact with the primary oncologist (18.6%, 13/70) and sharing information with them (38.5%, 5/13) (107). In contrast, countries with a high proportion of multidisciplinary employed CAM practitioners demonstrated a high degree of contact with the primary oncologist (Austria 47.4%, 18/38; USA 39.8%, 33/83) and information exchange (Austria 72.2%, 13/18; USA 72.7%, 24/33) (107).

3.2.3 Role of research in clinical practice

Across all countries, CAM practitioners reported a mean 59.8 (SD 26.1) on a scale of 0 to 100 regarding the importance of research in clinical practice, with higher scores reflecting a greater importance (107). Moreover, 87.4% (222/254) expressed an interest in research but only a relatively small proportion of CAM practitioners had ever participated in clinical research for either acupuncture (24.4%, 62/254) or herbal medicine (6.3%, 16/254) (107). Certified courses for continuing professional education were identified as the primary source of information by 33.1% (84/254), followed by online literature databases like PubMed (28.3%, 72/254), and webinars/seminars (11.8%, 30/254). In terms of reliability, practitioners considered expert opinions (37.0%, 90/254), research papers (32.7%, 83/254), and conferences (12.2%, 31/254) as the most trustworthy sources (107). The majority of CAM practitioners reported reading 10 to 20 research papers per year (34.3%, 87/254), and 62.6% (159/254) stated that a research paper had influenced their practice of acupuncture. In contrast, only 34.3% (87/254) reported that a scientific paper had influenced their practice of herbal medicine (107).

Compared on an international level, German CAM practitioners reported the lowest importance of research in clinical practice with 48.0 (SD 27.6) compared to Austria (58.5, SD 28.4), the USA (66.9, SD 20.4), and Australasia (64.1, SD 24.8) (Figure 2) (107).

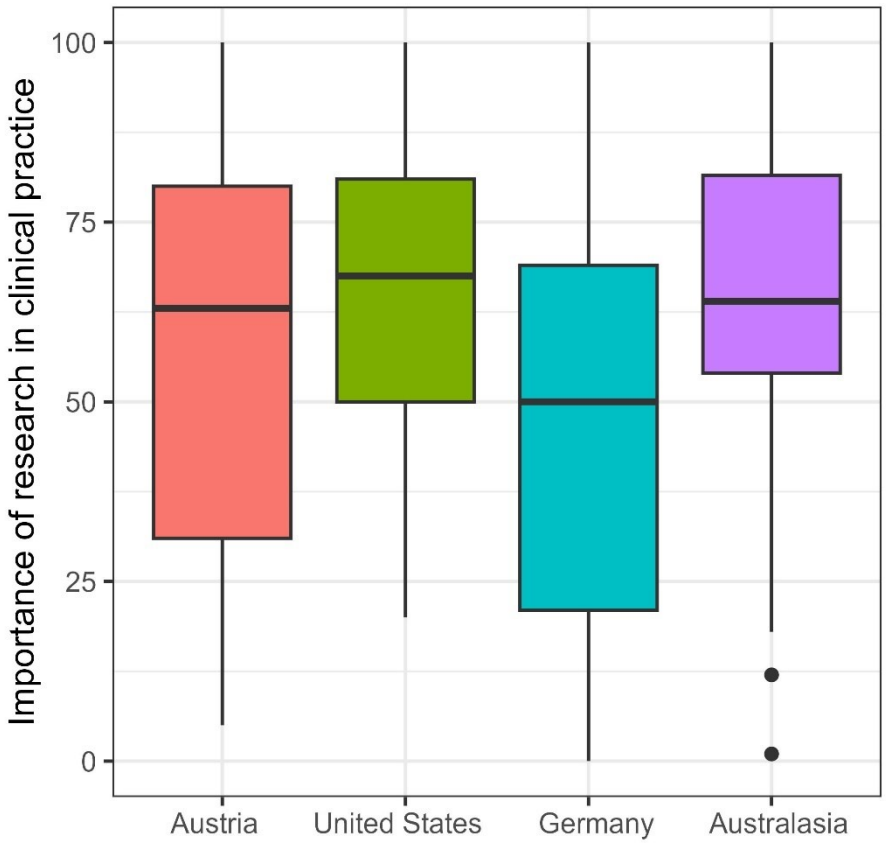

Figure 2: Importance of research rating by country.

While the interest in research was high across all countries, differences were observed for the active participation of CAM practitioners in research of acupuncture and herbs and the influence of clinical research in their daily clinical practice. Practitioners in the USA and Australasia participated most often in clinical research, which were mostly acupuncture studies (USA 32.5% 27/83, Australasia 39.0% 16/41). Research influenced German CAM practitioners the least, with 44.3% (31/70) reporting that research ever changed their practice of acupuncture compared to Austria (63.2%, 24/38), the USA (74.7%, 62/83), and Australasia (75.6%, 31/41).

