ELSEVIER

Contents lists available at ScienceDirect

# Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp



# Integrating conventional and complementary treatments in cancer care: The process within the public healthcare system of the region of Tuscany, Italy

Rossi Elio Giovanni <sup>a,\*</sup>, Bosinelli Francesca <sup>a</sup>, Navari Anna <sup>a</sup>, Noberasco Cristina <sup>a</sup>, Picchi Marco <sup>a</sup>, Nurra Linda <sup>a</sup>, Guido Carmelo Pasquale <sup>b</sup>, Firenzuoli Fabio <sup>c</sup>, Ferreri Rosaria <sup>d</sup>, Cracolici Franco <sup>d</sup>, Di Stefano Mariella <sup>e</sup>, Conti Tommaso <sup>e</sup>, Menicalli Chiara <sup>e</sup>, Sacco Irene <sup>e</sup>, Baccetti Sonia <sup>e</sup>, De Simone Luigi <sup>f</sup>, Bosco Filippo <sup>f</sup>, Martella Francesca <sup>g</sup>, Pennucci Cristina <sup>h</sup>, Signorini Alessandra <sup>i</sup>, Tucci Enrico <sup>i</sup>, Amunni Gianni <sup>j</sup>

- <sup>a</sup> Clinic for Complementary Medicine and Diet in Oncology, Local Health Unit Tuscany North West, Lucca, Italy
- <sup>b</sup> Center for Acupuncture and Traditional Chinese Medicine, Local Health Unit Central Tuscany, Firenze, Italy
- <sup>c</sup> Integrative Medicine Center, CERFIT, University Hospital of Careggi Hospital, Firenze, Italy
- d Center for Integrative Medicine, Hospital of Pitigliano, Local Health Unit South East Tuscany, Grosseto, Italy
- e Tuscan Regional Center for Integrative Medicine, Firenze, Italy
- f Breast Unit, AOUP, University Hospital of Pisa, Italy
- <sup>g</sup> Oncology Department, Local Health Unit Central Tuscany, Italy
- <sup>h</sup> Oncology Department, Local Health Unit Tuscany North West, Carrara, Italy
- i Oncology Department, Local Health Unit South East Tuscany, Arezzo, Italy
- <sup>j</sup> Coordinator for the Tuscan Oncology Network, University Hospital of Careggi, Firenze, Italy

# 1. Background

Recent research in the field of oncology has yielded important contributions concerning all the cancer disease phases. A growing amount of data is available regarding patient needs related to the physical and psychosocial sequelae of cancer and their association with overall quality of life (QoL) [1]. Such needs may be related to specific therapeutic steps and services provided (e.g., patients' need for more information on their health status), as well as specific symptom management (e.g., pain, emotional distress). These needs have been documented worldwide, both in early- and advanced-stage illness, in adult and pediatric populations, and in survivors (Arnaboldi, 2022; Bonacchi et al., 2015; Chen et al., 2021; Karadag and Yüksel, 2021; Wang et al., 2021) [2,3,4,5,6]. Moreover, studies have also identified specific care necessities (including those associated with cancer-related cognitive impairment due to both cancer pathogenesis and conventional treatments) (Chang et al., 2019; Edwards et al., 2018; Harrison and Wefel, 2018) [7–9]. Additionally, research has highlighted the fact that the additional allostatic burden associated with the SARS-CoV2 pandemic requires further steps in managing cancer patients' needs (Ebrahimabadi et al., 2021; Jones et al., 2020) [10,11].

Given these areas of need, it is not surprising to see a growing interest in complementary medicine (CM), with prevalence of use rates up to 51% among adults and ranging from 6% to 91% among children (Bishop et al., 2010; Keene et al., 2019) [12,13]. Patients seem to be using CM to better manage possible adverse effects of conventional anticancer treatments and cancer-related symptoms (Grant et al., 2019; Rossi et al., 2018; Rossi et al., 2018) [1,14,15].

In Italy, patient interest in CM use has grown significantly in recent decades, especially after the 2000s [3,16–19]. A study conducted in five oncology departments in Tuscany highlighted that 37.9% of patients in the sample had been using one or more types of CM, with 66.3% informing their physicians of this and 89.6% experiencing benefits (Bonacchi et al., 2014) [16]. Given this context, a better understanding of the impact of CM therapies on conventional therapies and on patient well-being is crucial for providing patients with effective therapeutic options and discouraging word-of-mouth-based self-treatment.

Integrative oncology (IO) is an innovative field of cancer care with a patient-centered, evidence-based approach focused on the implementation of CM practice into conventional oncological treatments (Ben-Arye et al., 2022; Bonacchi et al., 2015; Grant et al., 2019) [20,3,

E-mail addresses: eliogiovanni.rossi@uslnordovest.toscana.it, medicinaintegrata.lucca@uslnordovest.toscana.it (R.E. Giovanni).

<sup>\*</sup> Corresponding author. Clinic for Complementary Medicine and Diet in Oncology, Cittadella della Salute-Campo di Marte Hospital, Local Health Unit Tuscany North-West, Lucca, Italy.

# List of abbreviations

(ARTOI) Association for Research on Integrated Therapies in Oncology

(AIOM) Associazione Italiana di Oncologia Medica

(CanCon) Cancer Control Action Project

(CM) Complementary Medicine

(CME) Continuous Education in Medicine

(DTCP) Diagnostic and Therapeutic Care Pathway

(ECIBC) European Commission Initiative on Breast Cancer

(IO) Integrative Oncology

(ISPRO) Istituto per lo Studio, la Prevenzione e la Rete

Oncologica

(ITT) Istituto Toscano dei Tumori

(EPAAC) Joint Action European Partnership for Action Against Cancer

(MERGIO) Middle Eastern Research Group in Integrative Oncology

(MOG) Multidisciplinary Oncology Group (MTB) Multidisciplinary Tumor Board

(QASDG) Quality Assurance Scheme Development Group

(QoL) Quality of Life

(EUREGHA Network) Reference Network for European Regional and Local Health Authorities

(RCIM) Tuscan Regional Center for Integrative Medicine

(TCM) Traditional Chinese Medicine (AOUP) University Hospital of Pisa

1]. The aim of IO is twofold. On the one hand, it aims to reduce the main side effects of conventional treatments and improve patient compliance, thus enhancing therapeutic efficacy. On the other, it aims to boost patient empowerment, QoL, and overall well-being by allowing patients to have a more proactive role in the therapeutic process. A recent resolution by the European Parliament further stressed the potential supportive role of a holistic approach in cancer care and stated that evidence-based CM may play a role in controlling both illness-related and treatment-related adverse effects [21].

Recent evidence suggests that the growing interest in CM in cancer patients is a global, transcultural phenomenon. High CM use rates seem to be related to specific patient needs regarding therapeutic steps and the management of cancer-related symptoms. As a result, CM use management becomes of primary importance to ensure safe, effective treatments and to prevent word-of-mouth-based self-care. In this view, the field of IO is focused on integrating CM practice within mainstream care to achieve multiple goals. Implementing IO services within conventional oncological facilities might provide a crucial contribution in enhancing patient adherence to treatments and boosting QoL.

