

Travel Burden and Clinical Profile of Cancer Patients Admitted to the Cancer Institute of Iran in 2012

Fatemeh Sadeghi MSc^{1,2}, Atefeh Ardestani MD¹, Maryam Hadji MSc¹, Mohammad Ali Mohagheghi MD¹, Ali Kazemian MD³, Mehrzad Mirzania MD⁴, Habibollah Mahmoodzadeh MD¹, Mahdi Aghili MD³, Kazem Zende del MD PhD^{1,5}

Abstract

Background: Burden of cancer is increasing in developing countries, where healthcare infrastructures and resources are limited. Evaluating the pattern of care would provide evidence for planning and improvement of the situation.

Materials and Methods: We studied the pattern of residential place and clinical information of cancer patients who were admitted to the Cancer Institute of Iran from January 1, to May 31, 2012.

Results: We studied 1,705 consecutive cancer patients admitted to the Cancer Institute in the study period. The most common cancers were breast (29.2%), colorectal (9.0%), stomach (8.3%), head & neck (8.0%) and esophageal (3.8%) cancers. Radiotherapy was the main treatment (52.1%) followed by chemotherapy (43.8%) and surgery (29.1%). We found that 60% of the patients presented in the loco-regional or advanced stages. About 35% of patients travelled from other provinces mainly from Mazandaran (13.4%), Lorestan (10.6%), Zanjan (7.8%) and Ghazvin (6.6%). On average, the cancer patients travelled about 455 kilometers to receive care in the cancer institute. We found more than 38% patients who were referred from other provinces had an early stage tumor.

Conclusion: Establishment of comprehensive cancer centers in different geographical regions and implementation of a proper referral system for advanced cancer patients is needed to improve the patient outcomes and mitigate the burden of travel of patients for cancer care.

Keyword: Cancer patients, developing countries, diagnosis, Iran, travel burden, treatment

Cite this article as: Sadeghi F, Ardestani A, Hadji M, Mohagheghi MA, Kazemian A, Mirzania M, Mahmoodzadeh H, Aghili M, Zende del K. Travel burden and clinical profile of cancer patients admitted to the cancer institute of Iran in 2012. *Arch Iran Med.* 2017; **20(3)**: 147 – 152.

Introduction

Cancer is among the leading causes of death in both developed and developing countries. However, the burden of this lethal disease is more prominent in developing countries, where more than 80% of the world population live and the increasing trend is more striking.¹ In spite of higher incidence rates of cancers in developed countries, the mortality to incidence ratio is considerably higher in developing countries. The disparity in cancer mortality is mainly due to detection of patients at later stages and inadequate resources for diagnosis and treatment of patients in developing countries.^{2,3}

Access to effective and multidisciplinary approaches for diagnosis, treatment and palliative care would mitigate premature death and improve the quality of life among cancer patients.⁴⁻⁶ While developing countries have to deal with more than half of the world's patients, they only possess 5% – 10% of the global resources for cancer treatment.^{2,7}

Authors' affiliations: ¹Cancer Research Center, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran, ²Department of Immunology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran, ³Radiotherapy Research Center, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran, ⁴Department of Hematology and Medical Oncology, Cancer Research Center, Cancer Institute of Iran, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran, ⁵Cancer Biology Research Center, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran.

***Corresponding author and reprints:** Kazem Zende del MD PhD, Cancer Biology Research Center, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98-21-66581638, E-mail: kazendeh@tums.ac.ir. Accepted for publication: 25 January 2017

The I. R. of Iran is located in the Middle East and experiences a cancer epidemic similar to other developing countries. According to Globocan 2012, about 85,000 cancers occurred in Iran, which claimed more than 50,000 died of it in 2012.⁸ The most common cancers in Iran include stomach, bladder, prostate and colorectal cancers among men and breast, colorectal, stomach and esophageal cancers among women. Iran is a large country and within-country disparities exist in access to diagnostic and treatment facilities. Although detailed information is not available on access to treatment, it has been reported that only 50% – 70% of patients needing radiotherapy have access to this treatment in Iran.⁹ Iran is divided into 30 provinces and high quality treatment service, including cancer surgery, chemotherapy and radiotherapy is lacking in some of these regions. Therefore, cancer patients should travel to other provinces to receive appropriate diagnosis and treatment.