3.2.4 Reasons for not treating cancer patients

In total, 150 CAM practitioners (37.1%, 150/404) indicated that they do not treat cancer patients, with almost half of them (47.3%, 71/150) providing detailed reasons. Using qualitative text analysis, we condensed the open-end text answers to meaning units and grouped the results in thematic categories (Table 12). We identified six categories of reasons for not treating

cancer patients: "time issues," "no referrals," "other clinical focus," "missing experience," "personal reasons," and "concerns."

Table 12: Thematic categories of reasons for not treating cancer (107)

Reason for not treating cancer patients	Total (N=71)	%
Time issues	5	7.0
No referrals	36	50.7
Other clinical focus	23	32.4
Missing experience	13	18.3
Personal reasons	5	7.0
Concerns	7	9.9

Just over half (50.7%, 36/71) of the respondents stated that the main reason for not seeing patients with cancer in their clinics was due to having no referrals, while almost one-third (32.4%, 23/71) focused their clinical practice on other conditions. Reasons for not treating cancer patients also related to a lack of both clinical experience and training in oncology (18.3%, 13/71), as well as personal reasons (7.0%, 5/71), and concerns about interactions with cancer-specific conventional interventions (9.9%, 7/71) (Table 12).

Examples of statements provided by CAM practitioners are (as partly published in (107)):

- *"I am specialized in fertility treatment and pain relief. If I were to treat oncology patients, I would need further training, and I don't know if I have the mental strength to handle oncology patients. I had only one patient in 7 years. It was quite a challenge, but in the end, it went well."* — Germany, acupuncturist and herbalist, age 56-65 years old. (as published in (107))

- *"No local demand or referral mechanism. I will occasionally treat people undergoing chemotherapy or radiotherapy for symptoms like nausea, but these are casual referrals rather than from the nearest oncology center, which is 30 km away and fairly conservative."* — Australia, acupuncturist and herbalist, age 56-65 years old. (as published in (107))

- *"I treated my father with oncology-related symptoms and through his treatments; however, did not feel that the training in my degree covered anything specific to this and the medications—so just focused and treated the patterns that presented at the time. Would like to have had more training in this area. In Australia, I think that access to acupuncturists is an issue. I know that my father would have taken up this option if offered within the hospital setting or within his at-home palliative care team."* — Australia, acupuncturist, age 46-55. (as published in (107))

- *"In the beginning I had a few. I'm cancer patient my own and 'cured' for 6 years, which is way I had a good connection to the patients. Then, my focus moved to stress and burnout. Also, constant warnings about treating cancer patients as licensed CAM practitioner being against the law, led me to not educating myself further within this field"* — Germany, acupuncturist and herbalist, age 46-55. (as published in (107)).

- *"I focused my practice and research on fertility and gynecological problems. Ther are a few patients with breast cancer, but rarely, so that I cannot say that I treat cancer patients. So, it's a question of specialization."* — Germany, acupuncturist and herbalist, age 36-45. (as published in (107))

- *"It is not my main focus. Patients come because of other conditions; the cancer diagnosis is sometimes additive. I integrate it in my treatment, then."* — Germany, acupuncturist and herbalist, age 46-55. (as published in (107))

- *"Because of personal reasons. To me, it is also too much work, to sufficiently educate myself, to do professional work."* — Germany, acupuncturist and herbalist, age 56-65. (as published in (107)).

- *"I treat oncology patients, but I don't treat cancer. Hard question to answer."* — United States of America, acupuncturist and herbalist, age 46-55. (as published in (107))

- *“The topic of oncology is exciting; acupuncture and herbal medicine are good therapy options to improve the quality of life of the patients, but this topic affects me too deeply.”* — Austria, acupuncturist and herbalist, age 36-45. (as published in (107))

- *“Few cancer patients call me. There is also a little shy from me, to treat within an oncological setting (adverse effects with chemotherapy and other drugs etc.)”* — Austria, acupuncturist and herbalist, age 36-45. (as published in (107))

Across all the countries included in our analysis, practitioners expressed generally similar reasons for not treating cancer patients. However, a minor difference was observed in the qualitative analysis of responses, especially concerning the topics of “no referrals” and “concerns” among practitioners from the USA and Australasia (107). Practitioners who reported receiving limited or no patient referrals often cited additional concerns about legal issues or restrictions within their countries as the primary reasons for this situation. Furthermore, some practitioners noted that while they occasionally treated cancer patients, they did not consider themselves experts in CAM in an oncological setting. They expressed a need for further education before incorporating supportive cancer treatment into their practice (107).

