Cancer pain... who cares?  
International and national patterns of evidence-based global guidelines recommendations for physicians on the Web (2011 vs. 2018)

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Summary

Purpose: Although pain is a common event during treatment of cancer, its assessment and management remains suboptimal in everyday clinical practice at global level.

Methods: Considering both the important role of internet in daily life and that clinical guidelines are important for translating evidence in clinical practice, we performed a prospective study to scrutinize the magnitude of updated evidence-based cancer-pain guideline recommendation for physicians on the web. Changes over-time at a global level were scrutinized at two time points: 2011 for baseline and 2018 at first follow-up. Both anesthesiology and oncology societies were analyzed.

Results: In 2011 we scrutinized 181,000 WebPages and 370 eligible societies were identified; 364 of these were eligible for analyses both in 2011 and 2018. The magnitude of cancer pain updated and evidence-based guideline recommendations on the web for health care providers was extremely low at global level and at any time point considered: 1.1% (4/364) in 2011 and 4.7% (17/364) in 2018. Continental and inter-continental patterns, National’s highest developmental index, oncology tradition and economic-geographic areas were not found to influence cancer pain web-guideline provision. In 2018, pain & supportive care societies provided the highest rate of updated evidence-based cancer-pain guidelines for clinicians. Only 3/25 medical oncology societies and 1/34 radiation oncology societies, provided own or e-link (to other societies’) evidence-based guidelines in their websites.

Conclusions: Major medical oncology and radiation oncology societies - at global level - fail to produce updated cancer pain recommendations for their physicians, with most of these providing no or inconsistent or outdated guidelines.

Key words: cancer pain, global awareness, guideline implementation, web, medical societies, oncology, anesthesiology

Introduction

Stepwise improvements in cancer treatment efficacy have been cumulatively achieved across decades and major survival improvements in both palliative and radical treatment settings have been reached. Nonetheless, cost-effectiveness remains a strong determinant of rationalized oncology prac-
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Billions are spent each year for prematurely approved costly treatments of uncertain benefit [1] as well as for genomic diagnostic tests of equivocal utility [2], with most of these being potentially beneficial only for very few and selected group of patients.

But what happens with cancer pain? It affects more than half of cancer patients, with a prevalence of 55% among patients on anticancer treatment, 66.4% among those with advanced metastatic or terminal phases of the disease, and 59.3% following curative treatment [3]. Moderate to severe pain is reported by 38% of all patients [3], with severe impact on quality of life and performance of normal daily activities [4,5]. To date, one third of the patients still do not receive pain medication proportional to their pain intensity levels [6]. Pain research, pain assessment and management remain suboptimal in everyday clinical practice with half of the patients believing that their quality of life is not considered a priority in their overall care by their health care professionals [5,7]. Thus, cancer pain is a serious public health problem and a major concern for more than 10 million people yearly diagnosed with cancer worldwide [8].

How to ameliorate the management of cancer pain, and how to improve and assist the physicians' awareness in cancer pain management in daily clinical activities remains a hostile cornerstone to be solved.

Clinical practice guidelines are important for translating evidence in medical decision making and reducing undesirable practices encouraging services of proven efficacy [9]. Medical guidelines/recommendations provision in websites has been of extreme importance in improving patients' safety, reducing complications and shortening the length of stay among Medicare beneficiaries [10].

Since most recognized medical societies have very extensive membership, organize a large number of educational meetings worldwide, and have substantial influence upon their members, subscribers, and visitors; we hypothesized that one of the possible causes of current medical mismanagement of cancer pain might stem from a low number of web guidelines implementation among oncology, educational and policymaker medical societies. Thus, we set to examine the global coverage of cancer pain guidelines recommendations on the web for clinicians produced by international and national oncology societies. The magnitude of cancer pain guideline production on the web and its changes over time (2011 vs 2018 estimates) were scrutinized in a prospective web-based study. Since different level of development and economy might largely influence clinical daily practice and priorities in guideline implementation, we further separately scrutinized differences in cancer pain guideline implementation among the 10 highest developed countries [11], the 10 countries with long lasting tradition in medical oncology, and 6 different economic-geographic areas.

Methods

Identification of pertinent societies and caregivers

In 2011, 181,200 WebPages were scrutinized in order to identify anesthesiology, oncology and pain societies/organizations that might have provided web guidelines regarding cancer pain. We retrieved both international societies (intercontinental, African, Asian, European, Oceanian, North American, South American) and national organizations belonging either to one of the top 10 countries with the highest development index (Norway, Australia, New Zealand, USA, Ireland, Liechtenstein, Netherlands, Canada, Sweden, Germany) [11], or to 10 countries with a long lasting tradition in medical oncology but not included in the top 10 high developed countries (Australia, Belgium, China, Denmark, France, Japan, Italy, UK, Spain, Switzerland) [appendix_1 methods]. Due to notable economy and development differences between South and North American countries, the continental entities were separately searched and analyzed for North and South America.

