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USE OF ORAL CHEMOTHERAPEUTIC MEDICATIONS IN NON-TRADITIONAL AMBULATORY SETTINGS

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MASTER OF PUBLIC HEALTH RESEARCH PROJECT

**“USE OF ORAL CHEMOTHERAPEUTIC MEDICATIONS
IN NON-TRADITIONAL AMBULATORY SETTINGS”**

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Table of Contents

I. Abstract

II. Introduction

1) Subject Background

2) Purpose

3) Objectives

III. Methods

1) Study Design and Data Variables

2) Sample Description

3) Data Analysis

IV. Results

V. Discussion

VI. Conclusion and Recommendations

VII. Appendix

Tables

References

Abstract

Background: Cancer is the second leading cause of death in economically developed countries. The use and availability of oral treatment for cancer has increased dramatically in the past 10 years. Few studies have described the use of oral chemotherapy in non-traditional ambulatory settings by health care professionals across different specialties.

Objective: The purpose of this study is to describe the usage of oral chemotherapeutic medications in ambulatory settings.

Methods: Cross sectional study of 2007 NAMCS Survey analysis involving 21,761 subjects aged 18 years and above with cancer who participated in the 2007 National Ambulatory Medical Survey (NAMCS).

Main Outcome Measure: Physician-reported use of oral chemotherapeutic medications (includes all major drug classes) as indicated on questionnaire for 2007 NAMCS survey.

Results: Health care providers in non-traditional settings are less likely to prescribe oral chemotherapy than in traditional ambulatory settings (Adjusted odds ratio (AOR)=0.65{95% confidence interval: 0.59-0.68}). The study results suggest that oncologists are prescribing oral anti-cancer drugs the most as compared to other physician specialties.

Conclusion: Health care providers in non-traditional settings are less likely to prescribe oral chemotherapy than in traditional ambulatory settings. Primary care physicians may have limited experience in monitoring and prescribing these potentially toxic medications. Clear guidelines are required for the use of oral chemotherapy medications, considering the potential for their use in non-traditional ambulatory settings and by non-oncologists.

Keywords: Cancer, Oral Chemotherapeutic medications, cancer surveillance patient setting - Traditional/Non-Traditional, Physician specialty, oral cytotoxic drug, oral hormonal drug, targeted and biological treatment.

Background/Introduction

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells and is a leading cause of death worldwide. According to latest estimates, provided by World Health Organization (WHO) 7.4 million people died of cancer in 2004 (approx. 13% of all deaths worldwide). If measures are not in place to curtail the growth of cancer diseases, then 10 million people will be dead by 2030.¹ In terms of prevalence, lung cancer is the most common cancer worldwide, followed by cancer of the breast and colorectal cancer.^{1,2} Cancer is the second leading cause of death in economically developed countries and in U.S.¹ In U.S, according to most recent report published by American Cancer society about 1,437,180 new cancer cases were diagnosed in 2008. These did not include carcinoma in situ, basal and squamous cell skin cancers.¹

Oral Chemotherapy refers to the oral use of chemicals or popularly the use of antineoplastic drugs to treat cancer and other illnesses such as connective tissues disorders, diseases of immune system etc. Chemotherapy is administered traditionally both in the hospital and in the outpatient settings including physicians' offices and outpatient hospital departments using drugs prepared by the physicians' staff or the hospital pharmacy. Patients who receive chemotherapy in outpatient settings may be more vulnerable to medication errors due to lack of facilities for clinical monitoring, inappropriate dose administration, frequent changes in the doses based on the body surface area, and lack of computerized and advanced information technologies.³⁻⁶ Other reasons such as lack of recognition of these errors, existing communication problems, high patient load, busy time schedule and fragmentation of care only make the problems worse.^{5,7,8} There are also instances when oncologists prescribe oral chemotherapy on an off label basis.⁹⁻¹³

This may be due to lack of sufficient medications for rare diseases and the reimbursement policies that constrain the prescription of these medications.¹⁴⁻¹⁶