4 Discussion

This section includes parts of the content that has been previously published in *PLOSE ONE (Huemer et al., 2023)* (106) and the *Journal of Integrative Medicine (Huemer et al., 2023)* (107) as part of my dissertation thesis, and certain portions are presented identically.

In this dissertation project, we conducted a comprehensive exploration of the landscape of CAM therapies in Austria, examining both patient and CAM practitioner perspectives. Furthermore, we undertook a comparative analysis of the practice patterns in acupuncture and herbal medicine on an international scale. The following discussion delineates the outcomes of each study individually, while jointly summarizing the findings in a comprehensive conclusion.

4.1 Patient survey

Parts of this section were reproduced from or similarly published in Huemer et al. (106).

Several previous studies have investigated the prevalence, role, and patterns of CAM utilization among patients in oncology (11, 34-44). However, the use of complementary therapies changed over time and varies considerably depending on geographical and cultural factors (121). Consequently, the generalizability of findings from these studies to the unique circumstances of a single country is limited. Molassiotis et al. conducted the only European survey investigating CAM utilization among cancer patients, but this study was published over a decade ago in 2005 and did not include an Austrian sample (38). Following the recommendations of the WHO to explore and delineate country-specific variations (13), we undertook the most comprehensive survey in Austria to date, aiming to elucidate the characteristics of Austrian cancer patients utilizing CAM in addition with their cancer treatment (106).

We found a surprisingly high prevalence of 63.7% of CAM utilization in our study sample compared to a small study previously reporting a prevalence of 27.0% among Austrian cancer patients (106, 112). The difference may be explained by an increasing popularity of CAM therapies over the past 20 years. Our results complement the findings of other authors showing an increased use of CAM by cancer patients over the previous decades (121). Additionally, our study was conducted during the coronavirus disease 2019 (COVID-19) pandemic, which led to a greater uncertainty for cancer patients regarding the availability of tumor-specific

treatment, the risk of COVID-19 infection, and potential interference with their treatment plans. The resultant stress associated with the pandemic amplified the perceived symptom burden and increased the incidence of anxiety and depression (122-125). Moreover, the pandemic introduced new barriers to accessing healthcare services for cancer patients, leading to delays in the initiation of tumor-specific treatment and reduced access to symptom management (126, 127). These circumstances likely influenced the information-seeking behavior of the patients in our study, promoting a greater motivation to independently find ways to manage their occurring symptoms through alternative sources.

Among the frequently utilized CAM therapies in our study were biologically-based practices like vitamin and mineral supplementation, herbal medicine, and medical teas, along with manipulative body-based therapies such as massage and acupuncture the most popular (106). While certain components of these modalities, like acupuncture and massage, are currently recommended by clinical guidelines, caution is warranted for many biologically-based practices, as they lack a sufficient evidence-base and general recommendations for concurrent use with cancer-specific treatments (55). Our findings underscore the urgent need for comprehensive guidance on CAM for cancer patients and emphasize the importance of discussing CAM utilization during oncological care. Given the popularity of acupuncture in our study sample and its compliance with clinical guidelines, providing directed recommendations for its use and facilitating referrals to reliable acupuncturists could be a meaningful strategy for safely guiding cancer patients in their wish to utilize CAM within a clinical setting (106).

Further, the proportion of cancer patients actively disclosing and discussing their CAM use with their treating oncologist stood at only 42.2%, highlighting the need for improved communication about CAM (106). Moreover, the noteworthy 19.2% of respondents that chose not to answer this question suggest a significant communication gap. This item might be susceptible to social desirability bias due to fears of facing negative consequences when admitting to the use of CAM, potentially resulting in underreported outcomes. Additionally, a majority of patients acquire information about CAM from their close social environment (friends 45.0%, family 37.6%) and through media channels (internet 16.5%, other media 18.3%), with notably lower proportions seeking guidance from medically trained professionals (family physician 21.1%, CAM practitioner 11.9%, oncologist 9.2%, radiologist 0.9%) (106). Considering the skewed information-seeking behavior toward non-professional sources, risks associated with CAM due to misinformation may arise from this communication gap between physicians and patients (106).