National associations identified were further grouped by geographical-economic areas: Australia-New Zealand, Benelux, United Kingdom of Great Britain and Ireland, German speaking countries, North American, Scandinavian, South European and East Asian countries. Further methodological details are reported in Appendix_1 methods (Table 1).

Web searches identified 370 potentially eligible societies. Since one society was double reported and 5 societies ceased, 364 societies/organizations were eligible for analyses. (Figure 1. research flow chart). (appendix 2. List of analysed societies).

Screening of the 364 eligible societies’ web-sites for guideline recommendations was performed in June 2011 and in June 2018.

Outcomes

To scrutinize the global magnitude of “updated” and “evidence-based” guideline recommendations for cancer pain for physicians on the web and its changes over time. We considered as “updated” all the web guidelines that have been produced or revised or lastly adjourned within the last 5 years. Evidence-based were considered all guidelines including randomized controlled trials and/or meta-analyses in their references. Furthermore, we considered eligible only cancer pain guideline pertaining the general assessment and management of cancer pain. “Solo” specialist guideline (such as “solo” radiation protocols for bone pain among radiotherapy societies, or “solo” intrathecal use of opioids among anesthesiology societies) were not included in the final analyses.
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Results

A statistical improvement in the production of evidence-based and updated web-recommendations for cancer pain was observed over time (2011 vs 2018) at global level ($x^2=8.2866$, $p=0.039$). Nonetheless, the magnitude of recommendation provision was inquiringly low for any outcome considered. Only 16 and 44 societies / health providers provided some form of cancer pain web-recommendations (any setting considered) in 2011 and 2018; of these, only 4 societies in 2011 [12-15] and only 17 in 2018 [16-32] were providing “updated and evidence-based” cancer pain recommendations for physicians in their web sites (Table 1). Thus, the proportion of medical societies implementing cancer pain updated evidence-based guidelines for clinicians were almost null either in 2011 and 2018 (1.1 vs 4.7%).

In 2011, the 4 societies provided recommendations both for cancer pain assessment and cancer pain treatment [12-15], while in 2018 all the 17 societies were providing recommendations for cancer pain treatment [16-32], but only 10 provided recommendations for cancer pain assessment [21,23,24-27,30-32].

At their best (2018 analyses), only one intercontinental [16], 3 European [17,18,26], 4 North American [19-22], 3 Dutch [27-29], 2 German [30,31], 1 Japanese [32], 1 Italian [24], 1 Spanish [25], 1 UK [23], and 3 US medical societies (3/56) [20-22] were providing evidence-based updated guidelines for cancer pain in their web sites. No evidence-based updated recommendations for clinicians were found across African, Asian, Oceanian, South American medical societies, and the societies analyzed of the resting 13 countries (Table 1). Guideline release for clinicians was not influenced by the continent analyzed, the national high developmental index and the national high oncology tradition. Similarly, when the countries were grouped and analyzed by economic-geographic areas (Australia-New Zealand vs Benelux vs German speaking countries vs North American vs Scandinavian vs South European vs Great Britain and Ireland vs East Asian), no statistical differences were found in the proportion of societies providing updated evidence-based web-recommendation for cancer pain (2011: Yates’ $x^2=3.719$, $p=0.811$; 2018: Yates’ $x^2=3.429$, $p=0.843$).

Only the society type (anesthesiology vs oncology vs supportive care & pain societies) was found to influence cancer pain web-guideline provision in 2018 (Yates’ $x^2=6.994$, $p=0.030$). Nonetheless, despite a higher proportion of evidence-based updated web cancer pain guidelines was found among pain and supportive care medical societies (16.6%, 4/24) [16-19], while web-guideline delivery among oncology and anesthesiology societies did not overcome the 4.3% (Table 1).