#### 1.1. Aim

The present study describes the process for implementation of IO practice within the public healthcare system of the Region of Tuscany, Italy, which represents a successful example of IO practice both at a national and international level.

# 1.2. Design

This is a narrative report.

#### 1.3. Methods

The Region of Tuscany has pursued a progressive integration of CM in mainstream cancer care over the past 15 years, thus providing an

operational roadmap for other clinical and research facilities (Rossi et al., 2018) [15]. The Region's goals in this area can be divided into four key areas: 1) evidence-based research on IO and dissemination of the results; 2) legislative steps for IO services implementation in the Tuscan territory; 3) education and information on CM for healthcare providers and the general public; 4) IO clinical activities within the regional public health system. The present study provides a narrative report of the process of integration, which includes these four areas.

# 2. The process of integration

# 2.1. Evidence-based research on IO and dissemination of the results

Continual evidence-based research in CM and dissemination of the results for healthcare professionals, patients, and citizens is one of Tuscany's macro-objectives. The Region has thus implemented multiple national and international initiatives in this area. At a national level, the integration process began with the creation of a Working Group of oncologists and CM experts in 2008–2010, in order to establish a dialogue among different approaches and to write a literature review on the use of CM in oncology. The Working Group was reconstituted in 2020 [22].

Tuscany also promoted the 2018 Regional Call on Health Research, which dedicated a sub-line to research on the effectiveness of CM in oncology, with a budget of €1,200,000. Among the proposals granted funding, one project aimed at comparing the effects of homeopathy, acupuncture, and homeopathy plus acupuncture with a standard treatment, consisting of cognitive rehabilitation and add-on dietary advice, for cancer-related cognitive impairment in breast cancer patients (the CHEMOCIM Project). Two other projects that were awarded grants focused on the efficacy of *Cannabis indica* for aromatase-related articular pain (TOSCANNABIS) and the efficacy of acupuncture for radiotherapy-related fatigue (FAIR AC), respectively [23].

At the international level, the Region of Tuscany participated in the 2011–2014 Joint Action European Partnership for Action Against Cancer (EPAAC) and successively conducted a survey on European oncology centers that offered CM treatments to patients [25]. Based on scientific evidence in the literature, the document "Complementary and alternative medicine (CAM) in cancer care: Development and opportunities of integrative oncology" was published as one of the EPAAC deliverables (www.epaac.eu) and a book on complementary medicine for the oncological patient (in Italian) was published and distributed among Tuscan healthcare professionals [26].

Another noteworthy initiative involved the Tuscan Tumor Institute (Istituto Toscano dei Tumori or ITT, the regional authority in cancer care, prevention and research), now called the Institute for Study, Prevention, and Oncological Network (Istituto per lo Studio, la Prevenzione e la Rete Oncologica or ISPRO), and the Central Tuscany Local Health Unit (Azienda USL Toscana Centro), which signed a Memorandum of Understanding for Integrative Oncology with the Department of Integrative Medicine of the Memorial Sloan Kettering Cancer Center (MSKCC) in New York, USA. The document had a specific focus on research and education in CM practice. The collaboration with the MSKCC began with their support of the research projects promoted by the Region of Tuscany's Health Research Call 2018 and a joint participation in a European project fostering cooperation between Europe and China in personalized medicine (EU SinoEU PerMed project), which was however discontinued due to the Covid-19 pandemic.

Furthermore, a Tuscan CM expert joined the Quality Assurance Scheme Development Group (QASDG) Working Group promoted by the European Commission Initiative on Breast Cancer (ECIBC) [27] and managed by the Joint Research Center in Ispra, Varese, Italy. The QASDG Working Group published a Manual for Breast Cancer Services in April 2021, which highlights that "Breast Cancer Services must have a written policy to ask patients about and to discuss the use of complementary and integrative medicine" and that "Use of Complementary Integrative Medicine can have an impact on treatment. Patients should

be free to discuss this subject without any prejudice" (p. 63) [28]. Subsequently, the Region of Tuscany contributed to the Cancer Control Action (CanCon] EU Project [29] for defining general criteria for breast cancer services.

Another important contribution by the Region regarding a "Multi-disciplinary and integrative approach to cancer patients and diseases" was made in the "Booklet of Best Practices in Cancer 2021" [30] published by the reference network for European Regional and Local Health Authorities (EUREGHA Network) [31]. The booklet was officially presented to the European Commission and the European Parliament in 2021. On that occasion, the recently approved Diagnostic and Therapeutic Care Pathway (DTCP) "Integrative medicine for the oncological patient" was presented as the Region's best practice in cancer care [32].

The Tuscany International Health Cooperation also supported the organization of the workshop "Refugees with Chronic Diseases between the Middle East and Europe: The Role of Traditional and Integrative Medicine in Bridging Gaps" promoted by the Middle Eastern Research Group in Integrative Oncology (MERGIO) in Berlin in May 2017, during the 1st World Congress on Integrative Medicine and Health. Clinicians, researchers, and medical educators from Italy, Germany, Turkey, Israel, Palestine, Iran, Lebanon, Jordan, Egypt, and Sudan attended the workshop. The conclusions of this workshop underscored the need to advance collaborative regional and international initiatives and design educational and training programs for oncologists, nurse oncologists, psychooncologists, and other health practitioners from Europe and the Middle East, with a focus on palliative and supportive cancer care [33]. The first initiative resulting from this workshop was the organization, once again supported by Tuscany (Tuscany Local Health Unit North-West), of a three-day workshop titled "Multi-disciplinary Training Program in Anthroposophic and Integrative Manual Therapies in Integrative Oncology Practice," the primary objective of which was to provide nurses and practitioners with skills-oriented training in CM manual techniques.

Finally, the Region has had contacts and engaged collaboration with several international and European CMs federations and associations.

# 2.2. Legislative steps for IO services implementation in the tuscan territory

Specific legislative steps supported the integration process of CM therapies into conventional cancer care. First of all, Resolution 418/2015 ("CM Integration in the Tuscan Tumor Institute Oncological Network") stressed that cancer patients accessing the Tuscan Network of Oncology Departments should always be ensured evidence-based CM treatments [34].

This resolution led to the creation of a regional Working Group specifically aimed at integrating CM practice within conventional treatments in the Tuscan territory [35], which was recently reconstituted (see ISPRO note, 03/29/22). Currently, the Working Group is composed of nine oncologists and eight CM experts. This initiative is in line with recommendations by the Italian Association of Medical Oncology (Associazione Italiana di Oncologia Medica or AIOM, which has included specific sections on IO in its guidelines since 2018, and with the 2004 report created through the European Society of Mastology (EUSOMA) Workshop that was conducted in Florence, Italy [36].