The objective of this study was to study the clinical profile and referral pattern of cancer patients who were admitted to the cancer institute of Iran, the most comprehensive cancer center in the country.

Materials and Methods

Cancer Institute of Iran

The Cancer institute of Iran was established in 1949 based on collaboration between School of Medicine of Tehran University and the Red Crescent Organization of Iran. The details about history and activities of cancer institute of Iran have been

published elsewhere.¹⁰ In summary, the cancer institute of Iran is the center of excellence for cancer in Iran, which is located in the capital city of Tehran and provides cancer care to patients referred from the entire country. Annually, about 10,000 cancer patients receive inpatient and outpatient care in different departments of the cancer institute of Iran. Several multidisciplinary tumor boards, including general, head and neck, gastroenterology, breast and sarcoma tumor boards discuss complicated patients and make decisions about the best treatment options for the presenting patients. In terms of education, the cancer institute of Iran provides residency and fellowship programs, including pathology, radiation oncology, medical oncology, cancer surgery and palliative care. In addition, nurses, radiotherapy technicians and biophysicists spend some of their training periods in the cancer institute of Iran. Three research centers including Cancer Research Center (2003), Cancer Model (Biology) Research Center (2014), and Radiation Oncology Research Center (2015) have been established in the cancer institute of Iran and coordinate cancer research in different fields including basic, epidemiology, and clinical research.

Patient information

In a case series, we reviewed archived files for all cancer patients who were successively admitted to the cancer institute of Iran between January 2012 and May 2012 and included those who fulfilled the selection criteria. Inclusion criteria were adult cancer patients who were older than 18 years old and we excluded patients with a benign tumor or non-melanoma skin cancers and those for whom the diagnosis was missing. We collected personal and clinical information of the patients including, age, sex, place of residence, cancer site, stage, and type of treatment from the information archived in the hospital.

Statistical analysis

We performed descriptive statistics to study travel burden among Iranian cancer patients. We used SSER staging method and classified the patients into four groups including 1) local (tumors are localized and there is no indication for extension outside the tumor), 2) regional (direct extension to the adjacent organ or/and regional lymph nodes) and distant metastasis to other organs including lung, brain, bone, liver, etc. , and 4) unknown stage.¹¹ We used the International Classification of Diseases for Oncology (ICDO) codes to define cancer sites. Overall, we collected five months data and estimated the average number of cancer patients

admitted to the cancer institute of Iran in 2012 and applied descriptive statistics to report the frequency of different cancer types, stage of patients at diagnosis, and different treatment types including surgery, radiotherapy, chemotherapy, hormone therapy and immunotherapy. We estimated the travel distance for each patient based on the distance between their residential places to Tehran. Alborz province is located in the western part of Tehran province and recently became an independent. There is very short distance from capital city of Alborz (Karaj) to Tehran and people may commute for work or life between Tehran and Alborz and use their home or work address interchangeably in the medical records. In addition, all cancer patients travel to Tehran for diagnosis and treatment were from the capital city of Karaj. Therefore, we combined patients from Alborz province with Tehran patients in this study. Statistical analyses were performed using STATA software (Special Edition, Ver. 11.2, Stata corporation, Texas, 2009).

Results

We reviewed data from 1,705 consecutive patients who were admitted to the hospital in the first five months. We excluded 170 non-cancerous patients, 91 non-melanoma skin cancer patients and 16 patients who had no diagnostic information. From the 1428 eligible cases, 537 (38%) patients initiated their treatment in the cancer institute of Iran and the rest of them received initial treatment in other centers and were referred to our center to complete their treatment or for management of complications. Women were more frequent (N = 852, 59.7%) and the median age for all patients was 52.9 years. The most common cancer sites were breast (29.2%), colorectal (9.0%), stomach (8.3%), head & neck (8.0%) and esophageal (3.8%) cancers (Table 1).

In total, 35% of the patients were referred from other provinces, including Mazandaran (13.4%), Lorestan (10.6%), Zanjan (7.8%) and Ghazvin (6.6%) provinces for treatment in the cancer institute of Iran (Figure 1). On the average, the cancer patients had to travel about 455 kilometers to reach the cancer institute of Iran for treatment (Table 2), ranging from 132 KM travel from Ghom province to 1567 KM from Sistan-Baluchestan. Analyses by cancer sites showed that the patients were referred from other provinces for all types of cancer (Table 3). However, the main cancers referred from other provinces included melanoma, uterus, head and neck cancer, and soft-tissue sarcoma.