When the societies’ sub-types were analyzed, a higher proportion of web recommendations for physicians was evident for supportive care (50%) [17-19], and medical oncology societies (12%) [21,24,25], and were null or almost null across other societies subtypes (Table 1).
Table 1. Demographics of the scrutinized societies and caregivers organizations

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Discussion

Our analysis provides strong evidence for lack of web-guidelines for physicians for the assessment and management of cancer-related pain. Astonishingly, even in 2018, in our study, only 6.8% (4/59) of the “gate-keepers” specialties (medical oncology and radiation oncology) involved in the management of cancer patients provided evidence-based updated recommendation for cancer pain in their web-sites. Of note, ASCO (American Society of Clinical Oncology – the major medical oncology society worldwide) provided evidence-based pain guidelines only for the restricted sub-setting of cancer survivors [21], while no guidelines were provided for patients with active disease in any setting considered (under treatment, under follow-up or palliation). At the same time, ESMO (European Society of Medical Oncology – the European counterpart for medical oncology and second worldwide provider) presented outdated guidelines, thought new cancer pain guidelines were in press at the time of writing of our report [33].

Neither ASTRO (American Society for Therapeutic Radiology and Oncology), nor ESTRO (European Society for Therapeutic Radiology and Oncology) provided relative recommendations in their web sites (Table 1).

Cancer pain is a major public health problem. The crucial question is why this low level of priority exists, especially when the prevalence of cancer-related pain appears to be very high, and considering that it may severely jeopardize quality of life and performance of normal daily activities [3-5]. In some cases, patients may fear pain more than potential death from their cancer and this fear has aided the drive for the agenda of physicians-assisted suicide [34].

For all the above-mentioned threats the World Health Organization (WHO) developed guidelines to assist in the management of cancer pain more than 30 years ago [35]. Nonetheless, the cancer pain threat is far from being solved. To date, one third of the patients still did not receive pain medication proportional to their pain intensity levels [6], pain research, pain assessment and management remain suboptimal in everyday clinical practice with half of the patients believing that their quality of life is not considered a priority in their overall care by their health care professional [5-7]. Consequently, cancer patients’ dissatisfaction is very high. Inevitably, patients and their family members are prone to find their solutions by themselves, frequently by surfing blindly in the internet [36]. Nonetheless, these blind internet searches are of particular threat and may jeopardize the same patients’ outcomes since the cancer pain and cancer-cachexia Web information is largely dominated by the extremely strong market of para-medicine and counterfeit drugs [36,37].

Recently, the European Association for Palliative Care (EAPC) defined the untreated cancer pain as “scandal of global proportion”, as a combined action of EAPC, European Society of Medical Oncology (ESMO), the Pain Policy Studies Group (PPGS), the Union International Cancer Control (UICC) and the WHO underscored a lack of access to opioids medication at global level [38].

Can scarcity in guideline implementation modify medical thought in decision-making and generate deficits in cancer pain assessment / management in daily practice?
What triggers a determined medical society to establish guidelines on a certain subject?

An impressive number of medical, anesthesiology, and oncology societies have been developed over time and are engaged in providing flourishing professional and scientific activities. Many of these organizations have extensive membership bases and organize large meetings. In 2018, half of these societies provided guidelines, recommendations and position statements within their websites that have substantial influence upon their members, subscribers, and websites visitors [39-41]. Web clinical practice guidelines are important for translating evidence in medical decision-making and clinical practice applications, reducing undesirable practices, encouraging services of proven efficacy, improving patients’ safety and reducing complications [10]. Nonetheless, billions of dollars are spent each year for guidelines recommending prematurely approved costly treatment of uncertain benefit [1] and for guideline recommending genomic diagnostic tests of equivocal utility [2]. One may thus wonder why these societies do not prioritize guideline implementation for a pivotal and common problem (cancer pain) in daily clinical practice?

Diverging causes, such as scarce funding, lack of motivation, lack of impact on professional development, no interest from stakeholders, conflicting roles or educational deficits in pre- or postgraduate settings should be examined. Thus, in some clinical situations, the flourishing of high professional activity of medical societies might not be translated in an equal benefit for patients.

Prevalence and severity of a determinate clinical entity, as well as the patients’ expectancies from physicians might be substantially different from priorities of physicians and medical professional societies. Nowadays oncologists resemble more and more to molecular biologists, while patients are more and more seeking for a doctor who cares for them.

How to solve these discrepancies? To positively impact the development of clinical practice guidelines and put them on the web might represent a new challenging field for the future.