Another important milestone for IO practice implementation in Tuscany is a 2016 Resolution by the regional government, which indicated IO as the first priority field of CM treatment [37]. Furthermore, the 2019 and 2021 regional DTCP versions on breast cancer included a section on CM use in supportive cancer care [38]. In particular, the document highlights that patients should be presented with their treatment proposal during their meeting with the Multidisciplinary Tumor Board (MTB), "which also includes the use of integrative complementary medicine to treat the adverse effects of chemotherapy such as nausea, vomiting and asthenia" (p. 44). Moreover, the MTB includes a variety of professionals who support patients based on their needs: plastic surgeon, psycho-oncologist, geneticist, nuclear doctor,

physiotherapist, and "integrative medicine doctor (i.e., acupuncturist, phytotherapist, homeopath)" (p. 42). Therefore, after an agreement is reached on treatment options during the MTB, patients are referred to acupuncture, phytotherapy, and homeopathy facilities based on the possible side effects of conventional treatments. This decision-making process also takes into account patient preferences and the latest regional guidelines on IO. In addition, patients with signs and/or symptoms suggesting psychosocial distress may be referred to psycho-oncologists, psychiatrists, and CM experts for the treatment of mild mood and sleep disorders (pp. 54–55). The DTCP concludes with the chapter "Integrative medicine for the treatment of adverse effects of therapy" (pp. 74–77), entirely devoted to CM in oncology.

In 2021 the above-mentioned DTCP "Integrative Medicine for Oncological Patients" clearly stated the role of IO practice in Tuscany [32]. First of all, the document reports the epidemiological data on CM use among cancer patients (about 40% in Europe and Italy). Second, it stresses the need for a multidisciplinary, patient-centered approach in oncology—that is, a multidisciplinary professional équipe that has to include CM experts (Fig. 1). Furthermore, it states that patients should be guaranteed adequate information on available CM therapies at every stage of their disease by the referring oncology department and/or the CM outpatient clinic. Third, it evaluates the adverse effects of integrative medicine (acupuncture, herbal medicine, and homeopathy). Of note, the DTCP states that CMs can play a supportive role through all stages of the disease, from the diagnosis onward. In fact, a cancer diagnosis has a major negative impact on patients and their families and causes distress far beyond the wide range of physical symptoms in approximately 30% of patients [39]. Moreover, the DTCP lists evidenced-based CMs for treating the adverse effects of anticancer therapies as supportive care before and after surgery, during and after chemotherapy, and during hormonal therapy and radiotherapy. CMs can also have a positive effect during the follow-up phase, especially in promoting lifestyle changes and helping to reduce or remove unhealthy habits such as smoking, alcohol abuse, obesity, and others, improving the patient's diet and promoting physical exercise. Finally, CMs can contribute to palliative and end-of-life care through body-mind techniques that do not require physical effort.



Fig. 1. Interrelations among healthcare professionals in the Tuscan Regional Cancer Network.

# 2.3. Education and information on CM for healthcare providers and the general public

Promoting education, training programs, and evidence-based information on IO for healthcare providers is another macro-objective of the Tuscan Healthcare System. Since 2007, Regional Law [40] has recognized education and training courses for doctors, dentists, veterinarians and pharmacists in acupuncture, herbal medicine and homeopathy, which formed the basis for the approval in 2013 of the National Agreement between the State, Regions, and Autonomous Provinces [41]. Multiple Master's Degree courses on CM were held during the last 15 years, especially at the Tuscan universities of Florence and Siena. Thanks to a collaboration with the Foundation for Research on Integrated Therapies in Oncology (ARTOI), several physicians with expertise in IO employed in public clinics of the Tuscan healthcare system participated as lecturers in the IO Master's Degree courses held at several Italian universities, including La Sapienza University in Rome, the largest university in Europe.

It should be noted that the Continuous Education in Medicine (CME) system has recognized every scientific event on CM and IO promoted by the Tuscan Local Health Authorities since 2005. The collaboration of Tuscan experts in the writing and publication of the book *Principles of Integrative Oncology* published in 2021 [42] (constitutes another step in dissemination at the national level.

Additionally, the Tuscan Region organized two international congresses held in Florence in 2016 and in 2018, both attended by hundreds of oncologists and healthcare professionals.

Numerous training and refresher courses on these topics took place over time, including "Epigenetic and cancer diseases" in Lucca in 2016 and 2017 and the online course "Integrative oncology: organizational principles and models, treatment protocols and clinical outcomes" through the North-West Tuscany Local Health Authority (Azienda USL Toscana Nord-Ovest) in 2020.

Several initiatives for educating patients and the general public have also been implemented. A section on CM was added to the Region of Tuscany's website [43]. Another section on CM services specifically is

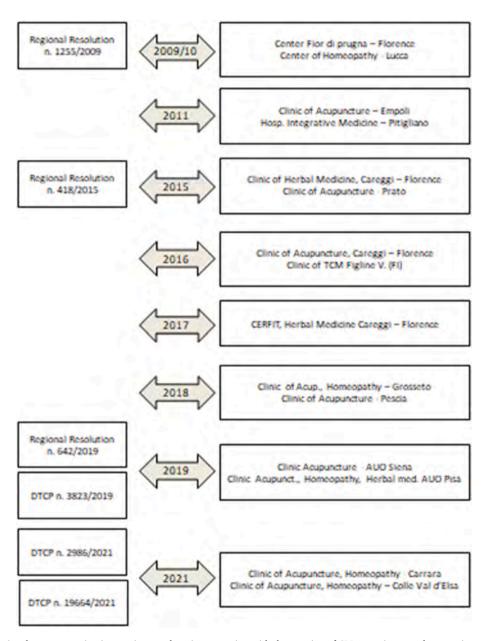


Fig. 2. Chronology of regional acts concerning integrative oncology in connection with the creation of CM outpatient oncology services within the regional public health service of Tuscany.

now featured on the ISPRO oncology institute website [44]. The region publishes a CM bulletin, MC Toscana [45], which is distributed at various conferences and events. Moreover, in 2018, oncology departments and CM outpatient clinics of the regional hospitals distributed a brochure to oncology patients titled "Integrative Medicine for Cancer Patients" containing guidance on the appropriate use of CM in oncology [24].

# 2.4. IO clinical activities within the tuscan regional public healthcare system

The first pilot project in IO was approved by the Region of Tuscany in 2009 with Regional Council Resolution N. 1255/2009 [46]. The first IO visits began in 2010 at the Homeopathic Clinic of the Local Health Unit of Lucca and the Acupuncture and Traditional Chinese Medicine Clinic "Fior di Prugna" in Campi Bisenzio (now in Florence), and the Herbal Medicine Clinic of Empoli (now in Careggi University Hospital). Afterward, IO activities were implemented at the Santa Chiara Hospital in Pisa and at the Pitigliano Hospital for Integrated Medicine (Grosseto), the regional reference center for "Integrative medicine for hospitalized natients" (Fig. 2)

Each IO clinic has its own prevailing clinical specialty consistent with its origin. In fact, the majority of the clinics started out as acupuncture, herbal medicine, or homeopathy clinics and then, in most cases, progressively integrated other therapies and/or complementary therapeutic protocols. Detailed information regarding the location, services, structural organization and contact details of all public CM clinics operating in Tuscan hospitals is available from the Annual Census published on the official regional website [47].

Access to CM visits is usually direct (i.e., patients may call to book an appointment), but in almost all cases patients are referred by their oncology departments. The CM visit, as well as acupuncture treatment and any other healthcare service for cancer patients, is free of charge. However, patients pay for herbal supplements/botanicals, medical devices, homeopathic medicines and other natural substances used. Along with the routine IO clinical services (acupuncture, herbal medicine and homeopathy), other CM services (dietary advice, support for physical activity including Tai Chi and Qi Gong, art and music therapy, etc.) are provided as well.