The use and availability of oral treatment of cancer has increased dramatically in the past 10 years^{13,17,18} and may represent up to 25% of all medication used for treatment of cancer in the next 5 years.¹⁹ Yet little or no information is surveyed through the traditional mechanisms of cancer surveillance reporting on the use of these medications. The prescribing of oral therapies for cancer is expanding to non-oncologic specialties including primary care physicians, who may have limited experience in monitoring and prescribing these potentially toxic agents.^{3-18,16-19} Surveying the use of these agents by primary care and other non-oncologic specialties is equally or perhaps even more important than surveying information from traditional oncologic practices. The new oral treatments require novel approaches to dosing, monitoring of patient adherence to prescribed treatment regimens, and monitoring outcomes for which these providers may be inadequately trained.^{16,19-21} One of such newer treatments are the targeted therapies which have recently become popular and their use is increasing rapidly.^{17,22} These are also known as “small molecular drugs”, act at the cellular receptors level, and are administered orally, due to which they have significant risks associated with their use. Targeted drugs are likely to represent a major proportion (nearly 85%) of anti-neoplastic oral chemotherapy use in the near future.^{17,22}

Currently existing cancer surveillance systems do not typically take into consideration the usage of oral chemotherapy drugs in traditional hospital outpatient settings, physician offices and in non-traditional ambulatory settings.^{3,5,8,16,19} We hypothesize that the prescribing of such medications in non-traditional ambulatory settings is non-trivial. Few studies^{3-6,8,13,18,23} compare

the safety and efficacy outcomes for the use of oral chemotherapy in non-traditional ambulatory settings by non-oncologists. Considering the challenges involved with monitoring and oversight of the home administration of these agents outside a controlled clinical environment, such studies are warranted. The risk of associated complications coupled with the challenges posed by the dosing and monitoring of oral chemotherapy agents highlights the necessity for creating a system to capture the data for cancer surveillance on a population basis. The purpose of this study is to describe the usage of oral chemotherapeutic medications in non-traditional ambulatory settings. The proposed study will attempt to answer the following questions to contribute to the knowledge and understanding of the use of chemotherapeutic medications: (1) to estimate the prevalence of oral cancer therapy use occurring in non-traditional ambulatory settings (2) to analyze the patterns and frequency of use of oral cancer treatment according to insurance status, patient settings and by physician specialty.

Methods

Study Design and Data Variables

The Institutional Review board of the Virginia Commonwealth University approved this study. We used cross-sectional data from the 2007 National Ambulatory Medical Care Survey (NAMCS). Briefly, NAMCS is a national probability sample survey of visits to the office-based physicians and community health center (CHC). National Center for Health statistics (NCHS) and Center for Disease Control and Prevention (CDC) conducts these surveys annually. The surveys are intended to provide useful information on national health statistics and health indicators to advance professional education, to serve as a guide for formulation of health policy and for quality assurance purpose.²⁴ Further, data collected from these surveys also serve as a

valuable tool to characterize the changes in utilization and practice of various health care related parameters such as changes in diagnosis, tests/procedures and prescribing practices.^{24,25}

The basic sampling unit for NAMCS is the physician-patient visit. Traditionally, only visits to the offices of nonfederal employed physicians classified by the American Medical Association (AMA) or the American Osteopathic Association (AOA) as "office-based, patient care" are included in NAMCS. Physicians in the specialties of anesthesiology, pathology, and radiology are not included in the survey. Starting in 2006, in addition to the traditional sample, NAMCS included a sample of community health centers, using information from the Health Resources Services Administration and the Indian Health Service to construct a sampling frame. Visits not included in the 2007 NAMCS are following: visits made by telephone, outside the physician's office (for example, house calls), visits made in hospital settings, visits made in institutional settings by patients for whom the institution has primary responsibility over time (for example, nursing homes), and visits to doctors' offices that are made for administrative purposes only. The 2007 NAMCS sample included 3,540 physicians: 3,301 Medical Doctors and 239 Doctors of Osteopathy. A total of 1,141 physicians did not meet all of the criteria and were ineligible for the study. Of the 2,399 eligible physicians, 1,568 participated in the study. Of these, 1,357 completed 32,778 Patient Record forms (PRFs). Of the 1,357 physicians who completed PRFs, 1,266 participated fully or adequately and 91 participated minimally, (i.e. fewer than half of the expected number of PRFs were submitted). The 2007 NAMCS used a multistage probability design that involved probability samples of primary sampling units (PSUs), physician practices within PSUs, and patient visits within practices. The first-stage sample included 112 PSUs. A PSU consists of a county, a group of counties, county equivalents (such as parishes and