In our study, we found no statistical association between CAM utilization and single symptoms or summative scores like the ESAS total score representing the experienced total symptom burden (43, 44). However, CAM utilization was 3.83-fold higher in patients with the symptom-cluster "drowsiness-depression-anxiety" compared to low-symptomatic cancer patients (106). Our results suggest an amplifying nature of cooccurring psychological symptoms, potentially resulting in higher symptom distress and interference with daily life, which, in turn, increases the willingness to use CAM. In total, we found four distinct symptom-clusters: "drowsiness-depression-anxiety", "moderate fatigue-drowsiness-sleep", "anorexia-nausea-breathlessness-constipation-emesis", and "all-low symptoms". Notably, both clusters entailing drowsiness are associated with a higher chance of using CAM (OR 3.83, p=0.039, and 2.09, p=0.062, respectively), although only one of them showed statistical significance according to our analysis (106). It could be that the "moderate fatigue-drowsiness-sleep" cluster is a precursor of the "drowsiness-depression-anxiety" cluster, since long-lasting fatigue and sleep issues are associated with a higher risk of developing depression in cancer patients (128, 129). Moreover, fatigue and depressive symptoms are among the most distressing for cancer patients with limited treatment options potentially motivating patients to take self-action and possibly explaining the higher prevalence of CAM use in our sample (130). In contrast, the cluster “anorexia-nausea-breathlessness-constipation-emesis” consisted mainly of gastrointestinal symptoms and had a lower chance of CAM utilization (OR 0.57, p=0.362) (106). Compared to psychological symptoms like depression and fatigue, gastrointestinal symptoms are relatively easy to manage, as a variety of conventional fast acting and potent treatments are widely available and easily accessible for patients. Additionally, health practitioners are more aware about gastrointestinal than psychological symptoms in cancer patients, the former are also routinely screened during cancer treatment, potentially explaining the lower chance of CAM utilization by patients facing this symptom cluster (131, 132).

Our cluster analysis aligns with previous studies investigating the occurrence of symptom clusters in cancer patients (117, 133-135). In their systematic review, So et al. identified clusters including fatigue-sleep disturbance and psychological symptoms as the most prevalent in cancer patients (135). Other common symptom clusters encompass fatigue and pain and gastrointestinal symptoms including anorexia, nausea and emesis (133). Our results support the previous findings of the existence and clinical relevance of such clusters (106). However, the etiology and pathophysiology of symptom clusters in cancer patients is not fully understood to date. Previous studies found that chronic inflammation may contribute to the development of a psychoneurological symptom cluster as proinflammatory cytokines may be involved in the pathophysiology of cancer-related fatigue, depression, and cancer pain (136,

137). Additionally, symptom clusters may arise from a single "trigger" symptom with secondary effects leading to the development of other symptoms, eventually forming a cluster (133). For example, cancer pain may interfere with the sleep quality, causing fatigue and depression. Both, in turn, are known to influence cancer pain through a disturbance of neurotransmitters, enhancing the experienced pain (133). In this way, a vicious circle may arise maintaining a stable symptom cluster of more than two symptoms occurring together (133). Our results support this established hypothesis, as the co-occurring symptoms in our clusters, particularly cancer-related fatigue and depression, are known to be intercorrelated (128, 129).

The strong statistical association between symptom clusters encompassing mainly psychological symptoms and utilization of CAM in cancer patients is also reflected by the patient-reported reasons for CAM use in our sample. The most reported reasons are the wish “to strengthen the body” (47.7%), “to improve quality of life” (45.9%), “to lower treatment side effects” (33.9%), and “to try everything” (31.2%) (106). Moreover, patients felt that CAM mainly improved “treatment side effects” (34.9%), “physical well-being” (33.9%), and their “Quality of Life” (25.7%) (106).

Previous studies have also suggested that the utilization of CAM is often driven by active problem-solving coping behavior or dissatisfaction with the treating physician, rather than solely by psychological distress (39, 40). Patients may turn to CAM due to unmet needs in symptom management, motivating them to seek assistance beyond the boundaries of conventional medicine. In some cases, this tendency towards CAM may even lead to the refusal of conventional cancer treatment, raising the risk of death among CAM users who omit traditional treatments in favor of CAM (101). The high prevalence of CAM use in our study, as well as in many other countries, may reflect the widespread demand for professional symptom management and an integrative approach encompassing rehabilitative, early palliative, and supportive care, along with evidence-based complementary medicine, particularly during the course of oncological treatment (106).

Symptoms associated with cancer and tumor-specific therapies evolve throughout the disease trajectory, potentially worsening in severity and significantly impacting the patient's quality of life as the disease progresses (135). Critical events and changes in the disease trajectory may further include the diagnosis of progressive disease, initiation of a new cancer-specific therapy, or severe changes in the experienced symptoms, urging a patient to take action (33). Although the discussion of CAM should be initiated early with every cancer patient, a notable shift in symptom burden, such as the emergence of the drowsiness-depression-anxiety cluster, can serve as a crucial indicator for oncologists to reconsider the use of CAM in this patient

population (106). To facilitate effective discussions about CAM in an oncology setting, Schofield et al. have provided guidance based on a systematic review (105). According to their recommendations, assessing CAM use at critical points during a patient's disease trajectory, particularly during the initiation of a new treatment regimen and the onset of new symptoms, is essential (105). This proactive approach enables healthcare professionals to address evolving patient needs and preferences and promote a more comprehensive and patient-centered approach to cancer care, which may prevent potential interactions or, in extreme cases, treatment refusal (106).