Our study presents some limitations. First of all, since there are no established validated searches for unearthing professional societies and organizations, some of them may have been missed by our searches. However, given the multiple layers of our search, and the large number of oncology societies retrieved, it is unlikely that prominent entities were missed and that missed societies might change the global patterns of web-guideline provision. Details on this study methodology had been already published in the literature [36,37,42-44]. Secondly, the human development index (HDI) changes over time. Thus, in June 2018 (at the time of data extraction) [45], countries’ position varied compared to the top 10 positions available in June 2011 [11]. Among the 188 nations analyzed by the HDI, 7 countries included of the top 10 HDI at the time of our analyses in the 2011 (Norway, Australia, USA, Ireland, Netherland, Canada, Germany) [11] continued to be in the top 10 at the time of our data extraction in June 2018 [45]. The remaining three countries continue to rank at the top of the list, all included in the top 15 positions (New Zealand 13/188, Sweden 14/188, and Liechtenstein 15/188) [45]. Thereafter, no significant biases may be attributed to country highest developmental national index migration at the two time-point of analyses.

In conclusion, our study outlined that overall cancer pain updated and evidence-based web-guidelines for physicians are remarkably scarce despite they seem to improve overtime. Moreover, the phenomenon is independent of continent, developmental index of the nation analyzed, oncology tradition and economic-geographic area.

Despite the fact one third of cancer patients did not receive adequate pain medications, medical oncology and radiotherapy societies fail to regularly produce updated cancer pain recommendations for their physicians, with most of these providing no or inconsistent or outdated guidelines. Cancer pain, who cares?

Conflict of interests

Study concept and study design (DM, NPP, AV, KK); internet screening for available societies in 2011 (TL, KK); scrutiny of relative web sites in 2011 (TL, KK); discussion upon scrutiny uncertainties 2011 (DM, NPP, AV, TV); protocol review and amendment in 2017 (DM, NPP, AV, GZV, TL, KK, TV, PN); scrutiny of relevant web sites in 2018 (PF, CG, GZF, MY); discussion upon scrutiny uncertainties in 2018 (NP, FK); critical appraisal of the results 2011, 2018 and analyses (DM, GP, GZV, DV, EP, ET, PN); manuscript writing (DM, GZV); Final details in manuscript editing: GP.

Conflict of interests

Authors have no conflicts of interest and no financial interest to declare.
References


2. Prasad V. Why the US Centers for Medicare and Medicaid Services (CMS) should have required a randomized trial of Foundation Medicine (F1CDx) before paying for it. Ann Oncol 2018;29:298-300.


24. Italian Institute of Medical Oncology (AIOM) (lastly accessed June 2018).


33. European Society for Medical Oncology (ESMO) Guidelines 2012 article (lastly accessed April 2018).


Appendix 1

Methods

Identification of pertinent societies and caregivers

In 2011 we constructed a database of anesthesiology, oncology and pain societies/organizations (educational, professional, health policymaker, caregivers) that might provide guidelines for cancer pain. We considered societies and organizations that were intercontinental (with a global outlook), continental (including two or more countries in the same continent), or national belonging to one of the top 10 countries with the highest development index [1].

Countries with a long lasting tradition in medical oncology (countries in which were performed the largest number of chemo/hormonal therapy randomized trials for advanced malignancies, based our previous meta-analyses [2-5]) but not included in the top 10 high developed countries, were further included in the internet searches (Table of main manuscript).

We performed internet searches (last search June 2011) involving possible combinations of 11 subject matters (“anesthesiology”, “anesthesiological”, “cancer”, “oncology”, “medical oncology”, “clinical oncology”, “radiation oncology”, “radiotherapy”, “surgical oncology”, “cancer research”, “supportive oncology”), 3 terms for educational and policy maker societies (“society” or “association” or “organization”), and 30 terms of geographic identifiers (10 pertaining to continents: “American”, “North American”, “South American”, “America Latina”, “African”, “European”, “Australian”, “Oceania”, “International”); 10 pertaining to eligible countries by the highest development index [1]: “Norway”, “Austria”, “Australia”, “New Zealand”, “USA”, “Ireland”, “Liechtenstein”, “Netherlands”, “Canada”, “Sweden”, “Germany”; and 10 pertaining to countries with a long lasting tradition in oncology but not included in the top 10 high developed countries: “Austria”, “Belgium”, “China”, “Denmark”, “France”, “Japan”, “Italy”, “UK”, “Spain”, “Switzerland ”). Due to notable economy and development differences between South and North American countries, the continental entities were separately searched and analyzed for North and South America [1]. This methodology for the identification of pertinent societies and caregivers had been previously used and described [6-8].

National associations identified were further grouped by geographical-economic areas a) Australia-New Zealand, b) Benelux (Belgium and Netherland), c) Germanophone (Austria, Germany, Liechtenstein Switzerland), d) North America ( US and Canada), e) Scandinavian (Denmark, Norway and Sweden), f) South European (France, Italy and Spain), g) United Kingdom of Great Britain and Ireland, h) East Asian (Japan and China).