independent cities), towns, townships, minor civil divisions (for some PSUs in New England), or a metropolitan statistical area (MSA). The first-stage sample consisted of 112 PSUs that comprised a probability subsample of the PSUs used in the 1985-94 National Health Interview Survey (NHIS). The NHIS PSU sample was selected from approximately 1,900 geographically defined PSUs that covered the 50 States and the District of Columbia. The 1,900 PSUs were stratified by socioeconomic and demographic variables and then selected with a probability proportional to their size. The second stage consists of a probability sample of practicing physicians selected from the master files maintained by the American Medical Association (AMA) and American Osteopathic Association (AOA). Within each PSU, all eligible physicians are stratified into fifteen specialty groups: general and family practice, osteopathy, internal medicine, pediatrics, general surgery, obstetrics and gynecology, orthopedic surgery, cardiovascular diseases, dermatology, urology, psychiatry, neurology, ophthalmology, otolaryngology, and "all other" specialties. NAMCS sample for 2007 was slightly larger than previous years, as the CDC's National Center for Chronic Disease and Prevention and Health Promotion sponsored the inclusion of an additional 200 primary care physicians (general/family practice, internal medicine, obstetrics/gynecology, and pediatricians), and the National Cancer Institute (NIH) sponsored a supplementary sample of 200 oncologists. The final stage was the selection of patient visits within the annual practices of sample physicians. This involved two steps. First, the total physician sample was divided into 52 random subsamples of approximately equal size, and each subsample was randomly assigned to one of the 52 weeks in the survey year. Second, the physician selected a systematic random sample of visits during the assigned week. The physician aided by his /her office staff when possible carried out the actual data collection for NAMCS. As per instructions, Physicians kept a daily listing of all patient visits during the

assigned reporting week using an arrival log, optional worksheet, or similar method. This list was the sampling frame to indicate the visits for which data were to be recorded. It was to include both scheduled and unscheduled patients. Visits were selected from the list using a random start and a predetermined sampling interval based on the physicians estimated visits for the week and the number of days the physician was expected to see patients that week. The sampling procedures were designed so that about 30 Patient Record forms were completed during the assigned reporting week. Some missing data items was imputed by randomly assigning a value from a patient record form with similar characteristics. Imputations, in general, were based on physician specialty, geographic region, and 3-digit ICD-9-CM codes for primary diagnosis. All drugs recodes used Multum drug categories, even those drugs not found in Multum's drug database also used the same. Statistics produced from the 2007 NAMCS were derived by a multistage estimation procedure. The procedure produces essentially unbiased national estimates and has four components: 1) inflation by reciprocals of the probabilities of selection, 2) adjustment for no response, 3) a ratio adjustment to fixed totals, and 4) weight smoothing. Physician and patient responses as indicated on a total of 32,778 patient record forms (PRF) comprised of self reported data.

We included data available from 2007, the most recent data available. We believe that using the latest dataset will help us to get the most accurate picture of current practices related to oral chemotherapy prescribing in various physician settings, as oral chemotherapeutic agents have been available since decades.⁴⁷

Adults of age 18 years and above with cancer were eligible for our study. This age group was the cut-off for our study as there are significant differences in the , spectrum of cancer and its treatment for those aged 18 years and above versus the ones below age 18.^{23,26-28}

Determinant

As a part of our literature review, we found that in certain physician settings, oral chemotherapy is administered traditionally and delivery of oral anti-cancer drugs in such settings is deemed relatively safe as compared to other clinical settings where there administration poses great risk and is not free of dangers related drug side effects and other adverse events.^{3-6,8,16,19,23} Therefore based on the findings from our literature review, we defined **traditional ambulatory setting** as physician private solo or group practice. On the other hand, all other settings including freestanding clinic/Urgicenter, community health center, mental health center, non-federal government clinic, family planning clinic, Health Maintenance organization (HMO) or other prepaid practice and faculty practice plan are defined as **non-traditional Ambulatory settings**.

Outcome Variable

Based on the literature review^{3-6,8,16,19,23} we categorized Oral chemotherapeutic medications into 3 categories as 1) oral cytotoxic/anti-neoplastic medications 2) oral hormonal medications and 3) orally administered Biological/targeted medications includes oral targeted therapy and small molecular agents (Table 1).