Table 1. Relative frequency of different cancer types by sex in the Cancer Institute of Iran for 5 month from January to May 2012

Female		Male	
Cancer Site	N (%)	Cancer Site	N (%)
Breast	407 (47.8)	Stomach	87 (15.1)
Colorectal	53 (6.2)	Colorectal	76 (13.2)
Head & Neck	47 (5.5)	Head & Neck	67 (11.6)
Cervix	35 (4.1)	Prostate	43 (7.5)
Ovary	33 (3.9)	Esophagus	36 (6.3)
Uterus	33 (3.9)	Lymphoma	31 (5.4)
Melanoma	32 (3.8)	Soft tissue	25 (4.3)
Stomach	31 (3.6)	Lung	22 (3.8)
Soft Tissue Sarcoma	22 (2.6)	Brain	20 (3.5)
Esophagus	18 (2.1)	Hodgkin	18 (3.1)
All cancer sites	852 (100)	All cancer sites	576 (100)

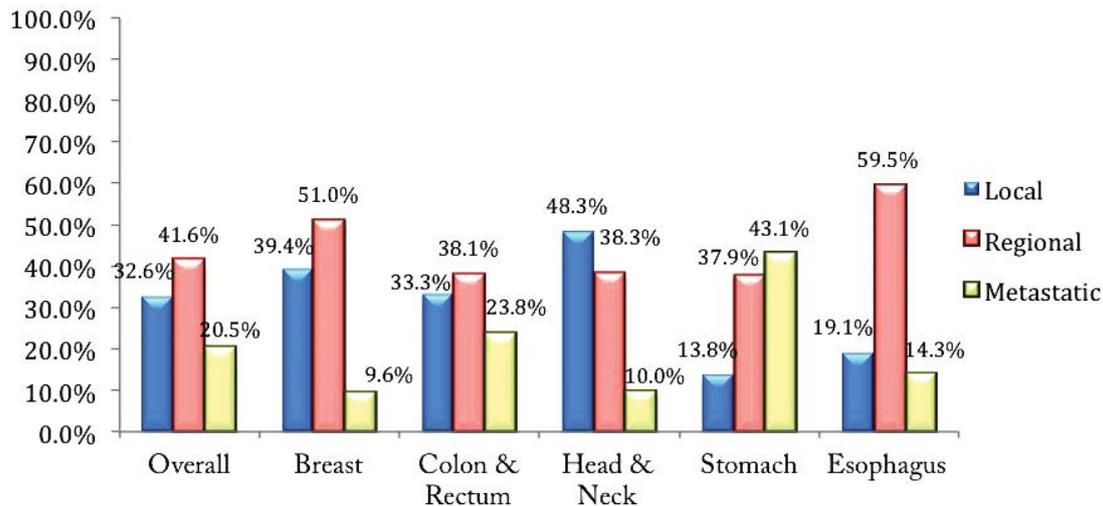


Figure 2. Stage distribution of different cancer types of cancer patients who were admitted to the Cancer Institute of Iran from January to May 2012 (Only 537 patients who received initial treatment in the cancer institute were analyzed for this figure)

Table 4. Stage distribution of different cancer types of cancer patients who initiated their cancer treatment in the Cancer Institute of Iran stratified by residential place from January to May 2012, (Only 537 patients who received initial treatment in the cancer institute were analyzed for this Table).

Cancer type	Tehran					Other provinces				
	Local	Regional	Metastatic	Unknown	Total	Local	Regional	Metastatic	Unknown	Total
Breast	28 (37.4%)	40 (53.3%)	7 (9.3%)	0 (0.0%)	75 (100%)	13 (44.8%)	13 (44.8%)	3 (10.3%)	0 (0.0%)	29 (100%)
Colorectal	15 (34.1%)	15 (34.1%)	12 (27.3%)	2 (4.5%)	44 (100%)	6 (31.6%)	9 (47.4%)	3 (15.8%)	1 (5.2%)	19 (100%)
Stomach	3 (9.7%)	12 (38.7%)	16 (51.6%)	0 (0.0%)	31 (100%)	5 (18.5%)	10 (37.1%)	9 (33.3%)	3 (11.1%)	27 (100%)
Head & Neck	15 (50.0%)	10 (33.3%)	3 (10.0%)	2 (6.7%)	30 (100%)	14 (46.7%)	13 (43.3%)	3 (10.0%)	0 (0.0%)	30 (100%)
Esophagus	6 (20.7%)	16 (55.2%)	5 (17.2%)	2 (6.9%)	29 (100%)	2 (15.4%)	9 (69.2%)	1 (7.7%)	1 (7.7%)	13 (100%)
All Cancer Types	98 (29.2%)	144 (43.0%)	78 (23.3%)	15 (4.5%)	335 (100%)	77 (38.1%)	79 (39.1%)	32 (15.9%)	14 (6.9%)	202 (100%)