Evidence concerning the benefits of this progressive integration of CM in mainstream cancer care in Tuscany have been described in retrospective observational studies over the years, and published in national and international peer-reviewed journals [14,15,48–54].

In addition to the above-mentioned CM reference centers (Florence, Careggi Florence, Lucca and Pitigliano), 21 public outpatient clinics provide IO services in Tuscany (see Table 1). In recent years, Tuscan public CM clinics have performed more than 30,000 CM visits each year, and at least one third of such services are specifically dedicated to cancer

A recent, not yet published regional survey conducted among public IO clinics has assessed the number of patients visited yearly, with a specific focus on those symptoms for which patients required CM treatments more frequently. According to preliminary data, around 2300 patients with cancer were seen at public integrative oncology clinics in Tuscany in 2021. Among these, 55.9% received acupuncture, 29.7% herbal therapy, 12.4% homeopathy, and 1.9% TCM techniques. In total, the visits or treatments were more than 11,600, with 78.7% specifically for acupuncture, 14.0% for herbal therapy, 5.1% for homeopathy, and 2.1% for TCM techniques) (Fig. 3).

The general trend is a gradual increase in the number of cancer patients turning to IO clinics. For example, the number of patients with cancer visited by the Fior di Prugna Center in Florence went from 131 in 2015 to 439 in 2021, with a total of 2262 cancer patients treated with acupuncture and TCM from 2010 to 2021. In Lucca's IO Clinic, the number of patients visited went from 72 in 2015 to 182 in 2021, with 856 patients visited from 2013 to July 2022. Moreover, according to

Table 1

Location	CM Services Provided
Northwestern Tuscany	
Azienda USL Toscana Nord ovest Cittadella	Acupuncture, Dietary Advice,
della salute Campo di Marte – Lucca	Homeopathy, Traditional Chinese
	Medicine
Azienda USL Toscana Nord ovest Day	Acupuncture, Homeopathy
Hospital Oncologia Centro Polispecialistico	
Achille Sicari IV piano – Carrara	
AOU Pisana – Santa Chiara	Acupuncture, Herbal Medicine,
	Homeopathy, Traditional Chinese
	Medicine
AOU Pisana – Ospedale Cisanello	Acupuncture, Traditional Chinese
	Medicine
Central Tuscany	
Azienda USL Toscana Centro	Acupuncture, Traditional Chinese
Ex CPA poliambulatorio specialistico - Pistoia	Medicine
SS Cosma e Damiano – Pescia	
Azienda USL Toscana Centro	Acupuncture, Traditional Chinese
Ex Ospedale Misericordia e Dolce – Prato	Medicine
Azienda USL Toscana Centro	Acupuncture, Homeopathy,
Centro di MTC Fior di Prugna – Firenze	Traditional Chinese Medicine
Azienda USL Toscana Centro Ospedale	Acupressure, Auriculotherapy, Plun
Serristori DH Oncoematologia – Figline	Blossom
Valdarno	
Azienda USL Toscana Centro Ospedale S.	Acupuncture, Traditional Chinese
Giuseppe - Centro Donna – Empoli	Medicine
AOU Careggi – Firenze	Acupuncture, Traditional Chinese
	Medicine
AOU Careggi – CERFIT, Firenze	Herbal medicine
AOU Careggi – Integrative medicine for	Herbal medicine
women's health in iatrogenic menopause,	
Firenze	
Southeastern Tuscany	
Azienda USL Toscana sud est	Acupuncture
Hospice Arezzo	
Azienda USL Toscana sud est	Acupuncture, Homeopathy,
Ospedale Misericordia di Grosseto	Traditional Chinese Medicine
Azienda USL Toscana sud est	Acupuncture, Traditional Chinese
Ospedali riuniti Nottola	Medicine
Azienda USL Toscana sud est	Acupuncture, Traditional Chinese
Ospedale della Gruccia – Montevarchi	Medicine
Azienda USL Toscana sud est	Acupuncture, Traditional Chinese
	ricupuncture, rituarionar omnese
Ospedale di Campostaggia – Poggibonsi Azienda USL Toscana sud est	Medicine Medicine

Acupuncture, Homeopathy, Traditional Chinese Medicine Acupuncture, Traditional Chinese

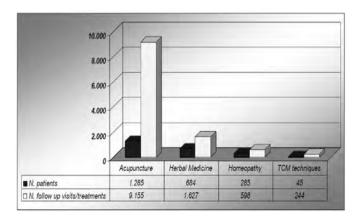


Fig. 3. Number of cancer patients (2,299) and number of follow-up visits/ treatments (11,624) carried out in public outpatient clinics of Integrative Oncology in Tuscany by type of Complementary Medicine in 2021.

Ospedale di Orbetello

AOU Senese

Azienda USI, Toscana sud est

Ospedale Petruccioli - Pitigliano

Policlinico "Santa Maria alle Scotte"

data from Lucca, the average age of oncological patients was 56 years, with breast cancer representing the most frequent diagnosis (about 64.3%), followed by colon/rectal cancer (8.8%), gynecological cancer (5.9%), and lung cancer (4.2%). Moreover, 28.4% of patients exhibited metastases and 9.9% had received a second cancer diagnosis, while 7.8% of them exhibited a recurrence [55].

In addition, the Careggi University Hospital (Regional Reference Center in Herbal Medicine), in 2021 visited 264 cancer patients for 936 oncological visits for patients treated with medicinal plants and botanicals. The clinic also aims to study the possible interactions between botanical products and anticancer drugs.

A specific center for the treatment of secondary symptoms from iatrogenic menopause operates at Careggi University Hospital (the "Integrative medicine for the health of iatrogenic menopausal women" service). An outpatient acupuncture clinic for the treatment of adverse symptoms of cancer therapy has also been operative at Careggi for several years, alongside an outpatient acupuncture and homeopathy clinic for breast cancer patients and an outpatient clinic for gynecological cancer patients in the Breast Unit at Pisa University Hospital.

To date, the South-East Tuscany Local Health Authority provides most of the CM services to cancer patients in the region. These services are operative in all the most important hubs in the area, such as Grosseto, Siena, and Arezzo, and in smaller hospitals, such as Campostaggia, Orbetello, and Nottola. In addition, the first CM hospital in Tuscany, the Petruccioli Hospital in Pitigliano, is still operational.

In April 2017, the oncology department of Central Tuscany Local Health at Serristori Hospital in Figline Valdarno implemented Traditional Chinese Medicine activities (auriculotherapy, acupressure, moxibustion, etc.), which are mainly managed by nurses. During the first two years of activity (2017–2018), nursing professionals performed 791 TCM treatments on patients who were mostly suffering from lung cancer and lymphoma. Chemotherapy-related nausea, vomiting, insomnia, and anxiety were the most frequently treated symptoms. It is also worth mentioning that at the University Hospital of Pisa (AOUP) there is an integrated approach to surgical anesthesia for frail breast cancer patients, consisting of electro-acupuncture and homeopathic medicines during the pre-surgical, surgical, and post-surgical phases to improve general well-being of patients undergoing breast cancer surgery, and to reduce or eliminate the use of opioids. To date, more than 100 surgical interventions of this type were performed [56].