Analyses

For our study, we analyzed the quantitative survey data using SAS Version 9.2. Analysis included descriptive statistics on demographic, socio-economic and health care characteristics for the eligible study population. Analysis also included calculation of estimates of association between various patient treatment settings and usage of oral chemotherapeutic agents weighting for the complex sampling design. We performed the following statistical tests: frequency procedures, crude and adjusted logistic regression analysis. The measure of effect was an odds ratio for estimating the likelihood of usage of oral chemotherapy in the non-traditional ambulatory setting vs. traditional ambulatory settings. We included confounders in the logistic regression model if their presence resulted in greater than 5% change in the estimates of odds ratio.

Results

After preliminary data analysis, we found a total of N=21,761 (weighted N=661,763) patients aged 18 years and above with cancer, suitable for oral cancer therapy administration. Table 2 shows the distribution of exposure groups and various confounders by oral chemotherapy usage in traditional and non-traditional ambulatory settings. It appears that oral chemotherapy use is more prevalent in traditional ambulatory settings as compared to non-traditional ambulatory setting (Figure 1). Various patient characteristics are associated with increasing oral chemotherapy use (Table 2). For example, patient's Age (prescribed more if patients are aged 65 years and above), Gender (females prescribed more than males), type of health care coverage (prescribed more for private and government sponsored insurance than others), Access to primary physician (prescribed less if patients have access to at least one primary care physician)

and prescribed more if seen earlier in practice. Forty-seven percent of users were over age 65 whereas only 31% of non-users of oral agents were in this age group. Eighty percent of users were women as compared to 61% of non-users. Racial/ethnic distributions appeared similar regardless of oral chemotherapy use. Oncologists are prescribing oral anti-cancer drugs the most as compared to other physician specialties (Fig 1). Age was determined to be the only confounder in our study and after adjusting for it, we found that health care providers are less likely to prescribe oral chemotherapy in non-traditional ambulatory settings as compared to traditional ambulatory settings (Adjusted OR=0.65{95% confidence interval: 0.61-0.69})(Table 3). It is also evident from (Fig 2) that primary care, surgical care and other physician specialties are mainly prescribing oral hormonal, targeted/biological therapy and oral cytotoxic drugs respectively. Table 4 provides the crude estimates of potential confounders in our study by use of oral chemotherapy. Use of oral agents was less in persons less than 65 years of age as compared to elderly persons. Women had 2.5 times the odds of receiving oral agents relative to men (odds ratio: 2.53; 95% confidence interval: 2.42-2.65). Patients not seen in the practice before were less likely to use oral agents (odds ratio: 0.48; 95% confidence interval: 0.44-0.51). Lack of primary care doctor presence was associated with increased odds of an oral agent (odds ratio: 1.38; 95% confidence interval: 1.33-1.44).

Discussion

Magnitude of the Problem

Some of the causes of increased patient visits to physicians' offices are patient non-compliance with self-administered therapy, longer duration of hospital stay and increased physician visits, which not only poses hindrance to successful chemotherapy but also results in higher

hospitalization rates^{29,30}. Lebovits et al³¹ found that patients coming for treatment to private clinics and physician offices were significantly less likely to adhere than the patients coming for treatment to university hospitals and other academic settings. Further, in regards to the patient taking oral chemotherapy, the study found that patients from lower income and socioeconomic status were non-adherent to their treatment in non-oncology settings.^{27,31,32} Another factor for non-adherence is the increasing costs incurred to the patient either indirectly such as non-medical cost including transportation³³ or from direct medical cost. For example, recent changes in Medicare are responsible for changes in the reimbursement policy for physicians, which in some manner can affect the practice patterns leading to visits to non-oncologist doctors for chemotherapy.¹⁴⁻¹⁶