More than 60% of the patients presented at loco-regional or advanced stages. More than 30% of the breast, colorectal, and head and neck cancers were diagnosed with a local tumor. However, about 40% of the stomach cancers were diagnosed at the advanced stage (Figure 2). We found that more than 38% of referral patients from other provinces who initiated their cancer treatment in the cancer institute of Iran had an early stage tumor (Table 4). In fact, almost there was no differences in the stage distributions of the patients who came from Tehran and those who were referred from other provinces.

Radiotherapy was the main treatment (52.1%) followed by chemotherapy (43.8%) and surgery (29.1%) and hormone therapy or immunotherapy were prescribed for about 10% of the patients (Figure 3).

Discussion

In this paper, we reported the demographic and clinical characteristics as well as the type of treatment provided for cancer patients who were admitted to the cancer institute of Iran in 2012. Breast and stomach cancers were the main cancer types treated in 2012. About 65% of patients were residents of Tehran, and 35% of the patients travelled about 455 kilometers from different

provinces, mainly Mazandaran (13.5%), Lorestan (10.7%), Zanjan (7.9%), Ghazvin (6.7%) and Gilan (6.2%) to receive care in the cancer institute of Iran.

The cancer patients were referred from different cities for treatment because of several reasons. The most important reason for referring to the cancer institute of Iran is lack of an organized referral system in the country and patients may prefer to initiate their treatment in the cancer institute of Iran or come to this hospital to complete their treatment or for management of complications from previous treatments. In addition, the cancer institute of Iran is a high volume hospital for surgery, radiotherapy, and chemotherapy. Some cancers, like soft tissue sarcoma and melanoma that need critical decisions and complicated care, may generally refer to the cancer institute of Iran for initial treatment, while other cancers, like breast and prostate cancers, may be referred if the initial treatment fails. Finally, some patients may be advised to travel to Tehran for their treatment because treatment facilities such as cancer surgery, chemotherapy or radiotherapy are not available in their residential place. Although we reported that patients had travelled a long journey for treatment in the cancer institute of Iran, they may not complete treatment because of the long duration of chemotherapy and radiotherapy for most cancer patients and the high economic and social burden for

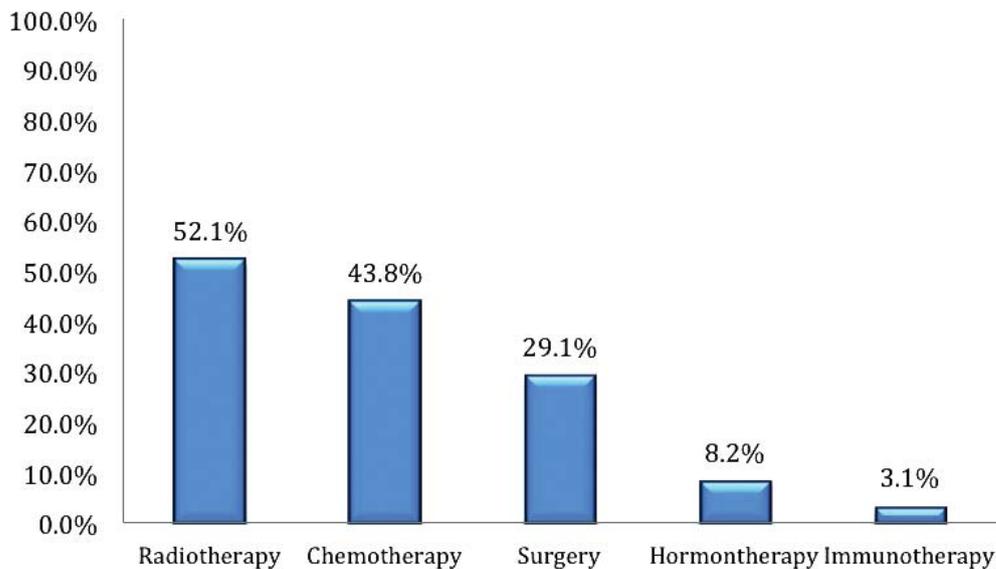


Figure 3. Treatment modality of cancer patients who were admitted for treatment to the Cancer Institute of Iran from January to May 2012