The first 100 results for each internet search were scrutinized. We included both societies with accessible web pages, as well as those whose presence was mentioned in some URL but did not have a webpage or their link was not functional (under construction or not working).

Outcomes

To scrutinize the global magnitude of updated and evidence-based guideline recommendations for cancer-pain for physicians on the web and its changes over-time. Both anesthesiology and oncology societies were analyzed.

We considered as “updated” all the web guidelines that have been produced within five years or the web page should have been reviewed or lastly adjourned within five years by the implementing organization. If time period was higher than five years we considered the guidelines as outdated. Evidence-based were considered all guidelines including randomized controlled trials and/or meta-analyses in their references.

Furthermore, we considered eligible only cancer pain guideline pertaining the general assessment and management of cancer pain. “Solo” specialist guideline (such as “solo” radiation protocols for bone pain among radiotherapy societies, or “solo” intrathecal use of opioids among anesthesiology societies) were not included in primary outcome analyses.

Data extraction from eligible website

From each pertinent anesthesiology / oncology / pain society and caregiver website we recorded its name, the URL, continent and/or country, sub-specialty setting (anesthesia research, comprehensive anesthesia managing, pain, supportive oncology, medical oncology, surgical oncology, radia-
tion oncology, cancer research) and whether they provided any guideline on any subject matter (any setting) and on cancer pain related guideline (last update for baseline screening June 2011, last updated for first interim analyses June 2018, next analyses are programmed for 2025). Whenever there was availability to perform electronic battle-searches within the website, we used the terms “guidelines” or “recommendations” or “position statements” in English. For non English websites, we translated these terms into the language the website used.

Whenever any eligible guidelines were available, we recorded whether recommendations were freely accessible through the website and whether they provided separate information developed by the society/organization itself or a link to another society/organization’s guidelines.

For each cancer pain guideline retrieved, we further addressed if it was implemented for patient or for physicians, whether it pertained cancer pain assessment or treatment setting. In order to evaluate guidelines consistency we further extract whether references were provided to support the guidelines statements, whether the evidence from randomized controlled trials and/or meta-analyses were provided to support the guidelines statements.

At each time point of analyses (2011, 2018) at first screening, we did not use a strict definition for guideline and any kind of recommendation (“guidelines” or “recommendations” or “position statements” or “suggestions” or “indications”) both for patients and physicians were recorded. However in the analyses for primary outcomes only evidenced based and updated guidelines for physicians were considered of value. Guidelines from web pages to be updated for more than five years were considered outdated.

Since all medical societies may have not the possibility to produce “own” guidelines, and considering that medical societies in their websites may provide guidelines either as “own produced guidelines”, either as a “link” to guidelines produced by other medical societies, we considered of value both guideline produced by “own” and/or as a “link” to a specific web site of another society with web recommendation for cancer pain.

### Analyzes

We evaluated whether the proportion of associations/organizations present intercontinental and international variations and the possible role played by the society type and subtype in guideline implementation. Group comparisons for categorical variables used chi-square, Fisher’s exact test, and Yates’ $x^2$. Whenever data scarcity was too high to allow analyses we used descriptive statistics.

#### Protocol amendment in 2017

In November 2017, considering the scarcity of updated cancer pain web-guidelines available, the board of primary investigators decided to recognize as updated all guidelines produced or adjourned within a period of five years (in the initial protocol updated guidelines/recommendations should have been provided or adjourned within a period of three years).