Additionally, promoting open communication about CAM can enhance the physician-patient relationship and increase patient satisfaction with cancer care. Therefore, incorporating discussions about CAM into routine history-taking is crucial (33). When addressing the topic of CAM, it is essential to elucidate relevant concerns from a scientific standpoint while acknowledging and respecting patients' cultural diversity and epistemological belief systems (33). Physicians are advised to choose a patient-centered communication style and encourage shared decision-making, respecting the patient's autonomy when guiding cancer patients in their choice of supportive CAM therapies (138). When inquired about the wish to utilize CAM, oncologists may suggest complementary therapies that were shown to benefit cancer patients. Clinical guidelines concerning the management of cancer pain, cancer-related fatigue, nausea and emesis, and supportive care in breast cancer patients published by leading oncological societies, including the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), and the AWMF have incorporated complementary therapies in their recommendations and provide evidence-based guidance for oncologists for discussing CAM therapies with their patients (139-144). Based on these recommendations, oncologists may suggest CAM therapies aimed at the patients’ concerns. Further, patients prefer referrals to CAM practitioners by their treating oncologist rather than from outside sources (145). Hence, Schofield et al. recommended the collaboration with local qualified CAM practitioners to facilitate the referral of patients to trustworthy professionals, ensuring the delivery of safe CAM treatments (105). In Austria, the Austrian medical chamber provides certification programs for the most widely used CAM modalities (20). Referring patients to CAM practitioners holding a certificate issued by the Austrian medical chamber may be a meaningful way for health care practitioners to assess their educational background and reputation.

Notably, our study revealed that most participants utilized relatively safe CAM modalities, such as physical therapies like massage and acupuncture (89, 106). Despite the predominance of safe practices, it is crucial to acknowledge that the reported therapies also encompassed

biological-based treatments like herbs and medical teas. This category of CAM modalities carries the potential for interactions with tumor-specific treatments (95). The results of our study show that cancer patients were predominantly assigned to the clusters including cancer-related fatigue, depression, anxiety, and sleep disorders (Cluster 2 [n=83] and Cluster 1 [n=23]) (106). Acupuncture is recommended by all major clinical guidelines to manage and support patients experiencing these psychological symptoms including ASCO (139, 140), NCCN (142), and AWMF (55). Considering the results of our cluster analysis, acupuncture was found to effectively reduce the severity of symptom clusters involving neuropsychological symptoms, especially pain-fatigue-sleep disturbances in cancer patients (146). In contrast to herbal therapies, acupuncture has a favorable safety profile provided it is delivered by qualified practitioners, additionally supporting its utilization in supportive and palliative care (89). Additionally, acupuncture is currently the most investigated CAM therapy in general and among cancer patients to date (56). When addressing the topic of CAM in cancer patients, practitioners may suggest using acupuncture instead of other CAM therapies given its established evidence, preferable safety profile, wide applicability and availability.

Finally, some limitations of the study should be discussed. First, we used a single-center design, which restricts the generalizability of our findings concerning cultural and socio-demographic factors. Therefore, our results may not be applicable in areas where traditional and complementary medicine constitutes a significant portion of the local public health care system (106). However, the primary intention of the study was to assess the patterns of CAM utilization among Austrian cancer patients. Additionally, we utilized a validated measurement tool (HCAMQ) to assess attitudes toward CAM, and we found no statistically significant difference between CAM users and non-users in our sample, suggesting that individual cultural preoccupation did not exert a significant influence on the motivation to utilize CAM (106). Second, our study only included patients currently receiving oncological or palliative care at our clinic. Consequently, our associations are relevant only to patients using CAM in conjunction with conventional medicine, not those solely relying on CAM instead of conventional medicine, which could represent a distinct patient cohort with different socio-demographic, clinical, and motivational characteristics (106). Nonetheless, our study has strengths such as a prospective design, robust sample size, a diverse participant group, and validated patient-reported outcome measures, all supporting our conclusion that symptom clusters are a noteworthy and measurable predictor of CAM utilization in oncology patients (106).

In summary, the results of our survey show a high prevalence of CAM utilization within our study sample and a significant communication gap between oncologists and cancer patients concerning CAM (106). Cancer patients frequently use safe CAM therapies which should be promoted by their treating oncologists according to current clinical guidelines, focusing on non-pharmacological procedures like acupuncture. However, the delivery of acupuncture should be made by reputable acupuncturists holding a certificate by the Austrian medical chamber to ensure an adequate training and education in this procedure.