Another important issue that may be related to the prescription of anti-cancer drugs by non-oncologists is use on an off-label basis, which denotes the use of drugs in populations or disease states not listed as indications on the drug's package insert.^{9,10} A drug or medical device that is used to treat a disease or condition not listed on its label, or used in such a way that is not outlined in the label, is referred to as off-label. The FDA has not officially approved many medications that are on the market due to lack of clinical trials and studies on their safety and efficacy. Since off-label prescribing happens more often in the ambulatory setting as compared to an academic setting, this may be one of the reasons for visits to non-oncologist physician practices.⁹⁻¹² Another study¹¹ showed that off-label prescribing is widespread in the acute hospitalized oncology population, with approximately 22% of all prescriptions for off-label or unlicensed medication. Further, off-label prescriptions are mostly for patients with metastatic or advanced cancer treated with palliative intent.^{5,12}

Walsh et al²³, found that 7% of adult chemotherapy visits and 19% of children's visits were associated with an error in medications used in the clinic or at home. Further, administration of chemotherapy medications made up for more than half of the errors detected. Home administration errors were more common in children and clinic administration errors more common in adults²³. Gandhi TK et al⁸ reviewed 10,112 medication orders from 1,606 patients including adults and children in an ambulatory chemotherapy setting and found that 302 orders (3%) were associated with a medication error. The majority of errors occurred in adults with a potential for harm, as a result, they were labeled as potential adverse drug events. Another study⁶ has shown that inpatient medical-surgical error prevalence estimates are 5% i.e. slightly lower as compared to the medication errors made in the primary care settings (approximately 8%). Taylor et al observed that a medication error occurred in approximately 10% of cases in which chemotherapeutic medications were prescribed for children with ALL in an ambulatory setting. Further, more than two-third of the errors were due to faulty prescribing of these medications.²⁸

Oral Chemotherapy provides significant advantages from the patients' perspectives. These advantages include patient comfort, flexibility, and no need for repeated and lengthy visits to physicians' offices, convenience associated with home administration, and the improved quality of life that is typical for patients treated in palliative setting.⁵ A majority of patients prefers the oral form of chemotherapy rather than the intravenous form especially if the efficacy is comparable to the intravenous route.^{3,4} However, very little scientific data is available on the true safety and efficacy of these drugs for use in general population due to lack of clinical trials. In addition, due to insufficient clinical trials, there is no adequate information and guidelines for

their appropriate administration to patients. Moreover, very few studies have been conducted in the past for directly comparing the safety and efficacy of oral and parental chemotherapeutic treatments.^{20,21}

Despite the potential benefits, oral chemotherapeutic agents are not free from risks similar to those associated with traditional infusion therapy including serious adverse sequel.^{5,18,35} Other risks associated with their usage about which patients are often not aware include drug-drug interactions, problems related to absorption and other complications resulting from the oral route of drug administration.^{5,36} The problem becomes even worse for the oral chemotherapeutic agents as there is less standardization in dose calculation and prescribing practices as well as availability of fewer other safeguards, standard for the routine infusion therapy. All these complications are difficult to monitor when delivered outside the traditional health care settings.⁵ Financial implications for the patients include rising health care costs due to out of pocket payments for drug prescription. In addition, the related out of pocket payments may be responsible for creating barriers, which further exacerbates the disparities associated with access to the care and outcomes for cancer patients. Disparities related to access to care might affect elderly patients with Medicare Part D Insurance, as well as those with lower incomes.^{19,37} On the other hand, the overall health care costs to the health care insurance providers/payers for oral treatment may be substantially lower than for traditional intravenous infusion therapy since they do not require a clinical setting in which these drugs are administered. Therefore, for the health care reimbursement system, the cost effectiveness of these medications may be positive.³⁸⁻⁴⁰ From the health care provider's perspective, it appears that due to the differences in methods of reimbursement between Europe and the U.S, American Oncologists may be less enthusiastic

about oral chemotherapy medicines as Medicare generally does not reimburse the cost of oral chemotherapy except when it is in intravenous form.¹⁴⁻¹⁶ Further, there is often overlap between health professionals from different specialties and there is often no clear distinction as to who can prescribe and monitor oral chemotherapy due to the lack of guidelines and information on the same.¹⁹