Lastly, in 2022 a new acupuncture and homeopathy facility was opened at the Carrara hospital.

# 2.5. Challenges

Several challenges were met in this process of integration and implementation over the years and at different stages. Giving some indications of possible solutions, however, we must take into account the specific nature of the Italian regional healthcare system, which is 'national' but also 'federalistic', i.e. with great organizational autonomy of the Italian regions. The first and main challenge was undoubtedly oncologists' mistrust of unknown therapies and their fear that these could be proposed as alternative, and not as complementary, treatments. However, this initial attitude has diminished over time both with the progressive publication of EBM studies supporting integrative medicine in oncology and the collaborative attitude of physicians with expertise in complementary techniques, who clarified the possibility of being allies in the same battle in support of patients.

There were also the usual bureaucratic administrative problems encountered in public healthcare when dealing with innovation—among them, difficulties in the recruitment of professionals, delays in the scheduling of follow-ups, and challenges regarding the definition and approval of protocols. Furthermore, the spread of the Covid-19 pandemic greatly impacted the availability of economic resources. Luckily, the cooperation of the regional government of Tuscany has permitted the resolution of most of these issues.

#### 3. Discussion

The prevalence of CM use rates among cancer patients in Italy and Europe is very high, and patients seem to exhibit multiple motivations for CM use [3,16]. In particular, CM use seems to be motivated by patients' unmet needs (i.e., those needs which are not satisfied due to a perceived gap between the level of service provided and patients' desired support and outcomes). Additionally, CM use seems to have a striking impact on patients' sense of empowerment and overall well-being.

That said, according to a survey conducted within the framework of the Joint Action European Partnership for Action against Cancer (EPAAC) [25], the percentage of oncology services providing CM treatments for cancer patients in European facilities is only 20%, with considerable differences from country to country, and a higher percentage of facilities in Italy and the U.K [57].

Patients' unmet needs often relate to specific therapeutic steps, including the need for more information, as well as symptomatology management and psycho-emotional support related to speaking with people who have had a similar experience [3]. Therefore, implementing an IO service may respond to patients' demand for CM therapies and provide safety and equity of therapeutic access within public healthcare systems.

The European Commission Initiative on Breast Cancer (ECIBC) is an important attempt to recognize such needs, when it states that "The Breast Cancer Services must have a written policy to ask the patient about and discuss the use of complementary and integrative medicine for breast cancer" [27]. Equally important is the above-mentioned resolution of the European Parliament "Strengthening Europe in the fight against cancer" of February 16, 2022. In particular, the resolution highlights that scientifically recognized integrative medicine approved by public health authorities can bring benefits to patients in relation to the parallel effects of several diseases, such as cancer, and their treatment. It also stresses the importance of developing a holistic, integrative, and patient-centered approach encouraging the complementary use of these therapies under the supervision of healthcare professionals, where appropriate [58].

In this context, IO outpatient clinics can play a key role in providing appropriate information regarding available CM treatments for patients who refuse conventional treatments and ask for "alternative" treatments, a scenario that can negatively impact prognosis and life expectancy [21]. It has also been suggested that an outpatient IO clinic might contribute to changing refusers' attitude in about 6% of patients, who often have a personal and family history of serious adverse effects from anticancer therapies, especially chemotherapy [59].

Relatedly, it is important to emphasize the importance of an IO service within a comprehensive cancer center towards disseminating correct and useful information on the role of CM in reducing the adverse effects of anticancer therapies and improving patients' sense of empowerment and quality of life, while also counteracting the fake news spread through social media among the general population.

In addition to the achievements in Tuscany, some promising steps have been made in other Italian Regions and Autonomous Provinces (Piedmont, Emilia-Romagna, Lazio, and Bolzano), which have implemented IO services. Among them, the Region of Abruzzo has approved its first regional guidelines for breast cancer that include CM therapies as supportive care [60].

# 4. Conclusions

The implementation of IO services is crucial for providing patients with safe, effective, and high-quality treatments and it has a relevant impact on their QoL, empowerment, and overall well-being. The operational methods utilized within the Tuscan public healthcare system are feasible and easy to apply to other Italian regions and European countries that have a similar regional healthcare system organization.

#### 5. Limitations

The present article has some limitations. First of all, it provides only limited details about the implementation of the initiatives discussed, which merits a more exhaustive discussion in a dedicated monograph. Second, it is possible that patient attitudes and needs in relation to complementary therapies are significantly affected by cultural factors that have not been explored. Third, although we have collected information about patient needs and desires via our ongoing relationship with them in our clinics and by contacting cancer patient associations, these needs should be further investigated via specific questionnaires. Future research should investigate all these areas above.

#### **Author contributions**

Rossi, E. G. Clinical and organizational work, conceptualization. working group participation, original version writing, review and editing., Bosinelli, F. Investigation, original version writing, review and editing., Di Stefano, M. Investigation, original version writing, review and editing., Navari, A. Investigation, organizational work., Noberasco, C. Clinical work, conceptualization, writing, review and editing., Picchi, M. Clinical work, conceptualization, writing, review & editing., Nurra, L. Writing - original draft writing, review & editing, Guido, C. P. Clinical and organizational work, working group participation, review and editing, Firenzuoli, F. Clinical and organizational work, working group participation, review and editing, Cracolici, F. Clinical and organizational work, working group participation, review and editing., Ferreri, R. Clinical and organizational work, review and editing., De Simone L. Clinical and organizational work, review and editing, Bosco F. Clinical and organizational work, review and editing, Conti, T. Investigation, data analysis, organizational work., Menicalli, C. Clinical and organizational work, writing, review and editing, Sacco, I. Clinical and organizational work, writing, review and editing., Baccetti, S. Working group coordination, organizational work., Martella, F. Clinical and organizational work, working group participation, review and editing., Pennucci, C. Clinical and organizational work, working group participation, review and editing., Signorini, A. Clinical and organizational work, working group participation, review and editing., Tucci, E. Clinical and organizational work, working group participation, review and editing., Amunni, G. Group coordination, clinical and organizational work, conceptualization.

#### Disclosure

No competing financial interests exist.

# Declaration of competing interest

The Authors declare that they have no competing interests. All the costs for this study were supported by the Region of Tuscany.

# Acknowledgements

The Authors would like to thank first of all the General Health, Welfare and Social Cohesion Directorate of the Region of Tuscany. They would also like to thank all the oncologists of the cancer departments within Tuscany's health authorities and university hospitals who collaborate daily with complementary medicine experts to improve the health and quality of life of patients with cancer.

# References

[1] S.J. Grant, J. Hunter, D. Seely, L.G. Balneaves, E.G. Rossi, T. Bao, Integrative oncology: international perspectives, Integr. Cancer Ther. 18 (2019), 1534735418823266.