4.2 Practitioner survey

Parts of this section were reproduced from or similarly published in Huemer et al. (107).

Acupuncture is one of the most frequently used CAM therapies by Austrian cancer patients, aiming to relieve their cancer-related symptoms (106). The delivery of acupuncture is considered safe when performed by a trained and experienced acupuncturist (89). However, acupuncturists and other CAM practitioners need to comply with modern research principles and evidence-based medicine like any other health care practitioner in order to delivere safe and effective treatments and to prevent interactions with conventional cancer treatments. Previous studies have shown that a significant proportion of Austrian CAM practitioners, mainly Homeopaths, had a low trust in modern science (26). Other studies in Australia, New Zealand and the USA found similar results of low to moderate research literacy among acupuncturists (147, 148). Furthermore, the case of Dr. Ryke Geerd Hamer is a cautionary example of a CAM practitioner holding a medical degree but using practices contradicting the current state of science causing tremendous harm to patients (24). In order to offer and recommend patients acupuncture and other CAM procedures as suggested by current clinical guidelines, it is important for oncologists to consider the practice patterns of acupuncturists and other CAM practitioners (32). Hence, we performed a multinational online survey aiming to investigate the evidence-informed practice, research literacy and role of research among Austrian acupuncturists and herbalists treating cancer patients and compare the practice patterns across other western countries (107). The results help to understand the current landscape of how acupuncture is provided in Austria to better guide oncologists in their treatment referrals of cancer patients. Additionally, our results provide important insights for the development and improvement of educational programs for acupuncturists and CAM practitioners aiming to enhance their research literacy (107).

To our knowledge, our study is the largest survey on an international scale assessing the clinical practice of CAM practitioners focusing on acupuncture and herbal medicine in cancer care (107). We could also map and compare the landscape of CAM practice across five western countries, enabling to draw comparative conclusions. In general, treating cancer patients is common (62.9%) among acupuncturists and herbalists which complements the findings of our survey among cancer patients showing a high prevalence of CAM utilization (106, 107). All practitioners were acupuncturists with 57.1% also practicing herbal medicine. However, only 23.6% were medical doctors of which the most practiced in Austria and Germany while it seems to be uncommon for acupuncturists and herbalists to hold a medical degree in the USA and Australasia (107). This demographical difference is explained by the legal regulations of each country. In Austria, any invasive or pharmacological practice claiming to influence a person's health or disease is legally restricted to medical doctors (19). In contrast, non-academic trained disciplines are allowed to perform acupuncture and herbal medicine after appropriate training and registration in Germany, the USA, Australia, and New Zealand (149-151). A legal restriction of CAM practices to medical doctors may be a meaningful way to prevent a fraudulent use and the delay of diagnosis and treatment of serious diseases, but does not assure an evidence-informed practice of CAM, as previously shown in a sample of Austrian medical doctors (26). However, the main focus of CAM practitioners' treatment was supportive and palliative care in conjunction to conventional medicine. Only 6.7% reported that "to cure the cancer itself" was the main reason for patient consultation, suggesting a realistic appraisal of the capabilities of acupuncture and herbal medicine by the CAM practitioners in our sample (107).

Most patients consulting CAM practitioners have breast cancer (61.8%) at any tumor stage and see them mainly before, during, or right after cancer-specific treatment. The most reported reason for consultation was "to alleviate treatment-related side effects" (52.4%) (107). The practitioner-reported patient characteristics and reasons for consultation align with previous studies. Patients identifying as women were repeatedly reported to use CAM alongside conventional medicine more often than other patients, potentially explaining the high proportion of breast cancer patients reported by our study participants (35-38). Moreover, our results concerning the reasons for consulting CAM practitioners also complement the findings of these studies, with symptom management being the most prevalent intention for seeing an acupuncturist or herbalist (35-38). Furthermore, we assessed the most frequently treated symptoms with fatigue and drowsiness being the most prevalent (21.7%) followed by pain (16.1%) and depressive symptoms (7.5%) (107). We found similar results in our survey among cancer patients, revealing a 3.83-fold higher chance to use CAM among cancer patients with

the symptom cluster “drowsiness-depression-anxiety” (106). The reported symptoms are also the most common studied symptoms in the field of integrative oncology (152, 153). The respondents within our study sample rated pain (34.4%), nausea/emesis (21.3%), depression/anxiety (20.1%), and fatigue/drowsiness (16.1%) to be treated most effectively using acupuncture, which also reflects the current scientific evidence and recommendations of leading oncological associations (107, 139-144). In contrast, constipation was the top-rated indication for herbal medicine, which is currently not recommended according to current clinical guidelines (107, 139-144). Moreover, the diverse and personalized nature of herbal prescriptions challenge the evaluation of both its effectiveness and safety, strictly limiting general recommendations for the utilization of herbal medicine especially in cancer care (88). However, our results suggest that the participating CAM practitioners are aware of the current indications and use the available evidence for acupuncture in the treatment of cancer-related symptoms (107).