The risk of complications coupled with the challenges in dosing and monitoring the use of oral chemotherapeutic agents highlights the necessity for creating a system to capture these data for cancer surveillance. Hospitals are working to improve the chemotherapy related prescription processes using technologies like e-prescription and electronic medical records but many traditional outpatient and physician office practices lack these. Another critical reason to create a system to capture data on oral cancer treatment relates to its potential economic impact. While the overall health care costs for administration of oral agents may be lower than for traditional office based administration; the costs of these medications are exorbitant¹⁹ with a 30-day supply costing as much as \$2000. It is also very important to realize that these drugs are often prescribed in combination with other medications, which entails their use over extended periods, probably for years, which translates to significant financial costs for both the patient and the health care system¹⁹. Lack of medical insurance and/or out-of-pocket payments may be responsible for creating barriers and further exacerbating the disparities linked to access and outcomes for cancer patients as per their insurance.¹⁹

Traditional systems for cancer surveillance, such as hospital based cancer registries; capture traditionally administered systemic therapy only 50-75% of time.⁴¹⁻⁴⁸ A potential solution to

supplement traditionally administered systemic therapy reporting is to capture data directly in the setting where the treatment is provided i.e. physician offices. Systems for monitoring and conducting surveillance on the usage of oral chemotherapeutic medications can be developed and built upon the existing infrastructure used currently for electronic reporting of controlled substances. Systems like these are currently operating in more than 38 states, and are planned for an additional 11 states.⁴⁰ Information as gathered from the use of these systems on surveillance and monitoring of these drugs will be useful for developing important guidelines and recommendations for the usage of oral chemotherapeutic medications in various settings(especially non-traditional ones). Health care providers especially in primary care can play a key role by facilitating discussion on the important aspects of oral chemotherapy administration with the patients in order to guide them and reduce the chances of possible harm resulting from their administration. There is also a need for better communication between the patients and their providers, to ameliorate the errors resulting from oral chemotherapy administration. Incorporating training on these issues for residents and physicians in the form of continuous medical education (CME) and educational workshops will also help in preventing medication errors and ultimately improve patient care. There is a need for standardizing the dosing for these medications distinct from the parenteral therapy and establishing certain guidelines to ensure their safe administration. Some solutions for improving patient outcomes include double-checking the dose before administration, checking patient identity, use of template orders in hospitals and outpatient settings to prevent the medication errors until necessary safeguards and guidelines are in place.^{3,4,7}

Strengths and Limitations

Our study has the following strengths: First, the data is analyzed from the National Center for Health Statistics (NCHS) database, which includes the National Ambulatory Medical Care Survey (NAMCS). NAMCS is a national probability sample survey of visits to office-based physicians in the United States and since the sample data are weighted to produce national estimates of office visits, the results of this study are generalizable to the U.S. population. Second, the study follows a cross-sectional study design, which helps in estimating the current weight of the problem and serves as a guide for future public health planning and for designing interventions to improve patient care. Some of the limitations of the study are discussed below. First; recall bias may be present as responses on questionnaires that were determined at the time of the interview. Second, the measures of chemotherapy usage and physician characteristics were determined based on self-report. Non-differential misclassification might dilute estimates of effect. Nevertheless, this study will serve as a basis for designing more robust research designs.

Conclusion and Future Recommendations:

More research is needed in the future, considering the fact that an increasing number of oral chemotherapeutic medications are being introduced every year in the form of complex regimens, which patients have to follow. Clear guidelines are needed for the use of oral chemotherapy medications, considering the potential for their use in non-traditional ambulatory settings and by non-oncologist specialties. There are currently no robust surveillance mechanisms to monitor the use of these medications and capture the information available for them. This certainly calls for development of surveillance mechanisms to monitor the use of oral chemotherapeutic

medications. In the current era of informational technology and use of electronic prescription practices, which hold enormous potential for future, there is a strong need for further exploration of these modalities to improve the delivery of oral chemotherapy medications and thereby improve patient care. There is also a need for effective legislation and policy making to formulate specific guidelines for the use of oral chemotherapy. Associations such as the Food and Drug Administration (FDA), the American Cancer Society, and other professional medical associations can play a pivotal role in collaboration with various government and private organizations, including the pharmaceutical companies, in devising suitable legislation and policies.

We believe that the findings of the study are novel and will help to devise interventions and formulate guidelines to reduce the occurrence of inappropriate oral chemotherapeutic prescribing practices especially for non-traditional ambulatory settings.