### References

1. Human development reports. Human development index (HDI) - Rankings.

### Appendix 2

#### List of the 364 societies/organizations scrutinized

- World Federation Societies of Anesthesiologists
- ACORN CRO
- Africa Oxford Cancer Consortium
- African Cancer Organization
- African Organisation for Research and Training in Cancer
- African Radiation Oncology Group
- African Women’s Cancer Awareness Association
- Age Anaesthesia Association
- Alles Over Chemotherapie
- Alliance mondiale contre le cancer
- American Academy of Pain Management
- American Anti-Cancer Society
- American Association for Cancer Education
- American Association for Cancer Research
- American Brachytherapy Society
- American Cancer Society
American College of Oncology Administrators
American College of Radiation Oncology
American Institute for Cancer Research
American Pain Society
American Society for Therapeutic Radiology and Oncology
American Society of Clinical Oncology
American Society of Preventive Oncology
American Society of Regional Anesthesia and Pain Medicine
American-Italian Cancer Foundation
Anaesthetic Patient Safety Foundation
Anaesthetic Research Society
Arbeitsgemeinschaft Internistische Onkologie
Asian American Network for Cancer Awareness
Asian Clinical Oncology Society
Asian Federation of Organizations for Cancer Research and Control
Asian Fund for Cancer Research
Asian-Oceanian Clinical Oncological Society
Asian Pacific Organization of Cancer Prevention
Association for Directors of Radiation Oncology Programs
Association for International Cancer Research
Association for Research on Treatment against Cancer
Association for the International Development of Anesthesia
Association Latin American for Therapeutic Radiation Oncology (ALATRO)
Association of Physician Assistants in Oncology
Association of American Cancer Institutes
Association of Anesthesia Clinical Directors
Association of Burns and Reconstructive Anaesthetists
Association of Cancer Executives
Association of Community Cancer Centers
Association of European Cancer Leagues
Association of Freestanding Radiation Oncology Centers
Association of Integrative Oncology and Chinese Medicine
Association of Residents in Radiation Oncology
Association of University Anaesthesiologists
Associazione Anestesisti Rianimatori Ospedalieri Italiani
Australasian Society of Anaesthesia Paramedical Officers
Australian Cancer Research Foundation
Australian Society of Anaesthetists
Austrian Cancer Aid Society
Austrian cancer association
Austrian Society of Anaesthesiology, Resuscitation and Intensive Care
Austrian Society of Hematology and Oncology
Austrian Society of Oncology
Austrian Society of Oncology Pharmacy
Austrian Society of Radiation Oncology
Austrian Society of Surgical Oncology
Belgian Association for Cancer Research
Belgian Association for Radiotherapy and Oncology
Belgian Federation Against Cancer
Belgian Pain Society
Belgian Society of Medical Oncology
Belgian Society of Surgical Oncology
Berufsverband Deutscher Anaesthesisten
British Accelerator Science and Radiation Oncology Consortium
British Anaesthetic & Recovery Nurses Association
British Association of Cancer Research
British Association of Cancer United Patients
British Association of Surgical Oncology
British Oncological Association
British Oncology Pharmacy Association
Canadian Association of General Practitioners in Oncology
Canadian Association of Medical Oncologists
Canadian Association of Nurses in Oncology
Canadian Association of Pharmacy in Oncology
Canadian Association of Provincial Cancer Agencies
Canadian Association of Radiation Oncologists
Canadian Cancer Action Network
Canadian Cancer Advocacy Network
Canadian Cancer Research Alliance
Canadian Cancer Society / National Cancer Institute of Canada
Canadian Oncology Societies
Canadian Partnership Against Cancer
Canadian Society for Surgical Oncology
Cancer Advocacy Coalition of Canada
Cancer assistance network
Cancer Association of South Africa
Cancer Australia
Cancer care, Inc.
Cancer Control New Zealand
Cancer Council Australia
Cancer Care Foundation
Cancer Federation Inc.
Cancer Foundation of China / FORMER= Chinese Cancer Research Foundation
Cancer Federation Inc.
Cancer Research Foundation
Cancer Research Initiative of South Africa
Cancer Research Institute
Cancer Research Society of Canada
Cancer Research UK
Cancer Society of New Zealand
Cancer Support Association of Western Australia
Cancer Support France
Cancer Trials New Zealand
Cancérologues Sans Frontières” / “Oncologists Without Borders
Canteen Ireland
Central European Cooperation Oncology Group
China East Radiation Oncology Group
Chinese American Society of Anesthesiology
Chinese Anti-Cancer Association
Chinese Cancer Association
Chinese Cancer Federation Inc.
Chinese Cancer Cure Foundation
Chinese Cancer Research Foundation
Chinese Cancer Research Institute
Chinese Cancer Research Initiative of South Africa
Chinese Cancer Society
Chinese Cancer Control New Zealand
Chinese Cancer Council
Chinese Cancer Research Foundation (China)
Chinese Cancer Research Network
Chinese Center for Disease Control and Prevention
Chinese Medical Association
Chinese Medical Association Society of Oncology
Chinese Oncology Society (Taiwan)
Chinese Preventive Medicine Association
Chinese Society of Anesthesiologists
Chinese Society of Clinical Oncology
Chinese Society of Therapeutic Radiology and Oncology