patients and their relatives who may temporarily stay in the capital city of Tehran or frequently travel between the cancer institute of Iran and their hometown. Travel burden may lead to delayed or incomplete treatment for cancer patients and compromise the efficiency and survival of these patients.

We found that more than 38% referral patients from other provinces that initiated their cancer treatment in the cancer institute of Iran had an early stage tumor. These results indicate that many patients can be treated in their hometown and it is not necessary to travel for treatment and a referral system needs to be defined for cancer patients. Many studies have reported that distance could be an important barrier to cancer care.¹²⁻¹⁵ Increasing travel requirements may cause delay in the diagnosis of cancer, and progression of tumors to an advanced stage, thereby reducing patient survival.¹⁶ In addition, it will increase economic burden to patients and the society.^{17,18} Previous studies have reported professional delays in diagnosis and treatment of oral cancer²⁰ and leukemia.¹⁹ COSA (2006) found large disparities in cancer outcomes between people living in metropolitan versus non-metropolitan regions in Australia.²⁰ Likewise, cancer patients in remote areas were sub-optimal for continuing their cancer treatment such as adjuvant radiotherapy, hormonal therapy and conserving surgery²¹ and did not seek formal supportive care.²²

Although breast cancer and stomach cancer were respectively the most common cancers among male and female patients who were admitted for diagnosis and treatment in the cancer institute of Iran, the relative frequencies of different cancer types were not completely matched with the pattern of cancer incidence in the country. The cancer institute of Iran admits a large number of head and neck cancers, malignant melanomas, and sarcomas that are not common cancers in Iran.⁸ In addition, radiotherapy was the main treatment provided to the cancer patients in the cancer institute of Iran due to the large radiotherapy department, which provides radiotherapy service for patients referred from the cancer institute and other hospitals. After excluding non-melanoma skin cancers, we estimated that this center annually admits about 400 head and neck cancer patients for treatment. Although the incidence rate of

head and neck cancer is not high in Iran, the high volume of head and neck cancers in the cancer institute of Iran could be due to the fact that these patients need a multidisciplinary approach, which is not available in most hospitals, in particular in other provinces.²³ As recommended by the National Comprehensive Cancer Network (NCCN),²⁴ a multidisciplinary team including oncosurgeons, otorhinolaryngologists with subspecialty in oral and maxillofacial surgery, pathologists, and oncologists provide high quality care to these patients in the cancer institute of Iran. Previous studies have reported a positive association between volume of hospitals and patient survival for head & neck cancer.²⁵⁻²⁷ In addition, the cancer institute of Iran admits a considerable number of patients with soft-tissue sarcoma and malignant melanoma that are relatively rare and should be managed in high volume centers by a multidisciplinary approach.^{28,29} In the UK, the Calman-Hine report recommended that treatment for less common cancers and where treatment is technically demanding should be offered in regional cancer centers, where there are site-specialist and multidisciplinary teams.³⁰

The incidence rate of cancer is rising in the world, in particular in low-middle income countries,³¹ indicating that the number of patients and waiting time will increase in referral hospitals like the cancer institute of Iran.³² Yun, et al. showed that the waiting time is higher at high-volume hospitals compared to low- to medium-volume hospitals.³³ Iran and other middle-income countries should establish cancer centers in different parts of the country and be prepared for the increasing number of cancers in the coming years. Providing high quality cancer care in different regions would reduce the burden of patients' trip from remote areas to large cities like Tehran.