- [2] P. Arnaboldi, The caregiving cancer patient: a new expanding category among the cancer population? J. Psychosoc. Oncol. (2022) 1–4, https://doi.org/10.1080/ 07347332 2023 2020833
- [3] A. Bonacchi, A. Toccafondi, A. Mambrini, M. Cantore, M.G. Muraca, F. Focardi, G. Miccinesi, Complementary needs behind complementary therapies in cancer patients, Psycho Oncol. 24 (9) (2015) 1124–1130, https://doi.org/10.1002/ pop. 3773
- [4] D.W. Chen, D. Reyes-Gastelum, S.T. Hawley, L.P. Wallner, A.S. Hamilton, M. R. Haymart, Unmet information needs among hispanic women with thyroid cancer, J. Clin. Endocrinol. Metab. 106 (7) (2021) e2680–e2687, https://doi.org/10.1210/clinem/deabl128.
- [5] E. Karadag, S. Yüksel, Complementary, traditional and spiritual practices used by cancer patients in Turkey when coping with pain: an exploratory case study, J. Relig. Health 60 (4) (2021) 2784–2798, https://doi.org/10.1007/s10943-021-01276.0
- [6] T. Wang, A. Molassiotis, J.Y. Tan, B.P.M. Chung, H.Q. Huang, Prevalence and correlates of unmet palliative care needs in dyads of Chinese patients with advanced cancer and their informal caregivers: a cross-sectional survey, Support. Care Cancer 29 (3) (2021) 1683–1698, https://doi.org/10.1007/s00520-020-05657-w
- [7] L. Chang, L.S. Weiner, S.J. Hartman, S. Horvath, D. Jeste, P.S. Mischel, D.M. Kado, Breast cancer treatment and its effects on aging, Journal of geriatric oncology 10 (2) (2019) 346–355, https://doi.org/10.1016/j.jgo.2018.07.010.
- [8] B.J. Edwards, X. Zhang, M. Sun, H.M. Holmes, L. Ketonen, N. Guha, P. Khalil, J. Song, S. Kesler, J.B. Shah, D. Tripathy, V. Valero, R.E. Champlin, Neurocognitive deficits in older patients with cancer, Journal of geriatric oncology 9 (5) (2018) 482–487, https://doi.org/10.1016/j.jgo.2018.02.010.
- [9] R.A. Harrison, J.S. Wefel, Neurocognitive function in adult cancer patients, Neurol. Clin. 36 (3) (2018) 653–674.
- [10] M. Ebrahimabadi, F. Rafiei, N. Nejat, Can tele-nursing affect the supportive care needs of patients with cancer undergoing chemotherapy? A randomized controlled trial follow-up study, Support. Care Cancer 29 (10) (2021) 5865–5872, https://doi. org/10.1007/s00520-021-06056-5.
- [11] J.M. Jones, H. Saeed, M.S. Katz, M.B. Lustberg, V.J. Forster, L. Nekhlyudov, Readdressing the needs of cancer survivors during COVID-19: a path forward, J. Natl. Cancer Inst.: J. Natl. Cancer Inst. 113 (8) (2020) 955–961, https://doi.org/ 10.1093/inci/diaa200.
- [12] F.L. Bishop, P. Prescott, Y.K. Chan, J. Saville, E. von Elm, G.T. Lewith, Prevalence of complementary medicine use in pediatric cancer: a systematic review, Pediatrics 125 (4) (2010) 768–776, https://doi.org/10.1542/peds.2009-1775.
- [13] M.R. Keene, I.M. Heslop, S.S. Sabesan, B.D. Glass, Complementary and alternative medicine use in cancer: a systematic review, Compl. Ther. Clin. Pract. 35 (2019) 33–47, https://doi.org/10.1016/j.ctcp.2019.01.004.
- [14] E. Rossi, C. Noberasco, M. Picchi, M. Di Stefano, L. Nurra, L. Ventura, Homeopathy and complementary medicine to reduce adverse-effects of anti-cancer therapy in patients with breast cancer, OBM Integrative and Complementary Medicine 3 (3) (2018), https://doi.org/10.21926/obm.icm.1803017.
- [15] E. Rossi, C. Noberasco, M. Picchi, M. Di Stefano, A. Rossi, L. Nurra, L. Ventura, Complementary and integrative medicine to reduce adverse effects of anticancer therapy, J. Alternative Compl. Med. 24 (9) (2018) 933–941, https://doi.org/ 10.1089/acm.2018.0143.
- [16] A. Bonacchi, L. Fazzi, A. Toccafondi, M. Cantore, A. Mambrini, M.G. Muraca, G. Banchelli, M. Panella, F. Focardi, R. Calosi, F. Di Costanzo, M. Rosselli, G. Miccinesi, Use and perceived benefits of complementary therapies by cancer patients receiving conventional treatment in Italy, J. Pain Symptom Manag. 47 (1) (2014) 26–34.
- [17] M. Berretta, C. Della Pepa, P. Tralongo, A. Fulvi, F. Martellotta, A. Lleshi, R. Nasti, R. Fisichella, C. Romano, C. De Divitiis, R. Taibi, R. Fiorica, R. Di Francia, A. Di Mari, L. Del Pup, A. Crispo, P. De Paoli, A. Santorelli, V. Quagliariello, R. Iaffaioli, U. Tirelli, G. Facchini, Use of Complementary and Alternative Medicine (CAM) in cancer patients: an Italian multicenter survey, Oncotarget 8 (15) (2017), 24401, https://doi.org/10.18632/oncotarget.14224.
- [18] M. Berretta, L. Rinaldi, R. Taibi, P. Tralongo, A. Fulvi, V. Montesarchio, G. Madeddu, P. Magistri, S. Bimonte, M. Trovò, P. Gnagnarella, A. Cuomo, M. Cascella, A. Lleshi, G. Nasti, S. Facchini, F. Fiorica, R. Di Francia, G. Nunnari, G. F. Pellicanò, A. Guglielmino, M. Danova, S. Rossetti, A. Amore, A. Crispo, G. Facchini, Physician attitudes and perceptions of complementary and alternative medicine (CAM): a multicentre Italian study, Front. Oncol. 10 (2020 Apr 28) 594, https://doi.org/10.3389/fonc.2020.00594.
- [19] A. Longhi, E. Setola, C. Ferrari, E. Carretta, Complementary and alternative medicine in sarcoma patients treated in an Italian sarcoma center, J. Cancer Res. Therapeut. 17 (2) (2021) 516–522, https://doi.org/10.4103/jcrt.JCRT\_348\_20.
- [20] E. Ben-Arye, N. Nijk, O. Lavie, O. Gressel, E.S. Md, N. Samuels, Can integrative oncology increase adherence to chemotherapy in advanced gynecologic cancer? Support. Care Cancer (2022) https://doi.org/10.1007/s00520-022-06865-2, 10.1007/s00520-022-06865-2.
- [21] European, Parliament Resolution of 16 February 2022 on Strengthening Europe in the Fight against Cancer – towards a Comprehensive and Coordinated Strategy (2020/2267(INI)), 2022. TA-9-2022-0038\_EN. (Accessed 9 September 2022).
- [22] Tuscany Region, Decreto Regionale 11285/2020: istituzione gruppo di lavoro "Integrazione delle medicine complementari nella Rete oncologica" [ENG: regional Decree 11285/2020: institution of the "Complementary Medicines Integration within the Oncological Network" Working Group]. Atto pubblicato su Banca Dati (PBD), Available at:, 2020 http://www301.regione.toscana.it/bancadati/att i/DettaglioAttiD.xml?codprat=2020AD00000012112. (Accessed 20 September 2022).