Acupuncturists and herbalists gain general experience before starting to treat cancer patients as suggested by the difference in the reported time of total practice and time of treating cancer patients (107). Our qualitative analysis of the free-text responses given by our study participant for not treating cancer patients provides complementary insights to these results (107). In addition to lacking referrals or prioritizing other health conditions in their practice, many respondents refrain from treating cancer patients due to insufficient clinical experience and concerns about potential interactions (107). Treating cancer patients seems to be experienced by CAM practitioners as a complex and emotionally challenging task, requiring profound knowledge in their respective discipline and confidence in their expertise. Moreover, our results suggest a growing trend towards specialization among CAM practitioners. Additionally, our survey participants expressed a need for additional training before engaging in the treatment of cancer patients. Hence, our results suggest to establish further educational or licensing programs to develop a subdiscipline of integrative CAM oncologists (107). To address the reported gaps in knowledge, concerns, and lack of expertise, a structured educational program could be created. This program might encompass the biological and clinical principles of oncological diseases, evidence-based recommendations for CAM treatments, and skills in critically evaluating new research findings (107). By offering education in this specialized subdiscipline, CAM practitioners could be equipped with the necessary knowledge and competencies to safely and meaningfully support individuals undergoing cancer treatment. Such initiatives would contribute to enhancing the overall quality of care provided by CAM practitioners in oncology (107).

Currently, most respondents used certified courses to inform their clinical practice (33.1%) and research papers found on online literature databases like PubMed (28.3%), with only a small proportion of 35.0% who underwent focused oncology training (107). However, concerning the perceived reliability of educational sources, the CAM practitioners in our study sample rated experts (37.0%) as more trustworthy than research papers (32.7%), which contradicts the currently accepted hierarchical grading of evidence (29, 154). Notably, our results showed country-specific variations in the perception of reliability, particularly between Austria and Germany versus the USA and Australasia, where CAM practitioners from the latter reported a higher trustworthiness of research papers (107). This discrepancy could potentially be attributed to differences in the educational backgrounds of acupuncturists and herbalists across these regions. In Austria and Germany, an academic-level diploma in acupuncture or herbal medicine is not required, whereas in the USA and Australasia, licensure as a CAM practitioner mandates a college degree or higher in acupuncture or herbology (107, 149-151). Graduating from a higher level of education in CAM practices may contribute to a greater familiarity and appreciation for CAM research among practitioners in the USA and Australasia compared to Austria and Germany (107). However, the tendency to value expert opinions over research findings is not unique to CAM practitioners specializing in cancer care. A recent survey conducted among Australasian CAM practitioners focusing on fertility support yielded similar outcomes, revealing that peer-reviewed research was the least utilized source of knowledge to inform and change their clinical practices (147). Instead, courses and conferences led by experts had a more significant impact on how CAM practitioners approached the treatment and support of couples facing fertility issues (147, 155). In contrast to our study sample, CAM practitioners treating cancer patients still relied on research papers more frequently as a source of information (107). This discrepancy may be associated to a greater awareness and concerns about potential interactions with oncological treatments, yielding an increased interest in the latest research findings within the oncology field (107).

In general, CAM practitioners rated research as moderately important for their clinical practice but most of them (87.4%) are interested in research concerning acupuncture and herbal medicine (107). However, only a few acupuncturists (24.4%) and herbalists (6.3%) ever participated actively in research. Again, we found country-specific differences concerning the importance of research in clinical practice, with German CAM practitioners exhibiting the lowest while those from the USA and Australasia reported the highest ratings (107). These results are also reflected by the item asking if a research paper ever changed the practitioner's way of practice, which again received the lowest agreement among German acupuncturists and herbalists compared to all other countries (107). These results further support our

hypothesis, that the educational background plays a pivotal role in the research literacy and appreciation of research findings for CAM practitioners. Compared to all other participating countries, Germany stands out with a unique regulation of certification programs for CAM practitioners. In Germany, any non-medical trained person may become a “Heilpraktiker” and may practice health interventions on patients after attending an educational program. Despite legal regulations stipulating the delivery of basic evidence-based medical knowledge, a recent study investigating the quality of education and alignment of schools for non-medical practitioners to these legal regulations found, that 83.0% (137/165) did not meet the required standards (156). In contrast, Austria expects CAM practitioners to be medical doctors and the USA and Australasia requires at least a bachelor’s degree in acupuncture or herbal medicine to be registered as CAM practitioners, potentially leading to a higher research literacy among the subgroups of our study sample (107). Fostering a better understanding and skills of the methods of modern research within the training and qualification program of acupuncturists, herbalists and other CAM disciplines may improve the general acceptance of research and its incorporation into their clinical practice (107).