Figure 1. Use of Oral Chemotherapy by Patient Setting and physician specialty

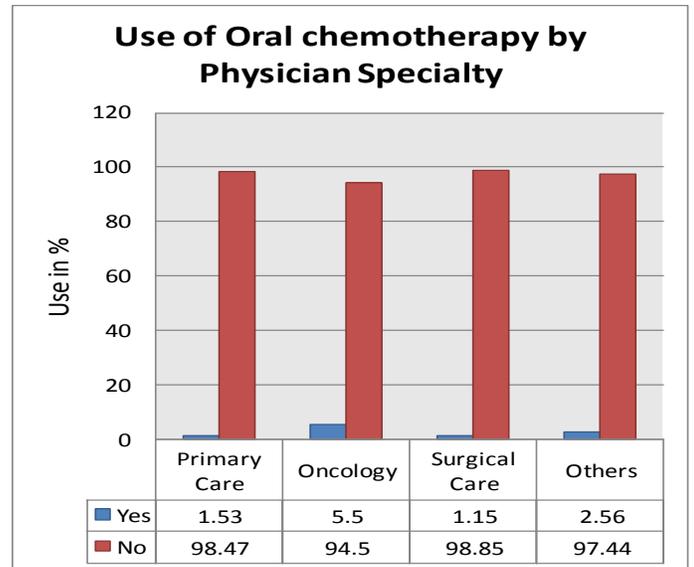
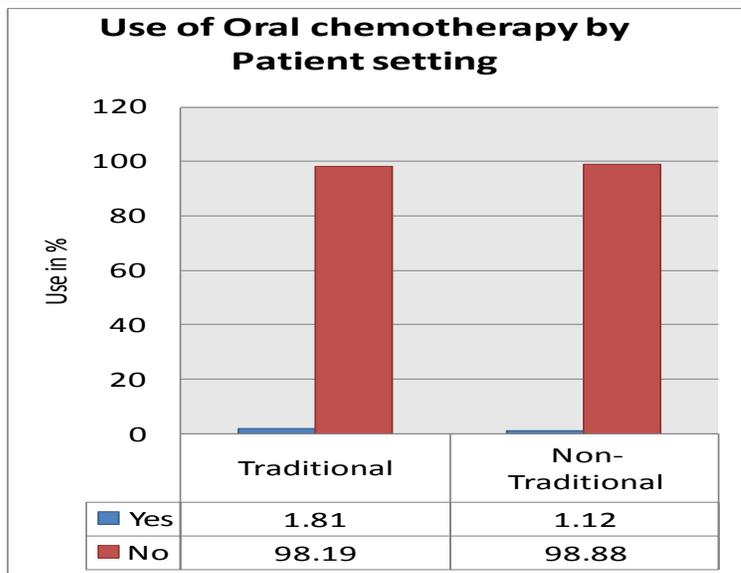