- [23] Tuscany Region, 2020. Decreto Regionale 975/2020: Bando Ricerca Salute 2018 (DD 15397/2018) Individuazione beneficiari e impegno di spesa [ENG: Regional Decree 975/2020: 2018 Regional Call on Health Research (DD 15397/2018). Recipient identification and Delivered Funding]. Atto pubblicato su BURT e Banca Dati (PBURT/PBD) Available at: http://www301.regione.toscana.it/bancadati/att i/DettaglioAttiD.xml?codprat=2020AD00000000510. (Accessed 20 September 2022).
- [24] Tuscany Region, ISPRO, Medicina integrata per malati oncologici [ENG: integrative medicine for oncological patients], Available at:, 2018 https://www.ispro.toscana.it/rete\_oncologica\_toscana. (Accessed 20 September 2022). Accessed in.
- [25] E. Rossi, A. Vita, S. Baccetti, M. Di Stefano, F. Voller, A. Zanobini, Complementary and alternative medicine for cancer patients: results of the EPAAC survey on integrative oncology centres in Europe, Support. Care Cancer 23 (6) (2015) 1795–1806, https://doi.org/10.1007/s00520-014-2517-4.
- [26] S. Baccetti, M. Di Stefano, E. Rossi, Le medicine complementari per il paziente oncologico. Sviluppo e opportunità dell'oncologia integrata, Felici Editore, Pisa, Italy. 2015.
- [27] European Commission, European commission initiative on breast cancer. Improving quality of care and reducing inequality in Europe, Available at: https://healthcare-quality.jrc.ec.europa.eu. (Accessed 5 February 2023).
- [28] European Commission, C.R. Center, Manual for Breast Cancer Services: European Quality Assurance Scheme for Breast Cancer Services: Publications Office. GEN-13: Complementary and Integrative Oncology, vol. 63, Pag, 2021.
- [29] European cancer patients coalition. Joint action on cancer Control (CanCon). Harmonising the way we fight cancer in Europe, Available at: https://ecpc.org/pclicy/joint-action-on-cancer-control-cancon/. (Accessed 5 February 2023).
- [30] European regional and local health authorities (EUREGHA), Available at: https://www.euregha.net/. (Accessed 5 February 2023).
- [31] European Regional and Local Health Authorities. Cancer. A Showcase of Best Practices from EUREGHA's Members, 2021. Available at: Available at: https:// www.euregha.net/publications/. (Accessed 5 February 2023).
- [32] Tuscany Region, Decreto Regionale 19664/2021: Rete oncologica regionale. Approvazione Percorso diagnostico terapeutico e assistenziale Medicina integrata per i malati oncologici [ENG: regional Decree 19664/2021: regional Oncological Network. Approval of the "Integrative Medicine fot Oncological Patients" Diagnostic and Therapeutic Care Pathway], Available at:, 2021 http://www301.re gione.toscana.it/bancadati/atti/DettaglioAttiD.xml?codprat=2021AD000000 222220. (Accessed 20 September 2022). Accessed in.
- [33] E. Ben-Arye, M. Bonucci, M. Daher, R. Kebudi, B. Saad, T. Breitkreuz, M. Rassouli, E. Rossi, N. Gafer, O. Nimri, M. Hablas, G.S. Kienle, N. Samuels, P. Silbermann, Refugees in conflict: creating a bridge between traditional and conventional health belief models, TheOncologist (2017) 1–4, https://doi.org/10.1634/theoncologist.2017-0490, 00.
- [34] Tuscany Region, Delibera 418/2015: integrazione delle medicine complementari nella Rete oncologica dell'Istituto Toscano tumori [ENG: resolution 418/2015: complementary medicines integration within the tuscan tumor institute oncological network], Available at, 2015 http://www301.regione.toscana.it/ban cadati/DettaglioAttiG.xml?codprat=2015DG00000000324. (Accessed 20 September 2022). Accessed in.
- [35] ISPRO note of the general director, Prot. Met.. 1200, 03/29/2022.
- [36] M. Baum, E. Ernst, S. Lejeunec, M. Horneber, Role of complementary and alternative medicine in the care of patients with breast cancer: report of the European Society of Mastology (EUSOMA) Workshop, Florence, Italy, J. Cancer 4 2 (2 0 0 6) (December 2004 European), 1 7 0 2 –1 0.
- [37] Tuscany Region, Delibera 1224/2016: approvazione del programma di attività triennale 2016-2018 della struttura di riferimento regionale per le medicine complementari e delle sue articolazioni e delle linee di indirizzo alle Aziende USL e AOU per la riorganizzazione delle attività di medicina complementare integrata prenotazione risorse anno 2016 [ENG: resolution 1224/2016: approval of the 2016-2018, triennial program by the Regional Referral Center for Complementary Medicine, as well as its Articulations, and of the Guidelines for Tuscan Local Health Units and Hospitals to reorganize Complementary 0. Medicine Services Resource Bokking Year 2016]. Atto soggetto a pubblicazione su Banca Dati (PBD): Direzione Diritti di Cittadinanza e Coesione Sociale (2016) Available at: http://www301.regione.toscana.it/bancadati/atti/DettaglioAttiG.xml?codprat=2016DG00000001489. (Accessed 20 September 2022) NO VOLUME, NOR PAGE. IT IS A RESOLUTION OF THE REGIONAL GOVERNMENT.
- [38] Tuscany Region, Decreto Regionale 2986/2021: Rete oncologica regionale. Approvazione percorsi diagnostico terapeutici assistenziali: tumori della mammella e tumori del colon-retto [ENG: regional Decree 2986/2021: regional Oncological Network. Approval of Diagnostic and Therapeutic Care Pathways: breast Cancer and Colon-Rectal Cancer], Atto pubblicato su Banca Dati (PBD) (2021) 2007). Legge regionale 19 febbraio 2007, n. 9: Modalità di esercizio delle medicine complementari da parte dei medici e odontoiatri, dei medici veterinari e dei farmacisti [ENG: Complementary Medicine Practice Modalities by Doctors, Dentists, Vets, and Pharmacists]. Bollettino Ufficiale n. 3, parte prima. Available at: http://www301.regione.toscana.it/bancadati/atti/DettaglioAttiD.xml?codprat = 2021AD0000000350835. Tuscany Region. (Accessed 20 September 2022) NO VOLUME, NOR PAGE. IT IS A TUSCAN REGIONAL RESOLUTION. raccoltanormativa.consiglio.regione.toscana.it/articolo?urndoc=urn:nir:regione. toscana:legge:2007-02-19;9.
- [39] L. Peters, J. Brederecke, A. Franzke, M. de Zwaan, T. Zimmermann, Psychological distress in a sample of inpatients with mixed cancer—a cross-sectional study of routine clinical data, Front. Psychol. 11 (2020), 591771, https://doi.org/10.3389/ fpsyc.2020.591771.