The most frequent place of practice for the majority of respondents was in their own solo clinics (107). Moreover, in Austria and the USA, a small fraction of CAM practitioners is also employed in hospital settings, indicating a growing acceptance of CAM therapies within hospitals and the broader public healthcare system. In Austria, this trend is again certainly linked to the substantial proportion of medical doctors practicing CAM, which may incorporate additional therapies like acupuncture into their daily routines while working in a hospital setting (107). In the USA, substantial efforts by various institutions to integrate acupuncture into the public healthcare system were made in recent years (157). The increasing recognition of acupuncture's clinical efficacy, together with the ongoing opioid crisis, resulted in its endorsement in clinical guidelines by leading medical associations and consequently to its inclusion in insurance coverage by Medicare and Veterans Health Administration. Following this, healthcare facilities began hiring more CAM practitioners to provide acupuncture, particularly for pain-related conditions (157).

Nevertheless, the interaction with oncologists remains infrequent for respondents (28.0%), limiting interdisciplinary information exchange and potentially constituting as a source of risk for adverse events or interactions with cancer-specific treatments (107). In addition to the results of our survey among cancer patients, this result suggest another communication gap leaving the utilization of CAM during cancer treatment mostly unrecognized by the treating oncologists (107). Further integration of acupuncturists into public healthcare facilities can

enhance interdisciplinary communication, strengthening a multidisciplinary environment aiming for a safe provision of integrative oncology (157).

We want to acknowledge certain limitations to this study. First, the overall response rate to the survey was low which is a common occurrence in surveys utilizing a convenience-sampling design (107). Factors contributing to this may include a lack of interest in actively participating in research and a lack of involvement in the field of oncology, leading to a reluctance to fill out the survey (158). This could introduce a self-selection bias, as the respondents may primarily were CAM practitioners treating cancer patients and those generally interested in research (107). However, our survey had a notably high response rate among practitioners not involved in cancer patient treatment, indicating a willingness to provide reasons for their choice of not treating cancer patients (107). Secondly, the selection of participating countries was based on the study team's connections within professional organizations, potentially limiting the representativeness of the results to the international practice within Western countries (107). Additionally, the low sample size per country should be considered when interpreting country-specific analyses. Lastly, we did not delve into further details about acupuncture or herbal therapy, such as the most frequently used acupuncture points, herbal prescription patterns, and their underlying rationale. Future studies should explore these aspects for a more comprehensive understanding of CAM practices (107).

In summary, we could provide deeper insight into the current landscape of CAM practice and research literacy among Austrian acupuncturists and herbalists and were able to compare them on an international level (107). Our results show that Austrian CAM practitioners are aware of the challenges and risks associated to treating cancer patients, but still require a better training in skills concerning modern scientific methods. Hence, we advocate a revision of current educational programs aiming to sensitize acupuncturists and herbalists for skills enabling them to translate research findings into their clinical practice.

4.3 Conclusion

Within this dissertation project, we were able to map the current patterns of CAM utilization of Austrian cancer patients and the clinical practice and research literacy of Austrian acupuncturists and herbalists for the first time. Our results indicate a high prevalence of CAM use during oncological treatment together with a lack of communication about its utilization between patients, CAM practitioners and oncologists, increasing the risk of adverse events and interactions with cancer specific treatments. A possible way of addressing the patient-wish to use CAM while simultaneously securing the safety of patients could be the integration of integrative oncology services into general medical practice and the Austrian public health care

system, together with educational programs for CAM practitioners strengthening their skills in research literacy. Oncologists should be aware of the varying tendency of their patients to use CAM, depending on significant changes in the disease trajectories including the appearance and worsening of symptom clusters like the “drowsiness-depression-anxiety” cluster. Hence, we endorse for a continuous pro-active monitoring of CAM utilization during and after cancer treatment. Acupuncture may currently be the most reliable CAM modality, as it showed favorable outcomes in clinical research concerning the its effectiveness in cancer symptom management, particularly for cancer pain and neuropsychological symptoms, and safety profile. Oncologists should therefore recommend its use to their patients instead of other CAM practices, as recommended by current clinical guidelines.

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