Chinese Society of Radiation Oncology
Clinical Cancer Research Center
Clinical Oncology Society of Australia
Coc Member Organization Cancer Care Initiatives
Community oncology alliance
Complementary and Alternative Medicine for Cancer
Confedercación Latinoamericana de Sociedades de Anestesiología
Confederation of European National Societies of Anaesthesiologists
Conseils pour la chimiothérapie
Cris Foundation for Cancer Research
Cure Cancer Australia Foundation
Danish Anaesthesiological Organisation
Danish Cancer Society
Danish Research School in Molecular Cancer Research
Danish Society of Intensive Care Therapy
Danish Society of Anaesthesiology and Intensive Care Medicine
Danish Society of Medical Oncology
Dansk Selskab for Cancerforsknin
Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin
Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin
Dutch Association of Medical Oncology
Dutch Association of Oncology Nurses
Dutch Belgian Hemato-Oncology Cooperative Group
Dutch Cancer Society
Dutch Society for Radiotherapy and Oncology
Dutch Society of Oncology
Dutch Society of Surgical Oncology
Eastern Cooperative Oncology Group
European (Spain) Website of Anaesthesia, Intensive Care and Pain Medicine
European Academy of Anaesthesiology
European Association for Cancer Education
European Association for Cancer Research
European Cancer Organisation
European cancer prevention organization
European Masters Program in Radiation Sciences for Oncology
European Organization for Palliative Care
European Organization for Research and Treatment of Cancer
European Palliative Care Research Collaborative
European School of Oncology
European Society for Hyperthermic Oncology
European Society for Intravenous Anaesthesia
European Society for Medical Oncology
European Society for Therapeutic Radiology and Oncology
European Society of Anesthesiology
European Society of Cancer Immunology and Immunotherapy
European Society of Intensive Care Medicine
European Society of Oncology Pharmacy
European Society of Surgical Oncology
Federación Panamericana e Ibérica de Sociedades de Medicina Crítica y Terapia Intensiva
Fédération Nationale des Centres de Lutte Contre le Cancer
Federation of Spanish Cancer Societies
Fight Cancer Foundation
Foundation for Anaesthesia Education and Research
Foundation for European Education in Anaesthesiology
Foundation of Geriatric Oncology Netherlands
Freesia Group for Cancer Charities Spain
French National Institute of Cancer
French Society of Radiation Oncology
French Society of Surgical Oncology
German Cancer Aid
German Cancer Research Center
German Cancer Society
German Society for Hematology and Oncology
German Society of Radiation Oncology
Italian Association of Cancer Patients
Intercultural Cancer Council
Intercultural Cancer Council Caucus
International Agency for Research on Cancer
International Anesthesia Research Society
International Association for the Study of Pain
International Cancer Biomarker Consortium
International Cancer Microenvironment Society
International Cancer Rehabilitation Association
International Network for Cancer Treatment and Research
International Organization for Cancer Prevention and Research
International Society for Biological Therapy of Cancer
International Society for Cell and Gene Therapy of Cancer
International Society for Oncology and Biomarkers
International Society of Cellular Oncology
International Society of Intraoperative Radiation Therapy
International Society of Oncology Pharmacy Practitioners
International Union Against Cancer
Ireland Cooperative Oncology Research Group
Irish Association for Cancer Research
Irish Association for Nurses in Oncology
Irish Cancer Data Association
Irish Cancer Society
Irish Institute of Radiography and Radiation Therapy
Irish Society of Medical Oncology
Irish Society of Surgical Oncology
Israel Cancer Association
Italian Association for Cancer Research
Italian Association for Radiation Oncology
Italian Cancer Society
Italian Foundation for Cancer Research
Italian Institute for Cancer Research
Italian League Against Cancer
Italian Society for Surgical Oncology
Japan Clinical Cancer Research Organization
Japan Society of Clinical Oncology
Japan Society of Therapeutic Radiology and Oncology
Japanese Cancer Association
Japanese Foundation for Cancer Research
Japanese Organization of Radiotherapy Quality Management
Japanese Society of Anesthesiologists
Japanese Society of Hyperthermic Oncology
Japanese Society of Medical Oncology
La Ligue Nationale contre le Cancer
La Sociedad Española del Dolor
La Sociedad Española de Anestesiología, Reanimación y Terapéutica del Dolor
l’Association Ensemble contre la douleur
l’Association pour la Recherche sur le Cancer (ARC)
Latin American and Caribbean Society of Medical Oncology
Latin American Association for Palliative Care
Latin American Cancer Research Coalition
Macmillan Cancer Support
Medical Oncology Group of Australia
Mediterranean School of Oncology
Multinational Association of Supportive Care in Cancer
National Association of Professional Cancer Coaches
National Cancer Institute
National Cancer Registrars Association
National Cancer Research Institute
National Cancer Research Network
National Coalition for Cancer Survivorship
National Comprehensive Cancer Network
National Foundation for Cancer Research
National Health and Medical Research Council
National Institute of Health and Excellence
Cancer pain... who cares?