The limitation of this study was that we used retrospective data from hospital files. It is important to conduct a prospective survey among cancer patients and figure out the reason for traveling from different parts of the country. In addition, we may need to analyze the outcome of patients treated in the cancer institute of Iran compared to those who stayed in their hometown and evaluate the benefits and harms of these travels for cancer patients. In addition,

it will also be interesting to compare the pattern of treatment in different hospitals and regions in the country. Unfortunately, there is no hospital-based cancer registry in Iran. Establishment of hospital-based cancer registries in different hospitals may help in regular monitoring of the pattern of care and patients' outcome in the country.⁸

In conclusion, we presented data on cancer patients who were referred to the cancer institute of Iran. The cancer institute of Iran admits patients from the entire country, in particular from the neighboring regions and the provinces that lack appropriate infrastructure for diagnosis and treatment of the patients. The cancer institute of Iran remains the main referral center in the country for diagnosis and treatment of rare and advanced cancers, which require high specialty and sophisticated care. While treatment of complicated patients and specific cancer types should be still undertaken centrally in large and high volume hospitals like the cancer institute of Iran, establishment of cancer hospitals and providing essential care to patients in different parts of the country is necessary. Further evidence on pattern of care and consequences of the travel burden for cancer patients in Iran and other low- and middle-countries is warranted.

Acknowledgement

This study was supported by a small grant from the Cancer Research Center of the Cancer Institute of Iran. The Research Ethics Committees of Tehran University of Medical Science approved the study proposal (No.: 92/D/130/924).