- [40] Tuscany region, tuscan regional Law no. 9/2007, Available at: http://jtest.ittig.cnr.it/cocoon/regioneToscana/xhtml?doc=/db/nir/RegioneToscana/2007/urn\_nir\_regione.toscana\_legge\_2007-02-19n9&css=&datafine=20121214. (Accessed 20 September 2022). Accessed in.
- [41] Conferenza permanente per i rapporti tra lo Stato, le Regioni e le Province Autonome di Trento e Bolzano, Accordo tra il Governo, le Regioni e le Province autonome di Trento e Bolzano concernente i criteri e le modalità per la formazione ed il relativo esercizio dell'agopuntura, della fitoterapia e dell'omeopatia da parte dei medici chirurghi ed odontoiatri [National Agreement among the State and the Regions and Autonomous Provinces on the rules for education and practice in complementary medicine by medical doctors, dentists, pharmacists and veterinarians] (2013) Codice: 4.10/2013/2 (Servizio III). Accordo ai sensi dell'articolo 4 del decreto legislativo 28 agosto 1997, n. 281 http://www.statoregioni.it/Documenti/DoC\_039735\_54%20%20csr%20punto%2010.pdf. (Accessed 5 February 2023).NO VOLUME, NOR PAGE. IT IS A TUSCAN REGIONAL RESOLUTION.
- [42] M. Bonucci, F. Marino, Principi di oncologia integrata, Tecniche Nuove, Milano,
- [43] Servizio Sanitario Toscana, Medicine complementari. [ENG:Tuscan healthcare system. Complementary medicine, Available at: https://www.regione.toscana.it/ sst/aree-di-intervento/medicina-complementare. (Accessed 5 February 2023).
- [44] Istituto per lo studio, la ricerca e la prevenzione oncologica. La Rete Oncologica Toscana. [ENG: institute for Study, Prevention, and Oncological Network, The Tuscan Oncological Network] Available at: https://www.ispro.toscana.it/rete\_oncologica\_toscana. (Accessed 5 February 2023).
- [45] Notiziario regionale delle medicine complementari. MC toscana. [ENG: region journal on complementary medicine], Available at: https://www.regione.toscana.it/-/notiziario-regionale-delle-medicine-complementari. (Accessed 5 February 2023).
- [46] Tuscany Region, Delibera Giunta Regionale 1255 del 28/12/2009: Destinazione fondo finalizzato all'integrazione delle Medicine Complementari negli interventi per la salute: anno 2009 [ENG: Regional Council Resolution 1225, in: 28/12/2009: End Use for the Fund for the Integration of Complementary Medicine in health-centered Interventions: Year 2009]. Atto soggetto a pubblicazione su Banca Dati (PBD): Direzione Diritti di Cittadinanza e Coesione Sociale, 2009. Available at: htt p://www301.regione.toscana.it/bancadati/atti/DettaglioAttiG.xml?codprat=200 9DG00000001146. (Accessed 20 September 2022). Accessed on.
- [47] Servizio Sanitario Toscana, Ambulatori di Medicine complementari. [ENG: tuscan healthcare system. Complementary medicine clinics], Available at: https://www. regione.toscana.it/-/ambulatori-di-medicine-complementari. (Accessed 5 February 2023).
- [48] F. Cracolici, S. Bernardini, R. Ferreri, Acupuncture in palliative care, OBM Integrative and Complementary Medicine 4 (1) (2019), https://doi.org/10.21926/ obm.icm.1901006.
- [49] R. Ferreri, S. Bernardini, F. Cracolici, F. Bechini, Integrated oncology in an integrated medicine hospital in Pitigliano (Grosseto, Italy), OBM Integrative and Complementary Medicine 4 (1) (2019), https://doi.org/10.21926/obm. jcm\_1901008
- [50] F. Firenzuoli, L. Gori, G. Corti, M. Manetti, Interferenza dei fitoestrogeni con il tamoxifene citrato nel trattamento del cancro mammario Gazzetta Medica Italiana 162 (4) (2003) 97–100.
- [51] L. Gori, F. Firenzuoli, Acupuncture for common physical symptoms in cancer patient care, J. Soc. Integr. Oncol. 1 (3) (2005) 130–133.
- [52] C. Guido, V. Selmi, C. Chelazzi, G. Borsotti, R. Giachetti, V. Limatola, V. Sicurani, A.R. De Gaudio, Acupuncture for chemo-related nausea and vomiting, OBM Integrative and Complementary Medicine 4 (1) (2019), 020, https://doi.org/ 10.21926/obm.icm.1901020, 2019.
- [53] E. Rossi, M. Picchi, C. Fonte, M. Pellegrini, E. Baldini, Integrative approach to the cancer patients with complementary medicine and diet in the Hospital of Lucca (Italy), Homeopathy 105 (1) (2016) 38–39.
- [54] F. Sivelli, E. Rossi, S. Baccetti, M. Di Stefano, E. Gallo, F. Firenzuoli, Herb-drug interactions in oncology: a clinical up-date, OBM Integrative and Complementary Medicine 4 (4) (2019), https://doi.org/10.21926/obm.icm.1904060.
- [55] E. Rossi, Complementary Therapies in Breast Cancer: the Tuscan Region's PDTA for Integrative Medicine in Oncology. Personal Communication at the Congress "BREAST CANCER UPDATE, in: Congress "Update Sui Tumori Della Mammella", Peschiera Del Garda (Vr), 24 June 2022.
- [56] F. Bosco, S. Cidin, F. Maceri, M. Ghilli, M. Roncella, L. De Simone, An integrated approach with homeopathic medicine and electro-acupuncture in anaesthesiology during breast cancer surgery: case reports, J. Pharmacopuncture 21 (2) (2018 Jun) 126–131, https://doi.org/10.3831/KPI.2018.21.016.
- [57] B. Egan, H. Gage, J. Hood, K. Poole, C. McDowell, G. Maguire, L. Storey, Availability of complementary and alternative medicine for people with cancer in the British National Health Service: results of a national survey, Compl. Ther. Clin. Pract. 18 (2) (2012 May) 75–80, https://doi.org/10.1016/j.ctcp.2011.11.003.
- [58] B. Johnson, H.S. Park, C.P. Gross, J.B. Yu, Complementary medicine, refusal of conventional cancer therapy, and survival among patients with curable cancers, JAMA Oncol. (2018), https://doi.org/10.1001/jamaoncol.2018.2487.
- [59] E.G. Rossi, C. Noberasco, M. Picchi, M. Di Stefano, F. Bosinelli, Integrative oncology and patients refusing conventional anticancer treatments, Compl. Ther. Clin. Pract. 48 (2022), 101608, https://doi.org/10.1016/j.ctcp.2022.101608. ISSN 1744-3881.
- [60] Abruzzo Region, DGR 546/2021: Garanzia dei Livelli Essenziali di Assistenza ed Adempimenti correlati al Recepimento del D.M. Salute 18, in: Maggio 2021: Presa d'Atto ed Approvazione del Documento Tecnico "Rete Senologica PDTA del Tumore della Mammella" [ENG: Essential Assistance Levels Guarantee and D. M.

Salute, May 18th, 2021, Fulfillment: Approval of the "Senological Network - Breast Cancer Diagnostic and Therapeutic Care Pathway Technical Document], 2021.

Retrieved from, https://www.regione.abruzzo.it/content/dgr-n-546-del -03092021. (Accessed 9 September 2022). Accessed on.