Navy Anesthesia Society
Nederlandse Vereniging voor Anesthesiologie
New Zealand Society for Oncology
New Zealand Society of Anaesthetists
Nordic Cancer Union
Norwegian Cancer Society
Norwegian Group on Inherited Cancer
Norwegian Society of Anaesthesiology
Oncology Nutrition Dietetic Group
Organisation of European Cancer Institutes
Organization for Oncology and Translational Research
Österreichische Gesellschaft für Internistische und Allgemeine Intensivmedizin
Peripheral Regional Anesthesia
Physician Assistants in Anesthesia
Prevent Cancer Foundation
Radiation Therapy Oncology Group
Royal Australian & New Zealand College of Radiologists
Royal College of Anaesthetists
Schweizerische Gesellschaft für Intensivmedizin-Société Suisse de Médecine Intensive
Scientific Association of Swiss Radiation Oncology
Scottish Intercollegiate Guidelines Network
Sino-American Network for Therapeutic Radiology and Oncology
Sociedad Española de Enfermería Oncológica
Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias
Società Italiana di Anestesia, Analgesia, Rianimazione e Terapia Intensiva
Société de Réanimation de Langue Francaise
Société Française d’Anesthésie et de Réanimation
Societe Francaise du cancer
Société suisse d’anesthésiologie et de réanimation/Schweizerische Gesellschaft für Anaesthesiologie und Reanimation
Society for Ambulatory Anesthesia
Society for Anesthesia and Resuscitation of Belgium
Society for Education in Anaesthesia
Society for Education in Anesthesia
Society for Integrative Oncology
Society for the Advancement of Geriatric Anesthesia
Society of Academic Anesthesiology Associations
Society of Neurosurgical Anesthesia and Critical Care
Society of Radiation Oncology Administrations
Society of Surgical Oncology
South African Oncology Consortium
South African Society of Clinical and Radiation Oncology
South African Society of Medical Oncology
South East Asian Radiation Oncology Group (SEAROG)
Southeast Anesthesiology Consultants
Spanish Association Against Cancer
Spanish Association for Cancer Research
Spanish Association of Radiotherapy and Oncology
Spanish Society of Chemotherapy
Spanish Society of Medical Oncology
Spanish Society of Surgical Oncology
Supportive and Rehabilitation Oncology
Swedish Cancer Society
Swedish Society for Anaesthesiology and Intensive Care
Swedish Society of Oncology
Swedish Surgical Society
Swiss Bridge Foundation
Swiss Cancer League, Swiss League Against Cancer
Swiss Cancer Research Foundation
Swiss Federation Against Cancer (Oncosuisse)
Swiss Group of Clinical Cancer Research
Swiss Institute for Experimental Cancer Research
Swiss Radiation Oncology Centers
Swiss Society for Oncology
Swiss Society of Medical Oncology
Swiss Society of Surgery
Taiwan Clinical Oncology Society
The American Academy of Pain Medicine
The American Board of Anesthesiology
The Association of Anaesthetists of Great Britain and Ireland
The Association of Anesthesia Clinical Directors
The Australian Organisation for Young People Living with Cancer
The Australian Pain Society
The Australian Patient Safety Foundation
The Australian Society of Post Anaesthesia and Anaesthesia Nurses
The Austrian Cancer league
The Belgian Society of Intensive Care Medicine
The British Medical Acupuncture Society
The British Pain Society
The Canadian Anesthesiologists’ Society
The Cancer Information and Support Society
The European Cancer Patient Coalition
The European Oncology Nursing Society
The European Society of Digestive Oncology
The European Society of Regional Anesthesia and Pain Therapy
The Global Regional Anesthesia website
The Intensive Care Society of Ireland
The International Society for Anesthetic Pharmacology
The International Spine Intervention Society
The Japan Cancer Society
The Japanese Association for Molecular Target Therapy of Cancer
The National Board of Anesthesiology
The Neuroanaesthesia Society of Great Britain and Ireland
The New Zealand Association of Cancer Specialists
TheRoyal College of Radiologists
The Society of Anaesthetists of Hong Kong
The South African Society of Anaesthesiologists
The South Asian Association for Regional Cooperation
The UK Society for Intravenous Society
Trans Tasman Radiation Oncology Group
World Anesthesia Society
World Cancer Research Fund International
World Federation Societies of Anesthesiologists
World Federation of Surgical Oncology Societies
World Institute of Pain