References

- Roshandel G, Merat S, Sotoudeh M, Khoshnia M, Poustchi H, Lao-Sirieix P, et al. Pilot study of cytological testing for oesophageal squamous cell dysplasia in a high-risk area in Northern Iran. *Br J Cancer*. 2014; 111(12): 2235 – 2241.
- Kanavos P. The rising burden of cancer in the developing world. *Annals of Oncology*. 2006; 17(suppl 8): viii15 – viii23.
- Farmer P, Frenk J, Knaul FM, Shulman LN, Alleyne G, Armstrong L, et al. Expansion of cancer care and control in countries of low and middle income: a call to action. *The Lancet*. 2010; 376(9747): 1186 – 1193.
- WHO. Cancer control: Knowledge into action: WHO guide for effective programmes. World Health Organization. 2007; 6: 2.
- Autier P, Boniol M, LaVecchia C, Vatten L, Gavin A, Héry C, et al. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. *BMJ*. 2010; 341: c3620.
- Zubizarreta EH, Fidarova E, Healy B, Rosenblatt E. Need for radiotherapy in low and middle income countries—the silent crisis continues. *Clinical Oncology*. 2015; 27(2): 107 – 114.
- Tanneberger S, Cavalli F, Pannuti F. Cancer in Developing Countries: The Great Challenge for Oncology in the 21st Century. *Indian Journal of Palliative Care*. 2004; 10: 80.
- Shakeri R, Malekzadeh R, Etemadi A, Nasrollahzadeh D, Abedi-Ardekani B, Khoshnia M, et al. Association of tooth loss and oral hygiene with risk of gastric adenocarcinoma. *Cancer Prev Res (Phila)*. 2013; 6(5): 477 – 482.
- Jemal A, Vineis P, Bray F. The cancer atlas: American Cancer Society; 2014.
- Shariat Torbaghan S, Mohagheghi M, Mosavi-Jarrahi A, Amanpour S, Zendehehdel K. The Cancer Institute of Iran. *Asian Pacific Journal of Cancer Prevention*. 2002; 3: 97 – 98.
- Ries LAG, Fritz AG, Hurlbut AA. SEER summary staging manual—2000: Codes and coding instructions. National Cancer Institute, SEER Program, *NIH Pub*. 2007: 62 – 84.
- Syed ST, Gerber BS, Sharp LK. Traveling towards disease: Transportation barriers to health care access. *Journal of Community Health*. 2013; 38(5): 976 – 993.
- Giambruno C, Cowell C, Barber-Madden R, Mauro-Bracken L. The extent of barriers and linkages to health care for head start children. *Journal of Community Health*. 1997; 22(2): 101 – 114.
- Guidry JJ, Aday LA, Zhang D, Winn RJ. Transportation as a barrier to cancer treatment. *Cancer Practice*. 1996; 5(6): 361 – 366.
- Nemet GF, Bailey AJ. Distance and health care utilization among the rural elderly. *Social Science & Medicine*. 2000; 50(9): 1197 – 1208.
- Ambroggi M, Biasini C, Del Giovane C, Fornari F, Cavanna L. Distance as a Barrier to Cancer Diagnosis and Treatment: Review of the Literature. *The Oncologist*. 2015; 20(12): 1378 – 1385.
- Stitzenberg KB, Sigurdson ER, Egleston BL, Starkey RB, Meropol NJ. Centralization of cancer surgery: Implications for patient access to optimal care. *Journal of Clinical Oncology*. 2009; 27(28): 4671 – 4678.
- Pietz K, Byrne MM, Daw C, Petersen LA. The effect of referral and transfer patients on hospital funding in a capitated health care delivery system. *Medical Care*. 2007: 951 – 958.
- Azad M, Biniiaz RB, Goudarzi M, Mobarra N, Alizadeh S, Nasiri H, et al. Short View of Leukemia Diagnosis and Treatment in Iran. *International Journal of Hematology-Oncology and Stem Cell Research*. 2015; 9(2): 88.
- Underhill C, Bartel R, Goldstein D, Snodgrass H, Begbie S, Yates P, et al. Mapping oncology services in regional and rural Australia. *Australian Journal of Rural Health*. 2009; 17(6): 321 – 329.
- Roder D, Zorbas H, Kollias J, Pyke C, Walters D, Campbell I, et al. Risk factors for poorer breast cancer outcomes in residents of remote areas of Australia. *Asian Pacific Journal of Cancer Prevention*. 2013; 14(1): 547 – 552.
- Pascal J, Johnson N, Dickson-Swift V, McGrath P, Dangerfield F. Understanding receptivity to informal supportive cancer care in regional and rural Australia: A Heideggerian analysis. *European journal of cancer care*. 2016; 25(3): 381 – 390.
- Wong RJ, Shah JP. The role of the head and neck surgeon in contemporary multidisciplinary treatment programs for advanced head and neck cancer. *Current Opinion in Otolaryngology & Head and Neck Surgery*. 2010; 18(2): 79 – 82.
- Pfister DG, Ang K, Brockstein B, Colevas AD, Ellenhorn J, Goepfert H, et al. NCCN practice guidelines for head and neck cancers. *Oncology* (Williston Park, NY). 2000; 14(11A): 163.
- Chen AY, Fedewa S, Pavluck A, Ward EM. Improved survival is associated with treatment at high-volume teaching facilities for patients with advanced stage laryngeal cancer. *Cancer*. 2010; 116(20): 4744 – 4752.
- Chen AY, Pavluck A, Halpern M, Ward E. Impact of treating facilities' volume on survival for early-stage laryngeal cancer. *Head & Neck*. 2009; 31(9): 1137 – 1143.
- Wuthrick EJ, Zhang Q, Machtay M, Rosenthal DI, Nguyen-Tan PF, Fortin A, et al. Institutional clinical trial accrual volume and survival of patients with head and neck cancer. *Journal of Clinical Oncology*. 2015; 33(2): 156 – 164.
- Gutierrez JC, Perez EA, Moffat FL, Livingstone AS, Franceschi D, Koniaris LG. Should soft tissue sarcomas be treated at high-volume centers?: An Analysis of 4205 Patients. *Annals of surgery*. 2007; 245(6): 952 – 958.
- Brennan MF. Management of extremity soft-tissue sarcoma. *The American Journal of Surgery*. 1989; 158(1): 71 – 78.
- Calman KC, Hine D. A Policy Framework for Commissioning Cancer Services. A Report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales: Guidance for Purchasers and Providers of Cancer Services: Department of Health; 1995.
- Nasrollahzadeh D, Kamangar F, Aghcheli K, Sotoudeh M, Islami F, Abnet CC, et al. Opium, tobacco, and alcohol use in relation to oesophageal squamous cell carcinoma in a high-risk area of Iran. *Br J Cancer*. 2008; 98(11): 1857 – 1863.
- van Lanschot JJB, Hulscher JBF, Buskens CJ, Tilanus HW, ten Kate FJW, Obertop H. Hospital volume and hospital mortality for esophagectomy. *Cancer*. 2001; 91(8): 1574 – 1578.
- Yun YH, Kim YA, Min YH, Park S, Won YJ, Kim DY, et al. The influence of hospital volume and surgical treatment delay on long-term survival after cancer surgery. *Annals of Oncology*. 2012; 23(10): 2731 – 2737.