Figure 2. Type of oral chemotherapy use by physician specialties

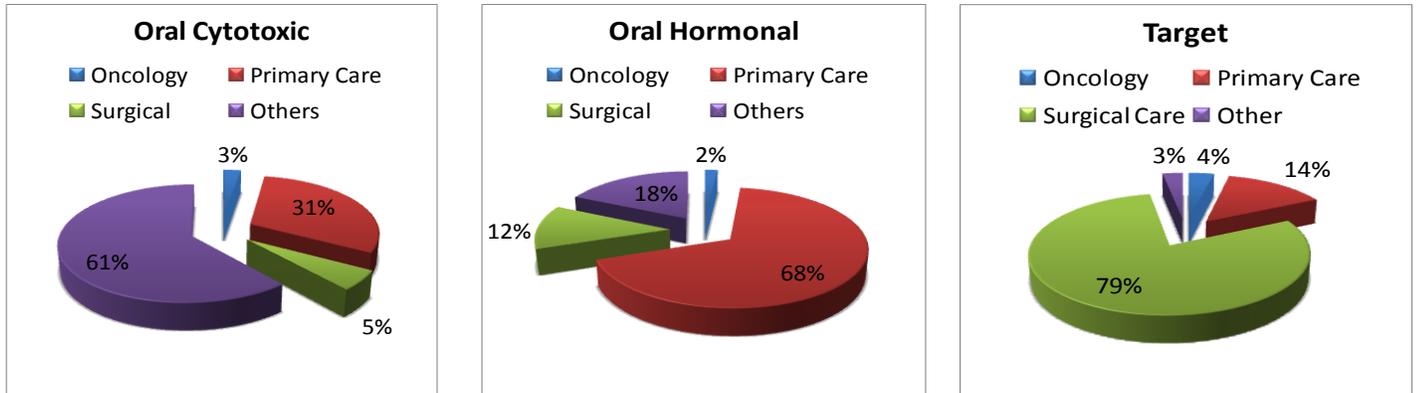


Table 1 Types of Oral Chemotherapy drug classes

Oral Cytotoxic/Anti-Neoplastic	Oral Hormonal Agents	Targeted therapy and Biological agents
Chlorambucil*	Anastrozole*	Bortezomib,
Cyclophosphamide*	Bicalutamide	Dasatinib*
Procarbazine	Diethylstilbestrol*	Imatinib*
Melphalan*	Exemestane	Lapatinib*
Busulphan	Raloxifen*	Nilotinib*
Lomustine*	Tamoxifen*	Sorefenib*
Temozolomide*	Letrozole	Sunitinib*
Azathioprine	Megestrol acetate*	Gefitinib*
Capecitabine*	Flutamide	Erlotinib*
5 -Flurouracil		Alemtuzumab
Tegafur/Uracil(UFT)		Bevacizumab
Thioguanine*		Gemtuzumab
Hydroxyurea*		Panitumumab
Methotrexate*		Rituximab
Hydroxycarbamide		Trastuzumab
6 Mercaptopurine*		
Thioguanine		
Idarubicin		
Etoposide		
Vinorelbine		
Sirolimus		
Thalidomide*		
Lenalidomide*		

*Approved by FDA

Table 2 Physician and Patient characteristics by use of oral chemotherapy

		Use of Oral Chemotherapy	
		Yes	No
		N=332	N=21429
		Wt N=11328	Wt N=650435
		Weighted %	Weighted %
Type of Setting			
	Traditional	91	86
	Non-Traditional	9	14
Physician Specialty			
	Oncology	2	1
	Primary care	51	57
	Surgical	13	20
	Others	34	22
Age of the Patient			
	18-24 years	6	7
	25-44 years	15	26
	45-64 years	32	36
	More than 65 years	47	31
Race			
	White NH	75	73
	Black NH	9	10
	Hispanic	10	12
	Asians	4	3
	Others	2	2
Patient's Gender			
	Male	20	39
	Female	80	61
Patient's Health care coverage			
	Private	47	53
	Medicare/Medicaid	47	37
	Others	6	10
Presence of Primary care physician			
	Yes	34	42
	No	66	58
Patient seen before in Practice			
	Yes	93	86
	No	7	14

**Table 3: Crude and Adjusted Regression Analysis
Use of Oral Chemotherapy**

Setting		Crude OR (95% CI)	Adjusted OR* (95% CI)	Full Model OR†(95%CI)
	Traditional	1.00	1.00	1.00
	Non-Traditional	0.61(0.58-0.65)	0.65(0.61-0.69)	0.63(0.59-0.68)

* Adjusted for Patients Age

† Adjusted for Physician Specialty, Patients Age, Gender, Race, Access to PCP, Seen before in Practice and health care coverage

Table 4: Crude estimates of potential confounders by Use of Oral chemotherapy

	Crude odds ratios (95% Confidence Intervals)
Age of the Patient	
18-24 years	0.56(0.52-0.61)
25-44 years	0.37(0.35-0.39)
45-64 years	0.59(0.56-0.61)
More than 65 years	1.00
Patient's Gender	
Female	2.53(2.42-2.65)
Male	1.00
Patient's Race	
White NH	1.28(1.09-1.50)
Black NH	1.12(0.95-1.33)
Hispanic	1.11(0.94-1.31)
Asian	1.29(1.07-1.55)
Others	1.00
Physician Specialty	
Oncology	2.16(1.89-2.47)
Primary care	0.60(0.58-0.63)
Surgical	0.44(0.41-0.46)
Others	1.00
Patient's Health care coverage	
Private	1.38(1.27-1.50)
Medicare/Medicaid	2.03(1.87-2.20)
Others	1.00
Presence of Primary care physician	
No	1.38(1.33-1.44)
Yes	1.00
Patient seen before in Practice	
No	0.48(0.44-0.51)
Yes	1.00

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